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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA,	**Civil Action No. 3:07-cv-06020 (MLC)(JJH)**
Plaintiffs,	**MOTION DATE: April 7, 2008**
vs.	**NOTICE OF MOTION FOR A TEMPORARY STAY**
AUROBINDO PHARMA LIMITED, and AUROBINDO PHARMA USA INC.	
Defendants.	

PLEASE TAKE NOTICE that Plaintiffs ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI

SEIYAKU KABUSHIKI KAISHA ("Plaintiffs") will move before this Court at the United States District Court for the District of New Jersey, 402 E. State Street, Trenton, New Jersey, on April 7, 2008, at 10 a.m., before the Honorable John J. Hughes, U.S.M.J. for entry of an Order to stay this proceeding pending resolution of jurisdictional issues in a substantially identical first-filed patent infringement action in the District of Delaware (Civil Action No. 1:07-cv-810, Dist. Delaware) and completion of any necessary proceedings before the Judicial Panel on Multidistrict Litigation (JPMDL) necessitated by a successful challenge to the jurisdiction of the Delaware court.

The Parties rely upon the Memorandum of Law and the Declaration of Jonathan M.H. Short submitted with this Motion, and upon all pleadings and proceedings on file herein.

A Proposed Order granting the Parties' motion is attached.

Respectfully submitted,

Dated: February 28, 2008

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that true copies of Plaintiffs' Motion to Stay with supporting papers were caused to be served on February 28, 2008, upon the following via ECF and/or Overnight Mail:

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA,	**Civil Action No. 3:07-cv-06020 (MLC)(JJH)**
Plaintiffs,	
vs.	
AUROBINDO PHARMA LIMITED, and AUROBINDO PHARMA USA INC.	
Defendants.	

MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFFS' MOTION FOR A TEMPORARY STAY

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I. INTRODUCTION

Plaintiffs, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals, Inc., and Shionogi Seiyaku Kabushiki Kaisha (collectively "AstraZeneca"), seek a temporary stay of this Hatch-Waxman patent infringement action against Defendants Aurobindo Pharma Limited ("APL") and Aurobindo Pharma USA Inc. ("APU") (collectively "Aurobindo"), pending resolution of jurisdictional issues in a substantially identical first-filed patent infringement action in the District of Delaware and completion of any necessary proceedings before the Judicial Panel on Multidistrict Litigation (JPMDL) necessitated by a successful challenge to the jurisdiction of the Delaware court. At least five related cases involving the same patent are pending in Delaware. Aurobindo's amenability to suit is currently being litigated in Delaware. Aurobindo is also participating in Delaware in the formulation of a coordinated discovery plan without prejudice to its jurisdictional allegations. Finally, AstraZeneca has committed to seek transfer of this action to Delaware by the JPMDL for participation in consolidated discovery in the event jurisdiction in Delaware is found to be improper.

Since no material prejudice can befall APL and APU by requiring them to proceed with discovery along with the other defendants in Delaware while these threshold procedural matters are being resolved, and since there is no compelling reason why AstraZeneca and this Court should be required to engage in redundant efforts in that regard, a temporary stay of these proceedings is warranted.

II. BACKGROUND

A. Nature and Stage of Proceedings

On October 31, 2007, Aurobindo sent AstraZeneca a notice ("Paragraph IV notice") that Aurobindo had filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug

Administration ("FDA"). In its ANDA, Aurobindo stated its intention to market and sell a generic version of AstraZeneca's well-known and highly successful drug Crestor® prior to the expiration of AstraZeneca's U.S. Patent No. RE37,314 ("the '314 patent"), which covers Crestor®. On December 11, 2007, AstraZeneca sued Aurobindo and six other generic drug manufacturers in the Federal District court of AstraZeneca's home state, Delaware (the "Delaware Action"), for infringing the '314 patent. (Civil Action No. 1:07-cv-810, Dist. Delaware). The timing of the Delaware suit was mandated by the statutory scheme, which provides for the initiation of a 30-month automatic stay of FDA final approval for an ANDA if the patent owner brings suit within 45 days of receiving notice of a Paragraph IV certification to allow adjudication of the patent issues. 21 U.S.C. § 355(j)(5)(B)(iii). The 30-month stay is an important benefit that might be lost if a timely patent infringement lawsuit is dismissed for lack of personal jurisdiction and then refiled in another jurisdiction after the 45 day period has run. *See* 21 U.S.C. § 355(j)(5)(B)(iii).

In order to protect itself from the prejudicial consequences of dismissal of its Delaware actions, AstraZeneca subsequently brought three "protective" suits, one in West Virginia, one in Florida, and this suit in the District of New Jersey (the "New Jersey Action", or "this case") for infringement of the same patent. AstraZeneca did so in anticipation that three of the defendants, including Aurobindo, might challenge jurisdiction in Delaware, as APL now has done. The three protective suits were filed but not served. The three affected defendants were notified of AstraZeneca's intention not to serve the complaints unless it became necessary to do so and that the cases would be dismissed upon establishment of jurisdiction in Delaware. (Short

Declaration, Ex. 2). There was no attempt at forum shopping.[1]

Two of the three defendants against whom protective suits were filed, recognizing the obvious judicial economies to be realized in handling this complex litigation in a single court, consented to jurisdiction in Delaware. Notwithstanding that APL is currently litigating another ANDA patent suit in Delaware before Judge Sleet,[2] APL filed a motion to dismiss the Delaware Action for lack of personal jurisdiction shortly after the assignment of that case to Judge Farnan.[3] That motion is currently pending and the parties have begun taking limited jurisdictional discovery. AstraZeneca's response is due April 21, 2008.

In an apparent attempt to further disrupt the orderly resolution of these cases, APU answered the unserved Complaint in this Court and has sought to push discovery forward in this case ahead of that in the main action.

B. Jurisdiction In Delaware

Jurisdictional discovery is underway in Delaware, and AstraZeneca cannot, therefore, fully articulate all of the bases for Delaware jurisdiction at this time. Suffice it to say that AstraZeneca brought the first-filed action in Delaware because it is AstraZeneca's home state,

---

[1] The Court in this District has recognized that filing a second, protective suit in ANDA cases is warranted. *Aventis Pharma S.A. v. Sandoz Inc.*, 2007 WL 1101228, *4 (D.N.J. 2007) (rejecting any allegation of judge or forum shopping). Courts in other districts similarly have stayed the second-filed case in favor of the first-filed case. *See, e.g. Schering Corp. v. Caraco Pharm. Labs., Ltd.*, 2007 WL 1648908 (E.D. Mich. Jun. 6, 2007); *PDL Biopharma, Inc. v. Sun Pharm. Indus., Ltd.*, 2007 WL 2261386 (W.D. Mich. Aug. 6, 2007); *Abbott Labs. v. Mylan Pharms., Inc.*, No 05-6561, 2006 U.S. Dist. LEXIS 13782 (N.D. Ill. Mar. 28, 2006).

[2] *Sanofi-Aventis et al. v. Actavis South Atlantic LLC* (Civil Action No. 1:07-cv-572, D. Del.).

[3] Apotex, Inc., one of the seven Delaware defendants who, like APL, has voluntarily litigated for years in Delaware with judges other than Judge Farnan, also moved to dismiss upon assignment of the case to Judge Farnan. No protective suit had been filed against Apotex because it had conceded general presence in Delaware not seven months earlier. If Apotex is successful, that action would be transferred to Florida and, in a rational world, transferred back to Delaware for consolidated discovery by the JPMDL.

because both Aurobindo defendants are believed to be subject to jurisdiction in Delaware, and because of the obvious judicial economies to be realized in discovering and trying these related cases together. The Delaware court should find general jurisdiction over both Aurobindo entities at least because (1) APU is a Delaware corporation subject to suit in Delaware, (2) APL, through its wholly-owned subsidiary APU, markets and sells APL's products throughout the U.S. and in Delaware, and (3) both Aurobindo entities are voluntarily conducting an important component of their ordinary business activities—the provocation and litigation of patent disputes in order to gain access to new markets—in Delaware.

If the personal jurisdiction issue in Delaware is resolved in AstraZeneca's favor, AstraZeneca intends to move for transfer of this case to Delaware or for its voluntary dismissal. Regardless, AstraZeneca has committed to the Delaware court to seek an order from the JPMDL to transfer this case to Delaware for coordinated pretrial proceedings in the event it remains pending here. (Short Decl., Ex. 1, Transcript of Feb. 20, 2008, Conference at p. 18, lines 20-21 and p. 21, lines 8-11).

C. Discovery In the Delaware Suits

As agreed during a February 20, 2008, status conference with the Delaware Court, AstraZeneca and the defendants in the Delaware suits, including APL and APU, will proceed with the development of a coordinated discovery plan in Delaware without prejudice to any jurisdictional challenges. A report is due to the Court on April 3, 2008, with a Rule 16 Conference to follow on April 10. It would be inefficient and duplicative if the other Delaware suits proceeded on a different schedule than the New Jersey Action. Additionally, any discovery taken in the Delaware Action can be utilized in the New Jersey Action if the personal jurisdiction motion should be decided in APL's favor and the JPMDL declines to transfer this case to Delaware for pretrial discovery.

III. ARGUMENT

A. The First-Filed Rule Directs the Second-Filed New Jersey Action to Be Stayed Absent Exceptional Circumstances

When two federal lawsuits addressing the same parties and issues are pending, the "first-filed" rule is applied. *The Violet Pot, LLC v. Lowe's Companies, Inc.*, 2007 WL 894187 at *2 (D.N.J. Mar. 20, 2007). The first-filed rule instructs that "[i]n all cases of federal concurrent jurisdiction, the court which has possession of the subject must decide it." *Crosley Corp. v. Hazeltine Corp.*, 122 F.2d 925, 929 (3d Cir. 1941); *EEOC v. Univ. of Pennsylvania*, 850 F.2d 969, 971 (3d Cir. 1988). Application of the first-filed rule encourages comity within the federal court system, promotes sound judicial administration, and limits the possibility of conflicting judgments. *See EEOC*, 850 F.2d at 971; *Crosley*, 122 F.2d at 930; *see also Continental Grain Co. v. Barge FBL-585*, 364 U.S. 19, 26 (1960) ("To permit a situation in which two cases involving precisely the same issues are simultaneously pending in different District Courts leads to the wastefulness of time, energy, and money."); *American Cyanamid Co. v. Eli Lilly and Co.*, 903 F. Supp. 781, 787 (D.N.J. 1995) (transferring second-filed action to the first-filed forum because application of the first-to-file rule favored transferring the case, related litigation was pending in the transferee forum, the convenience of the parties and the location of the documents weighed in favor of transfer, and the court in the transferee forum had already denied the accused infringer's motion to transfer the first-filed action).

Given the significant interests behind this rule, "invocation of the first-filed rule will usually be the norm, not the exception." *Violet Pot*, 2007 WL 894187 at *3. *See also American Cyanamid*, 903 F. Supp. at 787 (noting that application of the first-filed rule is particularly appropriate in patent cases). Only when presented with "exceptional circumstances" should a

court exercise its "discretion to depart from the rule." *EEOC*, 850 F.2d at 979. While there is no rigid definition, "exceptional circumstances" typically involve instances of bad faith, inequitable conduct, forum-shopping, or situations where the second-filed case is more fully developed than the first. *Nature's Benefit, Inc. v. NFI*, 2007 WL 2462625 at *4 (Aug. 27, 2007 D.N.J.). Those exceptional circumstances are not present here.

When applied, the first-filed rule permits a district court, in its discretion, to "stay, dismiss, or transfer the second-filed action to avoid duplicative litigation." *Nature's Benefit*, 2007 WL at *3. If, however, "the first-filed action is vulnerable to dismissal on jurisdictional grounds, the court in the second-filed action should stay or transfer said action rather than dismiss it outright." *Nature's Benefit*, 2007 WL 2462625 at *4 (*citing Alltrade, Inc. v. Uniweld Prods., Inc.*, 946 F.2d 622, 628 (9th Cir. 1991); *GT Plus, Ltd. v. Ja-Ru Inc.*, 41 F. Supp. 2d 421, 424 (S.D.N.Y. 1998).

There can be no dispute that application of the first-filed rule is warranted here. The New Jersey and Delaware actions involve the same issues, the same parties, and the two complaints are identical in substance. (*Compare* Complaint, Docket No. 1 *with* Short Decl., Ex. 3). Furthermore, as AstraZeneca filed its Delaware complaint on December 12, 2007 and its New Jersey complaint on December 18, 2007, the Delaware Action is clearly the first-filed.

Courts in other jurisdictions have explicitly recognized the propriety of the first-filed rule where, as here, the second-filed action is initiated only as a precautionary measure in a Hatch-Waxman case. For example, in *PDL Biopharma, Inc. v. Sun Pharm Indus., Ltd.*, the plaintiff first brought suit in the District of New Jersey accusing the generic defendant of patent infringement. 2007 WL 2261386 at *1 (W.D. Mich. Aug. 6, 2007). Like the instant case, plaintiff believed that the defendant might challenge jurisdiction in the first-filed case, so it

brought a second suit in the Eastern District of Michigan as a protective measure to preserve the 30-month stay of approval of the defendant's ANDA. *Id.* The Michigan court held that application of the first-filed rule was appropriate and stayed the second-filed action in Michigan pending proceedings in the first-filed New Jersey action. *Id.* at *2-3.

