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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also referred to as FORM PTO-1465)

REQUEST FOR *INTER PARTES* REEXAMINATION TRANSMITTAL FORM

Address to:
Mail Stop *Inter Partes* Reexam
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Attorney Docket No.: _____

Date: August 25, 2010

1. [X] This is a request for *inter partes* reexamination pursuant to 37 CFR 1.913 of patent number 7,148,359 issued December 12, 2006. The request is made by a third party requester, identified herein below.

2. [X] a. The name and address of the person requesting reexamination is:

Public Patent Foundation
55 Fifth Avenue, Suite 928
New York, NY 10003

b. The real party in interest (37 CFR 1.915(b)(8)) is: _____

3. [ ] a. A check in the amount of $_____ is enclosed to cover the reexamination fee, 37 CFR 1.20(c)(2);

[ ] b. The Director is hereby authorized to charge the fee as set forth in 37 CFR 1.20(c)(2) to Deposit Account No. _____; **or**

[X] c. Payment by credit card. Form PTO-2038 is attached.

4. [X] 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. [X] A copy of the patent to be reexamined having a double column format on one side of a separate paper is enclosed. 37 CFR 1.915(b)(5)

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. [X] A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included.

9. [X] Reexamination of claim(s) 1-7 is requested.

10. [X] 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.

12. [x] 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 1.915(b)(3)
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 1.915(b)(1) & (3).

13. [x] It is certified that the estoppel provisions of 37 CFR 1.907 do not prohibit this reexamination. 37 CFR 1.915(b)(7)

14. [x] a. It is certified that a copy of this request 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:

Abbott Laboratories

100 Abbott Park Rd D377/AP6A-1

Abbott Park IL 60064

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 2620.

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

[ ] The address associated with Customer Number: [ ]

OR

[x] Firm or Individual Name Public Patent Foundation

Address
55 Fifth Avenue, Suite 928

City	State	Zip
New York	NY	10003

Country USA

Telephone	Email
(212) 790-0442	info@pubpat.org

16. [x] 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. _____
[x] d. Copending litigation styled:
Abbott Laboratories v. Matrix Laboratories, et al.,
09-cv-1586 (N.D. Ill.).

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Daniel B. Ravicher
Authorized Signature

August 25, 2010
Date

Daniel B. Ravicher
Typed/Printed Name

47,015
Registration No., if applicable

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CONTROL NO.: 95/000,570

PATENT NO.: 7,148,359

ISSUED: Dec. 12, 2006

TO: Chemburkar et al.

FOR: POLYMORPH OF A PHARMACEUTICAL

CORRECTED ATTACHMENT TO FORM PTO/SB/58, REQUEST FOR *INTER PARTES* 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 *inter partes* reexamination under 35 U.S.C. §§ 311-318 and 37 C.F.R. § 1.913 of every claim of United States Patent No. 7,148,359 issued December 12, 2006 to Chemburkar et al. and assigned to Abbott Laboratories ("the '359 patent") because they are all invalid under 35 U.S.C. §§ 102 and 103 and their existence is causing significant public harm.[1]

THE '359 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

1 A copy of the '359 patent was included with the original filings in this matter, as Appendix A to the original ATTACHMENT TO FORM PTO/SB/58, REQUEST FOR INTER PARTES REEXAMINATION.

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

than one million Americans.[3] Every person afflicted with HIV/AIDS has the right to obtain the 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 '359 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 '359 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 '359 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 '359 patent merits review by your office.

