UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ORTHO-McNEIL PHARMACEUTICAL, INC., ORTHO-McNEIL, INC. and DAIICHI PHARMACEUTICAL CO., LTD., Plaintiffs, v. LUPIN PHARMACEUTICALS, INC. and LUPIN LTD., Defendants.	Civil Action No. 06-4999 (GEB)(TJB) **DOCUMENT FILED ELECTRONICALLY**

DEFENDANTS' MEMORANDUM IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT PURSUANT TO FED. R. CIV. P. 56

STERNS & WEINROTH, P.C.
50 West State Street, Suite 1400
Trenton, NJ 08607-1298
Telephone: (609) 989-5012
Facsimile: (609) 392-7956

LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
Chicago, IL 60601-6780
Telephone: (312) 616-5600
Facsimile: (312) 616-5700

Attorneys for Defendants Lupin Pharmaceuticals, Inc.and Lupin Ltd.

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Defendants Lupin Ltd. and Lupin Pharmaceuticals, Inc. (hereinafter, and collectively, "Lupin") submit this opening memorandum in support of their motion for summary judgment pursuant to Fed. R. Civ. P. 56, requesting invalidation of the patent term extension granted to U.S. Patent 5,053,407 ("the '407 patent") by the United States Patent and Trademark Office ("USPTO"), and reinstatement of the '407 patent's original expiration date of October 1, 2008.

I. NATURE AND STAGE OF THE PROCEEDINGS

Plaintiffs' complaint filed October 16, 2006, alleges that Lupin's Abbreviated New Drug Application ("ANDA") for levofloxacin tablets would infringe the '407 patent under 35 U.S.C. §§ 271(a), (b) and/or (c). *See Complaint* ¶¶ *17-21*. The complaint also seeks a judicial declaration that a term extension granted to the '407 patent under 35 U.S.C. § 156 (a) is valid, and that the '407 patent expires not on its original expiration date of October 1, 2008, but on December 20, 2010, pursuant to the 810-day term extension. *See Complaint* ¶¶ *35-41*.

Lupin filed its Answer and Counterclaims on February 15, 2007 (pursuant to a motion for an extension of time granted by this Court, and further agreements between the parties). In this pleading, Lupin alleges and seeks a judicial declaration that the grant of the term extension to the '407 patent is invalid, and

that the marketing of the levofloxacin tablets described in Lupin's ANDA after October 1, 2008 (*i.e.*, after the original expiration date of the '407 patent), would not infringe the '407 patent. *See Answer, Affirmative Defense and Counterclaim* ¶¶ *42-43; Counterclaim* ¶¶ *11-19.* Plaintiffs filed their Answer to Lupin's Counterclaim on March 7, 2007.

On June 11, 2007, this Court entered a Joint Stipulation and Order relative to the validity, enforceability and infringement of the '407 patent. In pertinent part, Lupin agrees therein that it "will not contest at trial or otherwise the validity or enforceability of the '407 patent or the infringement of claims 2 and 5 of the '407 patent" by the levofloxacin products described in Lupin's ANDA. *See Declaration of Karen A. Confoy ("Confoy Decl."), Exh. A, Joint Stipulation* at ¶ 5. Further, "Lupin will contest at trial only whether the '407 patent is entitled to the term extension granted to it by the PTO pursuant to 35 U.S.C. § 156." *Id.*

II. SUMMARY OF THE ARGUMENT

This action is premised on a single issue—the validity of the patent term extension granted to the '407 patent. As the relevant facts are not in dispute, and the issue is one of statutory construction, this case is appropriate for resolution via summary judgment.

Section 156 (a) of Title 35[1] states that in order to qualify for a patent term extension, the permitted (*i.e.*, FDA-approved) commercial marketing or use of the patented "product" must be the first such permitted marketing or use in the United States. 35 U.S.C. § 156 (a)(5). The term "product" is defined in the statute as a "drug product," the latter in turn being defined as an "active ingredient." 35 U.S.C. § 156 (f)(1) & (2). The FDA regulations define "active ingredient" as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease . . . . " 21 CFR §§ 210.3(b)(7) & 60.3(b)(2). Accordingly, to qualify for a patent term extension, the patented product must be the first permitted commercial marketing or use in the United States of that active ingredient, *i.e.*, a component that is intended to furnish pharmacological activity in the treatment of disease.

