IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC, PFIZER PHARMACEUTICALS, LLC, PFIZER LIMITED, C.P. PHARMACEUTICALS INTERNATIONAL C.V., PFIZER IRELAND PHARMACEUTICALS, WARNER-LAMBERT COMPANY, WARNER-LAMBERT COMPANY, LLC and WARNER-LAMBERT EXPORT LTD,	)	
Plaintiffs/Counterdefendants,	)	C.A. No. 07-138-JJF
v.	)	
RANBAXY LABORATORIES LIMITED, and RANBAXY INC.,	)	
Defendants/Counterclaimants.	)	

RANBAXY'S BRIEF IN OPPOSITION TO PFIZER'S MOTION TO DISMISS AND FOR PARTIAL JUDGMENT ON THE PLEADINGS PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 12(c)

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Defendants/Counterclaimants Ranbaxy Laboratories Limited and Ranbaxy Inc. (collectively "Ranbaxy") hereby oppose Pfizer's Motion To Dismiss and for Partial Judgment on the Pleadings Pursuant to Federal Rule of Civil Procedure 12(c).

I. INTRODUCTION

In this lawsuit, Pfizer seeks to delay the approval and marketing of Ranbaxy's generic version of Pfizer's Caduet® product. Pfizer's Caduet product is nothing more than a combination of two well-known, already-marketed drugs, combined for their intended purposes: Lipitor® (atorvastatin calcium) to treat high cholesterol and Norvasc® (amlodipine besylate) to treat high blood pressure. Pfizer asserts that Ranbaxy's Abbreviated New Drug Application ("ANDA") No. 78-747, for a generic version of Caduet, infringes U.S. Patent Nos. 6,455,574 ("the '574 patent") and 4,681,893 ("the '893 patent").

Pfizer's current Motion seeks to dismiss Ranbaxy's First Counterclaim and Third Affirmative Defense, which both assert that the '893 patent is invalid for obviousness under 35 U.S.C. § 103. Pfizer requests dismissal based on *res judicata* and/or collateral estoppel in view of *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, Civ. Action No. 03-209 (JJF), previously before this Court (the "Lipitor litigation"). That case involved an ANDA submitted by Ranbaxy Laboratories Limited, which sought approval to market a generic version of Pfizer's Lipitor product. However, the issue of obviousness of the '893 patent was not presented at trial or otherwise adjudicated in the Lipitor litigation.

Pfizer's assertion of *res judicata* and/or collateral estoppel fails in this new and distinct case because significant legal and factual changes have occurred that fundamentally alter the obviousness analysis of the '893 patent. At the time of the

Lipitor litigation, a party seeking to invalidate a patent for obviousness was rigidly required to show that there existed a "teaching, suggestion or motivation" to combine the prior art to arrive at the claimed invention, a burden referred to as the "TSM" test. However, in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), the Supreme Court recently dramatically lowered the bar of 35 U.S.C. § 103 by removing the TSM test as an absolute prerequisite for proving obviousness.

Additionally, a critical change in fact also renders the issue of obviousness fundamentally different than it was in the Lipitor litigation. During discovery in the Lipitor litigation, Pfizer withheld critical information about data it had relied on to gain issuance of the European counterpart to the '893 patent. This data purportedly demonstrated that the compounds of the '893 patent had unexpected activity compared to the compounds in the prior art. Ranbaxy was given no reason to challenge the reliability of this data until Pfizer, near trial and well after the close of discovery, revealed that the data was mislabeled as having been obtained using a test known as the "COR" test, but was actually obtained using a completely different test known as the "CSI" test. Thus, Ranbaxy was unable to timely analyze and compare this CSI data with other CSI test results — results which would have shown that no unexpected results existed for the compounds of the '893 patent.