THE SUBSTANTIAL NEW QUESTIONS OF PATENTABILITY

1. Whether claims 1-7 of the '359 patent were anticipated by U.S. Patent No. 5,635,523 to

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

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

Kempf et al. issued on June 3, 1997 ("the '523 patent");

2. Whether claims 1-7 of the '359 patent were anticipated by U.S. Patent No. 5,567,823 to Tien et al. issued October 22, 1996 ("the '823 patent");
3. Whether claims 1-7 of the '359 patent were rendered obvious by the '523 patent in view of Hancock, B., et al., "Characteristics and Significance of the Amorphous State in Pharmaceutical Systems", *Journal of Pharmaceutical Sciences*, 86(1):1-12 (1997) ("Hancock");
4. Whether claims 1-7 of the '359 patent were rendered obvious by the '523 patent in view of Royall, P., et al., "Characteristics of the Glass Transition of an Amorphous Drug Using Modulated DSC", *Pharmaceutical Research*, 15(7):1117-1121 (1998) ("Royall");
5. Whether claims 1-7 of the '359 patent were rendered obvious by the '523 patent in view of Hancock, and further in view of Royall;
6. Whether claims 1-7 of the '359 patent were rendered obvious by the '823 patent in view of Hancock;
7. Whether claims 1-7 of the '359 patent were rendered obvious by the '823 patent in view of Royall; and.
8. Whether claims 1-7 of the '359 patent were rendered obvious by the '823 patent in view of Hancock, and further in view of Royall.

These are new questions because neither Hancock nor Royall was of record during prosecution, and neither the '523 patent nor the '823 patent were applied during prosecution. A detailed explanation of the pertinency and manner of applying the cited patents and publications to the

claims of the '359 patent is set forth below.[5]

THE '523 PATENT ANTICIPATED THE '359 PATENT

The '359 patent application was filed May 4, 2005. The applicants claimed priority to several applications, including two provisional applications, numbers 60/137,535 (filed June 4, 1999) and 60/093,432 (filed July 20, 1998). Therefore, the earliest possible priority date for the '359 patent is July 20, 1998. The '523 patent issued on June 3, 1997. Accordingly, the '523 patent is 102(b) prior art to the '359 patent. As explained below, the '523 patent anticipates each claim of the '359 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 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,

5 A copy of the cited patents and publications was included with the original filings in this matter, as Appendix B to the original ATTACHMENT TO FORM PTO/SB/58, REQUEST FOR INTER PARTES REEXAMINATION.

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 '359 patent are directed to amorphous ritonavir. There are no limitations or requirements as to the quantity (by volume, or otherwise) of amorphous ritonavir.

Therefore, a very small amount of amorphous ritonavir is covered by the claims, and this is regardless of whether that amount of amorphous ritonavir is combined in mixture with crystalline ritonavir. In fact, those of skill in the art readily understood that, "[p]harmaceutical solids rarely exist as 100% crystalline or 100% amorphous." Hancock, 5. A single body of ritonavir can be (and actually would be expected to be) made of parts that are crystalline and parts that are amorphous. Those amorphous parts are themselves substantially pure amorphous ritonavir. Therefore, a prior art teaching of ritonavir that is not expressly 100% crystalline, inherently includes amorphous ritonavir.

Further, there are no limitations or requirements in the claims of the '359 patent that it be known or recognized that the ritonavir produced includes amorphous ritonavir. Referring to the "patent law principle" cited above, ritonavir in amorphous form (either by itself or in combination with ritonavir in crystalline form) would infringe the claims of the '359 patent, regardless of whether anyone was aware of the fact that it was in that form. Thus, a prior art teaching of ritonavir in any state other than 100% pure crystalline form anticipates the claims of the '359 patent even if that prior art reference does not disclose that the ritonavir would be partially (or completely) amorphous. The fact that it wasn't expressly recognized that ritonavir compositions would be partially crystalline and partially amorphous does not defeat this anticipatory effect.

The '523 patent is precisely such a reference. It discloses ritonavir compounds and it is not expressly shown that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently understand that at least some of the

'523 patent's compounds were partially or perhaps even completely amorphous, if not at the final state, then at least at one point during the process of producing the crystalline form. It is impossible to fathom that the entirety of teachings of the '523 patent are completely void of any inherent existence of amorphous ritonavir.

