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REQUEST FOR EX PARTE REEXAMINATION TRANSMITTAL FORM

Address to:

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 Alexandria, VA 22313-1450

Attorney Docket No.: _____

Date: August 25, 2010

1. This is a request for *ex parte* reexamination pursuant to 37 CFR 1.510 of patent number 6,037,157 issued March 14, 2000. The request is made by:
- patent owner. third party requester.
2. The name and address of the person requesting reexamination is:
- Public Patent Foundation
55 Fifth Avenue, Suite 928
New York, NY 10003
3. a. A check in the amount of \$_____ is enclosed to cover the reexamination fee, 37 CFR 1.20(c)(1);
- b. The Director is hereby authorized to charge the fee as set forth in 37 CFR 1.20(c)(1) to Deposit Account No. _____; or
- c. Payment by credit card. Form PTO-2038 is attached.
4. Any refund should be made by check or credit to Deposit Account No. _____ 37 CFR 1.26(c). If payment is made by credit card, refund must be to credit card account.
5. A copy of the patent to be reexamined having a double column format on one side of a separate paper is enclosed. 37 CFR 1.510(b)(4)
6. CD-ROM or CD-R in duplicate, Computer Program (Appendix) or large table
 Landscape Table on CD
7. Nucleotide and/or Amino Acid Sequence Submission
If applicable, items a. - c. are required.
- a. Computer Readable Form (CRF)
- b. Specification Sequence Listing on:
- i. CD-ROM (2 copies) or CD-R (2 copies); or
- ii. paper
- c. Statements verifying identity of above copies
8. A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included.
9. Reexamination of claim(s) 1-18 is requested.
10. A copy of every patent or printed publication relied upon is submitted herewith including a listing thereof on Form PTO/SB/08, PTO-1449, or equivalent.
11. An English language translation of all necessary and pertinent non-English language patents and/or printed publications is included.

[Page 1 of 2]

This collection of information is required by 37 CFR 1.510. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop Ex Parte Reexam, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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12. The attached detailed request includes at least the following items:
- a. A statement identifying each substantial new question of patentability based on prior patents and printed publications. 37 CFR 1.510(b)(1)
- b. An identification of every claim for which reexamination is requested, and a detailed explanation of the pertinency and manner of applying the cited art to every claim for which reexamination is requested. 37 CFR 1.510(b)(2).
13. A proposed amendment is included (only where the patent owner is the requester). 37 CFR 1.510(e)
14. a. It is certified that a copy of this request (if filed by other than the patent owner) has been served in its entirety on the patent owner as provided in 37 CFR 1.33(c).
The name and address of the party served and the date of service are:
Paul D. Yasger, Abbott Laboratories
100 Abbott Park Road, Dept. 377/AP6A
Abbott Park, IL 60064-6008
Date of Service: **August 25, 2010**; or
- b. A duplicate copy is enclosed because service on patent owner was not possible. An explanation of the efforts made to serve patent owner is attached. See MPEP 2220.

15. Correspondence Address: Direct all communications about the reexamination to:

 The address associated with Customer Number:

OR

 Firm or Individual Name **Public Patent Foundation**

Address

55 Fifth Avenue, Suite 928City **New York**State **NY**Zip **10003**Country **USA**Telephone **(212) 790-0442**Email **info@pubpat.org**16. The patent is currently the subject of the following concurrent proceeding(s):

- a. Copending reissue Application No. _____
- b. Copending reexamination Control No. _____
- c. Copending Interference No. _____
- d. Copending litigation styled: _____

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Daniel B. Ravicher
Authorized Signature

Daniel B. Ravicher
Typed/Printed Name

August 25, 2010
Date

47,015 For Patent Owner Requester
Registration No. For Third Party Requester

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT NO.: 6,037,157
ISSUED: Mar. 14, 2000
TO: Norbeck et al.
FOR: METHOD FOR IMPROVING PHARMACOKINETICS

