PTO/SB/57 (02-09)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also referred to as FORM PTO-1465)

REQUEST FOR *EX PARTE* REEXAMINATION TRANSMITTAL FORM

Address to:
Mail Stop *Ex Parte* 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 *ex parte* reexamination pursuant to 37 CFR 1.510 of patent number 5,635,523 issued June 3, 1997. The request is made by:
   [ ] patent owner. [x] third party requester.

2. [x] 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**
   [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 1.510(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. [x] A copy of any disclaimer, certificate of correction or reexamination certificate issued in the patent is included.

9. [x] Reexamination of claim(s) 1-10 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 1.510(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. [x] 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

[x] Firm or Individual Name Public Patent Foundation

Address

55 Fifth Avenue, Suite 928

City 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:

_____

_____

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.

[ ] For Patent Owner Requester
[x] For Third Party Requester

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT NO.: 5,635,523

ISSUED: Jun. 3, 1997

TO: Kempf et al.

FOR: RETROVIRAL PROTEASE INHIBITING COMPOUNDS

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. 5,635,523 issued June 3, 1997, to Kempf et al. and assigned to Abbott Laboratories ("the '523 patent") because they are all invalid under 35 U.S.C. §§ 102 and 103 and their existence is causing significant public harm.[1]

THE '523 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 '523 patent is attached hereto as Appendix A.
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 '523 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 '523 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 '523 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 '523 patent merits review by your office.

THE SUBSTANTIAL NEW QUESTIONS OF PATENTABILITY

1. Whether claims 1-10 of the '523 patent were anticipated or rendered obvious by U.S. Patent No. 5,142,056 to Kempf et al. issued on August 25, 1992 ("'056 patent");

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).

2. Whether claims 1-10 of the '523 patent were anticipated or rendered obvious by EP 337714A2, to Sigal et al. published on October 18, 1989 ("Sigal"); and
3. Whether claims 1-10 of the '523 patent were rendered obvious by Ho et al., Nature vol. 375 Jan. 12, 1995 "Rapid Turnover of Plasma Virions and CD4 Lymphocytes in HIV-1 Infection" ("Ho") in light of the '056 patent and/or Sigal.

These are new questions because neither the '056, Sigal nor Ho were cited as references, much less applied, during prosecution. A detailed explanation of the pertinency and manner of applying the cited patents and publications to the claims of the '523 patent is set forth below.[5]

THE '056 PATENT ANTICIPATED OR RENDERED OBVIOUS THE '523 PATENT

The '523 patent application was filed April 6, 1995. The applicants claimed priority to a series of applications, including application no. 07/998,114 (filed December 29, 1992) and application number 08/158,587 (filed December 2, 1993). However, the claims of the '523 patent are not entitled to those claims of priority because the specifications of those earlier applications were not sufficient to satisfy the written description requirement of 35 U.S.C. § 112 with respect to the ten claims of the '523 patent.

The Federal Circuit recently confirmed that the written description requirement is a separate statutory requirement from the best mode and enablement requirements. Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010). To satisfy the written description requirement, a specification must describe the claimed invention so that one of ordinary skill in the art can recognize what is claimed. Further, sufficient detail must be included in the specification to show one of ordinary skill in the art that the applicant possessed

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

the claimed invention at the time of the filing of the application.

In this case, the inventors did not possess the claimed invention at the time of filing of the claimed priority applications because the specifications lacked evidence that the claimed methods were effective *in vivo*. The only evidence of efficacy was *in vitro*. and no evidence of the correlation between the *in vitro* results and successful treatment in humans was provided. Many antiviral agents that provide exceptional results *in vitro* are ineffective *in vivo*. This principle is substantiated by a 1987 review article[6] indicating that *in vitro* testing performed on anti-viral compounds is useful as a screening tool but is not predictive of *in vivo* efficacy. The specifications of the purported priority applications lacked *in vivo* data supporting the efficacy of the claimed methods, which thus renders them insufficient to satisfy the written description requirement. Therefore, the '523 patent is not entitled to claim priority to those earlier applications. Thus, the effective filing date of the '523 patent is its specific filing date, April 6, 1995.

The '056 patent issued on August 25, 1992. Accordingly, the '056 patent is 102(b) prior art to the '523 patent. As explained below, the '056 patent renders each claim of the '523 patent invalid.