During prosecution of a parent application to the '359 patent (namely application 09/356,736), the issue of anticipation was raised by the Examiner in relation to another prior art reference, Kempf et al. U.S. Patent No. 5,541,206. This rejection was correct and ultimately forced the applicant to continue prosecution of claims relating to amorphous ritonavir in the instant application. In the prosecution of the instant application, the Examiner reversed course and accepted the argument that a single X-ray diffraction pattern comparison was sufficient to overcome the anticipatory rejection. Reexamination requesters here respectfully suggest this was error and that a more thorough investigation and inherent understanding of the '523 patent be applied.

The chart below compares all of the claims of the '359 patent to the teaching of the '523 patent. In essence, each claim of the '359 patent was inherently anticipated by the teaching of the '523 patent. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'523 patent**
1. Substantially pure amorphous ritonavir.	The '523 patent disclosed ritonavir compounds and it is not expressly proven that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently understand that at least some of the '523 patent's compounds were partially or perhaps even completely amorphous, if not at the final state, then at least

'359 patent	'523 patent
	at one point during the process of producing the crystalline form. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of amorphous ritonavir, a very small amount of amorphous ritonavir is covered by this claim, and this is regardless of whether that amount of amorphous ritonavir is combined in mixture with crystalline ritonavir. A single body of ritonavir can be (and actually would be expected to be) made of parts that are crystalline and parts that are amorphous. Those amorphous parts are themselves substantially pure amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that is not expressly 100% crystalline, inherently includes substantially pure amorphous ritonavir.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir inherent in the '523 patent has a glass transition temperature within the claimed range. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect.
3. A composition comprising amorphous ritonavir.	The '523 patent disclosed ritonavir compounds and it is not expressly proven that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently understand that at least some of the '523 patent's compounds were partially or perhaps even completely amorphous, if not at the final state, then at least at one point during the process of producing the crystalline form. Further, since there are no limitations or requirements as to the quantity (by volume, or

'359 patent	'523 patent
	otherwise) of amorphous ritonavir, a very small amount of amorphous ritonavir is covered by this claim, and this is regardless of whether that amount of amorphous ritonavir is combined in mixture with crystalline ritonavir. A single body of ritonavir can be (and actually would be expected to be) made of parts that are crystalline and parts that are amorphous. Those amorphous parts are themselves amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that is not expressly 100% crystalline, inherently includes amorphous ritonavir.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	It would be expected that the amorphous ritonavir inherent in the '523 patent would be substantially pure. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '523 patent that greater than 90% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 90% amorphous is covered by this claim, and this is regardless of whether that amount of 90% amorphous ritonavir is combined in mixture with ritonavir that is less than 90% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly amorphous. Those highly amorphous parts could themselves be greater than about 90%

'359 patent	'523 patent
	amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 90% amorphous, inherently teaches this claim.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '523 patent that greater than 95% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 95% amorphous is covered by this claim, and this is regardless of whether that amount of 95% amorphous ritonavir is combined in mixture with ritonavir that is less than 95% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly amorphous. Those highly amorphous parts could themselves be greater than about 95% amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 95% amorphous, inherently teaches this claim.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '523 patent that greater than 97% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect. Further, since there are no limitations or requirements as to the quantity (by volume, or

'359 patent	'523 patent
	otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 97% amorphous is covered by this claim, and this is regardless of whether that amount of 97% amorphous ritonavir is combined in mixture with ritonavir that is less than 97% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly amorphous. Those highly amorphous parts could themselves be greater than about 97% amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 97% amorphous, inherently teaches this claim.

THE '823 PATENT ANTICIPATED THE '359 PATENT

As discussed above, the earliest possible priority date for the '359 patent is June 29, 1995. The '823 patent was claims priority to an application filed as early as December 1992. Accordingly, the '823 patent is 102(e) prior art to the '359 patent. As explained below, the '823 patent anticipates each claim of the '359 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 '523 patent, the '823 patent is another prior art teaching of ritonavir compounds and it is not expressly proven that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently

understand that at least some of the '823 patent's compounds were partially or perhaps even completely amorphous, if not at the final state, then at least at one point during the process of producing the crystalline form. It is impossible to fathom that the entirety of teachings of the '823 patent are completely void of any inherent existence of amorphous ritonavir.