**ATTACHMENT TO FORM PTO/SB/57,
REQUEST FOR *EX PARTE* REEXAMINATION**

SIR:

The Public Patent Foundation ("PUBPAT"), a not-for-profit public service organization that works to protect the public from the harms caused by undeserved patents and unsound patent policy, respectfully requests *ex parte* reexamination under 35 U.S.C. §§ 302-307 and 37 C.F.R. § 1.510 of every claim of United States Patent No. 6,037,157 issued March 14, 2000 to Norbeck et al. and assigned to Abbott Laboratories ("the '157 patent") because they are all invalid under 35 U.S.C. §§ 102 and 103 and their existence is causing significant public harm.¹

THE '157 PATENT IS CAUSING SIGNIFICANT PUBLIC HARM

HIV/AIDS is one of the greatest threats to public health faced by the world today. As of the end of 2008, over 33 million people worldwide were living with HIV/AIDS,² including more than one million Americans.³ Every person afflicted with HIV/AIDS has the right to obtain the

¹ A copy of the '157 patent is attached hereto as Appendix A.

² <http://www.avert.org/worldstats.htm>, last visited August 3, 2010.

³ <http://www.avert.org/usa-statistics.htm>, last visited August 3, 2010.

best medical treatment available without any improper obstacles placed in their way. More specifically, American men, women, and children suffering from HIV/AIDS are entitled to access the best pharmaceutical treatments available without undeserved patents making those treatments either too expensive or too limited in supply.

Ritonavir is a retroviral protease inhibitor that is a significant treatment for HIV/AIDS patients. Today it is widely used as a booster for other protease inhibitors. Abbott Laboratories is the sole distributor of ritonavir in the United States (under the brand name Norvir) and is using the '157 patent – and seven other patents for which requests for reexamination are being filed concurrently herewith – to prevent anyone else from offering ritonavir to HIV/AIDS patients in the United States.⁴ Not only is the '157 patent being used to deny American HIV/AIDS patients fair access to the medical treatment that they need and deserve; it is also a barrier to further research on ritonavir here in the United States because there is no exception to patent infringement for such research. In these ways, the '157 patent is unquestionably causing significant public harm to the American people. Although these issues are not grounds to grant this request for reexamination, PUBPAT respectfully requests that they be considered when determining whether the validity of the '157 patent merits review by your office.

THE SUBSTANTIAL NEW QUESTIONS OF PATENTABILITY

1. Whether claims 1-18 of the '157 patent were anticipated by U.S. Patent No. 5,142,056 to Kempf et al. issued on August 25, 1992 (“the '056 patent”);

⁴ Approved Drug Products with Therapeutic Equivalence Evaluations, Food and Drug Administration (“Orange Book”), Application Number. N022417 (Approval Date February 10, 2010).

2. Whether claims 1-18 of the '157 patent were anticipated by U.S. Patent No. 5,886,036 to Kempf et al. issued March 23, 1999 (“the '036 patent”); and,
3. Whether claims 1-18 of the '157 patent were rendered obvious by the '056 patent alone or in view of J. Lin, et al., Time- and Dose-Dependent Pharmacokinetics of L-754,394, an HIV Protease Inhibitor, in Rats, Dogs and Monkeys, *J. Pharmacology and Experimental Therapeutics*, 274:264-269 (1995) (“Lin”).

These are new questions because neither the '056 patent nor Lin was of record during prosecution, and the '036 patent was not applied during prosecution. A detailed explanation of the pertinency and manner of applying the cited patents and publications to the claims of the '157 patent is set forth below.⁵

THE '056 PATENT ANTICIPATED THE '157 PATENT

The '157 patent application was filed June 26, 1996. The applicants claimed priority to two provisional applications, numbers 60/00,654 (filed June 29, 1995) and 60/003,849 (filed September 15, 1995). Therefore, the earliest possible priority date for the '157 patent is June 29, 1995. The '056 patent issued on August 25, 1992. Accordingly, the '056 patent is 102(b) prior art to the '157 patent. As explained below, the '056 patent anticipates each claim of the '157 patent.

