UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

OTSUKA PHARMACEUTICAL CO., LTD., *et al.*, Plaintiffs, v. SYLVIA MATHEWS BURWELL, *et al.*, Defendants.	Civil Action No. 1:15-cv-01688-KBJ

MEMORANDUM IN SUPPORT OF ALKERMES, INC.'S AND ALKERMES PHARMA IRELAND LIMITED'S UNOPPOSED MOTION TO INTERVENE

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Alkermes, Inc. and Alkermes Pharma Ireland Limited (collectively, "Alkermes") respectfully submit this memorandum of law in support of their motion to intervene as defendants. Alkermes seeks to intervene because on October 5, 2015, the federal Food and Drug Administration ("FDA") approved Alkermes, Inc.'s New Drug Application ("NDA") to market ARISTADA™, a long-acting, injectable atypical antipsychotic for the treatment of schizophrenia. ARISTADA contains a new and distinct molecule, aripiprazole lauroxil, which was specifically designed, developed, and optimized by Alkermes to function as a long-acting, injectable suspension which slowly releases medication over a multi-week period.

Through this lawsuit, Plaintiffs Otsuka Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Development & Commercialization, Inc., and Otsuka America Pharmaceutical, Inc. (collectively, "Otsuka") seek to reverse FDA's decision to grant marketing approval to ARISTADA. Otsuka seeks to take away Alkermes' legally protected interest in marketing its drug, and the Court should therefore grant Alkermes' timely motion to intervene as of right under Federal Rule of Civil Procedure 24(a). In the alternative, the Court should grant permissive intervention to Alkermes under Rule 24(b) because Alkermes' interests are implicated by Otsuka's action against FDA and Alkermes' involvement would not prejudice the interests of any existing parties. Plaintiffs do not oppose this motion, and the Federal Defendants take no position on it.

Because the Complaint was just filed yesterday and the time for the Federal Defendants to answer or move has not yet run (or, to our knowledge, begun running), it would be premature to require Alkermes to file an answer pursuant to Local Civ. R. 7(j). The Court should therefore provide that Alkermes' answer or other response to the Complaint shall be due on the same date as the Federal Defendants' answer or response.

BACKGROUND

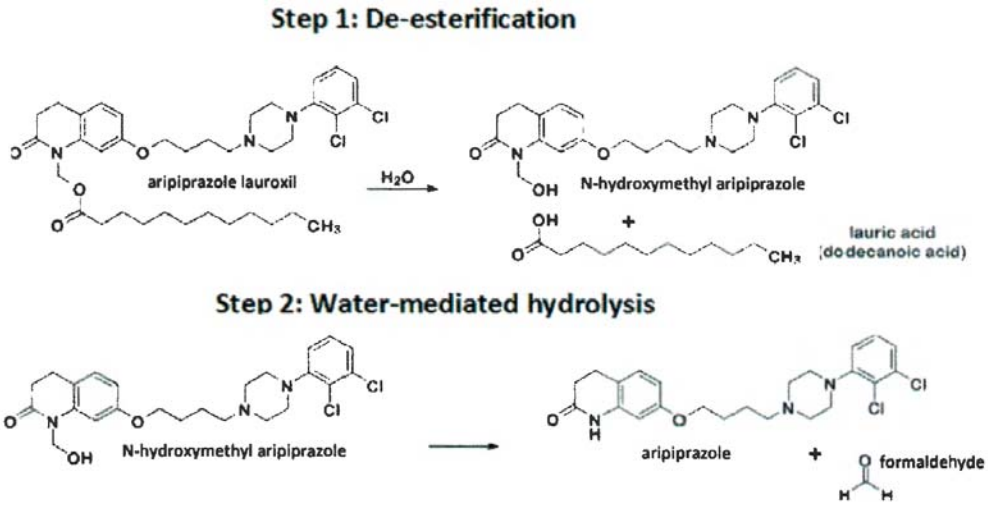
ARISTADA is an exceedingly important drug to Alkermes and represents the first time the company has both developed a drug in-house and launched it without a partner. Alkermes has spent the last seven years formulating, studying, and preparing to launch ARISTADA, a long-acting, injectable atypical antipsychotic drug that allows patients suffering from schizophrenia to receive treatment every four-to-six weeks instead of requiring this sensitive population to self-administer treatment daily. Its unique properties arise from its novel active ingredient, aripiprazole lauroxil, and the formulation and dosing of that active ingredient. Alkermes submitted its application for marketing approval to FDA on August 22, 2014, which FDA approved on October 5, 2015.

