NO. _____

In the
Supreme Court of the United States

JACOBUS PHARMACEUTICAL COMPANY, INC.,

Applicant,

v.

CATALYST PHARMACEUTICALS, INC.; XAVIER BECERRA, Secretary of Health and Human Services; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; JANET WOODCOCK, Acting Commissioner of Food and Drugs, U.S. FOOD AND DRUG ADMINISTRATION,

Respondents.

On Application to Stay the Mandate of the United States Court of Appeals for the Eleventh Circuit

APPENDIX TO EMERGENCY APPLICATION FOR A STAY

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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
>
> 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.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 19-cv-22425-BLOOM/Louis

CATALYST PHARMACEUTICALS, INC.,

Plaintiff,

v.

U.S. FOOD AND DRUG ADMINISTRATION, et al.,

Defendants.
_____/

ORDER

THIS CAUSE is before the Court on Magistrate Judge Lauren F. Louis's Report and Recommendations ("Report"), ECF No. [93], recommending the Court deny Plaintiff Catalyst Pharmaceuticals Inc.'s ("Catalyst") Motion for Summary Judgment, ECF No. [38]; grant Federal Defendants'[1] Cross-Motion for Summary Judgment, ECF No. [47]; grant Intervenor-Defendant Jacobus Pharmaceutical Company, Inc.'s ("Jacobus") Cross-Motion for Summary Judgment, ECF No. [46]; and dismiss the case. Catalyst timely filed Objections to the Report, ECF No. [94]. Federal Defendants and Jacobus thereafter filed Reponses to the Objections, ECF Nos. [98] and [99]. On September 22, 2020, the Court held a hearing on the Objections and had the benefit of the parties' further arguments. The Court has carefully considered the Report, the parties' submissions, the record in the case, the applicable law, and is otherwise duly advised. For the reasons set forth below, the Court agrees with the Report's analysis and conclusions and overrules

[1] The Federal Defendants consist of (1) the United States Department of Health and Human Services; (2) Alex Azar, Secretary of the United States Department of Health and Human Services; (3) the United States Food and Drug Administration ("FDA"); and (4) Norman Sharpless, Acting Commissioner of Food and Drugs.

the Objections.

I. BACKGROUND

The Court assumes the reader's familiarity with the facts underlying this case and set forth in the Report and does not repeat them at length. Catalyst challenges the Federal Drug Administration's ("FDA") approval of Jacobus's drug, Ruzurgi, for orphan drug status due to the FDA's earlier approval for orphan drug exclusivity to Catalyst's drug, Firdapse. Catalyst's legal challenge implicates the proper interpretation of the Orphan Drug Act, Pub. L. 97-414, 96 Stat. 2049 (1983); 21 U.S.C. §§ 360aa–360ee.

A. Orphan Drug Act

Lambert-Eaton Myasthenic Syndrome ("LEMS") is an "orphan disease" — a disease that affects so few people compared to the general population that drug companies do not have the financial incentive to develop drugs to treat it. To remedy this problem, Congress enacted the Orphan Drug Act, Pub. L. 97-414, 96 Stat. 2049 (1983); 21 U.S.C. §§ 360aa–360ee, which "amend[ed] the Federal Food, Drug, and Cosmetic Act to facilitate the development of drugs for rare diseases and conditions, and for other purposes." Pub. L 97–414 (HR 5238), Jan. 4, 1983.

Under the Orphan Drug Act, the term "rare disease or condition" means "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." 21 U.S.C. § 360bb. If a drug company (or "sponsor") develops a drug to treat a rare disease or condition, it "may request the Secretary to designate" it as such. *Id.* § 360bb(a)(1). If the Secretary finds that [the] drug . . . is being or will be investigated for a rare disease or condition" and "if an application for such drug is approved

under [21 U.S.C. § 355][2] . . . the approval, certification, or license would be for use for such disease or condition," and "the Secretary shall designate the drug as a drug for such disease or condition." 21 U.S.C. § 360bb(a)(1).

