IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

Otsuka Pharmaceutical Co., Ltd., et al.,	*	
Plaintiffs,	*	
v.		Case No. 15-1688
	*	
Sylvia Mathews Burwell, et al.,	*	
Defendants.		

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MEMORANDUM IN SUPPORT OF MOTION TO EXPEDITE PROCEEDINGS AND REQUEST FOR IMMEDIATE SCHEDULING CONFERENCE

Introduction

Plaintiffs Otsuka Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Development & Commercialization, Inc., and Otsuka America Pharmaceutical, Inc. (collectively, "Otsuka") respectfully move to expedite proceedings in this case. Otsuka seeks to have this case resolved on the merits before the end of the year. Without an expedited final decision by this Court, Otsuka will be significantly and irreparably harmed. Otsuka seeks the expedited filing of the agency administrative record and an expedited briefing and hearing schedule on Otsuka's intended motion for summary judgment.

Otsuka here challenges the U.S. Food and Drug Administration's ("FDA") denial of its citizen petition and approval of the New Drug Application ("NDA") submitted by Alkermes plc ("Alkermes") for aripiprazole lauroxil (marketed as Aristada®). This case involves no disputed issues of fact and only disputed questions of law. The case will be decided on the basis of the administrative record and without discovery. The legal issues here are precisely the kinds of questions the Court routinely resolves on motions for summary judgment. This case can and should proceed to the summary judgment stage as expeditiously as possible.

On October 5, 2015, FDA approved Alkermes's NDA for Aristada as a long-acting

injectable formulation that is a prodrug of aripiprazole indicated for the treatment of schizophrenia, with conditions of use that are the same as Otsuka's drug Abilify Maintena® (aripiprazole). (A prodrug is an inactive compound that requires metabolic conversion prior to becoming a molecule that actually acts in the body.) FDA's decision allows Alkermes to obtain a benefit under the Hatch-Waxman Amendments (*i.e.*, reliance on aripiprazole under an "intermediate" short-cut pathway that allows an NDA to rely on FDA's prior findings of safety and effectiveness for a particular drug, *see* Section 505(b)(2)), but not to be subject to the corresponding Hatch-Waxman tradeoff (*i.e.*, subject to three-year exclusivity for long-acting aripiprazole for the conditions of use of treatment of schizophrenia in acutely relapsing patients).

The Alkermes NDA for aripiprazole lauroxil relied on FDA's prior findings of safety and effectiveness for Otsuka's drug Abilify® (aripiprazole) to meet the drug approval requirements of the federal Food, Drug, and Cosmetic Act ("FDCA"). Yet, FDA allowed Alkermes to avoid the three-year exclusivity attaching to Otsuka's drug Abilify Maintena, with which Aristada shares the same conditions of approval. Abilify Maintena is a long-acting injectable formulation of aripiprazole for treatment of schizophrenia. Otsuka has three-year exclusivity that covers long-acting aripiprazole for the conditions of use of treatment of schizophrenia in both maintenance and acutely relapsing patients. The last of these exclusivities does not expire until December 5, 2017. Despite the fact that Aristada relied on FDA's prior findings of safety and effectiveness for aripiprazole to meet the FDCA's drug approval requirements; that aripiprazole is an active metabolite in aripiprazole; and aripiprazole provides the therapeutic benefit to patients taking aripiprazole, FDA determined that Aristada is not subject to aripiprazole's exclusivity.

With FDA approval in hand, Alkermes will flood the market with aripiprazole lauroxil – taking sales and profits of Abilify and Abilify Maintena – only to be stopped by this Court if it

ultimately determines FDA's approval was unlawful. If Otsuka is successful in this action, its harm will not be recoverable from FDA or Alkermes and its exclusivity period will be irretrievably shortened. Given the risk of harm to Otsuka, the alternative to moving to expedite the filing of the administrative record and its motion for summary judgment is for Otsuka to move for temporary and/or preliminary injunctive relief and thereafter to move for summary judgment. Otsuka respectfully submits that its proposed procedure of proceeding directly and expeditiously to the merits is more efficient, in the interest of judicial economy, and the proper way to proceed in this case.