Similarly, in *Schering Corp. v. Caraco Pharm. Labs. Ltd.*, the plaintiff filed first in New Jersey against twenty-one generic defendants and subsequently filed a second action in the Eastern District of Michigan against two defendants that it believed would—and in fact did—challenge jurisdiction in New Jersey. 2007 WL 1648908 at *1 (E.D. Mich. Jun. 6, 2007). As in *PDL*, the *Schering* court applied the first-filed rule and granted plaintiff's motion to stay the second-filed action. *Id.* at 3.

Furthermore, no exceptional circumstances exist here to justify departure from the first-filed rule. AstraZeneca's first-filed suit is in Delaware—its home forum—which does not constitute forum shopping. *See e.g., Shaw Family Archives, Ltd. v. CMG Worldwide, Inc.*, 434 F. Supp. 2d 203, 210 (S.D.N.Y. 2006). Nor can it be said that the second-filed suit is more fully developed than the first as both cases are at the same stage in the litigation—in both cases defendants have answered or otherwise moved to dismiss for lack of jurisdiction and discovery is only just beginning.[4] Finally, there is nothing to suggest any bad faith or inequitable conduct on behalf of AstraZeneca. The filing of AstraZeneca's second-suit in New Jersey was merely to preserve the statutory 30-month stay in the event that the Delaware Action were to be dismissed for lack of jurisdiction. *See Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 2007 WL 4284877 at *2 (D.N.J Dec. 3, 2007) (finding that the filing of a protective suit in another

[4] APL's refusal to agree to a stay of this case appears to be a thinly-veiled and improper attempt artificially to accelerate this case ahead of the main Delaware action and then eventually to try to transfer all of the Delaware suits to New Jersey. The attempt should fail.

jurisdiction in a Hatch-Waxman case is not indicative of bad faith or forum shopping).

B. Neither Defendants Nor the Public Will Be Prejudiced By a Temporary Stay

Neither Defendants nor the public will be harmed by the entry of a stay. Defendants do not yet have FDA approval of their ANDA. Therefore, even if this action could be resolved in Defendants favor tomorrow Defendants still could not sell their generic product. Nor will Defendants suffer any prejudice in their ability to adequately defend this litigation. They are voluntarily participating in pretrial proceedings in Delaware, subject to the resolution of their motions to dismiss. AstraZeneca moves only for a temporary stay of these proceedings pending resolution of Defendants' motion to dismiss for lack of personal jurisdiction in the Delaware Action and, resolution of any needed proceedings before the JPMDL. APL will be fruitfully engaged in Delaware discovery proceedings in the interim that will be fully utilizable in this Court if need be and will suffer no prejudice.

Further, granting this motion is consistent with the promotion of efficient judicial administration. By temporarily staying this action pending resolution of the jurisdictional disputes in the Delaware case, both the Court and the parties avoid the need to undertake duplicative efforts and incur unnecessary expenses. *See Adams*, 2007 WL 4284877 at *2 (noting that permitting the second-filed suit to proceed while jurisdictional challenges in the first-filed suit are pending would be a waste of judicial resources).

Finally, other courts have found that the harsh consequences facing Hatch-Waxman plaintiffs should the first-filed case be dismissed after the 45 day filing period has run weighs in favor of staying the second-filed action. *See Adams*, 2007 WL 4284877 at *2; *PDL*, 2007 WL 2261386 at *2. Clearly, AstraZeneca's protective suit in the District of New Jersey was a prudent approach to a statutory risk and the Court should stay this suit until the personal jurisdiction motion in the Delaware Action is resolved and any necessary proceedings before the

Judicial Panel on Multidistrict Litigation (JPMDL) necessitated by a successful challenge to the jurisdiction of the Delaware court are completed.

IV. CONCLUSION

For the foregoing reasons, the Court should grant the requested temporary stay and enter an Order in the form proposed.

Dated: February 28, 2008

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, **Plaintiffs,** **vs.** **AUROBINDO PHARMA LIMITED, and AUROBINDO PHARMA USA INC.** **Defendants.**	**Civil Action No. 3:07-cv-06020 (MLC)(JJH)** **DECLARATION OF JONATHAN M.H. SHORT IN SUPPORT OF PLAINTIFFS' MOTION FOR A TEMPORARY STAY**

Jonathan M.H. Short, of full age, hereby declares as follows:

1. I am a member of the bar of this court and am associated with the firm of McCarter & English, LLP, attorneys for Plaintiffs ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA ("AstraZecenca") in this matter.

2. I submit this declaration in support of AstraZeneca's Memorandum of Law in Support of Plaintiffs' Motion to Temporarily Stay These Proceedings.

3. Attached as Exhibit 1 hereto is a true and correct copy of the transcript of a conference call held before Judge Leonard P. Stark on February 20, 2008 for the cases bearing Civil Action Nos. 07-805 through 07-811 in the District of Delaware.

4. Attached as Exhibit 2 hereto is a true and correct copy of a December 18, 2007 letter from York M. Faulkner to counsel for defendants in the cases bearing Civil Action Nos. 07-805 through 07-811 in the District of Delaware.

5. Attached as Exhibit 3 hereto is a true and correct copy of the Complaint filed against the Aurobindo defendants in the case bearing Civil Action No. 07-810 in the District of Delaware.

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

Dated: February 28, 2008

Jonathan M.H. Short

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

- - -

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, Plaintiffs, v. MYLAN PHARMACEUTICALS, INC., Defendant.	:	CIVIL ACTION NOS. 07-805 (JJF-LPS)
ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, Plaintiffs, v. SUN PHARMACEUTICAL INDUSTRIES LTD., and SUN PHARMACEUTICAL INDUSTRIES INC., CARACO PHARMACEUTICAL LABORATORIES, LTD., Defendants.	:	and 07-806 (JJF-LPS)

- - -

Wilmington, Delaware
Wednesday, February 20, 2008 at 3:04 p.m.
TELEPHONE CONFERENCE

- - -

BEFORE: HONORABLE **LEONARD P. STARK**, U.S. MAGISTRATE JUDGE

- - -

(***Captions continue on page two***)

Brian P. Gaffigan
Registered Merit Reporter

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA,	:	CIVIL ACTION NOS.
Plaintiffs,	:	
v.	:	
SANDOZ, INC.,	:	
Defendant.	:	07-807 (JJF-LPS)
ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA,	:	
Plaintiffs,	:	and
v.	:	
PAR PHARMACEUTICAL, INC.,	:	
Defendant.	:	07-808 (JJF-LPS)
ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA,	:	
Plaintiffs,	:	and
v.	:	
APOTEX INC., and APOTEX CORP.,	:	
Defendants.	:	07-809 (JJF-LPS)

(***Captions continue on page three***)

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, Plaintiffs, v. AUROBINDO PHARMA LTD., and AUROBINDO PHARMA USA, INC., Defendants.	:	CIVIL ACTION NOS. 07-810 (JJF-LPS)
ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, Plaintiffs, v. COBALT PHARMACEUTICALS, INC., and COBALT LABORATORIES, INC., Defendants.	:	and 07-811 (JJF-LPS)

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and

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P R O C E E D I N G S

(REPORTER'S NOTE: The following telephone conference was held in chambers, beginning at 3:04 p.m.)

THE COURT: Good afternoon, counsel. This is Judge Stark. This is the time, as you know, for the status conference in seven different actions, all related. They have our civil case numbers beginning with 07-805 and ending 07-811.

I want to begin by learning who is on the call. So first, for AstraZeneca and the plaintiffs, who do I have on the line?

MS. BURKE: Good afternoon, Your Honor. This is Mary Burke from Connolly Bove representing the plaintiffs AstraZeneca and Shionogi. With me on the phone are Charley Lipsey and York Faulkner from Finnegan Henderson, Henry Renk from Fitzpatrick and Tom Stevens from AstraZeneca.

THE COURT: And who will be speaking for AstraZeneca plaintiffs on the call?

MR. LIPSEY: Your Honor, this is Charley Lipsey; and I'll be speaking for AstraZeneca.

THE COURT: Okay. Great. Is that all of the plaintiffs or are there other counsel for other plaintiffs?

MR. LIPSEY: That's it, Your Honor.

THE COURT: Okay. Great. Now, in Action No. 805 for the Mylan defendants, who is on the call?

MS. MAZZOCHI: Good afternoon, Your Honor, this is Deanne, D-E-A-N-N-E, Mazzochi, M-A-Z-Z-O-C-H-I, from the law firm Rakoczy Molino Mazzochi & Siwik in Chicago. Also with me from our firm is Tara Raghavan; and our local counsel is also here, and I'll have her introduce herself.

MS. MATTERER: Good afternoon. This is Mary Matterer from the law firm of Morris James.

THE COURT: Okay. And Ms. Mazzochi will be the

one speaking for the Mylan defendants?

MS. MAZZOCHI: Yes, Your Honor.

THE COURT: Okay. Thank you. And in Action No. 806, who is on the call for the Sun defendants?

MR. DROBNY: Good afternoon, Your Honor, this is Dane, D-A-N-E, Drobny, D-R-O-B-N-Y, at Winston & Strawn, as well as my partner, Chuck Klein.

MR. SEAMAN: And locally, John Seaman at Abrams & Laster.

THE COURT: Okay. And Mr. Drobny, you will be the one speaking?

MR. DROBNY: Yes, Your Honor.

THE COURT: Then Action No. 807, for the Sandoz defendants, who is on the call?

MR. PAVANE: Your Honor, this is Martin Pavane, P-A-V-A-N-E. And with me on the call is Darren Mogil, M-O-G-I-L; and in Delaware George Seitz, S-E-I-T-Z. And I will be speaking for the Sandoz defendants.

THE COURT: Great. Thank you very much.

In Action 808, that's the Par defendants. Who is on the call for them?

MR. BROWN: This is Dan Brown from Frommer Lawrence & Hague in New York representing Par. With me here in New York is Nick Giove from our firm; and in Delaware, Fred Cottrell from Richards Layton & finger.

THE COURT: Okay. And Mr. Brown, you will be the one speaking; correct?

MR. BROWN: Yes.

THE COURT: For the Apotex defendants in Action 809.

MR. HORWITZ: Your Honor, it's Rich Horwitz here in Wilmington at Potter Anderson; and with me from Welsh Katz, Robert Breisblatt, Laurie Haynie and Aron Carnahan; and I believe Mr. Breisblatt or Ms. Haynie will take the lead.

THE COURT: Mr. Breisblatt or Ms. Haynie, which one will it be?

MR. BREISBLATT: Your Honor, it will be Ms. Haynie doing the talking, but if there is no objection, I might chirp in from time to time.

THE COURT: Okay. We'll see how much chirping is necessary.

Okay. In Action 810, the Aurobindo defendants.

MR. KIRK: Your Honor, this is Richard Kirk from Bayard, P.A. here in Wilmington. My colleagues are Thomas Heneghan, H-E-N-E-G-H-A-N, Jeffrey Ward, and Edward Pardon, P-A-R-D-O-N, from Michael Best & Friedrich; and Mr. Heneghan will be our spokesman.

THE COURT: Okay. Thank you. And last, but not least, the Cobalt defendants in Action 811.

MR. HORWITZ: Your Honor, it's Rich Horwitz again. And with me for Cobalt, Steve Maddox from Foley & Lardner in DC.

THE COURT: Okay. And Mr. Maddox, you will be speaking for Cobalt?

MR. MADDOX: Yes, sir.

THE COURT: All right. Well, thank you, counsel. I have a court reporter with me. Obviously, it's imperative that before you speak, please identify yourselves so we can keep track of who is speaking, of course.

So as I understand it, all seven of these actions involve AstraZeneca and related entities as the plaintiffs. All seven of the cases claim that ANDA applications infringe the '314 patent and they all further are seeking a declaratory judgment of infringement pursuant to 35 U.S.C., Section 271(a). All of these cases, all seven have been assigned to Judge Farnan; and he, in turn, has referred them to me for all purposes, all pretrial purposes through, and including, the pretrial conference.

Have I said anything yet that is incorrect or that anybody disagrees with? Let me start with Mr. Lipsey.

MR. LIPSEY: No, Your Honor. You have it right so far.

THE COURT: And do any of the defense counsel think I have gotten anything wrong yet?

Okay. I'm hearing nothing so I will take that as a no. Thank you.

All right. Well, as I further understand, Mr. Lipsey, it appears that in five of the seven actions, there have been answers and counterclaims and by stipulation which I have ordered, AstraZeneca will be replying to any counterclaims by March 21st, 2008. Is that correct?

MR. LIPSEY: That is correct.

THE COURT: And, further, it appears that there are four actions which have motions to dismiss and with one exception, AstraZeneca will be replying to those motions by March 20th of this year, and the one exception is that Aurobindo has one motion to dismiss regarding the alleged lack of personal jurisdiction and a related joinder issue for which you are not going to respond until April 21st, 2008. Do I have that right, Mr. Lipsey?

MR. LIPSEY: Yes, Your Honor. That is correct. Two of those motions bear on whether the parties will be here in Delaware with us for trial. One of them is the Aurobindo motion you mentioned to which we have an agreement with Aurobindo for some limited jurisdiction discovery leading to our response on April 21st. There is a similar motion by Apotex and we have opened negotiations with Apotex hoping to get at least that motion on the same or approximately the same schedule as we have with Aurobindo,

and we will be chatting with them in the coming days trying to work that out.

THE COURT: Okay. Well, sticking with you, Mr. Lipsey, what, if anything, do the plaintiffs suggest I do with respect to scheduling at this point?

MR. LIPSEY: Well, we obviously were hoping to conduct all seven cases in the same court. All seven defendants appear to have contacts with Delaware. All seven defendants had conducted their ANDA litigation business before. We obviously would like to follow that through.