The Federal Circuit set forth the appropriate standard for anticipation, and in particular inherent anticipation in the pharmaceutical arts, in Schering Corp. v. Geneva Pharms., 339 F.3d 1373 (Fed. Cir. 2003). There, the Federal Circuit said that anticipation requires, “a single prior

⁵ Appendix B contains a copy of the cited patents and publications.

art reference [that] discloses each and every limitation of the claimed invention.” Id. at 1377. However, “a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference.” Id. Further, the court rejected “the contention that inherent anticipation requires recognition in the prior art,” and reconfirmed, “[t]he patent law principle ‘that which would literally infringe if later in time anticipates if earlier.’” Id. at 1377, 1379 (citing Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1378 (Fed. Cir. 2001)).

With respect to inherency, the court confirmed that it has broad and unlimited scope, saying:

Because inherency places subject matter in the public domain as well as an express disclosure, the inherent disclosure of the entire claimed subject matter anticipates as well as inherent disclosure of a single feature of the claimed subject matter. The extent of the inherent disclosure does not limit its anticipatory effect. In general, a limitation or the entire invention is inherent and in the public domain if it is the ‘natural result flowing from’ the explicit disclosure of the prior art.

Id. at 1379.

Applying these principles in Schering, the court held that a later patent claiming a metabolite formed in a patient's body upon ingestion of a pharmaceutical was anticipated by a prior art reference disclosing the pharmaceutical itself despite the fact that it was conceded that the formation of the metabolite in a patient's body was not known or recognized by those of skill in the art prior to the filing of the application leading to the patent on the metabolite. The court held that such recognition was not required to qualify for inherent anticipation. Id. at 1377 (“Other precedents of this court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. E.g.,

In re Cruciferous Sprout Litig., 301 F.3d 1343, 1351 (Fed. Cir. 2002); Mehl/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1366 (Fed. Cir. 1999) (“Where ... the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results.”); Atlas Powder, 190 F.3d at 1348-49 (“Because 'sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention. ... An inherent structure, composition, or function is not necessarily known.”)”)

Here, the claims of the '157 patent are directed to administering to a human a drug metabolized by cytochrome P450 monooxygenase and ritonavir. There is no limitation or requirement that the person performing the administration or the human receiving the administration know that the drug they are being given in combination with ritonavir is metabolized by cytochrome P450 monooxygenase. Referring to the “patent law principle” cited above, the administering of ritonavir with another drug that is metabolized by cytochrome P450 monooxygenase would infringe the claims of the '157 patent, regardless of whether anyone involved with that administering was aware of the fact that the other drug was metabolized by cytochrome P450 monooxygenase. Thus, a prior art teaching of the administration of a drug that is metabolized by cytochrome P450 monooxygenase in combination with ritonavir anticipates the claims of the '157 patent even if that prior art reference does not disclose, and even if those of skill in the art did not know at the time, that the other drug is metabolized by cytochrome P450 monooxygenase. The fact that the recognition that such drugs are metabolized by cytochrome P450 monooxygenase may not have existed at the time of the prior art reference does not defeat its anticipatory effect.

The '056 patent is precisely such a reference. Beginning at column 220, line 22 and continuing through line 59, the '056 goes into great detail regarding the administering of ritonavir in combination with other drugs, including specifically “one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines.” The '056 patent continues to teach that,

Any of a variety of HIV or AIDS vaccines can be used in combination with a compound of the present invention.

It will be understood that agents which can be combined with the compounds of the present invention for the treatment or prophylaxis of AIDS or an HIV infection are not limited to those listed above, but include in principle any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.

220:45-54.