During prosecution of a parent application to the '359 patent (namely application 09/356,736), the issue of anticipation was raised by the Examiner in relation to another prior art reference, Kempf et al. U.S. Patent No. 5,541,206. This rejection was correct and ultimately forced the applicant to continue prosecution of claims relating to amorphous ritonavir in the instant application. In the prosecution of the instant application, the Examiner reversed course and accepted the argument that a single X-ray diffraction pattern comparison was sufficient to overcome the anticipatory rejection. Reexamination requesters here respectfully suggest this was error and that a more thorough investigation and inherent understanding of the '823 patent be applied.

The chart below compares all of the claims of the '359 patent to the teaching of the '523 patent. In essence, each claim of the '359 patent was inherently anticipated by the teaching of the '523 patent. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'823 patent**
1. Substantially pure amorphous ritonavir.	The '823 patent disclosed ritonavir compounds and it is not expressly proven that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently understand that at least some of the '823 patent's compounds

'359 patent	'823 patent
	were partially or perhaps even completely amorphous, if not at the final state, then at least at one point during the process of producing the crystalline form. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of amorphous ritonavir, a very small amount of amorphous ritonavir is covered by this claim, and this is regardless of whether that amount of amorphous ritonavir is combined in mixture with crystalline ritonavir. A single body of ritonavir can be (and actually would be expected to be) made of parts that are crystalline and parts that are amorphous. Those amorphous parts are themselves substantially pure amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that is not expressly 100% crystalline, inherently includes substantially pure amorphous ritonavir.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir inherent in the '823 patent has a glass transition temperature within the claimed range. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect.
3. A composition comprising amorphous ritonavir.	The '823 patent disclosed ritonavir compounds and it is not expressly proven that each and every disclosed compound existed in 100% crystalline form. Therefore, one of ordinary skill in the art would inherently understand that at least some of the '823 patent's compounds were partially or perhaps even completely amorphous, if not at the final state, then at least at one point during the process of producing the crystalline form.

'359 patent	'823 patent
	Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of amorphous ritonavir, a very small amount of amorphous ritonavir is covered by this claim, and this is regardless of whether that amount of amorphous ritonavir is combined in mixture with crystalline ritonavir. A single body of ritonavir can be (and actually would be expected to be) made of parts that are crystalline and parts that are amorphous. Those amorphous parts are themselves amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that is not expressly 100% crystalline, inherently includes amorphous ritonavir.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	It would be expected that the amorphous ritonavir inherent in the '823 patent would be substantially pure. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '823 patent that greater than 90% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 90% amorphous is covered by this claim, and this is regardless of whether that amount of 90% amorphous ritonavir is combined in mixture with ritonavir that is less than 90% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly

'359 patent	'823 patent
	amorphous. Those highly amorphous parts could themselves be greater than about 90% amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 90% amorphous, inherently teaches this claim.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '823 patent that greater than 95% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect. Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 95% amorphous is covered by this claim, and this is regardless of whether that amount of 95% amorphous ritonavir is combined in mixture with ritonavir that is less than 95% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly amorphous. Those highly amorphous parts could themselves be greater than about 95% amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 95% amorphous, inherently teaches this claim.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	It was inherent in the ritonavir compounds taught by the '823 patent that greater than 97% of the ritonavir could be amorphous. Whether that fact was recognized by the reference, or even known by anyone at the time, does not defeat the reference's anticipatory effect.

'359 patent	'823 patent
	Further, since there are no limitations or requirements as to the quantity (by volume, or otherwise) of total ritonavir, a very small amount of ritonavir that is greater than 97% amorphous is covered by this claim, and this is regardless of whether that amount of 97% amorphous ritonavir is combined in mixture with ritonavir that is less than 97% amorphous. A single body of ritonavir can be (and actually would be expected to be) made of parts that are highly crystalline and parts that are highly amorphous. Those highly amorphous parts could themselves be greater than about 97% amorphous ritonavir as claimed here. Therefore, a prior art teaching of ritonavir that does not expressly exclude any portion of its volume from being greater than 97% amorphous, inherently teaches this claim.