There is obviously a certain amount of jurisdictional discovery we would like to take in order to tee those issues up. We would like not to delay everybody in the process of doing that. In part, even if we were to lose on the in personam jurisdiction issue on one or both of these defendants, we are planning on filing shortly a motion before the Multi-District Panel to send such actions as may not be here at least for pretrial discovery. And that being the case, we figure it highly likely that discovery is going to go forward in this court no matter what the outcome of those motions is.

What we would like is to have a series of Rule 26(f) conferences with counsel for the defendants during March where we can frame a discovery plan. An important component for us will be some kind of protection built in

there to deal with complex cases with multiple parties where we have some hopefully common discovery propounded, hopefully a lead counsel identified, hopefully some rational limits on interrogatories and depositions and deposition time; the sort of thing that is normally done in complex litigation. And we would propose then to have a Rule 16 conference with Your Honor in mid-April or thereabouts.

The Multi-District Panel, the next hearing that we can hope to get from them is in May, I am told, so it's almost certain that issue will be heard, if not resolved, by then. What we are hoping is the two defendants that are currently challenging jurisdiction will be invited to, and would accept, the right to participate in framing the discovery plan here without prejudice to their positions on in personam jurisdiction so their input can be had and they can enjoy such discovery as is available here while we're sorting out the jurisdictional issues.

So that, in a somewhat long winded form, is what we would propose.

THE COURT: Okay. I appreciate that background, and I think I understand where you are coming from. I think the best way to get all the defense positions and responses to that -- generally, the topic is scheduling, but I do want to hear specifically of what you think of what Mr. Lipsey has proposed -- is I'm just going to go in order of the

cases by number. So we'll start with the Mylan defendants, and I believe that is Ms. Mazzochi.

MS. MAZZOCHI: Yes. Good afternoon, Your Honor. Deanne Mazzochi. The general rule with this many defendants, we're certainly not going to be looking to do duplicative discovery. I think that we would certainly be willing to work with the other defendants to try to find areas where we do have some common ground so that we're not duplicating discovery; but by the same token, Mr. Lipsey talked about rational limits on depositions and interrogatories. My understandings is while the '314 patent is at issue in all of the cases, there are additional patents that are at issue in some cases and not in others. I believe there are some pending declaratory judgment claims by the other defendants to bring in other patents. So we just would want to make sure that there is no prejudice to any party in terms of being able to pursue discovery and that limits aren't going to be placed on any particular party for discovery.

Well, let me put it this way. I just don't want the defendants to be treated as if they are all one defendants with common interests because I think that there are going to be instances where the parties' common interests or the defendants' common interests are going to diverge.

THE COURT: Well, if I understood Mr. Lipsey, I think he intends to have separate Rule 26 conferences with each of the defendants. And I guess that would ultimately result in either multiple scheduling orders or at least one proposed scheduling order where the parties tried to agree on as much as they can but would presumably preserve the opportunity for each of the different defendants to indicate their specific individual needs on any particular type of discovery.

MS. MAZZOCHI: Right.

MR. LIPSEY: If I may, Charles Lipsey again. I actually was proposing meeting with all the defendants in which we could hash out exactly the kind of issue that just got raised. There may well be some individual needs that would have to be addressed, but I would hope to get some agreement amongst all of the defendants at least on how we're going to handle the common discovery.

THE COURT: Okay. I guess I didn't mean to impose whether it would be one meeting or seven meetings or some other number but that there would be a chance for all the defendants together, or individually, to air with the plaintiff what their view was on discovery and ultimately that would result in a document that I would see which would hopefully agree on most or all of the discovery issues, and to the extent that it didn't, we would have obviously the

scheduling conference and I would have to make some decisions.

Is that a fair characterization, Mr. Lipsey?

MR. LIPSEY: Absolutely, Your Honor.

THE COURT: And I think with that clarification, Ms. Mazzochi, that would not be shutting down your client from raising whatever issues they have. Am I right about that?

MS. MAZZOCHI: Right. I would hope not.

THE COURT: Okay. Was there anything more you wanted to add, Ms. Mazzochi?

MS. MAZZOCHI: No, Your Honor.

THE COURT: All right. For Sun, is it Mr. Drobny?

MR. DROBNY: Yes, Your Honor. And with Your Honor's clarification, we have no issues with what the plaintiffs have proposed.

THE COURT: Okay. For Sandoz, Mr. Pavane?

MR. PAVANE: Yes, we too are in agreement.

THE COURT: Okay. Mr. Brown for Par?

MR. BROWN: Likewise.

THE COURT: Okay. Was it Mr. Haynie for Apotex?

MS. HAYNIE: That was Ms. Haynie.

THE COURT: I apologize.

MS. HAYNIE: That's fine. With the

understanding there would no prejudice to our position, we would be willing to engage in preliminary discussions. However, we feel we should also mention we have filed a declaratory judgment action in the Middle District of Florida on a different patent, although it's related to the same underlying drug. It's a different patent, the '460 patent that we have filed in Florida. So that could raise different issues for our client.

THE COURT: Has that case proceeded at all yet?

MS. HAYNIE: No, it has not been answered yet. The answer is due March 26th.

MR. LIPSEY: Your Honor, Charles Lipsey again. That is one we would be approaching the judicial panel in Multi-District Litigation to send up here in the event that it needs to be litigated.

THE COURT: Okay. Thank you. But, Ms. Haynie, with my understanding at least that there is this other action out there which may cause some complications with you and your client, you are willing to sit down and talk with Mr. Lipsey about the possibility of a discovery plan and such here.

MS. HAYNIE: Yes. Under the conditions he discussed, yes.

THE COURT: For Aurobindo, is it Mr. Heneghan?

MR. HENEGHAN: Thank you, Your Honor. Our

situation is a little bit different in that we have the case pending here and the identical case is also pending in New Jersey. And unlike the situation with Apotex where the defendants filed its declaratory judgment in a different jurisdiction, the case in New Jersey was actually filed against us by the same plaintiffs on the exact same legal theory, the same patent. In fact, the complaints are word for word the same with the exception that the caption that identifies the court. That case already has an initial scheduling conference set for the end of March and it's going forward.

That being said, and without waiving any of our arguments on personal jurisdiction, we would be willing to cooperate in some sort of discussion about consolidating discovery regardless of how the cases go forward. I just want to make sure the court was aware that the situation with our motion to dismiss on personal jurisdiction is a little different in that it's a threshold issue that would possibly just take us out of Delaware completely.

With that being said, we are willing to cooperate in working together on a common discovery plan.

THE COURT: Okay. Thank you for that.

Mr. Lipsey, did you want to say anything about whether the New Jersey action impacts anything of this at this time?

MR. LIPSEY: Well, the New Jersey action is the other one that we would approach the Multi-District Panel on. And just to explain, that was what is called in this business a protective suit which we did not serve. Our intention was to proceed there only if the court were to determine that we did not have personal jurisdiction here in Delaware because there are substantive rights that turn on having the case pending. And while the court has the power to transfer it to where it should be, and we would expect that would happen if we were to be wrong on the jurisdictional issue, that suit was filed out of an abundance of caution. The answer was filed even without it being served. I don't want to wait until we resolve the jurisdictional issue here to approach the Multi-District Panel just because it takes so long to get on the docket there. So basically what we would like to do is proceed basically in parallel to fight the jurisdictional issue here. Hopefully, that will moot out the pleading that we filed with the Multi-District Panel.

THE COURT: I understand that. Okay. Finally, for Cobalt, was it Mr. Maddox?

MR. MADDOX: Yes, Your Honor. I beg your pardon?

THE COURT: I was just going to ask your position on meeting and talking about a discovery plan and

all that.

MR. MADDOX: My position is we've got the right sequence. I think everyone on this phone has been through these cases before, and it would be a miracle if there were no issues for you to resolve at a Rule 16 conference. And so I would propose that the sequence makes sense. The timing, I don't think we really need to wait until mid-to-late April for that. I think March is a long month. We can get a lot done there, and maybe have it at the end of March or beginning of April.

THE COURT: Okay. I won't, at this point, give up on the possibility of a miracle, but I certainly won't hold my breath for it. I appreciate the warning.

Well, just looking at my schedule, I could schedule a scheduling teleconference for the morning of April 4th, if you folks could get together and have your meeting or meetings and get me your proposal which outline any objections let's say by a week before that, which would be March 28th.

Mr. Lipsey, could you work with that schedule?

MR. LIPSEY: I unfortunately, have a deposition scheduled on the 4th. It might be a little easier if we could talk and make sure that we can get that covered for -- I am absolutely free on the 10th. I don't know whether that is something I can suggest.

THE COURT: No, I could do the morning of the 10th. And if I could get your submission a week before, by the 3rd?

MR. LIPSEY: Okay. That's fine with us. Is that okay with everybody else?

THE COURT: Anybody who has a problem with that date, please let me know by your name.

MR. HENEGHAN: Judge, this is Tom Heneghan on behalf of Aurobindo. We don't have a problem with that as long as it's clear we're happy to participate without any prejudice to our motion on personal jurisdiction.

THE COURT: Yes, nobody is waiving any rights or prejudicing any rights or at least that is not the intent. All I'm having you do is agree to talk without prejudice to your rights and to jointly submit something to me on April 3rd setting out a schedule or schedules, and everybody can again preserve their rights in writing in that filing and certainly should set out any objections that they have, and then we'll talk on April 10th and I'll try to resolve things.

With that background and understanding, does anybody have any objection to the timing of April 3rd for the submission and April 10th, let's say 10:00 a.m., for the teleconference?

Okay. I'm not hearing any objections.

MR. BREISBLATT: None, Your Honor. Robert Breisblatt for Apotex. The submission you want on April 3rd, do you want a single position with each parties or do you want each party to do their own submission?

THE COURT: I would prefer to have a single submission that laid out everybody's position, but I'd like to leave it to the discretion of all of you. My preference is one that assumes the document I would get would be something that would be manageable and would focus me on where there are disputes, and hopefully there aren't too many. If that assumption turns out to be incorrect and seven separate submissions are going to be, the parties feel, more appropriate, I want to leave you the opportunity to do that.

Is that enough guidance or do you need me to be more definitive?

MR. BREISBLATT: No, I think that is fine, Your Honor. Again, Bob Breisblatt. I think what I have seen lately where there are multiple defendants and a single plaintiff, and there isn't major agreement between the two, is that there is two submissions, one from the plaintiff and one from the defendants, and where the defendants have differing positions, they're placed in the defendants' order as well but if you would prefer a single, we can obviously do it that way.

THE COURT: Okay. So my preference is a single. If it's not going to be one, obviously two is better than seven, but I will accept up to eight different submissions, if need be, but I want them on April 3rd. And I am trusting the parties will work with their best good faith efforts to keep the submissions to the minimum number necessary to set out everybody's position for me. Okay?

Is there anything further?

MR. HENEGHAN: Judge, this is Tom Heneghan.

THE COURT: Yes.

MR. HENEGHAN: I just have a question. With all the advent of all the electronic filing we're doing these days, is there anything other than just filing it electronically that you want? Do you want a copy served to chambers or is the regular electronic filing sufficient? I'm just not sure what your preference is.

THE COURT: Yes. If you could deliver a courtesy copy, hand deliver a courtesy copy to chambers, that is very helpful even in the era of e-filing. I appreciate you asking.

Is there anything further that we should discuss at this point from anybody?

MR. LIPSEY: Charley Lipsey again. Not for the plaintiffs.

THE COURT: Okay. Any defendants want to speak

now?

I'm hearing silence again. Okay. I will take that as we've covered what we can cover today. I appreciate everybody's time, and I'll look for one or more submissions on April 3rd and we'll get an order out scheduling a scheduling teleconference for the morning of April 10th at 10:00 a.m., and I will look forward to that and thank you all for your time.

(The attorneys respond, "Thank you, Your Honor.")

THE COURT: Okay. Good-bye.

(Telephone conference ends at 3:29 p.m.)

EXHIBIT 2

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AstraZeneca Pharmaceuticals LP, et al. v.
Mylan Pharmaceuticals Inc., Docket No. 07-805;
Sun Pharmaceutical Industries Ltd., et al., Docket No. 07-806;
Sandoz Inc., Docket No. 07-807;
Par Pharmaceutical, Inc., Docket No. 07-808;
Apotex Inc., et al., Docket No. 07-809;
Aurobindo Pharma Ltd., et al., Docket No. 07-810; and
Cobalt Pharmaceuticals, Inc., et al., Docket No. 07-811

FINNEGAN
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Dear Counsel:

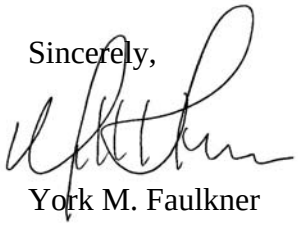
AstraZeneca and Shionogi ("Plaintiffs") recently filed the above-referenced actions in the U.S. District Court for the District of Delaware, alleging infringement of U.S. Patent No. RE 37,314, based on Abbreviated New Drug Applications submitted to the U.S. Food and Drug Administration. We represent Plaintiffs in those actions.

In an effort to simplify and expedite resolution of these issues, we have brought suit against each defendant in Delaware, where we believe personal jurisdiction is proper. To facilitate the efficient advancement of the actions, please confirm whether your respective clients will agree to consolidation of these actions.