It is now well known that many such drugs, including specifically those for the treatment of HIV/AIDS, are metabolized by cytochrome P450 monooxygenase. The '157 patent concedes this fact. '157 patent, 1:51-53 (“Some drugs and, in particular, HIV protease inhibitors are metabolized by cytochrome P450 monooxygenase”); 2:20-33. Therefore, since the '056 patent taught the administering of ritonavir in combination with other HIV drugs, which are now recognized to be metabolized by cytochrome P450 monooxygenase, the '056 patent inherently anticipated the claims of the '157 patent. The fact that it may not have been recognized at the time that such drugs taught by the '056 patent to be administered in combination with ritonavir were metabolized by cytochrome P450 monooxygenase is of no consequence.

The chart below compares all of the claims of the '157 patent to the teaching of the '056 patent. In essence, each claim of the '157 patent was inherently anticipated by the teaching of the '056 patent. Therefore each claim of the '157 patent is invalid and should be canceled.

'157 patent	'056 patent
<p>1. A method for improving the pharmacokinetics of a drug which is metabolized by cytochrome P450 monooxygenase comprising administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time.</p>
<p>2. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol , taxotere, clarithromycin, A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p>

'157 patent	'056 patent
	<p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>3. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's</p>

'157 patent	'056 patent
	<p>teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>4. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease</p>

'157 patent	'056 patent
	inhibitors, which are each an “agent useful for the treatment of HIV/AIDS,” one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.
5. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, saquinavir, falls within the classes of drugs taught by the '056 patent, as it is “agent useful for the treatment of HIV/AIDS,” one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
6. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is VX-478.	The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other

'157 patent	'056 patent
	<p>antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>7. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such</p>

'157 patent	'056 patent
	<p>knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>8. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's</p>

'157 patent	'056 patent
	<p>teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>9. A method for increasing human blood levels of a drug which is metabolized by cytochrome P450 monooxygenase comprising administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time.</p>
<p>10. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol , taxotere, clarithromycin, A-</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27.</p>

'157 patent	'056 patent
<p>77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>11. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450</p>

'157 patent	'056 patent
	<p>monoxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monoxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>12. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monoxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monoxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of</p>

'157 patent	'056 patent
	<p>a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>13. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim,</p>

'157 patent	'056 patent
	saquinavir, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.
14. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is VX-478.	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
15. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.	The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more

'157 patent	'056 patent
	<p>immunomodulators, antiviral agents, other anti-infective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>16. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other anti-infective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. It is now recognized that many of these drugs are metabolized by cytochrome P450</p>

'157 patent	'056 patent
	<p>monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '056 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '056 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>17. A method for inhibiting cytochrome P450 monooxygenase comprising administering to a human in need thereof an amount of ritonavir or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir. It is inherent in the '056 patent's teachings that the administration of ritonavir to a human would inhibit cytochrome P450 monooxygenase, even if that was not recognized at the time.</p>
<p>18. A method for inhibiting cytochrome P450 monooxygenase comprising contacting the cytochrome P450 monooxygenase with an amount of ritonavir or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir. It is inherent in the '056 patent's teachings that the administration of ritonavir to a human would inhibit cytochrome P450 monooxygenase as a result of contacting the cytochrome P450 monooxygenase with the ritonavir, even if that was not recognized at the time.</p>

THE '036 PATENT ANTICIPATED THE '157 PATENT

As discussed above, the earliest possible priority date for the '157 patent is June 29, 1995.

The '036 patent was claims priority to an application filed as early as December 1992. Accordingly, the '036 patent is 102(e) prior art to the '157 patent. As explained below, the '036 patent anticipates each claim of the '157 patent.

Referring to the discussion above regarding the appropriate standard for anticipation set forth by the Federal Circuit in Schering Corp. v. Geneva Pharms., and similar to the analysis performed above with respect to the '056 patent, the '036 patent is another prior art teaching of the administration of a drug that is metabolized by cytochrome P450 monooxygenase in combination with ritonavir. This teaching by the '036 patent anticipates the claims of the '157 patent even if it does not disclose, and even if one of ordinary skill in the art did not recognize at the time, that the other drug being administered with ritonavir is metabolized by cytochrome P450 monooxygenase. The fact that the recognition that such drugs are metabolized by cytochrome P450 monooxygenase may not have existed at the time of the prior art reference does not defeat the anticipatory effect of the '036 patent.