The '407 patent claims a chemical compound referred to as levofloxacin. There is no dispute that levofloxacin was a component in a commercial product previously approved by the FDA—FLOXIN®. Indeed, levofloxacin was an "active ingredient" in FLOXIN® because it furnished pharmacological activity (as an antimicrobial) in the treatment of disease. Because the product patented by the '407 patent (levofloxacin) is not the first FDA-approved commercial marketing or

[1] Section 156 was part of the 1984 "Hatch-Waxman Act," the latter formally known as the "Drug Price Competition and Patent Term Restoration Act of 1984." Other provisions of the Hatch-Waxman Act are codified at 21 U.S.C. §§ 355 *et seq*. *See Merck & Co., Inc. v. Kessler*, 80 F.3d 1543, 1543-44 (Fed. Cir. 1996).

use of that active ingredient (i.e., the definition of "product" under the statute), the grant of the term extension to the '407 patent is invalid.

III. CONCISE STATEMENT OF RELEVANT FACTS

A. FLOXIN® (ofloxacin)

Ofloxacin, a racemic mixture of two enantiomers, is disclosed and claimed in U.S. Patent 4,382,892 ("the '892 patent"). *See Paragraphs 1 and 6 of "Defendants' Concise Statement of Undisputed Facts Under L. Civ. R. 56.1 In Support Of Their Motion For Summary Judgment Pursuant to Fed. R. Civ. P. 56" (hereinafter DF ¶ __).* The '892 patent refers to ofloxacin as 9-fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4] benzoxazine-6-carboxylic acid). *See DF* ¶ 2. The '892 patent issued on May 10, 1983 and is assigned on its face to Daiichi Seiyaku Co., Ltd. *See DF* ¶ 3.

On December 28, 1990, the FDA approved tablets containing 200 mg, 300 mg and 400 mg ofloxacin under New Drug Application No. 019735 for commercial marketing in the United States. These tablets were marketed in the United States under the trademark FLOXIN®. *See DF ¶ 4.*

On December 30, 1991, the USPTO granted an application for patent term extension under 35 U.S.C. § 156, extending the original term of the '892 patent by two years—from September 2, 2001 to September 2, 2003. *See DF ¶ 5.*

The ofloxacin in FLOXIN® is present as a racemic mixture of two enantiomers. *See DF ¶ 6.* In chemistry, the term the term "enantiomers" (from the Greek words for "opposite" and "portion") denotes chemical components that are complete mirror images of each other, much as one's left and right hands are "opposite." *See DF ¶ 7.*

In prior litigation involving the Plaintiffs and the '407 patent, a district court determined that the term "enantiomer" means "one of a pair of isomers that are non-superimposable mirror images of each other," and further that "an isomer is one of a number of molecules that have the same chemical formula (the same constituent atoms) but the atoms are arranged in a unique pattern." *See DF ¶ 8; Ortho-McNeil Pharm., Inc. v. Mylan Labs.*, 348 F. Supp. 2d 713, 720 (N.D.W.Va. 2004). This Court was involved in another case concerning Plaintiffs and the '407 patent, *i.e., Ortho-McNeil Pharm., Inc. v. Teva Pharm. USA*, 2006 WL 755995 (D.N.J. March 17, 2006).

There are different conventions that may be used to describe enantiomers. The letters "R" and "S," and symbols "+" and "-," may be used to indicate a particular enantiomer. *See DF ¶ 9.* A mixture of enantiomers in equal parts is a racemic mixture. *See DF ¶ 10; Ortho-McNeil*, 348 F. Supp. 2d at 721, 724.