In 2007 the Federal Circuit specifically addressed the standard for obviousness in another case involving a pharmaceutical composition. In that case, Pfizer v. Apotex, the patented besylate salt of the compound amlodipine was held obvious over a prior art patent that claimed a genus of pharmaceutically acceptable salts of amlodipine even though it did not disclose the besylate salt. 480 F.3d 1348 (Fed. Cir. 2007). The besylate salt was found obvious despite the

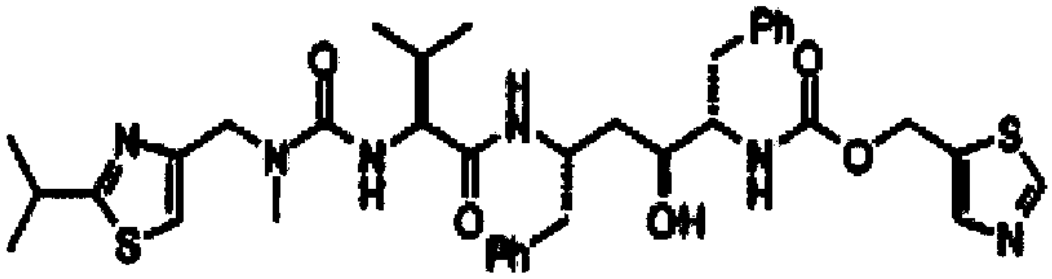
6 Sandstrom et al., "Antiviral Therapy In AIDS: Clinical Pharmacological Properties and Therapeutic Experience to Date," Drugs 34: 373-390 (1987).

fact that none of the anions listed in the prior art patent had a cyclic structure as does besylate and it was undisputed that one cannot reliably predict the influence of a particular salt species on the behavior of a parent compound. The Federal Circuit's obviousness decision was based on the skilled artisan's motivation to combine prior art teachings to achieve the claimed invention and reasonable expectation of success. *Id.* at 1361. The Pfizer v. Apotex case is instructive as to the obviousness of the '523 patent over the '056 patent.

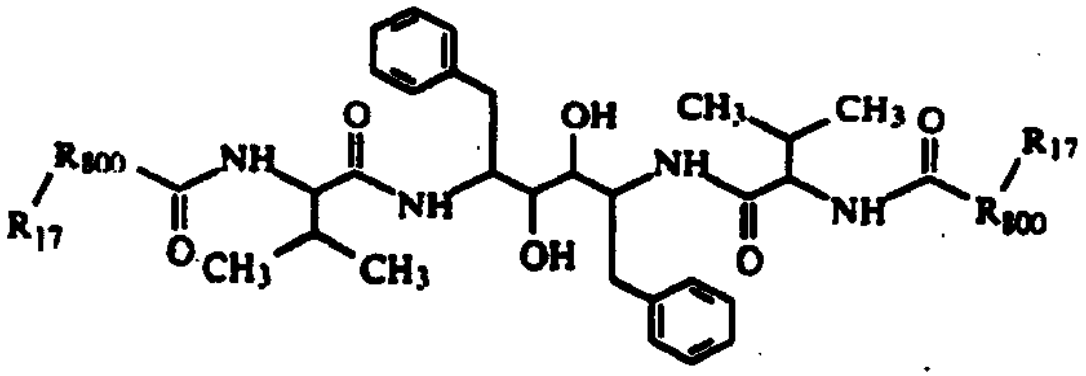
The '523 patent contains ten claims. Each one recites a method of inhibiting an HIV infection using a named retroviral protease inhibiting compound along with at least one reverse transcriptase inhibitor. Claim 1 is the broadest claim and reads as follows:

> 1. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a reverse transcriptase inhibitor.

The remaining claims vary only in the selection of reverse transcriptase inhibitor(s) used with the named compound. The compound having the formula recited in the claims is depicted as follows:



A compound disclosed in the '056 patent is depicted as follows:



The claimed compound and the compound taught by the '056 patent have the same central substituent. Therefore, the '056 patent anticipates the claims of the '523 patent. The additional hydroxyl group described in the '523 patent is inherent in or obvious in light of the '056 patent compound.

The chart below sets forth a comparison of all ten claims of the '523 patent to the teaching of the '056 patent. In essence, the formula recited in the method claims of the '523 patent represents a genus of or is rendered obvious by the class of compounds disclosed in the '056 patent, which have virtually the same central substituent and are described as being useful in the treatment of HIV/AIDS. The method of combining the compound with a retroviral protease inhibitor to inhibit HIV infection is explicitly disclosed in the '056 specification. Although the '056 patent may not have explicitly disclosed the exact compound recited in the '523 patent, each element of the '523 patent's claims is either inherent in or rendered obvious by the '056 patent's teachings. Therefore each claim of the '523 patent is invalid and should be canceled.