Otsuka markets Abilify®, a different drug. Abilify's active ingredient is aripiprazole, a distinct chemical compound from aripiprazole lauroxil, the active ingredient in ARISTADA. Abilify is available in several dosage forms, including immediate-release tablets that are taken orally and an extended-release injectable solution, which goes by the trade name Abilify Maintena®. Abilify Maintena is approved by FDA to treat schizophrenia. Otsuka has gone to extraordinary lengths to prevent competition with its Abilify products. This action is just the latest front in a coordinated regulatory and litigation battle by Otsuka to fight off all challengers to its billion-dollar Abilify empire. Through this action, Otsuka is expanding its fight to include not just aripiprazole products but also ARISTADA, which contains the distinct compound aripiprazole lauroxil. After a failed attempt at blocking ARISTADA's regulatory approval, Otsuka now implores this Court to take the extraordinary action of forcing FDA to rescind ARISTADA's approval.

I. ARISTADA AND ALKERMES' EFFORTS TO BRING IT TO MARKET

The development of ARISTADA is a major success for Alkermes, and Alkermes has

invested significant time, labor, and resources to bring the product to market. Alkermes began researching and developing the molecule that became aripiprazole lauroxil, the active ingredient in ARISTADA, more than seven years ago. Aripiprazole lauroxil was specifically designed, developed, and optimized to function as a long-acting, injectable suspension (liquid) that slowly releases medication over a multi-week period. The long-acting pharmacokinetic profile *in vivo* is governed by the slow dissolution properties of aripiprazole lauroxil (through the process shown below).



As shown above,[1] after dissolution, cleavage occurs, yielding lauric acid and the *N*-hydroxymethyl aripiprazole active moiety. *N*-hydroxymethyl aripiprazole then undergoes hydrolysis removing the hydroxymethyl group to form the aripiprazole metabolite. In recognition of its novelty, aripiprazole lauroxil was awarded U.S. Patent No. 8,431,576.

The finished drug product ARISTADA is composed of the aripiprazole lauroxil molecule, suspended in a solution, and then pre-loaded into a syringe. It comes in three doses—441 mg, 662 mg, and 882 mg. ARISTADA is indicated to treat patients living with

[1] Letter from J. Woodcock to W. H. Carson, at 18 Fig. 3 (Oct. 5, 2015) ["FDA Citizen Petition Denial"], Compl., Exh. 2, Dkt. No. 1-2.

schizophrenia, a serious, chronic, and often debilitating disease. Schizophrenia can impair a person's executive-functioning and decision-making capabilities, and those living with it frequently have difficulty remembering to take their medications every day.

ARISTADA fills an important need for those patients who suffer schizophrenia and who may be severely limited in their ability to adhere to a daily oral dosing regimen. Instead of a daily pill, ARISTADA allows patients to obtain treatment for schizophrenia by injection at four-to-six-week intervals (depending on dose) and permits a grace period of varying lengths (depending on dose) for patients who miss a scheduled injection. The six-week dosing interval and longer grace periods are distinct features of ARISTADA. The dosing intervals allow patients to go longer between injections, addressing potential adherence problems with more frequent dosing, and allow fewer overall injections, thereby limiting the risk of infection that any injection entails and reducing the frequency with which patients must experience the discomfort of injection. For patients who miss a scheduled injection, the longer grace period afforded by ARISTADA from reinitiation of daily oral lead-in therapy taken concurrently with the first injection addresses the practical reality of the disease state and also serves to address potential adherence issues with the daily dosing treatment regimen.