In the litigation involving Plaintiffs and the '407 patent mentioned previously, the Plaintiffs agreed that one of the ofloxacin enantiomers, *i.e.*,

(S)(-)ofloxacin, is levofloxacin. *See DF* ¶ 11; *Ortho-McNeil*, 348 F. Supp. 2d at 724. Plaintiffs further agreed in that same litigation that levofloxacin is one of two biologically active enantiomers present in ofloxacin, and that these enantiomers are present in ofloxacin in a 1:1 ratio. *See DF* ¶ *12*; *Ortho-McNeil*, 348 F. Supp. 2d at 721, 751. Ofloxacin may therefore be described as a racemic mixture of enantiomers, which mixture is known to chemists as (±)ofloxacin. *See DF* ¶ *13.*

The FLOXIN® product marketed in the United States included a racemic mixture of levofloxacin (*i.e.*, (S)(-)ofloxacin) and its enantiomer (*i.e.*, (R)(+)ofloxacin). *See DF* ¶ *14*; *Ortho-McNeil*, 348 F. Supp. 2d at 720-21.

B. LEVAQUIN® (levofloxacin)

The ’407 patent, issued on October 1, 1991, discloses and claims the (S)(-) enantiomer of ofloxacin, *i.e.*, levofloxacin. *See DF* ¶ *15.*

On December 20, 1996, the FDA granted marketing approval for injectable and tablet formulations comprising levofloxacin. *See DF* ¶ *16.* These levofloxacin formulations have been marketed under the trademark LEVAQUIN®. *See DF* ¶ *17.*

After the FDA approved LEVAQUIN®, Daiichi Pharmaceutical Co., Ltd. filed an application seeking an extension of the term of the ’407 patent. *See DF* ¶ *18.* The USPTO granted the patent term extension, and in doing so extended the

term of the '407 patent by 810 days. This extension moved the expiration of the '407 patent from October 1, 2008, to December 20, 2010. *See DF ¶ 19.*

In discussing the "optically active compounds of racemic ofloxacin," the inventors state in the '407 patent:

> the S*(-)-compound [i.e., levofloxacin*] possesses an antimicrobial activity of about 2 times higher than that of the (±)-compound [*i.e., ofloxacin*] and an acute toxicity (LD_{50}) weaker than that of the (±)-compound as determined in mice by intravenous administration. On the other hand, the present inventors found that the R(+)-compound exhibits an antimicrobial activity of only about 1/10 to 1/100 times that of the (±)-compound, whereas it possesses an acute toxicity substantially equal to that of the (±)-compound. That is, the S(-)-form of Ofloxacin [*i.e., levofloxacin*] has been found to have very desirable properties, i.e., increased antimicrobial activity and reduced toxicity, and is expected to be a very useful pharmaceutical agents as compared with the (±)-compound [*i.e., ofloxacin*].

See DF ¶ 20.

The foregoing passage confirms the finding by the district court in the prior case—that levofloxacin is a biologically active enantiomer present in ofloxacin, *i.e.*, it is a component that provides pharmacologic activity in the treatment of disease. *See DF* ¶ 21; *Ortho-McNeil*, 348 F. Supp. 2d at 751.

C. The Present Action

Plaintiff Daiichi Pharmaceuticals Co., Ltd. ("Daiichi") asserts it is the owner of the '407 patent in issue in this action. *See DF ¶ 22.* Plaintiff Ortho-McNeil, Inc. ("OMI") asserts it is an exclusive sublicensee of the '407 patent. *See DF ¶ 23.*

Plaintiff Ortho-McNeil Pharmaceutical, Inc. ("OMP") asserts it is the holder of approved New Drug Application ("NDA") No. 020634 for several pharmaceutical formulations of levofloxacin sold under the trademark LEVAQUIN®. *See DF ¶ 24.*

The '407 patent is listed in the FDA Orange Book for drugs marketed as LEVAQUIN®. *See DF ¶ 25.*

On July 14, 2006, Lupin Ltd. submitted ANDA No. 78-424 to the FDA seeking approval of levofloxacin tablet formulations. *See DF ¶ 26.*