Background

Otsuka holds an approved NDA for Abilify (aripiprazole), an atypical antipsychotic indicated for oral, once-daily treatment of schizophrenia and several other indications. Abilify Maintena, first approved in 2013, gave patients with schizophrenia quite a different treatment option. Abilify Maintena is approved and has exclusivity that covers long-acting aripiprazole for the conditions of use of treatment of schizophrenia in both maintenance and acutely relapsing patients. These exclusivities do not expire until December 2017.

On August 25, 2014, Alkermes announced that it had submitted an NDA to FDA seeking approval of aripiprazole lauroxil, a long-acting injectable for the treatment of schizophrenia. In its press release, Alkermes admitted that aripiprazole lauroxil converts to aripiprazole. The Alkermes NDA was supported by a single adequate and well-controlled clinical trial conducted on patients with schizophrenia currently experiencing an acute relapse. On July 13, 2015, Otsuka submitted a second citizen petition in which Otsuka requested (1) that FDA delay or withhold final approval of the Alkermes NDA pending the expiration of Otsuka's three-year exclusivity for the conditions of approval of aripiprazole on December 5, 2017; and (2) that FDA refuse to approve

the Alkermes NDA because it fails to satisfy the substantial evidence of effectiveness requirement. Alkermes submitted comments in opposition to Otsuka's petition. Otsuka filed supplements to its citizen petition to answer Alkermes's comments.

On October 5, 2015, FDA denied Otsuka's citizen petition on both grounds and granted approval to Aristada, a long-acting injectable formulation that is a prodrug of aripiprazole indicated for the treatment of schizophrenia, with conditions of use that are the same as Abilify Maintena.

Argument

A. Standard

"It is well established that district courts enjoy broad discretion when deciding case management and scheduling matters, a discretion that extends to determining how and in what order cases should be heard and determined." *Florida v. United States*, 820 F. Supp. 2d 85, 89 (D.D.C. 2011) (citation omitted) (citing *In re Vitamins Antitrust Class Actions*, 327 F.3d 1207, 1210 (D.C. Cir. 2003); *McSheffrey v. Exec. Office for the United States Attys.*, No. 00-5268, 2001 U.S. App. LEXIS 13898, *1 (D.C. Cir. May 4, 2001) (per curiam)). Expedition in these types of cases is not unprecedented. *See* Minute Order (paperless), *AstraZeneca Pharms. LP v. FDA*, No. 12-00388 (D.D.C. Mar. 14, 2012) (ordering defendants to file opposition to application for preliminary injunction by Mar. 15; plaintiff to file reply by Mar. 16; and defendants to file administrative record by Mar. 16); *AstraZeneca Pharms. LP v. FDA*, No. 12-472, 2012 U.S. Dist. LEXIS 54863, *13 (D.D.C. Mar. 28, 2012) (ordering that the parties submit "an expedited briefing schedule to govern the proceedings in this matter"); *Otsuka Pharm., Co. v. Burwell*, No. 8:15-cv-852 (D. Md.), ECF No. 6 (granting motion to expedite the proceeding).

Otsuka seeks expedited filing of the agency administrative record and an expedited briefing and hearing schedule on Otsuka's intended motion for summary judgment. For two core reasons, expedited review is necessary and appropriate. First, the parties do not need to engage in protracted litigation and FDA will not be prejudiced by expediting the proceedings. Second, Otsuka will be harmed during the pendency of this case by losing its limited period of exclusivity and suffering irretrievable lost profits and sales.

B. The Parties Do Not Need To Engage In Protracted Litigation, and FDA Will Not Be Prejudiced By Expediting The Proceedings.