'523 patent	**'056 patent**
1. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-	The '056 patent claims compounds and pharmaceutically acceptable salts of compounds having the same central substituent as the compound of claim 1, save the presence of a second hydroxyl group. The equivalence

'523 patent	'056 patent
amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a reverse transcriptase inhibitor.	of central substituents differing only by a second hydroxyl group was known in the art. The '056 specification teaches the utility of the disclosed compounds for the treatment of AIDS/HIV when administered in combination with one or more retroviral protease inhibitors including DDC and AZT (col. 220). The '056 specification also teaches that agents which can be combined with the disclosed compounds include any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.
2. The method of claim 1 wherein the reverse transcriptase inhibitor is selected from the group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, AzdU, carbovir, DDA, D4C, D4T, DP-AZT, FLT (fluorothymidine), BCH-189, 5-halo-3'-thiadieoxycitidine, PMEA, zidovudine (AZT).	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
3. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
4. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxycitidine.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
5. A method for inhibiting an HIV infection	As discussed above, the '056 patent disclosed a

'523 patent	'056 patent
comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxyinosine.	method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
6. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of D4T.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
7. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of 5-halo-3'-thia-dideoxycitidine.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
8. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.

'523 patent	'056 patent
combination with a therapeutically effective amount of BCH-189.	
9. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine and a therapeutically effective amount of one or more other reverse transcriptase inhibitors selected from the group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, DDA, D4C, D4T and DP-AZT.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
10. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine and a therapeutically effective amount of BCH-189.	As discussed above, the '056 patent disclosed a method of inhibiting HIV infection which included one or more reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.

SIGAL ANTICIPATED OR RENDERED OBVIOUS THE '056 PATENT

In addition to being anticipated or rendered obvious by the '056 patent, the '523 patent was also anticipated or rendered obvious by Sigal. The Sigal application was published October 18, 1989. Accordingly, it is 102(b) prior art to the '523 patent which has an effective filing date of April 6, 1995 as explained above. Pfizer v. Apotex is again instructive as to why the '523

patent is invalid over Sigal.

The chart below sets forth an element-by-element comparison of all ten claims of the '523 patent to the teaching of Sigal. In essence, the formula recited in the method claims of the '523 patent represents a genus of or is rendered obvious by the class of compounds disclosed in Sigal. Sigal discloses compounds having the identical central substituent as that of the compound named in the claims of the '523 patent and pharmaceutically acceptable salts thereof. Sigal at 42. It teaches the utility of such compounds in the inhibition of HIV protease, the prevention or treatment of infection by the human immunodeficiency virus (HIV) and the treatment of consequent pathological conditions such as AIDS. Id. Its invention is directed toward the combination of the disclosed compounds with other agents useful in the treatment of AIDS, such as the reverse transcriptase inhibitors DDC and AZT. Id. at 42-44. Although Sigal may not have explicitly disclosed the exact compound recited in the '523 patent, each element of the '523 patent's claims is either inherent in or rendered obvious by Sigal's teachings. Therefore each claim of the '523 patent is invalid and should be canceled.

'523 patent	**Sigal**
1. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a reverse transcriptase inhibitor.	Sigal discloses compounds and pharmaceutically acceptable salts of compounds having the identical central substituent as the compound of claim 1. Sigal teaches the utility of the disclosed compounds for the treatment of AIDS/HIV when administered in combination with one or more retroviral protease inhibitors including DDC and AZT. pp.42-44. Sigal also teaches that agents which can be combined with the disclosed compounds include other agents useful for the treatment of AIDS.
2. The method of claim 1 wherein the reverse transcriptase inhibitor is selected from the	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included

'523 patent	Sigal
group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, AzdU, carbovir, DDA, D4C, D4T, DP-AZT, FLT (fluorothymidine), BCH-189, 5-halo-3'-thiadieoxycitidine, PMEA, zidovudine (AZT).	reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
3. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
4. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxycitidine.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
5. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxyinosine.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
6. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not

'523 patent	Sigal
(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of D4T.	limit such reverse transcriptase inhibitors to those listed in the specification.
7. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of 5-halo-3'-thia-dideoxycitidine.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
8. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of BCH-189.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.
9. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine and a therapeutically	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.