We recognize that your clients have previously litigated in Delaware and assume that they will be content to do so again due to the efficiencies involved. In some instances, Plaintiffs either have or will file protective suits in alternative jurisdictions. We do not intend to serve the complaints in the protective suits, unless it becomes necessary to do so. Once these actions are underway in Delaware, Plaintiffs will dismiss the corresponding protective suits in the alternative jurisdictions.

We look forward to hearing from each of you and receiving the defendants' agreement to consolidate the actions in Delaware.

Sincerely,



York M. Faulkner

cc: Mary W. Bourke, Esq.

EXHIBIT 3

IN THE UNITED STATES DISTRICT COURT
FOR DELAWARE

ASTRAZENECA PHARMACEUTICALS LP, and ASTRAZENECA UK LIMITED, and IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, Plaintiffs, v. AUROBINDO PHARMA LIMITED, and AUROBINDO PHARMA USA INC., Defendants.	Civil Action No.: _____

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Limited, IPR Pharmaceuticals, Inc., and Shionogi Seiyaku Kabushiki Kaisha, for their Complaint against Aurobindo Pharma Limited and Aurobindo Pharma USA Inc., hereby state as follows:

Nature of the Action

1. This is a civil action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 100 et seq., and in particular under 35 U.S.C. §§ 271(e) and (a). This action relates to an Abbreviated New Drug Application ("ANDA") filed by and/or for the benefit

of Aurobindo Pharma Limited and Aurobindo Pharma USA Inc. ("the Aurobindo ANDA") with the United States Food and Drug Administration ("FDA") for approval to market generic versions of Plaintiffs' highly successful Crestor® pharmaceutical products that are sold in the United States.

Parties

2. Plaintiff AstraZeneca Pharmaceuticals LP ("AstraZeneca") is a corporation operating and existing under the laws of Delaware with its principal place of business at 1800 Concord Pike, Wilmington, Delaware 19803 USA.

3. Plaintiff AstraZeneca UK Limited is a corporation operating and existing under the laws of the United Kingdom with its principal place of business at 15 Stanhope Gate, London W1K 1LN, England.

4. Plaintiff IPR Pharmaceuticals, Inc. ("IPR") is a corporation operating and existing under the laws of Puerto Rico with its principal place of business at Carr 188 Lote 17, San Isidro Industrial Park, Canovanas, Puerto Rico 00729.

5. Plaintiff Shionogi Seiyaku Kabushiki Kaisha is a corporation operating and existing under the laws of Japan with its principal place of business at 1-8, Doshomachi 3-chome, Chuo-ku, Osaka 541-0045 Japan.

6. On information and belief, Defendant Aurobindo Pharma Limited ("Aurobindo Pharma") is a corporation operating and existing under the laws of India with its principal place of business at Plot # 2, Maitri Vihar, Ameerpet, Hyderabad — 500 038, Andhra Pradesh, India.

7. On information and belief, Defendant Aurobindo Pharma USA Inc. ("Aurobindo USA") is a wholly owned subsidiary of Aurobindo Pharma and is a corporation operating and existing under the laws of Delaware with its principal place of business at 2400 Route 130, North Dayton, New Jersey 08810 USA.

Background

8. IPR is the holder of approved New Drug Application ("NDA") No. 021366 for Crestor® Tablets, in 5 mg, 10 mg, 20 mg, and 40 mg dosage forms, containing rosuvastatin calcium. AstraZeneca is IPR's authorized agent for matters related to NDA No. 021366.

9. CRESTOR® (rosuvastatin calcium) is a prescription drug belonging to a group of medicines (called statins) that are used to treat high cholesterol. Crestor® is one of the most effective lipid-lowering statins available. Over 11 million patients have been prescribed Crestor®, and over 110 million prescriptions have been written worldwide for Crestor®.

10. Plaintiffs, among other things, manufacture, market, promote, educate the public and physicians about, and conduct research and development on existing and new indications for Crestor® Tablets. Plaintiffs financially benefit from sales of Crestor® Tablets in the United States.

11. On information and belief, Aurobindo Pharma and/or Aurobindo USA filed with the FDA, in Rockville, Maryland, ANDA No. 79-170 under 21 U.S.C. § 355(j) to obtain FDA approval for the commercial manufacture, use, importation, offer for sale, and sale in the United States of rosuvastatin calcium tablets in 5 mg, 10 mg, 20 mg, and 40 mg dosage strengths, which

are generic versions of Plaintiffs' Crestor® Tablets in 5 mg, 10 mg, 20 mg, and 40 mg dosage strengths, respectively.

12. By letter dated October 31, 2007, Aurobindo Pharma notified Plaintiffs that it had filed an ANDA seeking FDA approval to market rosuvastatin calcium tablets in 5 mg, 10 mg, 20 mg, and 40 mg dosage strengths (hereinafter referred to as "the Aurobindo Rosuvastatin Calcium Tablets"), and that it was providing information to Plaintiffs pursuant to 21 U.S.C. § 355(j)(2)(B)(ii) and 21 C.F.R. § 314.95.

13. On information and belief, Aurobindo Pharma is in the business of developing and manufacturing generic pharmaceutical products. On information and belief, Aurobindo Pharma sells and delivers its pharmaceutical products to Aurobindo USA in New Jersey. On information and belief Aurobindo USA is the agent, affiliate, representative, and/or alter ego of, and/or acts in concert with, Aurobindo Pharma for the purposes of marketing, distributing, and selling generic pharmaceutical products within the United States, including the State of Delaware.

14. On information and belief, Aurobindo USA, as the authorized agent of Aurobindo Pharma and/or in its own capacity, participated in the preparation and filing with the FDA of the Aurobindo ANDA for approval to market generic rosuvastatin calcium in the United States.

Jurisdiction and Venue

15. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

16. On information and belief, Aurobindo Pharma has developed a complete infrastructure in terms of marketing, sales, administration, finance and distribution in the United States. On information and belief, that infrastructure includes Aurobindo USA. On information and belief, Aurobindo Pharma develops and manufactures generic drugs and, directly or indirectly through Aurobindo USA, markets, distributes, and sells its generic drugs throughout the United States, including the State of Delaware.

17. Personal jurisdiction over Aurobindo Pharma is proper because it purposefully avails itself of the privilege of selling its generic products in the state of Delaware and can therefore reasonably expect to be subject to jurisdiction in Courts in Delaware. Among other things, upon information and belief, Aurobindo Pharma, directly or through its subsidiary Aurobindo USA, places goods into the stream of commerce for distribution throughout the United States, including the State of Delaware.

18. Personal jurisdiction over Aurobindo USA is proper because Aurobindo USA is incorporated in Delaware and has purposely availed itself of the privilege of doing business in this State. Further, Aurobindo USA maintains continuous and systematic contacts with the State of Delaware so as to reasonably allow jurisdiction to be exercised over it.

19. Venue is proper in this judicial district under 28 U.S.C. §§ 1391(c) and 1400(b).

Count I

Infringement of United States Patent No. RE37,314 Under 35 U.S.C. § 271(e)(2)

20. Plaintiffs incorporate by reference paragraphs 1-19 of this Complaint as if fully set forth herein.

21. United States Patent No. RE37,314 ("the '314 patent"), entitled "Pyrimidine Derivatives," was duly and legally reissued by the United States Patent and Trademark Office on August 7, 2001. Plaintiffs hold all substantial rights in the '314 patent and have the right to sue for infringement thereof. A true and correct copy of the '314 patent is attached as Exhibit A.

22. On information and belief, Aurobindo Pharma and Aurobindo USA filed ANDA No. 79-170 in order to obtain approval to market the Aurobindo Rosuvastatin Calcium Tablets in the United States before the expiration of the '314 patent. On information and belief, Aurobindo Pharma and Aurobindo USA also filed with the FDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) and 21 C.F.R. § 314.94(a)(12)(i)(A)(4), a certification alleging that the claims of the '314 patent are invalid.

23. On information and belief, Aurobindo Pharma and Aurobindo USA do not assert that Aurobindo Rosuvastatin Calcium Tablets are not covered by one or more claims of the '314 patent.

24. Under 35 U.S.C. § 271(e)(2)(A), the submission by Aurobindo Pharma and/or Aurobindo USA to the FDA of ANDA No. 79-170 to obtain approval for the commercial manufacture, use, or sale of the Aurobindo Rosuvastatin Calcium Tablets before the expiration date of the '314 patent constitutes infringement of one or more claims of the '314 patent, either literally or under the doctrine of equivalents.

25. Plaintiffs will be substantially and irreparably harmed by the infringing activities described above unless those activities are precluded by this Court. Plaintiffs have no adequate remedy at law.

Count II

Declaratory Judgment of Infringement of United States Patent No. RE37,314 Under 35 U.S.C. § 271(a)

26. Plaintiffs incorporate by reference paragraphs 1-25 of this Complaint as if fully set forth herein.

27. Upon information and belief, Aurobindo Pharma and Aurobindo USA have made substantial preparations to sell Aurobindo Rosuvastatin Calcium Tablets labeled for the same dosages as the Crestor® products.

28. Upon information and belief, Aurobindo Pharma and Aurobindo USA intend to commence sale of Aurobindo Rosuvastatin Calcium Tablets immediately upon receiving approval from the FDA.

29. The manufacture, importation, sale, and offer for sale of Aurobindo Rosuvastatin Calcium Tablets, once approved by the FDA, will directly infringe, induce and/or contribute to the infringement of one or more claims of the '314 patent under 35 U.S.C. § 271(a).

30. Plaintiffs will be substantially and irreparably harmed by the infringing activities described above unless those activities are enjoined by this Court. Plaintiffs have no adequate remedy at law.

31. An actual controversy exists relating to Aurobindo Pharma and Aurobindo USA's threatened infringement of the '314 patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment in its favor as follows:

(1) holding that the claims of the '314 patent are valid and enforceable;

(2) holding that the submission of ANDA No. 79-170 by Aurobindo Pharma and/or Aurobindo USA infringes one or more claims of the '314 patent under 35 U.S.C. § 271(e)(2);

(3) declaring that the manufacture, use, offering for sale, or sale of the Aurobindo Rosuvastatin Calcium Tablets within the United States or importing the Aurobindo Rosuvastatin Calcium Tablets into the United States before expiration of the '314 patent will infringe one or more claims of the '314 patent;

(4) ordering, pursuant to 35 U.S.C. § 271(e)(4)(A), that the effective date of any FDA approval of the Aurobindo Rosuvastatin Calcium Tablets shall be no earlier than the expiration date of the '314 patent;

(5) enjoining Aurobindo Pharma, Aurobindo USA, and all persons acting in concert with them, from commercially manufacturing, using, offering for sale, or selling the Aurobindo Rosuvastatin Calcium Tablets within the United States or importing into the United States the Aurobindo Rosuvastatin Calcium Tablets, prior to the expiration of the '314 patent;

(6) declaring this to be an exceptional case and awarding Plaintiffs their attorney fees under 35 U.S.C. § 285;

(7) awarding Plaintiffs their costs and expenses in this action; and

(8) awarding Plaintiffs any further and additional relief as this Court deems just and proper.

This 11th day of December 2007.

Respectfully submitted,

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580395

EXHIBIT A

(19) **United States**

(12) **Reissued Patent**

Hirai et al.

(10) **Patent Number: US RE37,314 E**

(45) **Date of Reissued Patent: Aug. 7, 2001**

(54) **PYRIMIDINE DERIVATIVES**

(75) Inventors: **Kentaro Hirai**, Kyoto; **Teruyuki Ishiba**, Osaka; **Haruo Koike**, Kyoto; **Masamichi Watanabe**, Shiga, all of (JP)

(73) Assignee: **Shionogi Seiyaku Kabushiki Kaisha**, Osaka (JP)

(21) Appl. No.: **09/141,731**

(22) Filed: **Aug. 27, 1998**

Related U.S. Patent Documents

Reissue of:

(64) Patent No.: **5,260,440**
Issued: **Nov. 9, 1993**
Appl. No.: **07/897,793**
Filed: **Jun. 12, 1992**

(30) **Foreign Application Priority Data**

Jul. 1, 1991 (JP) 3-188015

(51) **Int. Cl.**[7] **A61K 31/505**; C07D 239/34; C07D 239/38; C07D 239/42

(52) **U.S. Cl.** **514/316**; 544/318; 544/322

(58) **Field of Search** 514/756; 544/297

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,868,185	9/1989	Chucholowski et al.	514/256
4,925,852	5/1990	Kesseler et al.	514/256
5,026,708	6/1991	Fujikawa et al.	514/256

FOREIGN PATENT DOCUMENTS

0 330 057	8/1989	(EP) .
0 367 895	5/1990	(EP) .

OTHER PUBLICATIONS

Moore et al, J. Am. Chem. Soc., vol. 107, pp. 3694–3701, 1985.*

G. Beck et al., *J. Med. Chem.,* 33, 52–60 (1990).

B. Roth et al., *J. Med. Chem.,* 34, 463–466 (1991).

* cited by examiner

Primary Examiner—Richard L. Raymond

(74) *Attorney, Agent, or Firm*—Pillsbury Madison & Sutro, LLP Intellectual Property Group

(57) **ABSTRACT**

The compounds of the present invention inhibit the HMG-CoA reductase, and subsequently suppress the biosynthesis of cholesterol. And they are useful in the treatment of hypercholesterolemia, hyperlipoproteinemia, and atherosclerosis.

3 Claims, No Drawings

PYRIMIDINE DERIVATIVES

Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.

This application is a reissue of U.S. Pat. No. 5,260,440, issued Nov. 8, 1993.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor.