On September 29, 2006, pursuant to 21 U.S.C. § 355(j)(2)(B)(ii), Lupin Ltd. notified Plaintiffs by letter (this letter being received by Plaintiffs on October 2, 2006) that it had submitted ANDA No. 78-424 to the FDA, and that the application included a Paragraph IV certification with respect to the '407 patent. *See DF ¶ 27.* The Lupin Ltd. certification stated that in its opinion and to the best of its knowledge, Lupin Ltd.'s tablets would not infringe the '407 patent when marketed after October 1, 2008, *i.e.*, after the original (non-extended) expiration date of the '407 patent. *See DF ¶ 28.*

In response to this notice letter, Plaintiffs filed the Complaint in this Court, as described hereinabove. *See DF ¶ 29.*

IV. RELEVANT LEGAL FRAMEWORK CONCERNING TERM EXTENSIONS

A. 35 U.S.C. § 156 (Patent Term Extensions)

The statutory requirements under 35 U.S.C. § 156 for grant of a patent term extension state in relevant part:

> (a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent, which shall include any patent term adjustment granted under section 154(b), if—
>
> (5)(A) except as provided in subparagraph (B) or (C), **the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product** under the provision of law under which such regulatory review period occurred;
>
> * * *
>
> (f) For purposes of this section:
>
> (1) The term "**product**" means:
>
> (A) A **drug produc**t.
>
> * * *
>
> (2) The term "**drug product**" means the **active ingredient** of—
>
> (A) a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act), or
>
> * * *

> including any salt or ester of the active ingredient, as a single entity or **in combination with another active ingredient**.

35 U.S.C. § 156 (2004) (emphasis added). Section 156 was part of the Hatch-Waxman Act of 1984. *See Merck & Co.*, 80 F.3d at 1543-44.

The definition of the term "active ingredient" adopted by the FDA in the 1970s has remained unchanged to date—despite changes to the Hatch-Waxman Act since its enactment in 1984. *See, e.g., Confoy Decl., Exhs. C (¶ 33) & K* (21 CFR § 210.3(b)(7) (1979, 1984 & 2007)). The term "active ingredient" means "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man of or animals." 21 CFR § 210.3(b)(7). This same definition was specifically incorporated into the FDA regulations concerning patent term extensions when those regulations were first issued in 1988. The definition of "active ingredient" in the patent term extension regulations has also remained unchanged to date; it is the same as the definition set forth in 21 CFR § 210.3(b)(7). *See Confoy Decl., Exh. L* (21 CFR § 60.3(b)(2) (1988 & 2007)).

B. Summary Judgment Standard

In deciding a motion for summary judgment, a court should grant the motion if "there is no genuine issue as to any material fact and . . . the moving party is entitled to a judgment as a matter of law." FED. R. CIV. P. 56(c); *see also Celotex*

Corp. v. Catrett, 477 U.S. 317, 322-23 (1986); *Orson, Inc. v. Miramax Film Corp*., 79 F.3d 1358, 1366 (3d Cir. 1996). The threshold inquiry is whether "there are any genuine factual issues that properly can be resolved only by a finder of fact because they may reasonably be resolved in favor of either party." *See Anderson v. Liberty Lobby, Inc*., 477 U.S. 242, 250 (1986). In deciding whether triable issues of fact exist, the court must view the underlying facts and draw all reasonable inferences in favor of the non-moving party. *See Hancock Indus. v. Schaeffer*, 811 F.2d 225, 231 (3d Cir. 1987). In arguing against a motion for summary judgment, "an adverse party may not rest upon the mere allegations or denials of the adverse party's pleading, but the adverse party's response . . . must set forth specific facts showing that there is a genuine issue for trial." FED. R. CIV. P. 56(e).

C. Standard of Review Concerning Actions Taken by the USPTO

The USPTO is charged with administering the provisions of 35 U.S.C. § 156 and the underlying rules governing patent term extensions. *See* 35 U.S.C. § 156(d)(1). In determining the validity of a patent term extension, appropriate deference is to be given to the agency charged with this authority and responsibility. *See Dickinson v. Zurko*, 527 U.S. 150, 152 (1999) (principles of administrative deference apply to USPTO actions). Any deference owed to a USPTO decision arises not from force of law but rather from "the thoroughness of its consideration and the validity of its reasoning, *i.e.*, its basic power to persuade."

See Merck & Co., 80 F.3d at 1550 (*citing Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944)).

