IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

OTSUKA PHARMACEUTICAL CO., LTD., *et. al.* *Plaintiffs*, v. SYLVIA MATHEWS BURWELL, *et al.* *Defendants*.	**Case No.: 8:15-cv-00852-GJH**

ALEMBIC'S MEMORANDUM IN OPPOSITION TO OTSUKA'S MOTION FOR SUMMARY JUDGMENT

Intervenors-defendants Alembic Pharmaceuticals Limited; Alembic Limited; Alembic Global Holdings SA; and Alembic Pharmaceuticals, Inc. (collectively "Alembic") respectfully submit this memorandum in opposition to the motion for summary judgment submitted by plaintiffs Otsuka Pharmaceutical Co., Ltd.; Otsuka Pharmaceutical Development & Commercialization, Inc.; and Otsuka America Pharmaceutical, Inc. (collectively "Otsuka"). In addition, to the extent not inconsistent with any arguments set forth below, Alembic supports and incorporates any arguments made by federal defendants or by other intervenors-defendants.

Alembic has received "tentative approval" from the Food and Drug Administration ("FDA") for its abbreviated drug applications to market generic versions of Otsuka's Abilify® (aripiprazole) tablets and orally disintegrating tablets, signifying FDA's determination that Alembic's drug applications meet all substantive standards for approval. In the absence of the extraordinary relief sought by Otsuka, Alembic anticipates receiving final approval of its drug applications on or about April 20, 2015.

ARGUMENT

I. Otsuka's Claims Are Not Properly Before This Court.

For two independent reasons, Otsuka's claims are not properly before this Court.

First, the crux of Otsuka's case is that FDA's "reversal" of its approval decision (by changing the indication for Tourette's Disorder from a pediatric population to a general population) was unlawful.[1] Otsuka's Memorandum in Support of Motion for Summary Judgment ("Otsuka Mem.") at 17-29. In essence, Otsuka's contention is that FDA refused to approve its supplemental drug application seeking a pediatric indication for the treatment of Tourette's Disorder. The Federal Food, Drug, and Cosmetic Act ("FDC Act") sets forth a specific procedure for an adversely affected drug sponsor (like Otsuka) to challenge FDA's refusal to approve a drug application, involving an opportunity for a hearing with direct review in a Court of Appeals on a "substantial evidence" standard. 21 U.S.C. § 355(d) and (h). Under FDA's regulations, there is an opportunity for a formal evidentiary hearing before an Administrative Law Judge. *See* 21 C.F.R. § 314.201 and 21 C.F.R. Part 12.

Here, Otsuka should have pursued its objections to FDA's refusal to approve a pediatric indication for the treatment of Tourette's Disorder under those administrative hearing procedures. During such an administrative hearing, FDA can consider Otsuka's contention that

[1] FDA had the inherent authority to correct its approval decision by revising the patient population for the Tourette's Disorder indication. *See American Therapeutics, Inc. v. Sullivan*, 755 F. Supp. 1, 2 (D.D.C. 1990) (upholding FDA's authority to "rescind" a generic drug approval without going through the statutory withdrawal of approval administrative hearing process, where the agency had overlooked unfavorable compliance information in initially granting the approval; "This was a good faith mistake promptly discovered and corrected, nothing more.").

there was no factual or evidentiary support for the change in patient population, Otsuka Mem. at 23-26.

Because Otsuka did not invoke the statutory procedure for contesting FDA's refusal to approve a Tourette's Disorder pediatric indication for Abilify, Otsuka's claims are not properly before this Court. The Administrative Procedure Act ("APA") provides that "[a]gency action made reviewable by statute and final agency action for which there is no other adequate remedy in a court are subject to judicial review." 5 U.S.C. § 704. Here, Otsuka is not entitled to judicial review under the APA. FDA's refusal to approve a pediatric Tourette's Disorder indication for Abilify is not at this time, under the plain language of 21 U.S.C. § 355(d) and (h) and the reasoning discussed above, "agency action made reviewable by statute," 5 U.S.C. § 704. Because of the potential availability of direct review in a Court of Appeals under 21 U.S.C. § 355(d) and (h), the current posture is not "final agency action for which there is no other adequate remedy in a court," 5 U.S.C. § 704. Therefore, this Court does not have any jurisdiction under the APA to consider Otsuka's claims at this time. *See Sterling Drug, Inc. v. Weinberg*, 384 F. Supp. 557, 561 (S.D. N.Y. 1974), *aff'd*, 509 F.2d 1236 (2d Cir. 1975).