'523 patent	Sigal
effective amount of one or more other reverse transcriptase inhibitors selected from the group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, DDA, D4C, D4T and DP-AZT.	
10. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine and a therapeutically effective amount of BCH-189.	As discussed above, Sigal disclosed a method of inhibiting HIV infection which included reverse transcriptase inhibitors and did not limit such reverse transcriptase inhibitors to those listed in the specification.

THE '523 PATENT WAS RENDERED OBVIOUS BY HO IN VIEW OF THE '056 PATENT AND/OR SIGAL

Ho, published in January of 1995, predates the April 1995 filing of the '523 application and is thus prior art to the '523 patent under 102(a). Ho provides *in vivo* evidence that the compound recited in the claims of the '523 patent, referred to as ABT-538 in the article, was effective in treating HIV when administered to humans. Ho at 123. Ho thus rendered obvious the invention claimed in the '523 patent. The chart below sets forth an element-by-element comparison of all ten claims of the '523 patent to the teaching of Ho. Because Ho disclosed a method of treatment using the exact compound recited in the '523 patent, the '523 patent's claims are rendered obvious in light thereof. Although Ho did not explicitly disclose the combination of the compound with one or more reverse transcriptase inhibitors, this element of the invention was rendered obvious in light of the '056 patent and/or Sigal, both discussed above. Therefore

each claim of the '523 patent is invalid and should be canceled.

'523 patent	Ho in view of the '056 Patent and/or Sigal
1. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of a reverse transcriptase inhibitor.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
2. The method of claim 1 wherein the reverse transcriptase inhibitor is selected from the group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, AzdU, carbovir, DDA, D4C, D4T, DP-AZT, FLT (fluorothymidine), BCH-189, 5-halo-3'-thiadieoxycitidine, PMEA, zidovudine (AZT).	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
3. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
4. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not

'523 patent	Ho in view of the '056 Patent and/or Sigal
(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxycitidine.	specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
5. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of dideoxyinosine.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
6. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of D4T.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
7. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill

'523 patent	Ho in view of the '056 Patent and/or Sigal
pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of 5-halo-3'-thia-dideoxycitidine.	in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
8. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of BCH-189.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
9. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in combination with a therapeutically effective amount of zidovudine and a therapeutically effective amount of one or more other reverse transcriptase inhibitors selected from the group consisting of dideoxycitidine (DDC), dideoxyinosine (DDI), BCH-189, DDA, D4C, D4T and DP-AZT.	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to combine the teachings of these references because they each relate to the same field and problem.
10. A method for inhibiting an HIV infection comprising administering to a human in need thereof a therapeutically effective amount of (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl- 4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane or a pharmaceutically acceptable salt thereof in	Ho taught the efficacy of a method in which the claimed compound was administered to humans in need thereof. Although Ho did not specifically disclose the combination of the compound with a reverse transcriptase inhibitor, such combinations were obvious in light of prior art, including the '056 patent and Sigal, discussed above. One of ordinary skill in the art would have been motivated to

'523 patent	Ho in view of the '056 Patent and/or Sigal
combination with a therapeutically effective amount of zidovudine and a therapeutically effective amount of BCH-189.	combine the teachings of these references because they each relate to the same field and problem.

CONCLUSION

For the reasons set forth above, each of the claims of the '523 patent is invalid. Accordingly, PUBPAT respectfully requests that they be examined *ex parte* and subsequently canceled.

August 25, 2010

Date

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APPENDIX A

APPENDIX B

PTO/SB/08a (07-09)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 2

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

U. S. PATENT DOCUMENTS

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

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-Kind Code[5] (if known)	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]
		EP 0 337 714 A2	10-18-1989	Merck & Co. Inc.		

Examiner Signature		Date Considered	

*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.

PTO/SB/08b (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 2 of 2

Complete if Known	
Application Number	09/___,___
Filing Date	
First Named Inventor	Kempf, Dale J.
Art Unit	
Examiner Name	
Attorney Docket Number	

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
		HO et al., Rapid Turnover of Plasma Virions and CD4 Lymphocytes in HIV-1 Infection, Nature, 373: 123-126, January 1995.	

Examiner Signature		Date Considered	

*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 Applicant is to place a check mark here if English language Translation is attached.