This Court may reverse any USPTO decision if the decision is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law. *See Ray v. Lehman*, 55 F.3d 606, 608 (Fed. Cir. 1995). An abuse of discretion occurs when a decision is based on an erroneous interpretation of the law. *See In re Gartside*, 203 F.3d 1305, 1315-16 (Fed. Cir. 2000).

V. ARGUMENT

A. The Term Extension of the '407 Patent is Invalid For Failing to Satisfy 35 U.S.C. § 156 (a)(5)

Lupin does not dispute that the patent term extension granted to the '407 patent satisfies 35 U.S.C. § 156 (a)(1)-(4). What is disputed, however, is whether the fifth requirement of Section 156(a) is satisfied, specifically, whether the product claimed in the '407 patent (*i.e.*, Plaintiffs' levofloxacin tablet) is the "first permitted commercial marketing or use of the product" when the term "product" is properly construed. 35 U.S.C. § 156 (a)(5). Lupin contends that the USPTO improperly construed this term, and in doing so abused its discretion or otherwise acted not in accordance with the law when granting a patent term extension to the '407 patent. When this statute is properly construed and applied to the undisputed

facts, Lupin submits that the patent term extension granted to the '407 patent is invalid.

1. The Term "Product" Means an Active Ingredient of a New Drug Either Alone or in Combination with Another Active Ingredient

Statutory construction requires an initial examination of the statute, interpreting the words of the statute in accordance with their ordinary, common meaning unless otherwise defined by Congress. *See, e.g., Hoechst-Roussel Pharm., Inc. v. Lehman*, 109 F.3d 756, 758 (Fed. Cir. 1997). "It is well settled law that the plain and unambiguous meaning of the words used by Congress prevails in the absence of a clearly expressed legislative intent to the contrary." *See Hoechst Aktiengesellschaft v. Quigg*, 917 F.2d 522, 526 (Fed. Cir. 1990).

Section 156 (f) defines the term "product" as a "drug product," which is further defined in the statute as an "active ingredient of a new drug . . . including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." 35 U.S.C. § 156 (f)(2) (emphasis added). Substituting the statutorily-prescribed definition of "product" into the fifth subsection of Section 156 (a) yields the following:

> (a) The term of a patent which claims [**an active ingredient . . . as a single entity or in combination with another active ingredient**] . . . shall be extended in accordance with this section from the original expiration date of the patent . . . if—
>
> * * *

> (5)(A) . . . the permission for the commercial marketing or use of the [**active ingredient . . . as a single entity or in combination with another active ingredient**] after such regulatory review period is the first permitted commercial marketing or use of the [**active ingredient . . . as a single entity or in combination with another active ingredient**] under the provision of law under which such regulatory review period occurred . . . .

35 U.S.C. § 156 (emphasis added)

Thus, if the '407 patent claims an active ingredient (as a single entity or in combination with another active ingredient), the '407 patent term shall be extended if the permission for the commercial marketing [*i.e.*, FDA approval] is the first permitted commercial marketing or use of the active ingredient as a single entity or in combination with another active ingredient.

There is no factual dispute that the '407 patent claims levofloxacin, and that levofloxacin was a component in a FDA-approved product (FLOXIN®) marketed in the United States prior to the FDA grant of permission to market levofloxacin (as LEVAQUIN®).

Thus, the legal issue to be resolved is whether levofloxacin is an "active ingredient" under Section 156. If levofloxacin is an "active ingredient," there is no dispute that levofloxacin was a component of a product (FLOXIN®, as an enantiomer in the racemic mixture) which was approved well prior to the approval and marketing of Plaintiffs' levofloxacin product (LEVAQUIN®), and thus the

fifth requirement for a patent term extension would not be met. In other words, the marketing of levofloxacin would not be the "first permitted commercial marketing or use" of the active ingredient (levofloxacin) as either a single entity or in combination with another active ingredient.