Beginning at column 105, line 33 and continuing through column 107, line 16, the '036 patent goes into great detail regarding the administering of ritonavir in combination with other drugs, including specifically “one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines.” The '036 patent continues to teach that, “It will be understood that agents which can be combined with the compounds of the present invention for the treatment of prophylaxis of AIDS or an HIV infection are not limited to those listed above, but include in principle any agents useful for the treatment of for the treatment of prophylaxis of AIDS or an HIV infection.” 107:1-6. Even more specifically, the '036 patent teaches administering ritonavir

in combination with, “retroviral protease inhibitors (for example, HIV protease inhibitors such as [saquinavir] Ro 31-8959, SC-52151, KNI-227, KNI-272 and the like).” 105:46-48.

The '036 patent even claims the administration of a combination of ritonavir with “another HIV protease inhibiting compound.” Claim 1. The '036 claims such combination administration of ritonavir with another HIV protease inhibiting compound where they “are formulated as separate compositions” (claim 4), “are to be administered at the same time” (claim 5), and “are to be administered at different times” (claim 6). It also claims the specific combination of ritonavir with the specific HIV protease inhibitors saquinavir (referred to as Ro 31-8959), SC-52151, and KNI-272. Claims 2, 3, 7, 9, 10, 14, 16, 18 and 19. This is substantial teaching by the '036 patent of precisely what is claimed by the '157.

It is now well known that many such drugs, including specifically those for the treatment of HIV/AIDS, are metabolized by cytochrome P450 monooxygenase. The '157 patent concedes this fact. '157 patent, 1:51-53 (“Some drugs and, in particular, HIV protease inhibitors are metabolized by cytochrome P450 monooxygenase”); 2:20-33. Specifically, several of the drugs taught by the '036 patent to be co-administered with ritonavir, namely saquinavir (Ro 31-8959), SC-52151 and KNI-272, are acknowledged by the '157 patent to be metabolized by cytochrome P450 monooxygenase. '157 patent, 2:25-32. Therefore, since the '036 patent taught the administering of ritonavir in combination with other HIV drugs, which are now recognized to be metabolized by cytochrome P450 monooxygenase, the '036 patent inherently anticipated the claims of the '157 patent. The fact that it may not have been recognized at the time that such drugs taught by the '036 patent to be administered in combination with ritonavir were

metabolized by cytochrome P450 monooxygenase is of no consequence.

The chart below compares all of the claims of the '157 patent to the teaching of the '036 patent. In essence, each claim of the '157 patent was inherently anticipated by the teaching of the '036 patent. Therefore each claim of the '157 patent is invalid and should be canceled.

'157 patent	'036 patent
1. A method for improving the pharmacokinetics of a drug which is metabolized by cytochrome P450 monooxygenase comprising administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.	The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other anti-infective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33. Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time.
2. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol, taxotere, clarithromycin, A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011	The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other anti-infective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such

'157 patent	'036 patent
<p>BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), SC-52151 and KNI-272, three of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>3. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is</p>

'157 patent	'036 patent
	<p>now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), SC-52151 and KNI-272, three of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>4. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such</p>

'157 patent	'036 patent
	<p>knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), one of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>5. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p>

'157 patent	'036 patent
	<p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, saquinavir, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), the specific drug claimed in this claim. '036 patent, 105:46-48.</p>
<p>6. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is VX-478.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by</p>

'157 patent	'036 patent
	<p>cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48.</p>
<p>7. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease</p>

'157 patent	'036 patent
	inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48.
8. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.	<p>The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines.” 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a variety of classes of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would improve the pharmacokinetics of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48.</p>
9. A method for increasing human blood levels of a drug which is metabolized by cytochrome P450 monooxygenase comprising	The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more