In her Report, Judge Louis correctly summarizes the drug designation process, and the ensuing New Drug Application ("NDA") and approval process, as follows:

> During the development stage of a drug, a manufacturer or sponsor may request that the FDA designate its drug as one for use in a rare disease or condition under 21 U.S.C. § 360bb. The designation . . . under 21 U.S.C. § 360bb does not dictate the use or indication for which an orphan drug may ultimately be approved for marketing. The purpose of designation under §360bb is to allow the manufacturer or sponsor to qualify for tax incentives and federal assistance in the form of grants to defray the costs of qualified testing in the process of obtaining marketing approval. Later in development, after testing has occurred, the sponsor proposes a particular use or uses for a drug in its new drug application [("NDA")], which is then reviewed by the FDA to determine whether the application establishes that the drug is safe and effective for the proposed use or uses. *See* 21 U.S.C. § 355(d); 21 C.F.R. § 314.50(a)(1) (requiring a new drug application to include the new drug's proposed indications for use).

Report at 2–3.

To provide a financial incentive to develop orphan drugs, section 360cc of the Orphan Drug Act provides a seven-year Orphan Drug Exclusivity ("ODE") period to the drug sponsor that applies for and obtains approval to market an orphan drug:

> Except as provided in subsection (b), 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 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. Section 355(c)(2) of this title does not apply to the refusal to approve an application under the preceding sentence.

[2] 21 U.S.C. § 355 is entitled "New drugs" and, as explained in more detail below, sets forth the requirements for filing an application for approval to introduce a new drug into interstate commerce.

21 U.S.C. § 360cc.

Both sections 360bb and 360cc refer to section 355 of the Federal Food, Drug, and Cosmetic Act. Section 355(b) sets forth the requirements for filing an NDA. Section 355(b) requires, among other information, reports or investigations showing "whether or not such drug is safe for use and whether such drug is effective in use" and "specimens of the labeling proposed to be used for such drug." *Id.* § 355(b)(1)(A), (F). Under section 355(c), within 180 days (or as otherwise agreed) from the filing of the application under section 355(b), the Secretary shall approve the application if he finds none of the grounds under section 355(d) apply. Finally, under section 355(d), the Secretary may refuse the application if, among other reasons, "upon the basis of the information submitted to him as part of the application . . . he has insufficient information to determine whether such drug is safe for use under such conditions."

B. FDA Procedural History

Jacobus obtained an orphan drug designation for its amifampridine drug, Ruzurgi, in December 1990. *See* Sealed Joint Appendix, Vol. 1, ECF No. [66-1] at 8. In 2009, the FDA granted Catalyst's amifampridine drug, Firdapse, an orphan drug designation. *See* Sealed Joint Appendix, Vol. 2, ECF No. [66-2] at 247. The parties agree that the two drugs are the same, as Ruzurgi contains the same active moiety to that of the active ingredient in Firdapse.

In 2015, Catalyst submitted an NDA for approval to market Firdapse for the treatment of LEMS in adult patients. ECF No. [66-2] at 249–50. After its initial review, the FDA rejected the NDA. *See id.* at 289–92. In August 2017, Jacobus submitted its NDA for Ruzurgi for the treatment of LEMS in adult and pediatric patients. *See* ECF No. [66-1] at 53–56. As with Catalyst, the FDA reviewed the NDA and initially rejected it. *See id.* at 57–64. In March 2018, Catalyst resubmitted its NDA and, in November 2018, Firdapse was approved for treatment of LEMS in adults. *See*

ECF No. [66-2] at 487. Jacobus resubmitted its NDA in June 2018. *See* ECF No. [66-1] at 70. However, the FDA had already approved Catalyst's NDA for ODE of Firdapse for treatment of LEMS in adults. *See* ECF No. [66-2] at 487. The FDA administratively divided Jacobus's pending NDA into two parts — one for the treatment of adults and one for the treatment of pediatric patients. *See* Report at 5; ECF No. [66-1] at 434. Because Firdapse had already obtained ODE for LEMS in adults, the FDA's Exclusivity Board recommended denying approval of Ruzurgi with respect to the same. *See* ECF No. [66-1] at 424–33. The FDA thereafter approved Ruzurgi with respect to LEMS in pediatric patients, determining Firdapse did not have ODE with respect to that patient group because its NDA was limited to LEMS in adults. *See id.* at 424–43.