Constrained by both the prior TSM legal hurdle and the withheld information regarding Pfizer's test data, Ranbaxy could not have presented an obviousness challenge to the '893 patent in the Lipitor litigation. Now, given the drastic change in the legal and factual landscape present in the current Caduet litigation, however, Ranbaxy should not be prejudicially bound to an earlier judgment in a different case involving a different

cause of action and demand, rendered under significantly different circumstances that were out of Ranbaxy's control. Importantly, Ranbaxy is not seeking to re-litigate issues decided in the Lipitor litigation, but only to adjudicate the narrow issue of obviousness of the '893 patent in the present Caduet dispute. Accordingly, the Court should deny Pfizer's Motion and allow Ranbaxy to challenge the validity of the '893 patent under 35 U.S.C. § 103 in the present litigation.

II. NATURE AND STAGE OF THE PROCEEDING

Pfizer's brief sets forth the nature and stage of these proceedings. (D.I. 17 at 1-2). This is Ranbaxy's brief in opposition to Pfizer's Motion to dismiss Ranbaxy's Counterclaim and Affirmative Defense of invalidity of the '893 patent for obviousness, and for partial judgment on the pleadings.

III. SUMMARY OF ARGUMENT

1. Given the substantial intervening changes in law and fact, Ranbaxy's First Counterclaim and Third Affirmative Defense regarding the invalidity of the '893 patent for obviousness under 35 U.S.C. § 103 are not barred by *res judicata* and/or collateral estoppel based on the prior Lipitor litigation.

2. The Court should not enter judgment on the pleadings on Pfizer's First Claim for Relief, regarding infringement of the '893 patent, while the validity of the '893 patent is still in dispute.

IV. STATEMENT OF FACTS

Pfizer's brief sets forth certain facts underlying these proceedings. (*Id.* at 2-6). Ranbaxy provides the following additional facts:[1]

In 2003, Pfizer commenced the Lipitor litigation against Ranbaxy Laboratories Limited ("RLL") and Ranbaxy Pharmaceuticals Inc. ("RPI"). (D.I. 1 (Complaint), ¶¶ 26-29). The basis of that litigation was RLL's filing of an ANDA seeking approval to market a generic version of Pfizer's Lipitor product. (*Id.*). The present litigation concerns RLL's filing of an ANDA seeking approval to market a generic version of Caduet, a product that combines Lipitor (atorvastatin calcium) and Norvasc (amplodipine besylate). (*Id.* ¶¶ 16-18). Pfizer has sued RLL and Ranbaxy Inc. in the present litigation; RPI is not a party to this litigation. (*Id.* at Opening Paragraph).

In the Lipitor litigation, RLL's and RPI's Second Affirmative Defense asserted that the '893 patent "is invalid for violation of one or more provisions of 35 U.S.C. §§ 101, 102, 103, and/or 112." (Lipitor litigation D.I. 37, Answer ¶ 36). RLL and RPI also asserted invalidity of the '893 patent on various grounds, including obviousness, in its Second Counterclaim. (*Id.*, Counterclaim ¶ 15). The obviousness of the '893 patent was not presented at trial or decided in the Lipitor litigation.

In the present case, Ranbaxy's Affirmative Defense and Counterclaim of invalidity due to obviousness of the '893 patent are based, *inter alia*, on EP 179 559 ("the '559 publication"). *See* Attachment A ('559 publication, relevant portions attached

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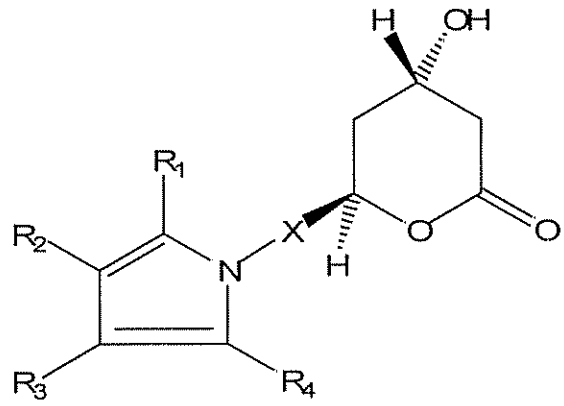
[1] As Pfizer notes in its Motion, a district court deciding a motion for judgment on the pleadings may take judicial notice of the factual record of a prior proceeding. (D.I. 17 at 8 (citing *Oneida Motor Freight, Inc. v. United Jersey Bank*, 848 F.2d 414, 416 & n.3 (3d Cir. 1988))). Ranbaxy will identify facts from the prior Lipitor litigation by their docket index number or trial exhibit number in that case.