2. Prior Art

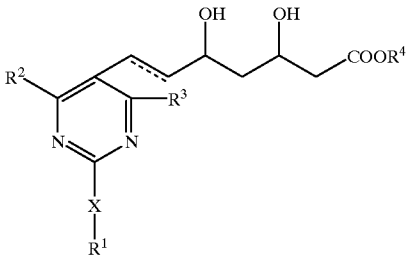
As the first generation of drugs for the treatment of atherosclerosis by inhibiting the activity of HMG-CoA reductase, there are known Mevinolin (U.S. Pat. No. 4,231,938), pravastatin sodium (U.S. Pat No. 4,346,227), and, simvastatin (U.S. Pat. No. 4,444,784), which are fungal metabolites or of the chemical modifications. Recently, synthetic inhibitors of HMG-CoA reductase such as fluvastatin (F. G. Kathawala et al., 8th Int'l Symp. on Atherosclerosis, Abstract Papers, p. 445, Rome (1988)) and BMY 22089 (GB Pat. No. 2,202,846) are developed as the second generation drugs.

SUMMARY OF THE INVENTION

The compounds of the present invention inhibit the HMG-CoA reductase, which plays a main role in the synthesis of cholesterol, and subsequently they suppress the biosynthesis of cholesterol. Therefore, they are useful in the treatment of hypercholesterolemia, hyperlipoproteinemia, and atherosclerosis.

DETAILED DESCRIPTION

The present invention relates to compounds of the formula (I):



wherein R^1 is lower alkyl, aryl or aralkyl, each of which may have one or more substituents: R^2 and R^3 each is independently hydrogen, lower alkyl, or aryl, and each of said lower alkyl and aryl may have one or more substituents; R^4 is hydrogen, lower alkyl, or a cation capable of forming a non-toxic pharmaceutically acceptable salt; X is sulfur, oxygen, or sulfonyl, or imino which may have a stubstituent; the dotted line represents the presence or absence of a double bond, or the corresponding ring-closed lactone. This invention also provides a pharmaceutical composition comprising the same.

In the specification, the term "lower alkyl" refers to a straight, branched, or cyclic C_1 to C_6 alkyl, including methyl, ethyl, n-propyl, isopropyl, cyclopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, cyclobutyl, n-pentyl, isopentyl, neopentyl, tert-pentyl, cyclopentyl, n-hexyl, and

isohexyl and the like. Further, the lower alkyl may be substituted by 1 to 3 substituents independently selected from the group consisting of halogen, amino, and cyano. Halogen means fluorine, chlorine, bromine and iodine.

The term "aryl" refers to C_6 to C_{12} aromatic group including phenyl, tolyl, xylyl, biphenyl, naphthyl, and the like. The aryl may have 1 to 3 substituents independently selected from the group consisting of lower alkyl, halogen, amino, and cyano. Preferred aryl is phenyl substituted by 1 to 3 halogens.

The term "aralkyl" refers to C_1 to C_6 lower alkyl substituted by C_6 to C_{12} aromatic aryl group defined above. Examples of them are benzyl, phenethyl, phenylpropyl and the like, each of which may have 1 to 3 substituents independently selected from the group consisting of lower alkyl halogen, amino, cyano, and the like.

The term "a cation capable of forming a non-toxic pharmaceutically acceptable salt" refers to alkali metal ion, alkaline earth metal ion, and ammonium ion. Examples of alkali metal are lithium, sodium, potassium, and cesium, and examples of alkaline earth metal are beryllium, magnesium, and calcium. Especially, sodium and calcium are preferred.

Examples of "acyl" are formyl acetyl, propionyl, butyryl, isobutyryl, valeryl, and isovaleryl.

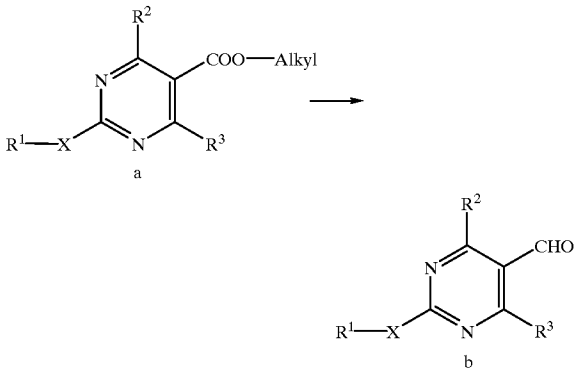
In the term "imino which may have a substituent", preferred substituents are acyl, optionally substituted amino, and substituted sulfonyl.

The term "substituted amino as substituent" means amino group substituted by sulfonyl and alkylsulfonyl. Examples of them are sulfonyl amino and methanesulfonyl amino.

The term "substituted sulfonyl as substituent" means sulfonyl group substituted by alkyl, amino, or alkylamino. Examples of them are methanesulfonyl, sulfamoyl, methylsulfamoyl, and N-methylsulfamoyl.

The compounds of the present invention can be prepared by the following method.

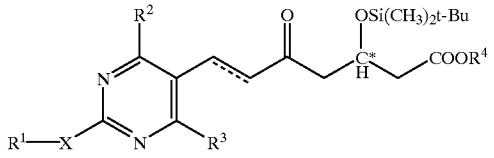
(1) The carboxylate group of the compound a is converted into the alcohol group by the reduction in an appropriate inactive solvent such as THF, ether, and toluene in the presence of the reductant such as LiAlH and DIBAL-H. The reaction is performed at −70° to 50° C., preferably at near room temperature, for 10 minutes to 10 hours, preferably for 30 minutes to 3 hours. Then the obtained alcohol is subjected to oxidation in an appropriate solvent such as methylene chloride in the presence of the oxidizing agent such as TPAP/4-methylmorpholin-N-oxide or pyridium chlorochromate to give aldehyde compound b. The reaction is performed at 0°–60° C., preferably at near room temperature, for 10 minutes to 10 hours, preferably 30 minutes to 3 hours.



wherein R^1, R^2, and R^3 each has the same meaning as defined above, and Alkyl means lower alkyl.

(2) The obtained compound b is subjected to reaction with (3R)-or (3S)-3-(tert-butyldimethylsilyloxy-5-oxo-6-triphenylphosphoranylidene hexanoic acid derivatives in an appropriate solvent such as acetonitrile, diethylether, tetrahydrofuran, and dimethylformamide to give the compound c. The reaction is performed for 1–30 hours, preferably for 10–15 hours under heating.

c



wherein C* means asymmetric carbon atom, the dotted line means the presence or absence of the double bond, R^1, R^2, R^3, and R^4each has the same meaning as defined above.

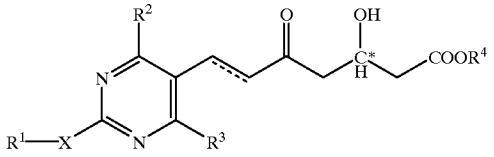
(3) The compound c is subjected to elimination of the tertbutyldimethylsilyl group in an appropriate organic solvent in the presence of hydrogen halogenide to give the compound d.

Every sort of halogen can be used for hydrogen halogenide. Amongst all, hydrogen fluoride is preferred.

The same organic solvents as used in the step (2) may be employed. Acetonitrile is especially preferred.

The reaction is performed in a range of from 0° to 60° C., preferably at room temperature, for 0.5–10 hours, preferably for 1–2 hours.

d



wherein C*, the dotted line, R^1, R^2, R^3, and R^4 each has the same meaning as defined above.

(4) The compound d is reacted with diethylmethoxyborane and $NaBH_4$ in an alcohol-organic solvent mixture and subjected to column chromatography of silica gel to give the compound (I) (in case R^4 is lower alkyl). The reaction is performed at a temperature between −100° to 20° C., preferably between −85° to −70° C. under cooling, for 10 minutes to 5 hours, preferably for 30 minutes to 2 hours.

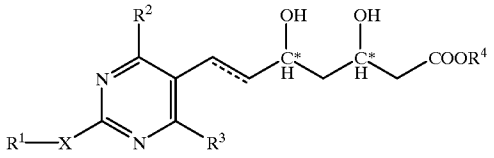
Here, the alcohol includes methanol, ethanol, propanol, and butanol; and the organic solvent includes the same as in the step (3).

Further, if necessary, the obtained compound may be subjected to saponification with the solution of metalic hydroxide (R^4: cation), and after the saponification, the reaction mixture is neutralized with an acid and extracted with an organic solvent (R^4: hydrogen). The saponification is performed in a popular solvent such as water, acetonitrile, dioxane, acetone, and the mixture thereof, preferably in the presence of a base, by a conventional method. The reaction is performed at 0° to 50° C., preferably at near room temperature.

As metalic hydroxide which may be used are sodium hydroxide, potassium hydroxide, and their analogue.

Acids which may be used include inorganic acids such as hydrochloric acid, sulfuric acid and the like.

(I)



wherein C*, the dotted line, R^1, R^2, R^3, and R^4 each has the same meaning as defined above.

Further, if necessary, the obtained compounds (I) are subjected to reflux under heating to give the corresponding lactones.

The compound of the present invention can be administered orally or parenterally. For example, the compound of the present invention may be orally administered in the form of tablets, powders, capsules and granules, aqueous or oily suspension, or liquid form such as syrup or elixir, and parenterally in the form of aqueous or oily suspension.

These preparations can be prepared in a conventional manner by using excipients, binders, lubricants, aqueous or oily solubilizers, emulsifier, suspending agents, and the like. And preservatives and stabilizers can be further used.

The dosages may vary with the administration route, age, weight, condition, and the kind of disease of the patients, but are usually 0.5–200 mg/day, preferably 1–100 mg/day through oral route, and 0.1–100 mg/day, preferably 0.5–50 mg/day through parenteral route. They may be used in a single or divided doses.

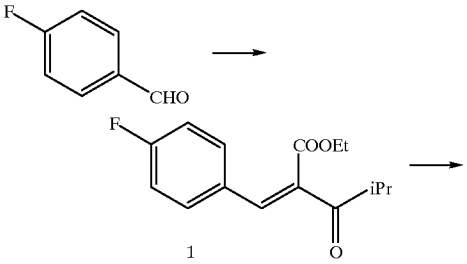
The present invention is illustrated by the following examples and reference examples, which are not to be considered as limiting.

The abbreviations used in examples and reference examples have the following meanings.

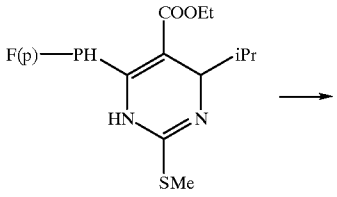
Me: methyl,
Et: ethyl,
i-Pr: isopropyl
t-Bu: tert-butyl,
Ph: phenyl,
DMF: dimethylformamide,
THF: tetrahydrofuran
DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
TPAP: tetrapropylammonium perruthenate
HMPA: hexamethylphosphoramide
DIBAL-H: diisobutylaluminum hydride.

REFERENCE EXAMPLE 1

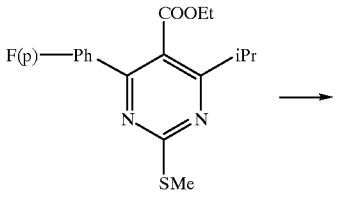
Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-methylthiopyrimidine-5-carboxylate (III-1) and Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-methylsulfonylpyrimidine-5-carboxylate (III-2)



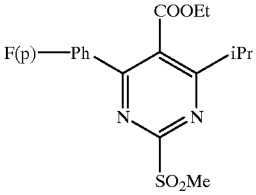
-continued



2



(III-1)



(III-2)

p-Fluorobenzaldehyde 81.81 g is reacted in the same manner as disclosed in the specification of JP Unexamed. Pat. Publn. No. 61-40272 to give 151.0 g (Yield: 86.7%) of the compound 1. Then the mixture of a solution of 44.68 g of the compound 1 in 65 ml of HMPA and 28.24 g of s-methylisourea hydrogen sulfate is stirred at 100° C. for 22 hours. Then the reaction mixture is extracted with ether, and washed with saturated sodium hydrogencarbonate and water in order. The organic layer is dried, and the solvent is distilled away. The obtained residue is subjected to column chromatography of silica gel to give 26.61 g (yield: 46.8%) of the compound 2.

To a solution of the obtained compound 2 in 400 ml of benzene is added 21.64 g (0.095 mmol) or DDQ, and the mixture is stirred for 30 minutes. Then the mixture is subjected to column chromatography of silica gel to give 24.31 g (Yield: 91.9%) of the compound (III-1).

NMR ($CDCl_3$) δ: 1.10 (t, J=7,3H): 1.31 (d, J=7,6 Hz); 2.61 (s, 3H); 3.18 (hept, J=7,1H); 4.18 (q, J=7,2H); 7.12 (m, 2H), 7.65 (m, 2H).

To a solution of 13.28 g (0.04 mmol) of the compound (III-1) in chloroform is added 17.98 g of m-chloroperbenzoic acid, and the reaction mixture is stirred at room temperature. Then it is washed with sodium sulfate and saturated sodium hydrogencarbonate in order. The solution is dried, and the solvent is distilled away and washed with n-hexane to give 13.93 g (Yield 95.7%) of the compound (III-2).

NMR ($CDCl_3$) δ: 1.16 (t, J=7,3H); 1.37 (d, J=7,6H); 3.26 (hept, J=7,1H); 3.42 (s, 3H), 4.28 (q, 2H); 7.18 (m, 2H); 7.76 (m, 2H).