Alkermes has made significant investments in ARISTADA's success. Alkermes' research and development costs were considerable, consisting of seven years of extensive product development, formulation, and safety and efficacy testing. Clinical testing alone consisted of one pivotal Phase III clinical trial and several Phase I trials that, in total, enrolled 880 people. Alkermes has also invested heavily in preparations for the market launch of ARISTADA. Alkermes' sales and administrative expenses have increased markedly over the last year, due in large part to the tripling in size of its sales and marketing organization to launch

ARISTADA. Exhibit 1 to Declaration of William M. Jay ("Jay Decl.") (Alkermes Form 10-Q Quarterly Report (July 30, 2015), at 25).

Following FDA approval on October 5, Alkermes brought the drug to market, and patients living with schizophrenia now have access to this important new therapy. Jay Decl., Exh. 3 (Alkermes Form 8-K Current Report (October 5, 2015), Exh. 99.1, at 1)).

II. OTSUKA'S EFFORTS TO BLOCK ARISTADA'S LAUNCH

Otsuka markets a different drug, called Abilify®. Unlike ARISTADA, which uses aripiprazole lauroxil as its active ingredient, Abilify's active ingredient is aripiprazole, a distinct chemical compound.[2] Abilify is available in several dosage forms. Immediate-release oral Abilify tablets have been on the market since 2002. But it was not until 2013 that Otsuka obtained FDA approval to market Abilify Maintena, the drug Otsuka asserts should have blocked ARISTADA's approval. Abilify Maintena is an extended-release injectable formulation of aripiprazole that allows for once-monthly dosing and is indicated to treat schizophrenia.

Abilify has produced billions of dollars in sales for Otsuka over the last thirteen years, and Otsuka has undertaken extensive efforts to protect it from potential competition. Those efforts focused first on generic competition. In April 2015, it was widely accepted that FDA might approve generic versions of oral aripiprazole when the period of pediatric exclusivity associated with Otsuka's U.S. Patent No. 5,006,528 (listed in the Orange Book as a drug product, drug substance, and method-of-use patent) expired. In April 2015, Otsuka sought and was denied a temporary restraining order from a New Jersey federal court to prevent the launch of

[2] Otsuka has acknowledged that ARISTADA and Abilify Maintena are different drugs, which have different chemical structures. *See* Otsuka Petition at 18, FDA Docket No. 2015-P-1354-0001 (July 13, 2015) (acknowledging that ARISTADA is a different drug than Abilify Maintena under FDA's "bright-line structural rule" and affirming that there are sound, scientific reasons underlying FDA's judgment, namely "the potential for unexpected clinical effects from the chemical differences between the two molecules"), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2014-P-1354-0001.

several generic versions of oral aripiprazole based on Otsuka's allegations of patent infringement. *See Otsuka Pharm. Co. v. Torrent Pharm. Ltd.*, Nos. 14-1078 *et al.*, 2015 WL 1782653 (D.N.J. Apr. 16, 2015). On the heels of that loss, Otsuka launched a regulatory offensive, seeking (and losing) a temporary restraining order and preliminary injunction from a Maryland federal court that sought to extend marketing exclusivity for a narrow orphan drug indication for oral Abilify into whole-drug exclusivity for an additional seven years. *See Otsuka Pharm. Co. v. Burwell*, No. GJH-15-852, 2015 WL 1962240 (D. Md. Apr. 29, 2015). In light of Otsuka's aggressive strategy to extend its exclusive hold on the market for aripiprazole, at least one court has allowed an antitrust counterclaim for sham litigation to proceed against Otsuka. *Otsuka Pharm. Co. v. Torrent Pharm. Ltd.*, No. 14-cv-1078 (JBS/KMW), 2015 WL 3869677 (D.N.J. June 22, 2015). Generic forms of Abilify tablets and orally disintegrating tablets became available to patients earlier this year.