THE '523 PATENT IN VIEW OF HANCOCK RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Hancock is a publication that was published in January 1997. Accordingly, Hancock is 102(b) prior art to the '359 patent. As explained below, the combined teachings of the '523 patent in view of Hancock rendered obvious each claim of the '359 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 still 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 '523 patent fully taught ritonavir and its use as an HIV protease inhibitor. Hancock taught that, "[t]he amorphous state is critical in determining the solid-state physical and chemical properties of many pharmaceutical dosage forms," and "[t]he high internal energy and specific volume of the amorphous state relative to the crystalline state can lead to enhanced dissolution and bioavailability." Hancock, Abstract and 2. Hancock further taught the four most common ways in which amorphous character can be induced in pharmaceutical systems, namely (i) vapor condensation, (ii) precipitation from solution, (iii) supercoolng of melt, and (iv) milling and compaction of crystals. Hancock, 1. Therefore, Hancock expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir, as Hancock teaches the four well known methods for doing so. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of the '359 patent were obvious in light of the combined teachings of the '523 patent in view of Hancock. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'523 patent in view of Hancock**
1. Substantially pure amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed.

'359 patent	'523 patent in view of Hancock
	Therefore, one of ordinary skill in the art would have pursued the creation of substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '523 patent in view of Hancock would have a glass transition temperature within the claimed range.
3. A composition comprising amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '523 patent in view of Hancock would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95% would be in amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

THE '523 PATENT IN VIEW OF ROYALL RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Royall is a publication that was received for publication in November 1997. Accordingly, Royall is 102(a) prior art to the '359 patent. As explained below, the combined teachings of the '523 patent in view of Royall rendered obvious each claim of the '359 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 still 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 '523 patent fully taught ritonavir and its use as an HIV protease inhibitor. Royall taught that, "[t]he significance of the amorphous state in pharmaceutical systems has been widely discussed" and then continued to specifically investigate the amorphous state of the HIV protease inhibitor saquinavir. 1117-1118. Therefore, Royall expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of

the '359 patent were obvious in light of the combined teachings of the '523 patent in view of Royall. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'523 patent in view of Royall**
1. Substantially pure amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '523 patent in view of Royall would have a glass transition temperature within the claimed range. Royall in fact specifically taught how to analyze the glass transition temperature of an amorphous HIV protease inhibitor.
3. A composition comprising amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '523 patent in view of Royall would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95% would be in

'359 patent	'523 patent in view of Royall
	amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

THE '523 PATENT IN VIEW OF HANCOCK AND FURTHER IN VIEW OF ROYALL RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Hancock is a publication that was published in January 1997 and Royall is a publication that was received for publication in November 1997. Accordingly, Hancock is 102(b) prior art to the '359 patent and Royall is 102(a) prior art to the '359 patent. As explained below, the combined teachings of the '523 patent in view of Hancock and further in view of Royall rendered obvious each claim of the '359 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 still 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 '523 patent fully taught ritonavir and its use as an HIV protease inhibitor. Hancock taught that, "[t]he amorphous state is critical in determining the solid-state physical and chemical properties of many pharmaceutical dosage forms," and "[t]he high internal energy and

specific volume of the amorphous state relative to the crystalline state can lead to enhanced dissolution and bioavailability." Hancock, Abstract and 2. Hancock further taught the four most common ways in which amorphous character can be induced in pharmaceutical systems, namely (i) vapor condensation, (ii) precipitation from solution, (iii) supercoolng of melt, and (iv) milling and compaction of crystals. Hancock, 1. Royall taught that, "[t]he significance of the amorphous state in pharmaceutical systems has been widely discussed" and then continued to specifically investigate the amorphous state of the HIV protease inhibitor saquinavir. 1117-1118. Therefore, Hancock and Royall each expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir, as Hancock teaches the four well known methods for doing so. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of the '359 patent were obvious in light of the combined teachings of the '523 patent in view of Hancock ad further in view of Royall. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'523 patent in view of Hancock and further in view of Royall**
1. Substantially pure amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed, and Royall taught, motivated and suggested