C. Case Procedural History

On June 12, 2019, Catalyst filed their Complaint against the Federal Defendants alleging the FDA's approval of Ruzurgi was arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law. Catalyst alleges that the FDA violated the Administrative Procedure Act as follows:

- the labeling that the FDA approved for Ruzurgi "implies and suggests that [Ruzurgi] may be used for adults," and thus encroaches on Catalyst's ODE (Count I);
- the approval of Ruzurgi for any patient population, adults or pediatrics, violated Catalyst's ODE (Count II);
- Jacobus's application for Ruzurgi impermissibly relied upon studies collected and submitted by Catalyst for Firdapse, and (Count III); and
- the FDA treated the NDAs for Firdapse and Ruzurgi differently, in a way that favored Ruzurgi, by (a) allowing Jacobus, but not Catalyst, to submit studies and clinical trials post-approval, and (b) accelerating Jacobus's application (Count VI).

See ECF No. [1].

On December 17, 2019, Jacobus moved to intervene in this action, *see* ECF No. [32], and was added as a Defendant. Catalyst filed a Motion for Summary Judgment, ECF No. [38], setting forth two pared-down arguments: (1) the FDA's approval of Ruzurgi violated Catalyst's ODE; and (2) the FDA violated its own labeling requirements in approving Ruzurgi. On December 20, 2019, the Court referred the matter to the Magistrate Judge Lauren F. Louis for all pre-trial proceedings. *See* ECF No. [41]. On January 17, 2020, Jacobus and the Federal Defendants filed separate Cross-Motions for Summary Judgment, *see* ECF No. [46], and ECF No. [47], respectively.

In her Report, Magistrate Judge Louis recommends that Catalyst's Motion for Summary Judgment be denied; both Jacobus and the Federal Defendants' Motions be granted; and the case be dismissed. The Report relies on *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984), which sets forth a two-step process for analyzing Administrative Procedures Act claims, known as the doctrine of "*Chevron* deference." Using the doctrine, described in this Order's "Legal Standards" section, the Report reasons:

1. The language in section 360cc of the Orphan Drug Act, specifically the phrase "disease or condition" is ambiguous under step one of the *Chevron* analysis; and
2. The FDA's interpretation of the statute, i.e. limiting Catalyst's ODE to LEMS in adults only, is reasonable under step two of the *Chevron* analysis.

Judge Louis also found the FDA's approval of Ruzurgi's labeling did not violation the Federal Food, Drug, and Cosmetic Act and the FDA did not inappropriately consider pricing in considering approval of Ruzurgi.

Catalyst filed Objections to the Report, averring it "inappropriately ignore[s] the plain language of the statute and the undisputed fact that LEMS in adults and pediatrics is the same disease[.]" ECF No. [94] at 16. In connection with this Objection, Catalyst argues the Report "misapplie[s]" the *Chevron* deference doctrine." *Id.* at 18. Catalyst further argues that the Report

misconstrues its challenge to the FDA's process of labeling Ruzurgi and that FDA's "reliance solely on adult studies on Jacobus's label falsely and misleadingly suggests the drug can be used *by* adults, in violation of the FDCA and FDA regulations." *Id.* at 25.

II. LEGAL STANDARDS

A. District Court Review of a Report and Recommendation

When a magistrate judge's "disposition" has been properly objected to, district courts must review the disposition *de novo*. Fed. R. Civ. P. 72(b)(3). Although Rule 72 is silent on the standard of review, the United States Supreme Court has determined Congress's intent was to require *de novo* review only when objections were properly filed, not when neither party objects. *See Thomas v. Arn*, 474 U.S. 140, 150 (1985) ("It does not appear that Congress intended to require district court review of a magistrate[] [judge]'s factual or legal conclusions, under a *de novo* or any other standard, when neither party objects to those findings." (alterations added)). A proper objection "identifie[s] specific findings set forth in the R & R and articulate[s] a legal ground for objection." *Leatherwood v. Anna's Linens Co.*, 384 F. App'x 853, 857 (11th Cir. 2010) (alterations added; citation omitted). "Frivolous, conclusive, or general objections need not be considered by the district court." *Id.* (quoting *Marsden v. Moore*, 847 F.2d 1536, 1548 (11th Cir. 1988) (internal quotation marks and other citation omitted)); *see also Russell v. United States*, No. 11-20557-Civ, 2012 WL 10026019, at *1 (S.D. Fla. Apr. 17, 2012) (declining to address general or blanket objections not specifically identifying aspects of the magistrate judge's report to which the petitioner objected).