Second, Otsuka contends that FDA's "corrected" labeling contains multiple aspects pertaining to pediatric use that cannot be omitted. Otsuka Mem. at 32-34. To the best of Alembic's knowledge, FDA has not made any final agency decision regarding appropriate "carve out" labeling for generic versions of Abilify that propose to omit the Tourette's Disorder indication.[2] Under these circumstances, there is no final agency decision on appropriate carve-

[2] Alembic, other intervenors-defendants, and other firms have received "tentative approvals" for their generic versions of Abilify, indicating FDA's judgment that their applications meet all substantive standards for approval. However, according to FDA's public website, those tentative approvals all predate the December 2014 approval of Tourette's Disorder indication for Abilify.

out labeling that is amenable to review by this Court under the APA, 5 U.S.C. § 704. *Hi-Tech Pharmacal Co. v. U.S. Food and Drug Administration,* 587 F.Supp.2d 1, 10 (D.D.C. 2008). Moreover, Otsuka's contentions are not ripe for adjudication. *See Pfizer, Inc. v. Shalala*, 182 F.3d 975, 980 (D.C. Cir. 1999).

II. FDA's Labeling Decisions Are Entitled To Substantial Deference From This Court

Otsuka contends there was no factual support for FDA's decision to correct the approved Tourette's Disorder indication for Abilify from pediatric patients to the general population. Otsuka Mem. at 23-26. However, Otsuka overlooks the fact that the selection of the appropriate patient population "rests on the agency's evaluations of scientific data within its area of expertise, and hence is entitled to a high level of deference" from this Court. *Serono Laboratories, Inc. v. Shalala*, 158 F.3d 1313, 1320 (D.C. Cir. 1998) (internal quotations and citations omitted). As the D.C. Circuit stated in *A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1490 (D.C. Cir. 1995), FDA's "judgments as to what is required to ascertain the safety and efficacy of drugs falls squarely within the ambit of FDA's expertise and merit deference from us" (internal quotations and citations omitted). FDA's judgment as to the appropriate patient population for a particular indication is an integral part of assessing the safety and efficacy of drugs, and thus is entitled to a high level of deference. Moreover, FDA's interpretations regarding the interplay between labeling and exclusivity are entitled to deference. *See AstraZeneca Pharmaceuticals LP v. Food and Drug Administration*, 872 F.Supp.2d 60, 86 (D.D.C. 2012), *aff'd*, 713 F.3d 1134 (D.C. Cir. 2013).

When viewed in this light, the fact that Otsuka apparently did not submit clinical trial data with non-pediatric patients (Otsuka Mem. at 5-7, 23) is hardly dispositive.

III. Otsuka's Orphan Drug Exclusivity Does Not Automatically Block The Final Approval Of Alembic's ANDA With The Tourette's Disorder Indication Carved Out

Even if FDA's decision to broaden the patient population for the treatment of Tourette's Disorder from a pediatric population to a general population was unlawful, Otsuka's exclusivity does not automatically block the final approval of generic products (such as Alembic's) with carved-out labeling (with Tourette's Disorder omitted) on or about April 20, 2015. This conclusion follows for three independent reasons.

First, Otsuka contends that Section 505A(o) of the FDC Act, 21 U.S.C. § 355a(o), sets forth the "only" circumstance when exclusivity-protected pediatric information can be omitted from the labeling of a proposed generic product. Otsuka Mem. at 28 and 30. However, the statute does not expressly use the word "only." Otsuka invokes the *expressio unius est exclusio alterius* (the expression of one thing is the exclusion of another) principle of statutory construction in an attempt to, in essence, insert the word "only" into section 355a(o). Otsuka Mem. at 30. This Court should reject Otsuka's proffered approach.

In *Adirondack Medical Center v. Sebelius*, 740 F.3d 692, 697 (D.C. Cir. 2014), the D.C. Circuit considered the *expressio unius* canon of construction, noting that "the canon's relevance and applicability must be assessed within the context of the entire statutory framework" (citations omitted). The D.C. Circuit stated: "The *expressio unius* canon is a 'feeble helper' in an administrative setting, where Congress is presumed to have left to reasonable agency discretion questions that it has not directly resolved." *Id*. (citations omitted). The D.C. Circuit rejected an argument, functionally identical to Otsuka's argument, which would have effectively inserted "only" into the relevant statutory provision, stating "Congress generally knows how to use the word 'only' when drafting laws." *Id*. (citations omitted).