Through this lawsuit, Otsuka is expanding its litigation strategy beyond aripiprazole and is now attempting to block sales of a different drug, ARISTADA. This lawsuit follows a series of Citizen Petition correspondence Otsuka initiated with FDA to attempt to block ARISTADA's approval. On September 9, 2014, Otsuka filed a Citizen Petition with FDA arguing that ARISTADA is a different drug than Abilify thus requiring an additional clinical study to prove ARISTADA's safety and efficacy, and that, as a result, FDA should refuse to review ARISTADA's marketing application. FDA accepted Alkermes' application for filing and substantive review on October 22, 2014, effectively denying Otsuka the relief it had requested. FDA officially denied Otsuka's petition on February 3, 2015.

Then in July 2015—just one month before ARISTADA's presumptive decision date from FDA—Otsuka filed another Citizen Petition making arguments about a claimed marketing

exclusivity. In this second Citizen Petition, Otsuka flipped its argument from one year prior, arguing that ARISTADA is no longer *different* than Abilify and instead is the *same* drug as Abilify, and therefore was blocked by a narrow marketing exclusivity held by Abilify Maintena. (Otsuka also reprised the September 2014 argument in July 2015, arguing that FDA should deny the application outright because ARISTADA is a *different* drug than Abilify Maintena and, it claimed, required an additional clinical trial.)

Otsuka's delay tactic worked, extending FDA's review of Alkermes' application past August 22, 2015, the presumptive date of approval based on statutory and federal guidelines, for another six weeks. But its substantive arguments failed. On October 5, 2015, FDA denied Otsuka's July 2015 petition. FDA determined that Abilify Maintena holds no exclusivity that blocks ARISTADA's launch, and that Alkermes has sufficiently demonstrated ARISTADA's safety and efficacy. FDA approved ARISTADA the same day it denied Otsuka's Citizen Petition.

In the action before this Court, Otsuka again seeks to stop Alkermes' launch of ARISTADA in its tracks and to block its sales for *more than two years*, until December 5, 2017, when the second of Abilify Maintena's two claimed marketing exclusivities for its aripiprazole product expires.

ARGUMENT

I. ALKERMES IS ENTITLED TO INTERVENE AS OF RIGHT

Alkermes has a right to intervene in this matter because it has an approved NDA for ARISTADA that Otsuka seeks, through this lawsuit, to rescind. Federal Rule of Civil Procedure 24(a) provides in relevant part that

> [o]n timely motion, the court must permit anyone to intervene who . . . claims an interest relating to the property or transaction that is the subject of the action, and is so situated that disposing of the action may as a practical matter impair or

> impede the movant's ability to protect its interest, unless existing parties adequately represent that interest.

Fed. R. Civ. P. 24(a)(2). Under this rule, a party has an absolute right to intervene in an action if it satisfies four requirements: (1) the motion is timely; (2) the applicant has "a legally protected interest in the action"; (3) denial of the motion would "threaten to impair" the applicant's ability to protect its interests; and (4) no party to the action will adequately represent the applicant's interests. *Karsner v. Lothian*, 532 F.3d 876, 885 (D.C. Cir. 2008) (quoting *SEC v. Prudential Secs.*, 136 F.3d 153, 156 (D.C. Cir. 1998)).

Alkermes easily satisfies these four requirements for intervention as of right. FDA has already granted final approval for ARISTADA and Alkermes has launched the drug. Jay Decl. Exh. 3 (Alkermes Form 8-K Current Report (October 5, 2015), Exh. 99.1, at 1). Unless Otsuka prevails in this Court, Alkermes will continue to provide patients with a product with unique benefits to patients living with schizophrenia. By contrast, if Otsuka obtains the relief it seeks in this action, then FDA will be required to rescind final approval of Alkermes' application and will be prohibited from approving ARISTADA for *over two years*, even though Alkermes has fully satisfied FDA that it has met all requirements for final approval to market its drug. Under these circumstances—*i.e.*, where one pharmaceutical manufacturer attempts to enjoin FDA from approving the marketing applications of a competitor—the courts of this Circuit have consistently recognized that the competitor's legal interests could be impaired by the litigation and have thus routinely allowed the competitor to intervene as of right. *See, e.g., Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1078-79 (D.C. Cir. 2001); *Ranbaxy Labs., Ltd. v. Burwell*, 82 F. Supp. 3d 159, 163 (D.D.C. 2015); *Biovail Corp. v. FDA*, 519 F. Supp. 2d 39, 43 (D.D.C. 2007); *Apotex, Inc. v. FDA*, 508 F. Supp. 2d 78, 80 n.2 (D.D.C. 2007); *Purepac Pharm. Co. v. Thompson*, 238 F. Supp. 2d 191, 192 (D.D.C. 2002); *Pfizer Inc. v. Shalala*, 1 F. Supp. 2d