'157 patent	'036 patent
<p>administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.</p>	<p>immunomodulators, antiviral agents, other antiifective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time.</p>
<p>10. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol , taxotere, clarithromycin, A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such</p>

'157 patent	'036 patent
	<p>treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), SC-52151 and KNI-272, three of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>11. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and</p>

'157 patent	'036 patent
	<p>ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), SC-52151 and KNI-272, three of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>12. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug,</p>

'157 patent	'036 patent
	<p>even if that was not recognized at the time. The specific drugs claimed in this claim fall within the classes of drugs taught by the '036 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), one of the specific drugs claimed in this claim. '036 patent, 105:46-48.</p>
<p>13. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines.” 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, saquinavir, falls within the classes of drugs</p>

'157 patent	'036 patent
	<p>taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48. Further, the '036 patent expressly taught administering ritonavir in combination with saquinavir (Ro 31-8959), the specific drug claimed in this claim. '036 patent, 105:46-48.</p>
<p>14. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is VX-478.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other anti-infective agents or vaccines." 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent,</p>

'157 patent	'036 patent
	105:35-37, 46-48.
<p>15. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 105:35-37. The '036 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48.</p>
<p>16. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 105:35-37. The '036 patent further specifically taught</p>

'157 patent	'036 patent
	<p>administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 107:4-6. It is now recognized that many of these drugs are metabolized by cytochrome P450 monooxygenase. The '157 concedes such knowledge is in the prior art. '157 patent, 1:51-53, 2:20-33.</p> <p>Thus, the '036 patent expressly disclosed administering to a human in need of such treatment a therapeutically effective amount of a combination of drugs metabolized by cytochrome P450 monooxygenase and ritonavir. It is inherent in the '036 patent's teachings that such co-administration would increase the human blood levels of the drug, even if that was not recognized at the time. The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '036 patent, as it is an HIV protease inhibitor, one of the classes of drugs expressly taught by the '036 patent as being co-administered with ritonavir. '036 patent, 105:35-37, 46-48.</p>
<p>17. A method for inhibiting cytochrome P450 monooxygenase comprising administering to a human in need thereof an amount of ritonavir or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir. It is inherent in the '036 patent's teachings that the administration of ritonavir to a human would inhibit cytochrome P450 monooxygenase, even if that was not recognized at the time.</p>
<p>18. A method for inhibiting cytochrome P450 monooxygenase comprising contacting the cytochrome P450 monooxygenase with an amount of ritonavir or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.</p>	<p>The '036 patent taught administering to a human in need of such treatment ritonavir. It is inherent in the '036 patent's teachings that the administration of ritonavir to a human would inhibit cytochrome P450 monooxygenase as a result of contacting the cytochrome P450 monooxygenase with the ritonavir, even if that</p>

'157 patent	'036 patent
	was not recognized at the time.

THE '056 PATENT IN VIEW OF LIN RENDERED THE '157 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '157 patent is June 29, 1995. Lin is a publication that was accepted for publication on March 24, 1995. Accordingly, Lin is 102(a) prior art to the '157 patent. As explained below, the combined teachings of the '056 patent and Lin rendered obvious each claim of the '157 patent.

The Supreme Court set forth the appropriate standard for obviousness in KSR v. Teleflex, 127 S.Ct. 1727 (2007). In KSR, the Supreme Court reaffirmed its holding in Graham v. John Deere that obviousness is principally a three-prong analysis whereby “the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved.” Id. at 1734 (citing Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18 (1966)). Since the KSR decision, the Federal Circuit has restated that the obviousness inquiry also requires a showing that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention and that the skilled artisan would have had a reasonable expectation of success in doing so. Pfizer v. Apotex, 480 F. 3d 1348, 1361 (Fed. Cir. 2007).