REFERENCE EXAMPLE 2

Another synthetic method of the compound (III-1)

To a solution of 200 mg (0.594 mmol) of the compound 2 in 5 ml of dichloromethane are added 0.5 g (6.10 equivalent) of potassium carbonic anhydride and 166 mg (1.1 equivalent) of iodine, and the mixture is stirred at room temperature for 2.5 hours. After reaction, to the mixture is added saturated sodium hydrogensulfite and extracted with ether. The organic layer is washed with water and dried. The solvent is distilled away under reduced pressure to give 166 mg (Yield: 83.6%) of the compound (III-1) as resinous substance.

NMR ($CDCl_3$) δ: 1.10 (t, 3H, J=7); 1.31 (d, 6H, J=7); 2.61 (s, 3H) 3.17 (heptet, 1H, J=7); 4.18 (q, 2H, J=7); 7.07–7.17 (m, 2H); 7.61–7.69 (m, 2H)

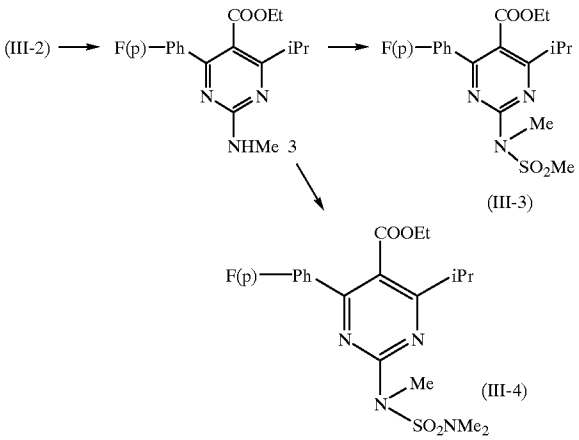
REFERENCE EXAMPLE 3

Another synthetic method of the compound (III-2)

To a solution of 1.0 g (2.97 mmol) of the compound 2 in 10 ml of acetone is added 1.5 g (9.48 mmol) of potassium permanganate, and the mixture is stirred at room temperature for 15 minutes. Acetic acid 1.0 ml is added thereto, and the mixture is stirred at room temperature for further 30 minutes and water is added thereto. The reaction mixture is extracted with ether, washed with saturated sodium hydrogencarbonate and saturated brine and dried over anhydrous magnesium sulfate. The solvent is distilled away under reduced pressure to give 1.07 g (2.94 mmol) (Yield: 99.1%) of the compound (III-2) as crystals.

REFERENCE EXAMPLE 4

Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methyl-sulfonylamino)pyrimidine-5-carboxylate (III-3) and Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-dimethylsulfamoylamino)pyrimidine-5-carboxylate (III-4)



To a solution of 52.7 g (144 mmol) of the compound (III-2) in 500 ml of absolute ethanol is added gradually a solution of 71.9 ml of 5N methylamine in ethanol under ice-cooling. The reaction mixture is warmed to room temperature, stirred for 1 hour and evaporated under reduced pressure. To the residue is added water, and the mixture is extracted with ether, dried and evaporated under reduced pressure to give 46.9 g (Yield: 100%) of the compound 3. mp. 85°–86° C.

Anal Calcd. (%) for $C_{17}H_{20}N_3FO_2$: C,64.34; H,6.35; N,13.24: F,5.99. Found: C,64.42, H,6.46: N,13.30; F,6.14.

To a solution of 370 mg (1.213 mmol) of the compound 3 in 5 ml of DMF is added 60 mg of 60% NaH under ice-cooling, and the reaction mixture is stirred for 30 min-

utes. Methanesulfonyl chloride 208 mg is added thereto, and the mixture is warmed to room temperature and stirred for 2 hours further. To the mixture is added ice-water, and the mixture is extracted with ether. The organic layer is washed with water and dried. The solvent is evaporated under reduced pressure, and the resulting residue is washed with ether-n-pentane to give 322 mg (Yield: 57.6%) of the compound (III-3).

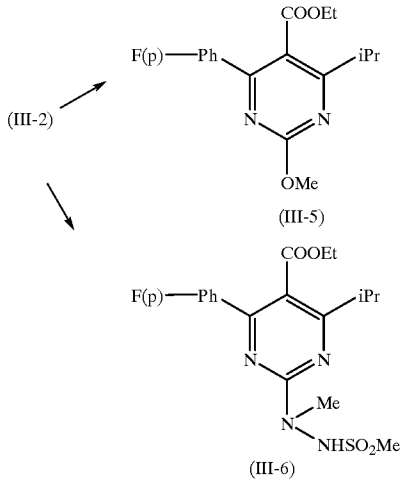
NMR ($CDCl_3$) δ: 1.10 (t, J=7,3H); 1.32 (d, J=7,6H); 3.24 (hept,J=7,1H); 3.52 (s,3H); 3.60 (s, 3H); 4.19 (q, J=7,2H); 7.14 (m, 2H); 7.68 (m, 2H).

To a solution of 4.13 g (13.0 mmol) of the compound 3 in 40 ml of DMF is added 0.57 g of 60% NaH under ice-cooling, and the mixture is warmed to room temperature and stirred for 1 hours. After cooling again, dimethylsulfamoyl chloride 2.43 g (16.9 mmol) is dropwise added thereto, and the mixture is stirred for 2.5 hours. To the mixture is added icewater, and the mixture is extracted with ether washed with water, dried and evaporated under reduced pressure to distill ether. The resulting residue is washed with ether-hexane to give 4.10 g (Yield: 74.2%) of the compound (III-4). mp. 114°–116° C.

Anal Calcd. (%) for $C_{19}H_{25}N_4SFO_4$: C,53.76; H,5.94; N,13.20; F,4.48. Found: C,53.74: H,5.96; N,13.19; F,4.78.

REFERENCE EXAMPLE 5

Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-methoxypyrimidine-5-carboxylate (III-5) and Ethyl 4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylhydrazino)pyrimidine-5-carboxylate (III-6)



To a solution of 1.39 g (3.8 mmol) of the compound (III-2) in 60 ml of absolute methanol is added a solution of 0.41 g (7.6 mmol) of sodium methoxide under ice-cooling. The reaction mixture is warmed to room temperature gradually and stirred for 1 hour. The mixture is neutralized with acetic acid and extracted with ether. The organic layer is washed with sodium bicarbonate and water in order, dried and evaporated under reduced pressure to distill ether. The residue is subjected to column chromatography of silica gel to give 1.17 g (Yield: 96.7%) of the compound (III-5).

NMR ($CDCl_3$) δ: 1.10 (t, 3H, J=7 Hz); 1.32 (d, 6H, J=6.6 Hz); 3.21 (m, 1H); 4.08 (s, 3H); 4.18 (q, 2H, J=7 Hz); 7.07–7.74 (m, 4H).

To a solution of 2.50 g (6.77 mmol) of the compound (III-2) in 50 ml of absolute ethanol is added 0.80 g (16.93 mmol) of methyl hydrazine under ice-cooling. The reaction mixture is warmed to room temperature and stirred for 2 hours and extracted with ether. The organic layer is washed with saturated brine and dried to distill the solvent. To a mixture of 2.37 g of the thus obtained compound and a mixture of anhydrous THF and anhydrous pyridine is added 1.03 g (7.84 mmol) of methanesulfonyl chloride under testing. The reaction mixture is warmed to room temperature and stirred for 1.5 hours. To the mixture are added 3 ml of anhydrous pyridine and 1.53 g (11.65 mmol) of methanesulfonyl chloride, and the mixture is stirred for 2 hours. To the reaction mixture is added ice-water and extracted with ether. The organic layer is washed with water and the resulting oily residue is subjected to column chromatography of silica gel to give 2.75 g (Yield: 94.0%) of the compound (III6).

NMR ($CDCl_3$) δ: 1.08 (t, J=7,3H); 1.29 (d, J=7,6H); 2.96 (s, 3H); 3.24 (hept, J=7,1H); 3.59 (s, 3H); 4.16 (q, J=7,2H); 7.14 (m, 2H), 7.63 (m, 2H).

REFERENCE EXAMPLE 6

Methyl (3R)-3-(tert-butyldimethylsilyloxy)-5-oxo-6-triphenylphosphoranylidene hexanate

(1) (3R)-3-(tert-butyldimethylsilyloxy)glutaric acid-1-((R)-(−)mandelic acid ester*[1] 65 g (164 mmol) is dissolved into 60 ml of methanol, a solution of sodium methoxide in methanol (28% methanol 310 ml, 1.6 mol) is added dropwise thereto under nitrogen atmosphere at 0° C. for 45 minutes at internal temperature under 7° C. The reaction mixture is stirred at 0° C. for 30 minutes and poured into a mixture of 150 ml of conc.HCl, 300 ml of water, and 500 ml of methylene chloride being stirred under ice-cooling and the organic layer is collected. The aqueous layer is extracted with 200 ml of methylene chloride, and each organic layer is washed with dil.HCl and brine in order. Each organic layer are collected and dried over anhydrous magnesium sulfate and evaporated to distill the solvent to give half ester compound.

*[1]: This compound can be prepared by the method described at page 10 in the specification of KOKAI 2-250852.

^{1}HNMR($CDCl_3$) δ: 0.08 (s, 3H); 0.09 (s, 3H); 0.86 (s, 9H); 2.52–2.73 (m, 4H); 3.08 (s, 3H); 4.55 (quint, 1H, J=6Hz).

IR ($CHCl_3$): 2880, 1734, 1712, 1438, 1305, 1096, 836 cm^{-1}.

[α]D=−5.0±0.4° (C=1.04, 23.5° C., $CHCl_3$).

Rf 0.32 ($CHCl_3$/MeOH=9/1).

(2) To a solution of the thus obtained half ester compound in 10 ml of ether are added dropwise triethylamine and ethyl chlorocarboxylate in order under nitrogen atmosphere at −78° C. The resulting white suspension is stirred at 0° C. for 1 hour and cooled to −78° C. The resulting precipitate is filtered under nitrogen atmosphere and the filtrate is washed with 15 ml of ether. To a suspension of 1.29 g (3.6 mmol) of methyl bromide triphenylphosphonium in 5 ml of THF is added dropwise butyllithium (1.6M hexane, 2.25 ml, 3.6 mmol) under nitrogen atmosphere at −78° C. The reaction mixture is stirred at 0° C. for 1 hour and cooled to −78° C. and added dropwise to the solution of thus obtained active ester compound in ether. The reaction mixture is washed with 5 ml of THF and stirred at 0° C. for 1 hour, and 10 ml of 5% sodium hydrogencarbonate is added thereto. The reaction mixture is stirred for 5 minutes and extracted with ethyl acetate and the organic layer is separated and the

remaining aqueous layer is extracted with ethyl acetate. Each organic layer is collected and washed with brine, dried over anhydrous magnesium sulfate and concentrated. The obtained residue is subjected to column chromatography of silica gel eluting with ether-ethyl acetate and crystallized from ether-hexane to give objective compound.

^{1}HNMR ($CDCl_3$)δ: 0.04 (s, 3H); 0.06 (s, 3H); 0.83 (s, 9H); 2.4–2.9 (m, 4H); 3.64 (s, 3H); 3.74 (d, 1H); 4.5–4.7 (m, 1H); 7.4–7.8 (m, 15H).

IR ($CHCl_3$): 2380, 1730, 1528, 1437, 1250, 1106, 835 cm^{-1}.

[α]D=−6.2° (C=1.27, 22.0° C., $CHCl_3$).

mp.:77.5°–78.5° C., Rf=0.48 ($CHCl_3$/MeOH=9/1).

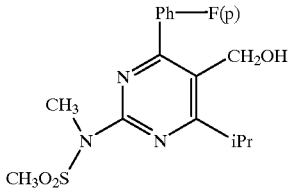
Anal Calcd. (%) for $C_{31}H_{39}O_4PS$: C, 69.63; H,7.35; P,5.79. Found: C, 69.35; H,7.35; P,6.09.

EXAMPLE 1

Sodium (+)-7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylaminopyrimidin)-5-yl]-(3R,5S)-dihydroxy-(E)-6-heptenate (I a-1)

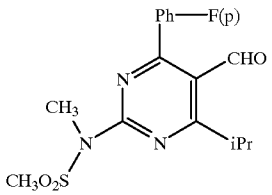
(1) To a solution of 322 mg of the compound (III-3) obtained in Reference Example 2 in 7 ml of anhydrous toluene is added dropwise 1.4 ml of DIBAL-H in 1.5M toluene at −74° C., and the reaction mixture is stirred for 1 hour and acetic acid is added thereto. The mixture is extracted with ether, and the organic layer is washed with sodium bicarbonate and water, dried and evaporated under reduced pressure to distil ether. The obtained residue is subjected to column chromatography of silica gel eluting with methylene chloride/ether (20/1) to give 277 mg (Yield: 96.1%) of [4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl]methanol 4.

4



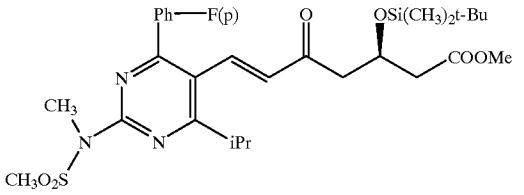
(2) A suspension of 277 mg of the thus obtained compound 4, 190 mg of 4-methylmorpholin-N-oxide, 6 mg of TPAP, 1.0 g of powder molecular sieve 4A, and 10 ml of methylene chloride is stirred for 2 hours. The insoluble matter is filtered off and the two-thirds of the filtrate is distilled away under reduced pressure. The resulting residue is subjected to column chromatography of silica gel eluting with methylene chloride to give 196 mg (Yield: 71.2%) of 4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)-5-pyrimidinecarbardehyde as crystals.