38, 39 (D.D.C. 1998), *aff'd in part, rev'd in part on other grounds*, 182 F.3d 975 (D.C. Cir. 1999).

Because Alkermes' motion is timely, Alkermes has significant interests at stake in this litigation, Otsuka's requested relief would impair Alkermes' interests, and no other party in this litigation can adequately represent Alkermes' interests, Alkermes is entitled to intervene as of right.

A. The Motion Is Timely

Alkermes is filing this motion to intervene just one day after Otsuka filed this action on October 15, 2015, making the motion unquestionably timely. *See, e.g.*, *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1076 (D.C. Cir. 1998) (motion filed a few weeks after the complaint was timely); *Appleton v. FDA*, 310 F. Supp. 2d 194, 197 (D.D.C. 2004) (motion filed within two months of notification of suit was timely). And intervention will not delay the proceedings or prejudice the parties in any way, as evidenced by their decision not to oppose Alkermes' motion. If permitted to intervene, Alkermes will adhere to the case management orders entered by this Court and coordinate, to the extent possible, with the Federal Defendants.

B. Alkermes Has A Substantial Legal Interest In This Action

A party has an interest within the meaning of Rule 24(a) if it has a "legally protected interest" in the outcome of the litigation, which may include an economic interest that is directly implicated by the plaintiff's claim. *See, e.g.*, *Dimond v. Dist. of Columbia*, 792 F.2d 179, 192 (D.C. Cir. 1986) (holding that the threat of economic loss satisfies the interest requirement under Rule 24(a)(2)).

Here, Alkermes has a protectable legal interest in this suit because it has already received final FDA approval of its application, has launched its drug, and has made a significant investment in a commercial, medical, and manufacturing workforce to ensure a successful

launch. Indeed, since June 30, 2014, Alkermes has tripled the size of its sales and marketing organization in preparation for the launch of ARISTADA in August 2015. Jay Decl. Exh. 1 (10-Q Quarterly Report (July 30, 2015), at 25). ARISTADA is an exceedingly important drug to Alkermes, as it represents the first time Alkermes both developed a drug in-house and launched it without a partner. As a result, Alkermes has invested a large portion of its company in its 2015 launch of ARISTADA—an investment that contributed to an operating loss of $87.1 million for Alkermes plc in 2014. Jay Decl. Exh. 2 (Alkermes 10-K 2014 Annual Report (Feb. 24, 2015), at 59). Uncertainty manufactured by Otsuka *through this very lawsuit* threatens Alkermes' ability to retain the investment in people recruited, trained, and poised to make Alkermes' launch of ARISTADA a success and to recoup the significant resources Alkermes has put into this endeavor.

C. Otsuka's Requested Relief Would Impair Alkermes' Interests

As discussed above, Otsuka's requested relief would directly impair Alkermes' substantial interests. If Otsuka's request for relief is denied, Alkermes will continue to market ARISTADA. But if Otsuka prevails, FDA will be forced to rescind ARISTADA's approval—regardless of FDA's conviction that Alkermes' application complies with all other statutory and regulatory requirements—and Alkermes will have to delay bringing a new drug to market for *more than two years*, until December 2017. The delay will deprive Alkermes of customers and sales, idle the sales force that Alkermes has assembled specifically to sell ARISTADA, and undermine the other significant investments Alkermes has made to launch the drug.