However, although the Federal Circuit may have in the past implemented a rigid rule that a patent claim cannot be rendered obvious merely because it was “obvious to try,” the Supreme Court in KSR expressly reversed that rule, saying:

The same constricted analysis led the Court of Appeals to

conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." ... When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

127 S. Ct. at 1742. Further, as the Federal Circuit has stated post-KSR, "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." Pfizer v. Apotex, 480 F. 3d at 1364. Thus, under binding recent Federal Circuit case law, there is a reasonable expectation of success and the claims are thus obvious if, (i) one of ordinary skill in the art would have been motivated to combine the teachings in the prior art, (ii) it was in fact obvious-to-try to do that, and (iii) there was only a limited number of parameters that one of ordinary skill in the art would have to try in order to successfully achieve the claimed invention. Pfizer v. Apotex, 480 F. 3d at 1366.

Here, the '056 patent fully teaches ritonavir and its use as an HIV protease inhibitor. Further, beginning at column 220, line 22 and continuing through line 59, the '056 goes into great detail regarding the administering of ritonavir in combination with other drugs, including specifically "one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." The '056 patent continues to teach that:

Any of a variety of HIV or AIDS vaccines can be used in combination with a compound of the present invention.

It will be understood that agents which can be combined with the compounds of the present invention for the treatment or prophylaxis of AIDS or an HIV

infection are not limited to those listed above, but include in principle any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.

220:45-54.

Lin taught a HIV protease inhibitor that substantially inhibited cytochrome P450 and, therefore, had improved pharmacokinetics. Thus, one of ordinary skill in the art would have been motivated to try to use ritonavir (a known HIV protease inhibitor) to inhibit cytochrome P450 to achieve improved pharmacokinetics. The motivation is provided by at least the desirability of improved pharmacokinetics well known in the field and also the specific suggestion of Lin to try to use HIV protease inhibitors in such a capacity. This is not the case where there would be an unlimited number of parameters to try, as the only combination to attempt is the use of ritonavir as a cytochrome P450 inhibitor. Therefore, the claims of the '157 patent were obvious in light of the combined teachings of the '056 patent and Lin.

The chart below compares all of the claims of the '157 patent to the teaching of the '056 patent in view of Lin. In essence, each claim of the '157 patent was obvious in light of the teaching of the '056 patent to co-administer ritonavir with other drugs and Lin's teaching that HIV protease inhibitors like ritonavir could inactivate cytochrome P450. Therefore each claim of the '157 patent is invalid and should be canceled.

'157 patent	'056 patent in view of Lin
1. A method for improving the pharmacokinetics of a drug which is metabolized by cytochrome P450 monooxygenase comprising administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically	The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such

'157 patent	'056 patent in view of Lin
<p>acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.</p>	<p>treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p>
<p>2. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol, taxotere, clarithromycin, A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an “agent useful for the treatment of HIV/AIDS,” one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>3. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more</p>

'157 patent	'056 patent in view of Lin
<p>consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>4. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p>

'157 patent	'056 patent in view of Lin
	<p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>5. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drug claimed in this claim, saquinavir, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>6. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is VX-478.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught</p>

'157 patent	'056 patent in view of Lin
	<p>administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '056 patent, as it is “agent useful for the treatment of HIV/AIDS,” one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>7. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '056 patent, as it is “agent useful for the treatment of HIV/AIDS,” one of the classes of</p>

'157 patent	'056 patent in view of Lin
	drugs expressly taught by the '056 patent as being co-administered with ritonavir.
<p>8. The method of claim 1 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.</p> <p>The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '056 patent, as it is “agent useful for the treatment of HIV/AIDS,” one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>9. A method for increasing human blood levels of a drug which is metabolized by cytochrome P450 monooxygenase comprising administering to a human in need of such treatment a therapeutically effective amount of a combination of said drug or a pharmaceutically acceptable salt thereof and ritonavir or a pharmaceutically acceptable salt thereof.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir “in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines.” 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with “any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.” 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to</p>