2. The Federal Circuit Declared the Term "Active Ingredient" to be "Well-Defined"

The Court of Appeals for the Federal Circuit has previously analyzed Section 156, and specifically the term "active ingredient" and two other terms, and concluded that these terms all "had well-defined, ordinary, common meanings when Congress enacted the [Hatch-Waxman] Act [in 1984]." *See Glaxo Oper. UK Ltd. v. Quigg*, 894 F.2d 392, 395 (Fed. Cir. 1990), *aff'g*, 706 F. Supp. 1224 (E.D. Va. 1989).

According to the Federal Circuit, there is no factual (or legal) dispute concerning the meaning of the term "active ingredient." It thus matters not what the Plaintiffs or Lupin believed this term meant at the time Lupin was preparing its ANDA on levofloxacin (or prior to that time), nor even what either party now believes (or contends) is the correct meaning of this term.

The well-defined, ordinary, common meaning of "active ingredient" in 1984 was, as it remains today, "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure of any function of the

body of man or of animals." 21 CFR § 210.3(b)(7)(1984); *see Confoy Decl., Exh. K.* Indeed, this was the definition of active ingredient at the time Plaintiffs applied for an extension of the '407 patent term, and was the very same definition referenced by the Federal Circuit when it analyzed the meaning of Section 156. *See, e.g., Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 347 F.3d 1367, 1373 (Fed. Cir. 2003).

To the extent Plaintiffs' propose a construction that conflicts with what the Federal Circuit has previously concluded is the plain meaning of the statutory language, Plaintiffs "may prevail only if a contrary legislative intent is clearly shown by the legislative history." *See LSI Computer Sys., Inc. v. United States Int'l Trade Comm'n*, 832 F.2d 588, 590 (Fed. Cir. 1987). As the Supreme Court stated:

> While we now turn to the legislative history as an additional tool of analysis, we do so with the recognition that only the most extraordinary showing of contrary intentions from those data would justify a limitation on the "plain meaning" of the statutory language. When we find the terms of a statute unambiguous, judicial inquiry is complete, except in " 'rare and exceptional circumstances,' " TVA v. Hill, 437 U.S. 153, 187, n.33 (1978), quoting Crooks v. Harrelson, 282 U.S. 55, 60 (1930).

See Garcia v. United States, 469 U.S. 70, 75 (1984). Thus, even assuming Plaintiffs were somehow able to overcome the Federal Circuit's conclusive statement concerning the meaning of the term "active ingredient," statements or opinions by any party to this action, those of a third party, or evidence other than

the legislative history, are irrelevant to resolving the meaning of the term "active ingredient." No "rare" or "exceptional" circumstances are present here.

It is undisputed that the levofloxacin in FLOXIN® provided pharmacological activity, and is thus an "active ingredient" under Section 156. For example, the '407 patent asserts that levofloxacin exhibits stronger antimicrobial activity than does the R(+)-enantiomer of ofloxacin, but that the R(+)-enantiomer exhibits antimicrobial activity nonetheless. In addition to the activity described in the '407 patent, a district court opinion in the prior levofloxacin case confirms the existence of the pharmacological activity of ofloxacin and its enantiomers, primarily the S(-)-enantiomer of ofloxacin. *See Ortho-McNeil,* 348 F. Supp. 2d at 751. Thus, FLOXIN® included levofloxacin as an active ingredient, either alone or in combination with the R(+)-enantiomer of ofloxacin. Because levofloxacin is an "active ingredient" as that term is properly defined (21 CFR § 210.3(b)(7)), the term extension granted to the '407 patent is invalid because "a patent is ineligible for extension if it is not the first permitted commercial marketing or use of the active ingredient contained in that approved patented product." *See Fisons PLC v. Quigg*, 876 F.2d 99, 100 (Fed. Cir. 1989), *citing Fisons PLC. v. Quigg*, 1988 WL 150851 *1, *5 (D.D.C. Aug. 19, 1988).