This is a case in which Otsuka challenges FDA's denial of its citizen petition and FDA's approval of the Alkermes NDA under the FDCA and the Administrative Procedure Act ("APA"). Otsuka's claims do not require the parties to engage in protracted litigation, and FDA will not be prejudiced by expediting these proceedings. The claims involve questions of whether the interpretation of Otsuka's three-year exclusivity, found in Section 505(c)(3)(E)(iii) and (iv) of the FDCA, is contrary to the statute and contrary to FDA's regulations and whether the new interpretation should have gone through formal notice-and-comment rulemaking under the APA.

The resolution of these claims does not require the resolution of disputed issues of fact. The factual record has been established at the agency, and the case will be decided on the administrative record without discovery. This case only presents disputed questions of law, precisely the kinds of questions the Court routinely resolves on motions for summary judgment and can be accomplished expeditiously under Otsuka's proposed scheduling order. FDA will not be prejudiced by Otsuka's proposed scheduling order, given the straightforward nature of this case (*i.e.*, no disputed issues of fact; no discovery) and because under the proposed schedule the agency will have its normal fourteen days to respond to Otsuka's motion for summary judgment.

C. Otsuka Will Be Harmed During The Pendency Of These Proceedings.

The immediate, and irreparable, consequence of FDA's decision is Otsuka's lost right to statutory exclusivity attaching to conditions of approval for aripiprazole. Where exclusivity is of limited duration, courts have recognized that loss of statutory exclusivity can constitute irreparable harm. *See Mylan Labs., Ltd. v. FDA*, 910 F. Supp. 2d 299, 313 (D.D.C. 2012) ("[C]ourts have held that a first applicant's loss of its statutory entitlement to 180-day exclusivity period is irreparable because once lost 'it cannot be recaptured' . . . ."); *Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 1, 11 (D.D.C. 2008) ("This Court has recognized, however, that a clear statutory entitlement is not 'merely economic' harm, and its loss may be sufficiently irreparable to justify emergency injunctive relief because '[o]nce the statutory entitlement has been lost, it cannot be recaptured."); *Apotex, Inc. v. FDA*, No. 06-627, 2006 U.S. Dist. LEXIS 20894, *58 (D.D.C. Apr. 19, 2006) ("[T]hey stand to lose a statutory entitlement, which is a harm that has been recognized as sufficiently irreparable. Once the statutory entitlement has been lost, it cannot be recaptured." (citation omitted)), *summarily aff'd on other grounds* 449 F.3d 1249 (D.C. Cir. 2006); *Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 131 (D.D.C. 1997) ("[D]epriving [first-filer] Mova of a 180-day statutory grant of exclusivity and giving [later-filer] Mylan an officially sanctioned head start in the market . . . will cause injury to Mova."). Expediting these proceedings will serve to protect Otsuka's exclusivity to a limited degree, ensuring that a decision comes sooner, rather than later, and if Otsuka is ultimately correct, preserves a lengthier period of Otsuka's exclusivity than otherwise might be possible without expediting the proceedings.

It is no secret that Alkermes intends to dominate the market of long-acting injectable drugs to treat schizophrenia and will take some of Otsuka's sales and profits. Alkermes has touted that the company "designed [aripiprazole lauroxil] to be the best in class of the long acting forms of

Aripiprazole." Richard Pops, Chairman and CEO, Alkermes CEO Presents at Citi Global Healthcare Conference (Feb. 25, 2013), *available at* http://seekingalpha.com/article/1222541-alkermes-ceo-presents-at-citi-global-helathcare-conference-transcript?part=single. Alkermes has stated publicly that patients taking aripiprazole are targets for aripiprazole lauroxil. *Id.*; *cf.* Richard Pops, Chairman & CEO, Alkermes' CEO Presents at Goldman Sachs Healthcare Conference (June 11, 2013), *available at* http://seekingalpha.com/article/1500922-alkermes-ceo-presents-at-goldman-sachs-healthcare-conference-transcript?part=single ("We were quite well aware of that molecule in that format [*i.e.*, Abilify Maintena]. So [w]e actually designed [aripiprazole lauroxil] to be . . . a generational advance over that."); Jim Frates, Sr. Vice President & CFO, Alkermes' Management Presents at Deutsche Bank 38th Annual dbAccess Health Care Conference (May 29, 2013), *available at* http://seekingalpha.com/article/1467941-alkermes-management-presents-at-deutsche-bank-38th-annual-dbaccess-health-care-conference-transcript (*hereinafter* May 29, 2013 Statements) ("Otsuka and Lundbeck have launched their own long-acting ABILIFY. . . Now we have to prove it out in our clinical studies but we think we can cover all the dosages, up from the low dose all the way through the high dose of Aripiprazole which is a [sic] used in a large number of schizophrenic patients right now. And that's something our competition can't do.").