This potential loss of commercial opportunities for Alkermes is an injury in fact directly traceable to the relief Otsuka seeks (and thus would be redressed by an order rejecting Otsuka's suit). It clearly gives Alkermes standing to intervene and satisfies the impairment prong for mandatory intervention. *See Fund for Animals, Inc. v. Norton*, 322 F.3d 728, 733 (D.C. Cir.

2003) (intervenor had standing and an interest sufficient to justify intervention because it "would suffer concrete injury" in the form of "[t]he threatened loss of tourist dollars" if "the court were to grant the relief the plaintiffs seek"); *Mova Pharm. Corp.*, 140 F.3d at 1076 (pharmaceutical company's interests were affected, and intervention was allowed, where the company "was in danger of losing market share" depending on the court's order).

D. The Existing Parties Cannot Adequately Represent Alkermes' Interests

Finally, the existing parties cannot adequately represent Alkermes' interests. A proposed intervenor as of right is required to show only that representation of its interests "'may be' inadequate," and "the burden of making that showing should be treated as minimal." *Trbovich v. United Mine Workers*, 404 U.S. 528, 538 n.10 (1972) (citation omitted). Alkermes easily clears this bar here, where the existing defendants comprise a federal agency and its officials.

Alkermes' interests are not adequately represented by the Federal Defendants. Courts have "often concluded that governmental entities do not adequately represent the interests of aspiring intervenors" because an agency's obligation "is to represent the interests of the American people" writ large, not the more particular interests of a company or organization. *Fund for Animals*, 322 F.3d at 736. Alkermes is concerned with protecting its own commercial interests and ensuring that it has the opportunity to commercialize ARISTADA. Those interests could easily diverge from the Federal Defendants' during the course of litigation; FDA has institutional interests that extend beyond this particular suit that may affect the arguments it is willing to put forward.

II. ALTERNATIVELY, ALKERMES SHOULD BE GRANTED PERMISSION TO INTERVENE UNDER RULE 24(B)

In the alternative, this Court should grant Alkermes permission to intervene under Rule 24(b). *See* Fed. R. Civ. P. 24(b)(1)(B) ("On timely motion, the court may permit anyone to

intervene who . . . has a claim or defense that shares with the main action a common question of law or fact."). The standard for intervention under this rule is a liberal one: "Rule 24(b) . . . provides basically that anyone may be permitted to intervene if his claim and the main action have a common question of law or fact," *Nuesse v. Camp*, 385 F.2d 694, 704 (D.C. Cir. 1967), so long as intervention would not "unduly delay or prejudice the rights of the original parties." *Acree v. Republic of Iraq*, 370 F.3d 41, 49 (D.C. Cir. 2004), *abrogated on other grounds by Republic of Iraq v. Beaty*, 556 U.S. 848 (2009). To intervene under Rule 24(b), a party is not required to show that existing parties will not adequately represent its interests. *See Sierra Club v. Van Antwerp*, 523 F. Supp. 2d 5, 10 (D.D.C. 2007) (granting intervention where the court found the movant "satisf[ied] the three threshold requirements for permissive intervention:" "(1) an independent ground for subject matter jurisdiction; (2) a timely motion; and, (3) a claim or defense that has a question of law or fact in common with the main action").

As explained above, Alkermes' intervention here is timely and would not prejudice the rights of the original parties or cause delay. *Supra* at 10. Moreover, Alkermes' claims certainly have "a . . . question of law or fact" in common with the main action, Fed. R. Civ. P. 24(b)(1)(B): in order to preserve FDA approval of its ARISTADA application (and thus to enter the market with this important drug), Alkermes opposes Otsuka's request for an order rescinding agency approval of its application.

CONCLUSION

For the foregoing reasons, Alkermes respectfully requests that the Court grant its motion to intervene as a defendant in this action.

Dated: October 16, 2015

Respectfully submitted,

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