To the extent it is argued that each enantiomer of ofloxacin possesses some level of pharmacological activity, and that the term extension is somehow justified

on this basis, the extension remains invalid. Section 156 defines the term "product" to mean "the active ingredient . . . as a single entity or in combination with another active ingredient." 35 U.S.C. § 156 (f)(2) (emphasis added). In other words, as levofloxacin indisputably exhibited pharmacological activity when present as a component of FLOXIN®, it matters not that the other enantiomer also may be deemed to be an active ingredient of FLOXIN®. The statute clearly prohibits a patent term extension when the basis for the extension is an active ingredient (levofloxacin) that previously was present in an earlier FDA-approved dosage form as an active ingredient, even if it was present in combination with another active ingredient (*e.g.,* the R(+)-enantiomer of ofloxacin). *See Arnold Partnership v. Dudas*, 362 F.3d 1338, 1341 (Fed. Cir. 2004)

B. Other Considerations

Although Plaintiffs were able to obtain FDA approval to market LEVAQUIN®, Section 156 does not provide for extension of patent term for every product that must undergo FDA approval. *See Fisons*, 876 F.2d at 101. The requirements for obtaining a patent term extension differ from those pertaining to patentability; the USPTO often grants patents on different polymorphic forms of drugs, controlled release dosage forms of drugs and combinations of drugs—and the FDA grants approvals for such products—but not all of these are entitled to patent term extensions. *See, e.g., Arnold Partnership*, 362 F.3d at 1341-43.

The USPTO routinely considers requests for patent term extensions, and has recently declined requests for extensions using an analytical framework consistent with that presented herein by Lupin.

In a decision concerning the product Symbicort®, an extension was sought for a product containing two active ingredients: formoterol fumarate dihydrate and budesonide. *See Confoy Decl., Exh. M.* FDA records indicated that each active ingredient had been approved by the FDA for commercial marketing or use in the U.S. prior to the approval of Symbicort®. *Id.* at 2-3. Because both active ingredients in Symbicort® were previously approved, the USPTO decided that the patent on Symbicort® was not eligible for a term extension. *Id*. The decision relied in part on *Arnold Partnership* which requires a court to examine a drug product's (dosage form's) patent extension eligibility on a component-by-component basis. *Id*. at 3-4. In the present case, the active ingredient in issue, levofloxacin, was a component in a prior FDA-approved product (dosage form), ofloxacin. Therefore, the '407 patent covering a component (*i.e.*, the active ingredient levofloxacin) in a previously-approved product is not entitled to a term extension.

The legislative history of Section 156 also is consistent with Lupin's position. The court in *Fisons v. Quigg*, in considering this legislative history, observed that the specific purpose of the term extension appears to have been

relatively narrow—to restore lost patent life only for "pioneer" drugs, *e.g.*, new chemical entities (compounds that were not known previously). The *Fisons* court thus found that "Congress's intent was to restore patent life only to new chemical entities," and not to new therapeutic applications of existing chemicals. *See* Fisons, 1988 WL 150851 at *7.

In a 2008 decision denying a patent term extension for METVIXIA™, the USPTO took the opportunity to explain why patent term extensions such as that granted for the '407 patent are not warranted. *See Confoy Decl., Exh. N* at 4-7. The USPTO retraced the history of the judicial precedent that supports Lupin's present position, concluding with the most recent Federal Circuit's decision that addresses the meaning of the term "active ingredient" in the context of patent term extensions, *Pfizer, Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004):

> Judicial precedent confirms that the USPTO's application of the definition of "product," as that term is used in section 156(a)(5)(A), is correct. In *Fisons v. Quigg*, 1988 WL 150851 (D.D.C. 1988) ("*Fisons I*"), the district court addressed the meaning of the term "product." The district court considered both the plain language of section 156(a)(5)(A) and its legislative history. With respect to the latter, the district court observed:
>
> > Upon examination, the specific purpose of Section 156(a)(5)(A) appears to have been relatively narrow– to restore lost patent life only for "pioneer" drugs. A report by the Congressional Office of Technology Assessment ("OTA") to the 97th Congress provided the factual foundation for the restriction of patent restoration benefits to new chemical entities. The

> OTA report stated: "Although important pharmaceutical innovations may result from new therapeutic applications of existing chemicals … many of the pharmaceutical breakthroughs that have occurred have resulted from NCE (new chemical entity) research and the development of NCEs generally has required more time and money than other types of innovation and has involved greater risks." The House Committee on Energy and Commerce explained that the bill "requires extensions to be based on the first approval of the product because the only evidence available to Congress showing that patent time has been lost is data on so-called class I, new chemical entity drugs."