5



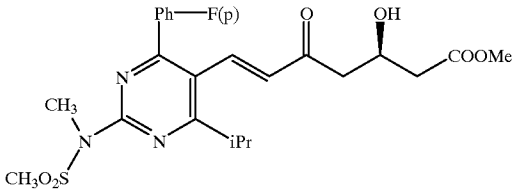
(3) A solution of 190 mg of the compound 5, 450 mg of methyl (3R)-3-(tert-butyldimethylsilyloxy)-5-oxo-6-triphenylphosphoranylidene hexanate (Reference Example 6), and 5 ml of acetonitrile is refluxed under heating for 14 hours and evaporated under reduced pressure to distill acetonitrile. The resulting residue is subjected to column chromatography of silica gel eluting with methylene chloride to give 233 mg (Yield: 71.3%) of methyl 7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl]-(3R)-3-(tert-butyldimethylsilyloxy)-5-oxo-(E)-6-heptenate 6 as syrup.

6



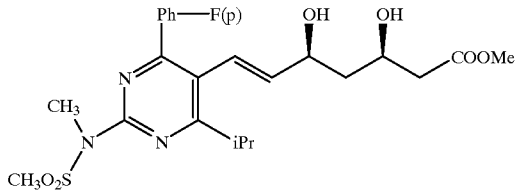
(4) To a solution of 16 g of the compound 6 in 100 ml of acetonitrile is added dropwise a solution of 48% hydrogen flouride in 400 ml of acetonitrile (1:19) under ice-cooling, and the mixture is warmed to room temperature and stirred for 1.5 hours. The reaction mixture is neutralized with sodium bicarbonate and extracted with ether. The organic layer is washed with sodium chloride, dried and evaporated under reduced pressure to distil ether to give 13 g (Yield: 100%) of methyl 7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl]-(3R)-3-hydroxy-5-oxo-(E)-6-heptenate 7 as syrup.

7



(5) To a solution of 13 g of the compound 7 in 350 ml of anhydrous THF and 90 ml of methanol is added a solution of 29.7 ml of 1M diethylmethoxyborane-THF at −78° C., and the mixture is stirred at the same temperature for 30 minutes. To the mixture is added 1.3 g of $NaBH_4$, and the mixture is stirred for 3 hours. Acetic acid 16 ml is added thereto, and the mixture is adjusted to pH 8 with saturated sodium bicarbonate and extracted with ether. The organic layer is washed with water, dried and evaporated ether under reduced pressure. To the resulting residue is added methanol and the mixture is evaporated under reduced pressure for three times. The resulting residue is subjected to column chromatography of silica gel eluting with methylene chloride/ether (3/1) to give 11.4 g (Yield: 85.2%) of methyl 7-[4-(4-fluorophenyl)-6-iso-propyl-2-methyl-N-methylsulfonylamino)pyrimidin-5-yl]-(3R,5S)-dihydroxy-(E)-6-heptenate as syrup.

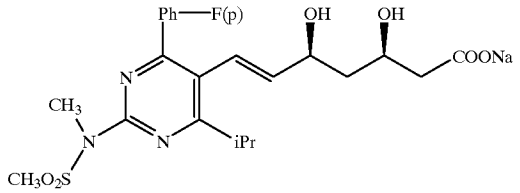
(Ib-1)



NMR ($CDCl_3$) δ: 1.27 (d, J=7,6H); 1.53 (m, 2H); 2.47 (d, J=6,2H); 3.36 (hept, J=2H); 3.52 (s, 3H); 3.57 (s, 3H); 3.73 (s, 3H); 4.20 (m, 1H); 4.43 (m, 1H); 5.45 (dd, J=5,16, 1H); 6.64 (dd, J=2,16, 1H); 7.09 (m, 2H); 7.64 (m, 2H).

(6) To a solution of 11.4 g of the compound (I b-1) in 160 ml of ethanol is added 223 ml of 0.1N sodium hydroxide under ice-cooling. The reaction mixture is warmed to room temperature and stirred for 1 hour. The solvent is distilled away under reduced pressure, and ether is added to the resulting residue and the mixture is stirred to give 11.0 g (Yield: 95.0%) of the objective compound (I a-1) as powdery crystals.

(Ia-1)



$[\alpha]_D$=+18.9±0.6° (C=1.012, 25.0° C., H_2O).

NMR ($CDCl_3$) δ: 1.24 (d, J=7,6H); 1.48 (m, 1H); 1.65 (m, 1H); 2.27 (dd,J=2,6.2H); 3.41 (hept, J=7,1H); 3.48 (s, 3H); 3.59 (s, 3H); 3.73 (m, 1H); 4.32 (m 1H); 5.49 (dd, J=7,16 1H); 6.62 (d, J=16,1H); 7.19 (m, 2H); 7.56 (m, 2H).

EXAMPLE 2

Sodium (+)-7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-acetyl-N-methylamino)pyrimidin-5-yl]-(3R,5S)-dihydroxy-(E)-6-heptenate (I a-2)

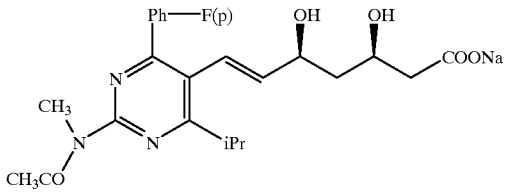
(1) Ethyl 4-(4-fluorophenyl-6-isopropyl-2-methylaminopyrimidine-5-carboxylate 3 838 mg obtained in Reference Example 4 is allowed to react in the same manner as in Example 1 (1) and (2) to give 157 mg of 4-(4-fluorophenyl)-6-isopropyl-2-methylaminopyrimidine-5-carbaldehyde.

(2) A solution of 157 mg of thus obtained aldehyde compound in 4 ml of anhydrous DMF is reacted with 25 mg of 60% NaH under ice-cooling for 30 minutes, 0.05 ml of acetylchloride is added thereto and the mixture is stirred for 1 hour. The mixture is added with ice and extracted with ether. The organic layer is washed with water and dried and concentrated to distill the solvent to give 167 mg (Yield: 93.4%) of 4-(4-fluorophenyl)-6-isopropyl-2-(N-acetyl-N-methylamino)pyrimidine-5-carbardehyde. Thus obtained aldehyde compound is reacted in the same manner as in Example 1 (3)–(5) to give methyl 7-[4-(4-fluorophenyl)-6-isopropyl-2-(N-acetyl-N-methylaminopyrimidin)-5-yl]-(3R,5S)-dihydroxy-(E)-6-heptenate (I b-2).

NMR ($CDCl_3$)δ: 1.27 (d, J=7,6H); 1.54 (m, 2H); 2.48 (d, J=6,2H); 2.52 (s, 3H); 3.39 (hept, J=7, 1H); 3.60 (s, 3H); 3.58 (brs, 1H); 3.74 (s, 3H): 4.21 (m, 1H); 4.48 (m, 1H); 5.50 (dd, J=5,16, 1H); 6.66 (dd, J=2,16); 7.11 (m, 2H); 7.61 (m, 2H).

(3) The thus obtained compound (I b-2) is reacted in the same manner as Example 1 (6) to give the objective compound (I a-2).

(Ia-2)



NMR ($CDCl_3$)δ: 1.27 (d, J=7,6H); 1.57 (m, 2H): 2.17 (s, 3H); 2.27 (d, J=6,2H); 3.72 (s, 3H); 3.50 (hept, J=7, 1H); 3.70 (m, 1H); 4.35 (q, J=6,1H); 5.59 (dd, J=5,16, 1H); 6.54 (d, J=16, 1H); 7.24 (m, 2H): 7.59 (m, 2H).

EXAMPLE 3–6

As a starting material, each pyrimidine carboxylate (III) obtained in Reference Example 1–3 is reacted in the same manner as Example 1 or 2 to give the compound (I b) and (I a). Their physical constants are shown in Table 1–3.

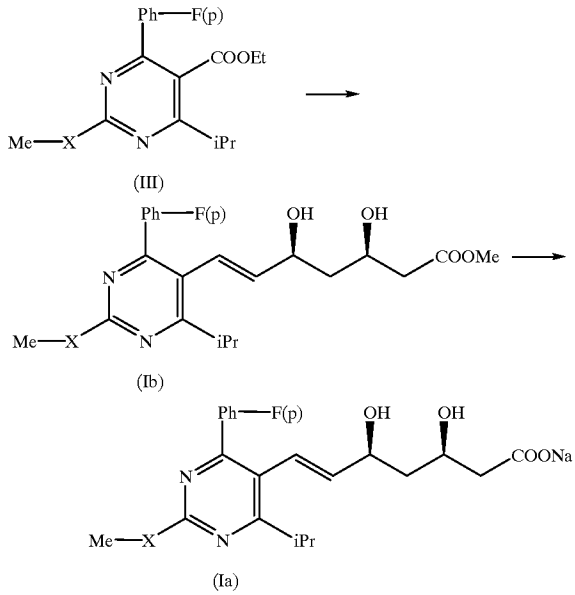


TABLE 1

Ex. No.	Startup material	Product NMR δ
3	(Ill-1)	1b-3(X: S)Yield 96.0% ($CDCl_3$, 1.26(d, J = 7.6H): 1.52(m, 2H): 2.47(d, J = 6, 2H): 2.60(s, 3H): 3.33(hept, J = 7, 1H): 3.73 (s, 3H): 4.18(m, 1H): 4.44(m, 1H): 5.44(dd, J = 5, 16, 1H): 6.60(dd, J = 2, 16, 1H), 7.07(m, 2H): 7.58(m, 2H) 1a-3(X: S)Yield 87.3% (D_2O) 1.20(d, J = 7, 6H): 1.47(m, 1H): 1.61(m, 1H): 2.26(m, 2H), 2.54(s, 3H): 3.36(hept, J = 7, 1H):

TABLE 1-continued

		3.71(m, 1H): 4.29(m, 1H): 5.43(dd, J = 6, 16, 1H): 6.55(d, J = 16, 1H): 7.16(m, 2H), 7.47 (m, 2H)
4	(Ill-2)	1b-4(X: SO_2): Yield 93.7% ($CDCl_3$) 1.31(d, J = 7, 6H): 1.52(m, 2H): 2.48(d, J = 6, 2H): 3.40(s, 3H); 3.47(hept, J = 7, 1H); 3.74 (s, 3H): 3.87(brs, 1H): 4.23(m, 1H): 4.49 (m, 1H); 5.59(dd, J = 5, 16H, 1H); 6.74(d, d, J = 2, 16, 1H); 7.12(m, 2H): 7.69(m, 2H) 1a-4(X: SO_2): Yield 70.9% (D_2O) 1.27(d, d, J = 7, 2, 6H); 1.60(m, 2H); 2.25(J = 6, d, 2H): 3.44(s, 3H): 3.51(hept, J = 7, 1H): 3.70(m, 1H): 4.33(q, J = 6, 1H): 5.65(d, d, J = 5, 16, 1H): 6.71(d, J = 16, 1H): 7.23(m, 2H); 7.60 7.60(m, 2H)

TABLE 2

Ex. No.	Starting material	Product NMR δ
5	(Ill-5)	1b-5(X: O): ($CDCl_3$) 1.27(d, 6H, J = 6.6 Hz): 1.35–1.68(m, 2H): 2.47 (m, 2H): 3.34(m, 1H): 3.78(s, 3H): 4.03(s, 3H): 4.19(m, 1H); 4.43(m, 1H): 5.43(dd, 1H, J = 5.6, 16 Hz): 6.59(dd, 1H, J = 1.4, 16 Hz): 7.03–7.64(m, 4H) 1a-5(X: O) Yield 57.7% ($CDCl_3$, CD_3OD) 1.27(d, 6H, J = 6.6 Hz): 1.35–1.68(m, 2H): 2.17–2.43(m, 2H): 3.36(m, 2H), 4.05(s, 3H): 4.37 (m, 2H): 5.48(dd, 1H, J = 5.6, 16 Hz): 6.54(dd, 1H, J = 1.4, 16 Hz): 7.06–7.65(m, 4H)
6	(Ill-4)	1b-6(X: N—SO_2NMe_2): ($CDCl_3$) 1.26(d, 6H, J = 6.6 Hz); 1.38–1.62(m, 2H): 2.47 (d, 2H, J = 5.8); 2.84(s, 6H), 3.35(m, 1H): 3.64(s, 3H); 3.74(s, 3H); 4.20(m, 1H): 4.44 (m, 1H); 5.42(dd, 1H, J = 5.4, 16 Hz): 6.60 (dd, 1H, J = 1.2, 16 Hz): 7.03–7.64(m, 4H) 1a-6: Yield: 91.2% ($CDCl_3$, CD_3OD) 1.26(d, 6H, J = 6.6 Hz); 1.36–1.69(m, 2H): 2.15–2.50(m, 2H); 2.85 (s, 6H); 3.41(m, 2H): 3.64 (s, 3H): 4.04(m, 1H): 4.37(m, 1H); 5.48 (dd, 1H, J-5.6, 16 Hz): 6.54(dd, 1H, J-1, 16 Hz): 7.05–7.66(m, 4H)

TABLE 3

Ex. No.	Starting material	Product NMR δ
7	(Ill-6)	1b-7(X: N—$NHSO_2Me$): Yield: 87.8% ($CDCl_3$) 1.24(d, J = 7, 6H): 1.51(m, 2H): 2.47(d, J = 6, 2H); 2.95(s, 3H); 3.35(hept, J = 7, 1H); 3.46 (d, J = 2, 1H): 3.55(s, 3H); 3.66(d, J = 2, 1H): 3.74 (s, 3H): 4.18(m, 1H): 4.44(m, 1H): 5.41 (dd, J = 5, 16, 1H); 6.58(dd, J = 2, 16, 1H); 7.09(m, 2H); 7.58(m, 2H), 7.70(s, 1H) 1a-7(X: N—$NHSO_2Me$): Yield: 74.7% (D_2O) 1.23(d, J = 7, 6H): 1.51(m, 2H): 2.26(d, J = 6, 2H) 3.10(s, 3H); 3.37(hept, J = 7, 1H): 3.44 (s, 3H): 3.70(m, 1H). 4.29(q, J = 6, 1H): 5.39 (dd, J = 5, 16, 1H): 6.58(d, J = 16, 1H): 7.19(m, 2H):7.52(m, 2H)

EXAMPLE 7

Calcium salt of the compound (I a-1) (sodium salt) 1.50 g (3.00 mmol) is dissolved in 15 ml of water and stirred at room temperature under nitrogen atmosphere, successively 3.00 ml (3.00 mmol) of 1 mol/L calcium chloride 3.00 ml (3.00 mmol) is added dropwise thereto over 3 minutes. The reaction mixture is stirred at the same temperature for 2 hours, and the resulting precipitate is collected, washed with water and dried to give 1.32 g of calcium salt as powdery. This compound started to melt at a temperature of 155° C., but the definitive melting point is ambiguous.