B. The Administrative Procedure Act

To prevail on an Administrative Procedure Act ("APA") claim, a plaintiff must prove an agency's decision was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); *see also Salmeron-Salmeron v. Spivey*, 926 F.3d 1283, 1286

(11th Cir. 2019). The Court's "role is to ensure that the agency came to a rational conclusion, not to conduct its own investigation and substitute its own judgment for the administrative agency's decision." *Defs. of Wildlife v. U.S. Dep't of Navy*, 733 F.3d 1106, 1115 (11th Cir. 2013) (internal quotation marks and citation omitted).

When reviewing an agency's interpretation of a statute, the Court is confronted with two questions. *See Chevron*, 467 U.S. at 842. The Court must "first ask whether congressional intent is clear." *Wilderness Watch & Pub. Emps. for Envtl. Responsibility v. Mainella*, 375 F.3d 1085, 1091 (11th Cir. 2004) (citation omitted). If Congress's intent is clear and 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." *Id.* (internal quotation marks omitted; quoting *Chevron*, 467 U.S. at 842–43).

If the statute is silent or ambiguous regarding a specific issue, then the Court must ask "whether the agency's answer is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. The agency's construction "governs if it is a reasonable interpretation of the statute — not necessarily the only possible interpretation, nor even the interpretation deemed most reasonable by the courts." *Entergy Corp. v. Riverkeeper, Inc.*, 556 U.S. 208, 218 (2009) (citation and emphasis omitted). At a minimum, the Court gives "an agency interpretation deference under *Skidmore v. Swift & Co*., [323 U.S. 134 (1944)] corresponding to the 'thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control.'" *Martin v. Soc. Sec. Admin., Comm'r*, 903 F.3d 1154, 1159 (11th Cir. 2018) (alteration added; quoting *Skidmore*, 323 U.S. at 140).

III. DISCUSSION

Catalyst sets forth two general Objections. First, Catalyst argues Magistrate Judge Louis

misconstrues the plain language of the Orphan Drug Act, specifically 21 U.S.C. § 360cc. In an expansion of this argument, Catalyst insists there are six specific instances in which Magistrate Judge Louis misapplies *Chevron* deference. Second, Catalyst argues Ruzurgi's FDA-approved label violates 21 U.S.C. section 355(d) and its implementing regulations because the Ruzurgi labeling implies it may be used for adult patients. The Court addresses each argument in turn.

A. Plain Language of 21 U.S.C. § 360cc

The crux of this case is whether the language of section 360cc is ambiguous. If it is, the Court need only determine whether the FDA's interpretation of the statute is reasonable. *See Chevron*, 467 U.S. at 843. A review of the statutory language is necessary. The full text of section 360cc(a) states:

> Except as provided in subsection (b), **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 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. Section 355(c)(2) of this title does not apply to the refusal to approve an application under the preceding sentence.

(emphasis added).

The Report focuses on the phrase "same disease or condition" and concludes "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. ECF No. [93] at 10. The statute's silence on this point, the

Report reasons, gives rise to an ambiguity under *Chevron* step one. *See id.* at 9–12.[3]

In its Objections, Catalyst insists the reasoning in the Report contravenes the plain language of section 360cc. *See* ECF No. [94] at 15. Catalyst emphasizes that all parties agree Firdapse and Ruzurgi are the "same drug" and both drugs are intended to treat the "same disease or condition" — LEMS. To elucidate its point, Catalyst points to a "readily diagrammable formula" used in a case it contends is instructive, *Eagle Pharmaceuticals, Inc. v. Azar*: "if x and y, then z." *Id.* at 16 (citing 952 F.3d 323, 328 (D.C. Cir. 2020) (internal quotation marks and citations omitted)).

In *Eagle Pharmaceuticals*, the D.C. Circuit questioned whether the plain language of section 360cc permitted "serial exclusivity," i.e. whether, after the expiration of the seven-year ODE for a certain drug, a *second* drug sponsor could take advantage of the exclusivity provision. *See* 952 F.3d at 328. More specifically, the Court questioned whether the FDA was permitted to require the sponsor of the second drug to demonstrate the drug's clinical superiority after its approval (a "post-approval clinical-superiority requirement") before awarding the sponsor ODE. *See id.* at 329. The Court found the FDA had no such authority, reasoning that by mandating the second drug sponsor demonstrate clinical superiority at the post-approval stage, the FDA created a requirement not intended, or written, by Congress. *See id.* at 331 ("the text leaves no room for the FDA to place additional requirements on a drug that has been designated and approved before granting its manufacturer the right to exclusivity.") Referring to the formula "if x and y, then z," the Court found the corresponding statutory text read, simply, "if designation and approval, then exclusivity." *Id.*