And Alkermes has marketed itself based on the success of Abilify, and undoubtedly will continue to do so. *See* Alkermes Press Release, Alkermes Announces Positive Topline Results From Pivotal Phase 3 Study of Aripiprazole Lauroxil for Treatment of Schizophrenia (Apr. 8, 2014), *available at* http://investor.alkermes.com/mobile.view?c=92211&v=203&d=1&id=1916604 ("Aripiprazole lauroxil is a new, long-acting injectable antipsychotic agent designed to provide patients with once-monthly dosing of a medication that, once in the body, converts to aripiprazole, a molecule

that is commercially available under the name ABILIFY®."); *cf.* May 29, 2013 Statements ("[W]hat we are trying to do is deliver Aripiprazole, native Aripiprazole, over the course of a month."); *id.* ("If we can move and provide the market with a long acting ABILIFY, we think this is going to be a very exciting opportunity to expand that market . . . .").

Given the opportunity, Alkermes will flood the market with its new long-acting injectable for the treatment of schizophrenia, stealing Otsuka's sales, profits, and market share. The harm that Otsuka experiences will not be recoverable. Because FDA enjoys sovereign immunity, Otsuka is without a remedy to recover money damages from the agency. *See Smoking Everywhere, Inc. v. FDA*, 680 F. Supp. 2d 62, 77 n.19 (D.D.C.) (Absent a waiver, sovereign immunity shields the federal government and its agencies, like FDA, from suit."), *aff'd on other grounds sub nom. Sottera, Inc. v. FDA*, 627 F.3d 891 (D.C. Cir. 2010). Nor can money damages be recovered from Alkermes. The FDCA expressly precludes private litigants from enforcing its provisions. *See* 21 U.S.C. § 337(a); *Iacangelo v. Georgetown Univ.*, 580 F. Supp. 2d 111, 118 (Sept. 17, 2008 D.D.C. 2008) ("It is well settled the Congress did not intend to create a private cause of action to enforce the Federal Food, Drug, and Cosmetic Act ("FDCA")."), *magistrate judge's report adopted and approved*, 580 F. Supp. 2d 111 (D.D.C. Sept. 30, 2008), *modified by* 595 F. Supp. 2d 87 (D.D.C. Feb. 3, 2009).

Otsuka filed its complaint and this motion to expedite soon after receiving FDA's decision denying its citizen petition and approving Alkermes's NDA. In its proposed scheduling order, Otsuka has shortened its own time to file its motion for summary judgment and reply, committing itself to a stringent schedule to reach a final judgment as expeditiously as possible.

Conclusion

For these reasons, the Court should grant Otsuka's motion to expedite the proceedings and request for immediate scheduling conference and enter a scheduling order as follows:

October 23:	Defendants shall file the administrative record
November 6:	Otsuka shall file its motion for summary judgment
November 20:	Federal Defendants shall file their opposition to plaintiffs' motion for summary judgment
December 1:	Otsuka shall file its reply to the Federal Defendants' opposition
Week of Dec. 7:	Hearing on Otsuka's motion for summary judgment

Dated: October 15, 2015

Respectfully submitted,

/s/ Ralph S. Tyler

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that the above motion to expedite was served electronically on counsel for FDA this 15th day of October, 2015 as follows:

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