'157 patent	'056 patent in view of Lin
	<p>attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p>
<p>10. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of cyclosporine, FK-506, rapamycin, taxol, taxotere, clarithromycin, A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>11. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478, AG1343, DMP-323, XM-</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27.</p>

'157 patent	'056 patent in view of Lin
450, BILA 2011 BS, BILA 1096 BS, BILA 2185 BS, BMS 186,318, LB71262, SC-52151, SC-629, KNI-272, CGP 53437, CGP 57813 and U-103017.	<p>The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
12. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is selected from the group consisting of A-77003, A-80987, MK-639, saquinavir, VX-478 and AG1343.	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the</p>

'157 patent	'056 patent in view of Lin
	<p>human blood levels of the co-administered drug.</p> <p>The specific drugs claimed in this claim fall within the classes of drugs taught by the '056 patent. For example, MK-639, saquinavir, VX-478, and AG1343 are each HIV protease inhibitors, which are each an "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>13. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is saquinavir.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drug claimed in this claim, saquinavir, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>14. The method of claim 9 wherein the drug which is metabolized by cytochrome P450</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in</p>

'157 patent	'056 patent in view of Lin
monooxygenase is VX-478.	<p>combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drug claimed in this claim, VX-478, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
15. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is MK-639.	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit</p>

'157 patent	'056 patent in view of Lin
	<p>cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drug claimed in this claim, MK-639, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>16. The method of claim 9 wherein the drug which is metabolized by cytochrome P450 monooxygenase is AG1343.</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir "in combination with one or more immunomodulators, antiviral agents, other antiifective agents or vaccines." 220:22-27. The '056 patent further specifically taught administering to a human in need of such treatment ritonavir in combination with "any agents useful for the treatment or prophylaxis of AIDS or an HIV infection." 220:47-54. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450, which would increase the human blood levels of the co-administered drug.</p> <p>The specific drug claimed in this claim, AG1343, falls within the classes of drugs taught by the '056 patent, as it is "agent useful for the treatment of HIV/AIDS," one of the classes of drugs expressly taught by the '056 patent as being co-administered with ritonavir.</p>
<p>17. A method for inhibiting cytochrome P450 monooxygenase comprising administering to a human in need thereof an amount of ritonavir</p>	<p>The '056 patent taught administering to a human in need of such treatment ritonavir. Lin taught a HIV protease inhibitor could inhibit</p>

'157 patent	'056 patent in view of Lin
or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.	cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.
18. A method for inhibiting cytochrome P450 monooxygenase comprising contacting the cytochrome P450 monooxygenase with an amount of ritonavir or a pharmaceutically acceptable salt thereof effective to inhibit cytochrome P450 monooxygenase.	The '056 patent taught administering to a human in need of such treatment ritonavir. Lin taught a HIV protease inhibitor could inhibit cytochrome P450, and therefore suggested and motivated one of ordinary skill in the art to attempt to use ritonavir to achieve the same pharmacological benefit. Thus, it would have been obvious to try to use ritonavir to inhibit cytochrome P450.

CONCLUSION

For the reasons set forth above, each of the claims of the '157 patent is invalid. Accordingly, PUBPAT respectfully requests that they be examined *ex parte* and subsequently canceled.

August 25, 2010
Date



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CERTIFICATE OF SERVICE

The undersigned certifies that a copy of this Request for Ex Parte Reexamination in its entirety, including all accompanying documents, is being deposited with the U.S. Postal Service as First Class Mail on the date of the signature below in an envelope addressed to the attorney of record for the assignee of U.S. Patent No. 6,037,157 as provided for in 37 C.F.R. § 1.33(c):

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APPENDIX A

APPENDIX B

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Complete if Known

Application Number	90/
Filing Date	
First Named Inventor	Kempf, Dale J.
Art Unit	
Examiner Name	
Attorney Docket Number	

Sheet 1 of 2

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
		US- 5,142,056	08-25-1992	Kempf et al.	
		US- 5,886,036	03-23-1999	Kempf et al.	
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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