[3] The Report notes that the FDA referred the analysis of Catalyst's ODE to the Exclusivity Board at the FDA's Center for Drug Evaluation and Research. The Exclusivity Board determined LEMS in adults is not the same disease or condition as LEMS in children for the purposes of its exclusivity analysis and recommended Ruzurgi be approved for pediatric patients. The FDA adopted the Exclusivity Board's recommendation. *See* Report at 6; ECF No. [66-1] at 424–33.

Catalyst applies the same formula to this case, contending that the resulting logic is: "if (x) FDA designates *and* (y) approves a drug under the Orphan Drug Act, *then* (z) under the plain language of this provision, the FDA is barred from approving another application for such drug." ECF No. [94] at 16 (alteration adopted, citation, internal quotation marks, and footnote call number omitted).

In this case, the reasoning of *Eagle Pharmaceuticals* is not as easy to import as Catalyst suggests. Catalyst is not wrong to urge the Court to focus on the plain language of the statute, as this is what the Court must do under *Chevron* step one. But Catalyst misses the mark by omitting a portion of section 360cc from its logic, which starts with approval under section 355. Returning to the text, section 360cc states "If the Secretary . . . ***approves an application filed pursuant to section 355*** . . . for a drug designated under section 360bb of this title . . . the Secretary may not approve another application under section 355 of this Title . . . for the same drug for the same disease or condition for a person who is not the holder of such approved application . . . ." On its face, the text of section 360cc refers the reader to section 355, which in turn sets forth the requirements to obtain approval for a drug, including evidence that the drug is safe and effective for its intended use. The drug's intended use — which drug companies must describe in the section 355 application — may be for a treatment of all patients with the disease or condition or, as in this case, for the manifestation of the disease in adult patients or pediatric patients only.

Importantly, Catalyst does not dispute its section 355 application was for the treatment of LEMS in adults only, *see* ECF No. [66-2] at 487, nor does Catalyst argue NDA applications do not (or should not have to) distinguish between adult and pediatric patients in the first instance. Thus, by virtue of section 360cc's reference to Section 355 — which in turn contemplates that drug companies must provide evidence of the effectiveness of their proposed drug for a specific *use* to obtain marketing approval — it is not clear whether the language "disease or condition" in

section 360cc refers to the *approved* disease or condition for which the sponsor applies in its NDA, or the disease or condition that was initially *designated* under section 360bb.

In this respect, Jacobus's reliance on *Spectrum Pharmaceuticals, Inc. v. Burwell*, is apt. In *Spectrum*, the D.C. Circuit considered whether the FDA should not have approved the defendant's generic version of the drug, levoleucovorin, used to treat liver damage caused by methotrexate therapy (a type of chemotherapy) and manage pain from colorectal cancer. *See* 824 F.3d 1062, 1064 (D.C. Cir. 2016). The plaintiff, Spectrum Pharmaceuticals — which had obtained ODE for the *colorectal* indication — sued the FDA when it approved the generic drug for *methotrexate* indications. *See id.* Spectrum argued the FDA knew, but ignored, that the generic drug would also be used to treat colorectal pain, thus trenching on Spectrum's ODE. *See id.* at 1065. The court rejected Spectrum's arguments, finding the FDA was permitted to approve the generic drug because the label for the same mentioned only the methotrexate indications and omitted (or "carved-out") the colorectal indication subject to Spectrum's ODE. *See id.* at 1065–67.

The court in *Spectrum* did not consider whether the Orphan Drug Act permits the FDA to limit ODE to adult or pediatric manifestations of a disease or condition. Nevertheless, the court's commentary on the text of the Orphan Drug Act is instructive.

> As the Fourth Circuit reasoned in *Sigma–Tau Pharmaceuticals, Inc. v. Schwetz*, 288 F.3d 141 (4th Cir. 2002), the words "for such disease or condition" suggest 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. *See id.* at 145 (reasoning that the statutory language is "directed at FDA approved-use, not generic competitor intended-use***"). The statute creates limits on the approval of an "application," which by implication directs FDA to evaluate what is written on the application***. 21 U.S.C. § 360cc. An application will necessarily include only stated indications, not intended off-label uses. *Id.* § 355(b).