'359 patent	'523 patent in view of Hancock and further in view of Royall
	investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '523 patent in view of Hancock and further in view of Royall would have a glass transition temperature within the claimed range. Royall in fact specifically taught how to analyze the glass transition temperature of an amorphous HIV protease inhibitor.
3. A composition comprising amorphous ritonavir.	The '523 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed, and Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '523 patent in view of Hancock and further in view of Royall would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95%

'359 patent	'523 patent in view of Hancock and further in view of Royall
	would be in amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

THE '823 PATENT IN VIEW OF HANCOCK RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Hancock is a publication that was published in January 1997. Accordingly, Hancock is 102(b) prior art to the '359 patent. As explained below, the combined teachings of the '823 patent in view of Hancock rendered obvious each claim of the '359 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 still 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 '823 patent fully taught ritonavir and its use as an HIV protease inhibitor. Hancock taught that, "[t]he amorphous state is critical in determining the solid-state physical and chemical properties of many pharmaceutical dosage forms," and "[t]he high internal energy and specific volume of the amorphous state relative to the crystalline state can lead to enhanced

dissolution and bioavailability." Hancock, Abstract and 2. Hancock further taught the four most common ways in which amorphous character can be induced in pharmaceutical systems, namely (i) vapor condensation, (ii) precipitation from solution, (iii) supercoolng of melt, and (iv) milling and compaction of crystals. Hancock, 1. Therefore, Hancock expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir, as Hancock teaches the four well known methods for doing so. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of the '359 patent were obvious in light of the combined teachings of the '823 patent in view of Hancock. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'823 patent in view of Hancock**
1. Substantially pure amorphous ritonavir.	The '823 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed. Therefore, one of ordinary skill in the art would have pursued the creation of substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '823 patent in view of Hancock would have a glass transition temperature within the claimed range.
3. A composition comprising amorphous	The '823 patent disclosed ritonavir compounds.

'359 patent	'823 patent in view of Hancock
ritonavir.	Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '823 patent in view of Hancock would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95% would be in amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Hancock taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

THE '823 PATENT IN VIEW OF ROYALL RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Royall is a publication that was received for publication in November 1997. Accordingly, Royall is 102(a) prior art to the '359 patent. As explained below, the combined teachings of the '823 patent in view of Royall rendered obvious each claim of the '359 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 still 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 '823 patent fully taught ritonavir and its use as an HIV protease inhibitor. Royall taught that, "[t]he significance of the amorphous state in pharmaceutical systems has been widely discussed" and then continued to specifically investigate the amorphous state of the HIV protease inhibitor saquinavir. 1117-1118. Therefore, Royall expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of the '359 patent were obvious in light of the combined teachings of the '823 patent in view of Royall. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'823 patent in view of Royall**
1. Substantially pure amorphous ritonavir.	The '823 patent disclosed ritonavir compounds. Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of

'359 patent	'823 patent in view of Royall
	substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '823 patent in view of Royall would have a glass transition temperature within the claimed range. Royall in fact specifically taught how to analyze the glass transition temperature of an amorphous HIV protease inhibitor.
3. A composition comprising amorphous ritonavir.	The '823 patent disclosed ritonavir compounds. Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '823 patent in view of Royall would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95% would be in amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