Here, section 355a(o) was added by the Best Pharmaceuticals For Children Act ("BPCA"), Pub. L. No. 107-109, enacted on January 4, 2002. The BPCA amended what are commonly called the 1984 Hatch-Waxman Amendments to the FDC Act. It is widely recognized that Hatch-Waxman represented a balance, with benefits accruing to both innovator pharmaceutical companies and generic pharmaceutical companies. *See, e.g., Abbott Laboratories v. Young*, 920 F.2d 984, 985 (D.C. Cir. 1990). Looking at the BPCA as a whole, it is apparent that its varied provisions sought to maintain that balance. For example, on the one hand, for the benefit of the innovator industry, the BPCA reauthorized 6-month pediatric studies exclusivity, which would have sunset in the absence of Congressional action. *See* former 21 U.S.C. § 355a(j) (sunset provision), added to FDC Act by Pub. L. No. 105-115 (Nov. 21, 1997). At the same time, the BPCA included provisions to benefit the generic industry. For example, the BPCA added 21 U.S.C. § 355a(m), which clarified that there is no loss of 180-day exclusivity when there is an "overlap" of 180-day exclusivity and 6-month pediatric studies exclusivity. 180-day exclusivity has been recognized as a very valuable benefit to the generic industry, as it serves as an incentive to challenge patents on innovator drugs by providing a period during which the first generic applicant or applicants to challenge an *Orange Book* patent on the reference product being copied face no (or limited) generic competition. *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 878-79 (D.C. Cir. 2004). In fact, the D.C. Circuit referred to 180-day exclusivity as an "Edenic moment of freedom from the pressures of the marketplace" for the generic firms benefitting from the exclusivity. *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998).

Looking at the BPCA as a whole, it is apparent that its purpose was to encourage – and reward – the study of drugs in pediatric populations, without giving innovator drug sponsors

unwarranted monopoly extensions. Nothing in the BPCA's legislative history[3] indicates that the BPCA was intended to somehow differentiate between the 3-year "new clinical studies" exclusivity and orphan drug exclusivity. Thus, this Court should decline to read the word "only" into section 355a(o), as Otsuka would have it. When viewed against this background, Otsuka's attempt to invoke the *expressio unius* canon should be rejected. Properly interpreted, Section 355a(o) sets forth ***some*** circumstances under which exclusivity-protected pediatric labeling can be carved out, but that list is not exclusive.

Second, the electronic *Orange Book* shows that Abilify has exclusivity I-700 ("treatment of pediatric patients with Tourette's Disorder (6-18 years)"), expiring December 12, 2017. Although not explained in the *Orange Book*, that exclusivity can only be 3-year "new clinical studies" exclusivity granted under 21 U.S.C. § 355(j)(5)(F)(iv) in connection with the December 12, 2014 approval of Otsuka's supplemental drug application for Abilify. Otsuka agrees that Abilify has 3-year "new clinical studies" exclusivity. *See* Otsuka Mem. at 30, n.7. Thus, the exclusivity associated with Otsuka's Tourette's Disorder supplemental approval is expressly within the scope of 21 U.S.C. § 355a(o), which allows the carve-out of "a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of section 355(j)(5)(F)."

[3] H.R. Rep. No. 107-277 (107th Cong., 1st Sess.); 147 Cong. Rec. E2368-01 (Dec. 20, 2001); 147 Cong. Rec. E2389-01 (Dec. 20, 2001); 147 Cong. Rec. H10200-01 (Dec. 18, 2001); 147 Cong. Rec. S. 13070-02 (Dec. 12, 2001).

Third and finally, Section 355a(o) simply does not apply to the current situation, as it was intended solely for situations where the innovator drug sponsor earns 6-month pediatric exclusivity pursuant to a "written request" for a pediatric study from FDA, *see* 21 U.S.C. § 355a(b) and (c). As explained in the Congressional report about legislation that eventually became the BPCA:

> *Section 11. Prompt approval of generic drugs when pediatric information added to labeling*
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> * * *
>
> Pursuant to a written request, the FDA can ask that manufacturers conduct pediatric studies which could give rise not only to the six months of exclusivity provided for in section 505A [21 U.S.C. § 355a], but also three years of exclusivity pursuant to the Hatch-Waxman Act. This Section does not prevent any manufacturer from earning six months of exclusivity and then claiming three years of supplemental exclusivity pursuant to section 505(j) [21 U.S.C. § 355(j)]. ***However, it does make clear that if a manufacturer does claim supplemental [pediatric studies] exclusivity under section 505(j), the terms of that exclusivity will not prevent generic competition for the indications or aspects of labeling which are not protected***.***

H.R. Rep. No. 107-277 (107th Congress, 1st Sess.) at 37-38 (emphasis added). Thus, the BPCA's history clarifies that section 355a(o) only applies in situations where ***both*** 6-month pediatric studies exclusivity ***and*** 3-year "new clinical studies" exclusivity are involved. Here, nothing indicates that Otsuka obtained 6-month pediatric exclusivity in connection with its Tourette's Disorder indication.

CONCLUSION

For the reasons discussed above, this Court should deny Otsuka's motion for summary judgment.

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Respectfully Submitted,

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on this 7th day of April, 2015, a copy of the Memorandum In Opposition to Otsuka's Motion for Summary Judgment by Alembic Pharmaceuticals Limited, Alembic Limited, Alembic Global Holdings SA, and Alembic Pharmaceuticals, Inc. (collectively "Alembic") was served via ecf on the following:

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