Id. at 1067. (emphasis added). The *Spectrum* court observed, as this Court does here, section 360cc refers to applications, and an application "necessarily includes" the proposed drug's specific use.

See id. Thus, that the FDA interprets section 360cc to refer to the *approved* disease or condition stated in the 355 application by no means contravenes the text of the statute.[4]

In sum, because there is more than one way to reasonably interpret section 360cc, the Court finds the statute is ambiguous under *Chevron* step one. *See* 467 U.S. at 842.

Following this conclusion, the six "fatal flaws" Catalyst identifies may be dealt with in relatively short order:

First, Catalyst argues "the term 'same disease or condition' is simply not ambiguous." ECF No. [94] at 19. For the reasons stated above, there is more than one reasonable interpretation of the words "same disease or condition" given section 360cc's reference to section 355.

Second, Catalyst argues "nothing about the interplay of other Orphan Drug Act provisions can render the straightforward term 'same disease or condition' ambiguous." *Id.* This objection refers only to section 360cc's interplay with section 360bb, glossing over section 355 entirely. In this respect, the Court agrees with the Federal Defendants that the words "same disease or condition" must be considered "in their context and with a view to their place in the overall

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[4] What is more, a case on which Catalyst relies, *Depomed, Inc. v. United States Department of Health & Human Services*, supports the Court's conclusion. In *Depomed*, the court considered whether a pharmaceutical company was entitled to ODE for a drug used to treat post-herpetic neuralgia ("PHN"), where the FDA had already granted marketing approval to a drug called Neurontin. *See* 66 F. Supp. 3d 217, 220 (D.D.C. 2014). The court began its analysis, as this Court does, by looking to the text of section 360cc. After reciting the same, the court noted:

> [T]he plain language of the statute sets forth **two procedural prerequisites for marketing exclusivity**: first, the FDA must have "designated" the drug as an orphan drug, upon request from the drug's sponsor, pursuant to 21 U.S.C. § 360bb and its accompanying regulations; and **second, the FDA must have "approved" the designated orphan drug for marketing to the public pursuant to 21 U.S.C. § 355, which is the section of the FDCA that provides the general procedure for marketing approval of all the pharmaceutical products that the FDA regulates**. **If both conditions are met, then the Act provides that the FDA "may not approve another" such drug for marketing to the public** for "seven years from the date" of the designated drug's approval. 21 U.S.C. § 360cc(a).

Id. at 221 (emphasis added; footnote call number omitted). Thus, in the *Depomed* court's view, section 360cc makes clear that ODE is tied to application approval under section 355.

statutory scheme." ECF No. [99] at 12 (citing *King v. Burwell*, 576 U.S. 473, 486 (2015) (other citations omitted)). Because section 360cc's interplay with section 355 is central to the Court's finding, Catalyst's argument is misplaced.

Third, Catalyst argues "although the R&R infers that the term 'same disease or condition' in 360cc(a) must be tied to the scope of Catalyst's approval in this case, no text in the provision supports this, either directly or indirectly." ECF No. [94] at 20. Not so. Section 360cc refers directly to section 355, and section 355 concerns NDAs, which may be limited in scope.

Fourth, Catalyst argues "although Congress used the terms 'indication' or 'uses' elsewhere in the FDCA to draw distinctions between specific approved uses of a drug, Congress chose not to use those terms in the ODE provision." ECF No. [94] at 21. Although this is true, Congress also specifically referred to section 355 in section 3600cc. Congress could have, but did not, omit reference to section 355, or make clear that the term "same disease or condition" refers only to the disease or condition *as designated* in section 360bb. For example, Congress could have written: "if the Secretary approves an application for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application for another drug with the same designation." Congress did not do so, and the Court cannot simply ignore its reference to section 355.

Fifth, Catalyst argues "other provisions of the Orphan Drug Act show that Congress explicitly did not intend for a 'disease or condition' to be sliced and diced by FDA according to 'subpopulations or 'subgroups.'" ECF No. [94] at 21. This argument does not hold up against the language of section 355, which requires a drug company to substantiate the effectiveness of its drug for a particular *use*. *See* 21 U.S.C. § 355(b). Catalyst points to section 360ee(b)(1)(C)(ii), which encourages research to "understand the full spectrum of the disease manifestations, including . . . identifying and defining distinct subpopulations affected by ***a*** rare disease or

condition.'" Yet this section of the statute does not explain away section 360cc's reference to section 355. Certainly, it does not give rise to the conclusion that the FDA's interpretation of section 360cc contravenes the plain meaning of the statute.