Fisons I, 1988 WL 15081 at *7. After making these observations, the district court found that "Congress's intent was to restore patent life only to new chemical entities." The district court thus construed section 156(a)(5)(A) in a straightforward way:

> In the definitional provision of Section 156, the term "product" is defined as a "human drug product." 35 U.S.C. § 156(f)(1)(A). This term is further defined in the next subparagraph as "the *active ingredient* of a new drug, antibiotic drug, or human biological product … including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." 35 U.S.C. § 156(f)(2) (emphasis added in original). Substituting this definition directly back into Section 156(a)(5)(A) yields the statement that a patent is ineligible for extension if it is not the first permitted commercial marketing or use of the active ingredient contained in that approved patented product.

Id. at *5.

The Federal Circuit affirmed the district court's interpretation. *See Fisons v. Quigg*, 876 F.2d 99 (Fed. Cir. 1989) ("*Fisons II*"). The Federal Circuit stated: "In sum, we

> hold that the district court correctly applied the definition given in 35 U.S.C. § 156(f) to the term 'product' used in section 156(a)(5)(A). We are convinced that such an interpretation comports with the intent of Congress as expressed in the statute." *Fisons II*, 876 F.2d at 102.
>
> The Federal Circuit later interpreted the term "active ingredient" in *Pfizer, Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004). There, the Federal Circuit accepted the FDA's definition of the term "active ingredient" as meaning "active moiety." *See id.* at 1366 (citing Abbreviated New Drug Application Regulations: Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,358 (F.D.A. Oct. 3, 1994)). It likewise accepted that "active moiety" means "the molecule or ion excluding those appended portions of the molecule that cause the drug to be an ester, salt … responsible for the physiological or pharmacological action of the drug substance," based upon the FDA's regulations. *Id.* (quoting 21 C.F.R. § 314.108(a)) (omission in original). Hence the Federal Circuit has construed the term "active ingredient" as used in section 156(f)(2) to mean the underlying molecule, *i.e.*, the molecule or ion responsible for the physiological or pharmacological action of the drug, excluding those appended portions of the molecule that cause the drug to be an ester or salt.

See Confoy Decl., Exh. N at 4-5.

LEVAQUIN® is not a pioneer drug, and does not contain a new chemical entity; Plaintiffs admit that its active ingredient (levofloxacin) was included in a FDA-approved product (i.e., FLOXIN®) years before FDA approval for LEVAQUIN® was sought. It is telling that enantiomers, such as the levofloxacin active ingredient in LEVAQUIN®, do not qualify for New Chemical Entity exclusivity if the corresponding racemic mixture containing that enantiomer was previously approved as a drug. The FDA formalized its position on this matter a

decade ago stating, "a single enantiomer of a previously approved racemate contains a previously approved active moiety and is therefore not considered a new chemical entity." *See* 54 Fed. Reg. 28872 at 28898 (July 10, 1989). For that same reason they do not qualify for patent term extensions.

Thus, the legislative history of Section 156 is consistent with the plain language of the statute—the term extension of the '407 patent is invalid.

VI. CONCLUSION

The patent term extension granted by the USPTO to the '407 patent is invalid because it fails to meet all of the statutory criteria set forth in 35 U.S.C. § 156. Lupin respectfully requests that its motion be granted, that the term extension granted to the '407 patent be invalidated, and that the '407 patent's original expiration date be reinstated.

Respectfully submitted,

STERNS & WEINROTH, P.C.
Attorneys for Defendants Lupin Pharmaceuticals, Inc. and Lupin Ltd.

Dated: September 26, 2008

By: /s/ Karen A. Confoy
Karen A. Confoy
kconfoy@sternslaw.com

Of Counsel:
Robert F. Green
Christopher T. Griffith
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
Chicago, IL 60601-6780
Telephone: (312) 616-5600
Facsimile: (312) 616-5700
Attorneys for Defendants
Lupin Pharmaceuticals, Inc. and Lupin Ltd.