THE '823 PATENT IN VIEW OF HANCOCK AND FURTHER IN VIEW OF ROYALL RENDERED THE '359 PATENT OBVIOUS

As discussed above, the earliest possible priority date for the '359 patent is July 20, 1998. Hancock is a publication that was published in January 1997 and Royall is a publication that was received for publication in November 1997. Accordingly, Hancock is 102(b) prior art to the '359 patent and Royall is 102(a) prior art to the '359 patent. As explained below, the combined teachings of the '823 patent in view of Hancock and further in view of Royall rendered obvious each claim of the '359 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 still 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 '823 patent fully taught ritonavir and its use as an HIV protease inhibitor. Hancock taught that, "[t]he amorphous state is critical in determining the solid-state physical and chemical properties of many pharmaceutical dosage forms," and "[t]he high internal energy and specific volume of the amorphous state relative to the crystalline state can lead to enhanced dissolution and bioavailability." Hancock, Abstract and 2. Hancock further taught the four most common ways in which amorphous character can be induced in pharmaceutical systems, namely (i) vapor condensation, (ii) precipitation from solution, (iii) supercoolng of melt, and (iv) milling and compaction of crystals. Hancock, 1. Royall taught that, "[t]he significance of the amorphous state in pharmaceutical systems has been widely discussed" and then continued to

specifically investigate the amorphous state of the HIV protease inhibitor saquinavir. 1117-1118. Therefore, Hancock and Royall each expressly taught, suggested and motivated the creation and investigation of amorphous forms of pharmaceuticals and specifically HIV protease inhibitors like ritonavir.

This is not the case where there would be an unlimited number of parameters to try in order to achieve amorphous ritonavir, as Hancock teaches the four well known methods for doing so. Therefore, one of ordinary skill in the art was expressly motivated to derive amorphous ritonavir in order to determine its pharmacological characteristics and was expressly taught how to do so. As such, and as set forth in the chart below, the claims of the '359 patent were obvious in light of the combined teachings of the '823 patent in view of Hancock ad further in view of Royall. Therefore each claim of the '359 patent is invalid and should be canceled.

'359 patent	**'823 patent in view of Hancock and further in view of Royall**
1. Substantially pure amorphous ritonavir.	The '823 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed, and Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of substantially pure amorphous ritonavir as claimed here.
2. The substantially pure amorphous ritonavir of claim 1 characterized by a glass transition from about 45° C. to about 49° C.	It would be expected that the amorphous ritonavir rendered obvious by the '823 patent in view of Hancock and further in view of Royall would have a glass transition temperature within the claimed range. Royall in fact specifically taught how to analyze the glass

'359 patent	'823 patent in view of Hancock and further in view of Royall
	transition temperature of an amorphous HIV protease inhibitor.
3. A composition comprising amorphous ritonavir.	The '823 patent disclosed ritonavir compounds. Hancock taught, motivated and suggested that the amorphous form of pharmaceutical compounds be derived and analyzed, and Royall taught, motivated and suggested investigation into the amorphous forms of specifically HIV protease inhibitors, like ritonavir. Therefore, one of ordinary skill in the art would have pursued the creation of amorphous ritonavir as claimed here.
4. The composition of claim 3, wherein said amorphous ritonavir is substantially pure.	The amorphous ritonavir rendered obvious by the '823 patent in view of Hancock and further in view of Royall would include substantially pure amorphous ritonavir.
5. The composition of claim 3, wherein greater than about 90% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 90% would be in amorphous form.
6. The composition of claim 3, wherein greater than about 95% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 95% would be in amorphous form.
7. The composition of claim 3, wherein greater than about 97% of ritonavir in said composition is amorphous ritonavir.	Both Hancock and Royall taught, motivated and suggested derivation and analysis of amorphous pharmaceutical compounds, including those wherein greater than 97% would be in amorphous form.

CONCLUSION

For the reasons set forth above, each of the claims of the '359 patent is invalid. Accordingly, PUBPAT respectfully requests that they be reexamined *inter partes* and subsequently canceled.

September 23, 2010
Date

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CERTIFICATE OF SERVICE

The undersigned certifies that a copy of this CORRECTED ATTACHMENT TO FORM PTO/SB/58, REQUEST FOR INTER PARTES REEXAMINATION, 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. 7,148,359 as provided for in 37 C.F.R. § 1.33(c):

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