Finally, Catalyst argues "the Orphan Drug Act explicitly provides three specific circumstances where FDA may actually approve a second 'same drug' for the 'same disease or condition' notwithstanding ODE[.]" ECF No. [94] at 22. Catalyst points to three exceptions enumerated in 21 U.S.C. section 360cc(b), including (1) if the company with ODE "cannot ensure the availability of sufficient quantities" of its drug," *id.* section 360cc(b)(1); (2) the entity with ODE consents "in writing," *id.* section 360cc(b)(2); or (3) a subsequent drug company can demonstrate its drug "clinically superior" to the drug with ODE, *id.* section 360cc(c). The Court agrees with the Federal Defendants that each of these exceptions pertains to whether a "sponsor's orphan drug exclusivity may be 'broken' by a second applicant, none of which apply here." ECF No. [99] at 14. As explained above, Catalyst only sought and obtained approval under section 355 with respect to the treatment of LEMS in adults, *not* LEMS for all patients. Had another sponsor arrived with a competing drug for LEMS in *adults*, the Court might scrutinize the foregoing exceptions. It need not do so here.

The Court emphasizes that Catalyst's view of section 360cc is not necessarily *wrong*, but it is not the only reasonable way to interpret the plain language of the statute. As noted, an agency's construction of a statute "governs if it is a reasonable interpretation . . . not necessarily the only possible interpretation, nor even the interpretation deemed most reasonable by the courts." *Entergy Corp*, 556 U.S. at 218 (citation and emphasis omitted).

B. Catalyst's Challenge to Ruzurgi's Label

Catalyst next argues Ruzurgi's label is "false or misleading," in violation of 21 U.S.C. section 355(a), because it implies or suggests Ruzurgi may be used for adults even though it has

only been approved for pediatric patients. *See* ECF No. [94] at 24. The label for Ruzurgi states "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." ECF No. [66-1] at 448. According to Catalyst, the "specific reliance solely on adult studies on Jacobus's label falsely and misleadingly suggests the drug can be used *by* adults, in violation of the FDCA and FDA regulations." ECF No. [94] at 25.

Catalyst points to (1) 21 U.S.C. section 355(d), providing the Secretary may refuse an NDA if he finds the labeling for the same is "false or misleading;" (2) 21 C.F.R. section 201.57(c)(2)(iv), providing "indications . . . must be supported by substantial evidence of effectiveness based on adequate and well-controlled studies as defined in [section] 314.126(b) of this chapter; " and (3) 21 C.F.R section 201.57(c)(15)(i), providing "any clinical study that is discussed in prescription drug labeling that relates to an indication for or use of the drug must be adequate and well-controlled as described in [section] 314.126(b) of this chapter and must not imply or suggest indications or uses or dosing regimens not stated in the 'Indications and Usage' or 'Dosage and Administration' section."

"As with all agency rules . . . regulations implementing [a statute] are accorded *Chevron* deference." *See Falken v. Glynn Cty., Georgia*, 197 F.3d 1341, 1346 (11th Cir. 1999); *Robertson v. Methow Valley Citizens Council*, 490 U.S. 332, 359 (1989) (noting an agency's interpretation of its own regulation is controlling if it is not "plainly erroneous or inconsistent with the regulation." (citation omitted)). Save for a general citation to the premise set forth in *Simmons v. Block*, 782 F.2d 1545, 1550 (11th Cir. 1986) (noting "the failure of an agency to comply with its own regulations" is unlawful under the APA), Catalyst fails to present any case law in support of its position. Certainly, it presents no authority that would call into question the FDA's interpretation of its regulation under *Chevron's* highly deferential standard.

With this standard in mind, the Court declines Catalyst's invitation to substitute its interpretation of "misleading" for the FDA's interpretation. The Court notes Ruzurgi's label does not affirmatively represent the drug is approved for adult patients, but merely discloses pediatric approval was based on adult studies. Moreover, as noted by Jacobus, *see* ECF No. [98] at 24, this disclosure is required under 21 C.F.R. section 201.57(c)(15): "[t]his section must discuss those clinical studies that facilitate an understanding of how to use the drug safely and effectively."