$[\alpha]D=+6.3° \pm 0.2°$ (C=2.011, 25.0° C., MeOH).

Anal Calcd. (%) for $C_{22}H_{27}N_3O_6SF$. 0.5Ca . $0.5H_2O$: C,51.85; H,5.53; N,8.25; F,3.73; Ca,3.93. Found: C,51.65; H,5.51; N,8.47; F,3.74; Ca,4.07.

Biological Activity

Experiment

The HMG-CoA reductase inhibitory effect

(1) Preparation of rat liver microsome

Sprague-Dawley rats, which were in free access to ordinary dietes containing 2% cholestyramine and water for 2 weeks, were used for the preparation of rat liver microsome. The thus obtained microsome was the purified according to the manner by Juroda et al., Biochem. Biophys. Act, 486, 70 (1977). The microsomal fraction obtained by centrifugation at 105,000×g was washed once with a buffered solution containing 15 mM nicotinamide and 2 mM magnesium chloride (in a 100 mM potassium phosphate buffer, pH 7.4). It was homogenized with a buffer containing nicotinamide and magnesium chloride at the same weight as the liver employed. The thus obtained homogenate was cooled down and kept at −80° C.

(2) Measurement of the HMG-CoA reductase inhibitory activities

The rat liver microsome sample (100 μl), which was preserved at −80° C., was fused at 0° C. and diluted with 0.7 ml of a cold potassium phosphate buffer (100 mM, pH7.4). This was mixed with 0.8 ml of 50 mM EDTA (buffered with the aforementioned potassium phosphate buffer) and 0.4 ml of 100 mM dithiothreitol solution (buffered with the aforementioned potassium phosphate buffer), and the mixture was kept at 0° C. The microsome solution (1.675 ml) was mixed with 670 μl of 25 mM NADPH (buffered with the aformentioned potassium phosphate buffer), and the solution was added to the solution of 0.5 mM [3^{-14}](HMG-CoA (3mCi/mmol). A solution (5 μl) of sodium salt of the test compound dissolved in potassium phosphate buffer is added to 45 μl of the mixture. The resulting mixture was incubated at 37° C. for 30 minutes and cooled. After termination of the reaction by addition of 10 μl of 2N·HCl, the mixture was incubated again at 37° C. for 15 minutes and then 30 μl of this mixture was applied to thin-layer chromatography of silica gel of 0.5 mm in thickness (Merck AG, Art 5744). The chromatograms were developed in toluene/acetone (1/1) and the spot, whose Rf value was between 0.45 to 0.60, were scraped. The obtained products were put into a vial containing 10 ml of scintillator to measure specific radio-activity with scintillation counter. The activities of the present compounds are shown in Table 4 as comparative ones based on the assumption that the activity of Mevinolin (sodium salt) as reference drug is 100.

TABLE 4

Test Compound	HMG-CoA reductase inhibitory activities
1a-1	442
1a-3	385
1a-5	279

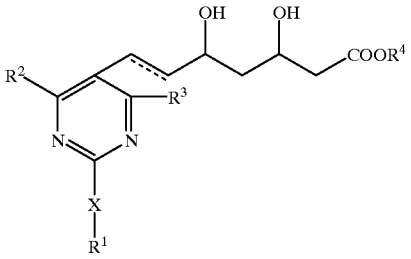
TABLE 4-continued

Test Compound	HMG-CoA reductase inhibitory activities
1a-7	260
Mevinolin Na	100

From the test data, the compounds of the present invention exhibit HMG-CoA reductase inhibition activities superior to Mevinolin.

What is claimed is:

[1. A compound represented by the formula (I):



wherein

R^1 is (1) lower alkyl which may have 1 to 3 substitutents independently selected from the group consisting of halogen, amino, and cyano, (2) C_6 to C_{12} aromatic group which may have 1 to 3 substituents independently selected from the group consisting of lower alkyl, halogen, amino, and cyano, or (3) C_1 to C_6 lower alkyl substituted by C_6 to C_{12} aromatic group which may have 1 to 3 substituents independently sel-ected from the group consisting of lower alkyl, halo-gen, amino, and cyano; R^2 and R^3 each is independently (1) hydrogen, (2) lower alkyl which may have 1 to 3 substituents independently selected from the group consisting of halogen, amino, and cyano, or (3) C_6 to C_{12} aromatic group which may have 1 to 3 substituents independently selected from the group consisting of lower alkyl, halogen, amino, and cyano; R^4 is (1) hydro-gen, (2) lower alkyl, or a cation capable of forming a non-toxic pharmaceutically acceptable salt; X is sulfur, oxygen, or sulfonyl, or imino which may be substituted by formyl, acetyl, propionyl, butyryl, isobutyryl, vale-ryl, isovaleryl, amino substituted by sulfonyl or alkyl-sulfonyl, and sulfonyl substituted by alkyl, amino or alkylamino, the dotted line represents the presence or absence of a double bond, or the corresponding ring-closed lactone.**]**

[2. The compound claimed in claim **1**, wherein X is imino which may be substituted by formyl, acetyl, pro-pionyl, butyryl, isobutyryl, valeryl, isovaleryl, amino substituted by sulfonyl or alkylsulfonyl, or sulfonyl substituted by alkyl, amino or alkylamino.**]**

[3. The compound claimed in claim **2**, wherein X is imino which may be substituted by formyl, acetyl, pro-pionyl, butyryl, isobutyryl, valeryl, isovaleryl, alkylsul-fonylamino, or alkylsulfonyl.**]**

[4. The compound claimed in claim **1** having the (3R, 5S)-dihydroxy configuration.**]**

[5. A pharmaceutical composition comprising an ef-fective amount of the compound claimed in claim **1** as an active ingredient, in combination with a pharmaceu-tical excipient.**]**

6. The compound 7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methyl-N-methylsulfonylamino)pyrimidin-5-yl)-(3R,5S)-dihydroxy-(E)-6-heptenoic acid in the form of a non-toxic pharmaceutically acceptable salt thereof.

7. The compound of claim 6 in the form of a sodium salt.

8. The compound of claim 6 in the form of a calcium salt.

* * * * *

JS 44 (Rev. 12/96)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

I. (a) PLAINTIFFS
ASTRAZENECA PHARMACEUTICALS LP, AND
ASTRAZENECA UK LIMITED, AND
IPR PHARMACEUTICALS, INC., AND
SHIONOGI SEIYAKU KABUSHIKI KAISHA

(b) COUNTY OF RESIDENCE OF FIRST LISTED PLAINTIFF
(EXCEPT IN U.S. PLAINTIFF CASES) NEW CASTLE COUNTY, DELAWARE

DEFENDANTS
AUROBINDO PHARMA LTD. AND
AUROBINDO PHARMA USA INC.

COUNTY OF RESIDENCE OF FIRST LISTED DEFENDANT
(IN U.S. PLAINTIFF CASES ONLY)

(c) ATTORNEYS (FIRM NAME, ADDRESS AND TELEPHONE NUMBER)
Mary W. Bourke
Connolly Bove Lodge & Hutz LLP
P.O. Box 2207, 1007 North Orange Street
Wilmington, Delaware 19899-2207
(302) 658-9141

ATTORNEYS (IF KNOWN)

II. BASIS OF JURISDICTION (PLACE AN "X" IN ONE BOX ONLY)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

III. CITIZENSHIP OF PRINCIPAL PARTIES (PLACE AN "X" IN ONE BOX FOR PLAINTIFF AND ONE BOX FOR DEFENDANT)
(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☐ 1	☐ 1	Incorporated *or* Principal Place of Business in This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business in Another State	☐ 5	☐ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. ORIGIN (PLACE AN "X" IN ONE BOX ONLY)

☒ 1 Original Proceeding | ☐ 2 Removed from State Court | ☐ 3 Remanded from Appellate Court | ☐ 4 Reinstated or Reopened | ☐ 5 Transferred from another district (specify) | ☐ 6 Multidistrict Litigation | ☐ 7 Appeal to District Judge from Magistrate Judgment

V. NATURE OF SUIT (PLACE AN "X' IN ONE BOX ONLY)

CONTRACT
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excl Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault. Libel & Slander
- ☐ 330 Federal Employers Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJURY
- ☐ 362 Personal Injury - Med. Malpractice
- ☐ 365 Personal Injury - Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 440 Other Civil Rights

PRISONER PETITIONS
- ☐ 510 Motions to Vacate Sentence

HABEAS CORPUS:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

FORFEITURE/PENALTY
- ☐ 610 Agriculture
- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 R.R. & Truck
- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor Mgmt Relations
- ☐ 730 Labor Mgmt Reporting & Disclosure Act
- ☐ 740 Labor Railway Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Empl. Ret. Inc. Security Act

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☒ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS - Third Party 26 USC 7609

OTHER STATUTES
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce/CC Rates/etc.
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 810 Selective Service
- ☐ 850 Securities/ Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 895 Freedom of Information Act
- ☐ 900 Appeal of Fee Determination Under Equal Access to Justice
- ☐ 950 Constitutionality of State Statutes
- ☒ 890 Other Statutory Actions

VI. CAUSE OF ACTION (CITE THE U.S. CIVIL STATUTE UNDER WHICH YOU ARE FILING AND WRITE BRIEF STATEMENT OF CAUSE. DO NOT CITE JURISDICTIONAL STATUTES UNLESS DIVERSITY.)

Action for infringement of U.S. Patent No. RE37,314 arising under 35 U.S.C. § 271.

VII. REQUESTED IN
COMPLAINT: ☐ UNDER F.R.C.P. 23

CHECK IF THIS IS A **CLASS ACTION**

DEMAND: Amount to be determined, Permanent Injunction sought

CHECK YES only if demanded in complaint:
JURY DEMAND: ☐ YES ☒ NO

SEE NEXT PAGE FOR RELATED CASES

VIII. RELATED CASE(S) (See instructions):

IF ANY: ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. COBALT PHARMACEUTICALS INC. AND COBALT LABORATORIES INC.; ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. APOTEX INC. AND APOTEX CORP.; ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. MYLAN PHARMACEUTICALS INC.; ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. PAR PHARMACEUTICAL, INC.; ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. SANDOZ INC.; ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., SHIONOGI SEIYAKU KABUSHIKI KAISHA VS. SUN PHARMACEUTICAL INDUSTRIES LTD., SUN PHARMACEUTICAL INDUSTRIES INC., CARACO PHARMACEUTICAL LABORATORIES LTD.

DATE SIGNATURE OF ATTORNEY OF RECORD

FOR OFFICE USE ONLY

RECEIPT # AMOUNT APPLYING IFP JUDGE MAG. JUDGE

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA, **Plaintiffs,** **vs.** **AUROBINDO PHARMA LIMITED, and AUROBINDO PHARMA USA INC.** **Defendants.**	**Civil Action No. 3:07-cv-06020 (MLC)(JJH)** **[PROPOSED] ORDER**

This matter having come before the Court on Plaintiffs ASTRAZENECA PHARMACEUTICALS LP, ASTRAZENECA UK LIMITED, IPR PHARMACEUTICALS, INC., and SHIONOGI SEIYAKU KABUSHIKI KAISHA's motion to stay this proceeding pending resolution of jurisdictional issues in a substantially identical first-filed patent infringement action in the District of Delaware (Civil Action No. 1:07-cv-810, Dist. Delaware) and completion of any necessary proceedings before the Judicial Panel on Multidistrict Litigation (JPMDL) necessitated by a successful challenge to the jurisdiction of the Delaware court., and

Upon consideration of all supporting and opposing papers, and oral arguments of the parties,

IT IS ON THIS ___ DAY OF _____, 2008, ORDERED AND ADJUDGED that:

1. Plaintiffs' motion is GRANTED; and

2. This proceeding is stayed pending resolution of jurisdictional issues in a substantially identical first-filed patent infringement action in the District of Delaware (Civil Action No. 1:07-cv-810, Dist. Delaware) and completion of any necessary proceedings before the Judicial Panel on Multidistrict Litigation (JPMDL) necessitated by a successful challenge to the jurisdiction of the Delaware court.

SO ORDERED.

_____

Hon. John J. Hughes, U.S.M.J.