The Court agrees with Judge Louis that the record reflects the FDA "reviewed the label for Ruzurgi after the application had been split for pediatric patients and adults and concluded that it was not misleading for pediatric patients." ECF No. [93] at 16.

IV. CONCLUSION

For the foregoing reasons, it is

ORDERED AND ADJUDGED that:

1. Magistrate Judge Louis's Report and Recommendations, **ECF No. [93]**, is **ADOPTED;**
2. Plaintiff Catalyst Pharmaceuticals Inc.'s Objections, **ECF No. [94]**, are **OVERRULED;**.
3. Plaintiff Catalyst Pharmaceuticals Inc.'s Motion for Summary Judgment, **ECF Nos. [38], [40]**, is **DENIED;**
4. Federal Defendants' Cross-Motion for Summary Judgment, **ECF No. [47]**, is **GRANTED;**
5. Intervenor-Defendant Jacobus Pharmaceutical Company, Inc.'s Cross-Motion for Summary Judgment, **ECF No. [46]**, is **GRANTED**; and
6. The Case is **DISMISSED**. The Clerk of Court shall **ADMINISTRATIVELY CLOSE** the case.

DONE AND ORDERED in Chambers at Miami, Florida, on September 29, 2020.

BETH BLOOM
UNITED STATES DISTRICT JUDGE

Copies to:
Counsel of Record

IN THE UNITED STATES COURT OF APPEALS

FOR THE ELEVENTH CIRCUIT

No. 20-13922-JJ

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 Food and Drugs,
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

ON PETITION(S) FOR REHEARING AND PETITION(S) FOR REHEARING EN BANC

BEFORE: LAGOA, ANDERSON, and MARCUS, Circuit Judges.

PER CURIAM:

The Petition for Rehearing En Banc is DENIED, no judge in regular active service on the Court having requested that the Court be polled on rehearing en banc. (FRAP 35) The Petition for Rehearing En Banc is also treated as a Petition for Rehearing before the panel and is DENIED. (FRAP 35, IOP2)

ORD-42

No. 20-13922

UNITED STATES COURT OF APPEALS FOR THE ELEVENTH CIRCUIT

CATALYST PHARMACEUTICALS, INC.,

Plaintiff-Appellant,

v.

XAVIER BECERRA, Secretary of Health and Human Services;
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES;
JANET WOODCOCK, ACTING Commissioner of Food and Drugs;
U.S. FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

JACOBUS PHARMACEUTICAL COMPANY, INC.,

Intervenor-Defendant-Appellee.

On Appeal from the United States District Court for the Southern District of Florida, No. 1:19-cv-22425-BB, Hon. Beth Bloom

DECLARATION OF LORI DUNHAM IN SUPPORT OF JACOBUS PHARMACEUTICAL COMPANY, INC.'S MOTION TO STAY THE MANDATE PENDING THE FILING AND DISPOSITION OF A PETITION FOR WRIT OF CERTIORARI

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Counsel for Jacobus Pharmaceutical Company, Inc.

DECLARATION OF LORI DUNHAM

I, Lori Dunham, pursuant to 28 U.S.C. § 1746, declare as follows:

I am a mother and advocate for G.D., a sixteen-year-old girl who has Lambert Eaton Myasthenic Syndrome (LEMS).

On June 16, 2020, I sent a letter (via email) to Judge Beth Bloom of the U.S. District Court for the Southern District of Florida. In that letter, I shared G.D.'s story and how Jacobus's LEMS drug, Ruzurgi, has impacted her life. The Court published the letter on its public docket. *See* R.78.

On November 19, 2021, acting through counsel, G.D. and I sought leave from this Court to file an *amicus curiae* brief in support of Jacobus's petition for rehearing *en banc*. The *amicus* brief also discussed G.D.'s struggles living with LEMS and how Ruzurgi has helped her live a better life. Although the Court unfortunately denied our request for leave to file the brief, I understand it is still available on the public docket.

Both the letter and the *amicus* brief truthfully and accurately recount G.D.'s struggles with LEMS and the impact Ruzurgi has had on her life. The factual content of both the brief and the letter are based

on, and accurately reflect, my own personal observations and experiences as G.D.'s mother.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on December 10, 2021

Lori Dunham