hereto, produced in the Lipitor litigation at P0267818-96). The '559 publication is a European patent application filed by Warner-Lambert Company (Pfizer's predecessor-in-interest, hereinafter "Warner-Lambert") that was published on April 30, 1986. (*Id.*). Its counterpart in the United States is Patent No. 4,647,576. (Lipitor litigation trial exhibit DTX-261). The '559 publication discloses compounds that are nearly identical to those claimed in the '893 patent, and which are taught to be useful for the same indication, *i.e.*, lowering blood serum cholesterol. (*Compare* Attachment A ('559 publication) at P0267819-21, *with* D.I. 1 (Complaint), Ex. A ('893 patent) at col. 1). The '559 publication discloses Formula I (below) and teaches that various substituents can be used for groups R_1, R_2, R_3, R_4 and X. (*Id.* at P0267821-23).



Formula I, disclosed in the '559 publication, is identical to Formula I disclosed and claimed in the '893 patent. (D.I. 1 (Complaint), Ex. A ('893 patent) at col. 2, Claim 1). Moreover, the similarities between the disclosure of the '559 publication and the '893 patent are even greater. The '559 publication discloses several compounds having the same substituents for R_1, R_2, R_4 and X as those of atorvastatin lactone, which is disclosed and claimed in the '893 patent. (*Compare* Attachment A ('559 publication) at P0267821-23, P0267831, *with* D.I. 1 (Complaint), Ex. A ('893 patent) at col. 2, ll. 3-38, Table 1 (Compound 1), col. 10, ll. 40-44, Claims 1, 2, 3, 4 and 5). Thus, the only

difference between the disclosure of the '559 publication and the atorvastatin lactone claimed in the '893 patent lies in the R_3 (lower left) substituent.

During the prosecution of the European counterpart to the '893 patent (EP 247 633, hereinafter "the '633 patent"), the Examiner rejected the claims as merely an obvious solution to the problem of providing active compounds similar to those described in the '559 publication. (Lipitor litigation trial exhibit DTX-331 at RA017527-28) (relevant portions attached hereto as Attachment B). The Examiner indicated, however, that if data were presented demonstrating that the claimed compounds showed surprising effectiveness compared to those in the '559 publication, the claims would be allowed. (*Id.* at RA017528).

In response, Warner-Lambert stated:

> Applicants generally accept the Examining Division's arguments saying that a person skilled in the art would expect that the pyrazole [sic] ring was susceptible to further substitutions at the 3 and 4 position including other carboxy derivatives . . . without leading to a significant change in qualitative properties.

(*Id.* at RA017516). To overcome the rejection, Warner-Lambert presented data allegedly showing unexpected results of the '893 patent compounds over the '559 publication compounds. (*Id.* at RA017520). Warner-Lambert represented that this data was from a test known as the "COR" test. (*Id.*).

On September 3, 2004, several months after the close of discovery in the Lipitor litigation, Pfizer revealed that the data submitted during prosecution of the '633 patent purporting to be "COR" data was actually data from a completely different test known as the "CSI" test, and specifically from CSI screen 124. (Lipitor litigation D.I. 191). As this Court is well-aware, at trial in the Lipitor litigation, the parties and the experts

strongly disagreed about the accuracy and reliability of Warner-Lambert's CSI test data as a whole. (*See, e.g.*, Lipitor litigation D.I. 292 (Ranbaxy's Opening Post-Trial Brief) at 40; *see generally* Lipitor litigation D.I. 289, 308 and 310). Moreover, when properly recognized as CSI data, the data relied upon by Warner-Lambert to show unexpected activity over the prior art can be compared with other Warner-Lambert data obtained using the same CSI test, but which were not disclosed to the European Patent Office. (*See, e.g.*, Lipitor litigation trial exhibit DTX-3347). Such a comparison reveals that no unexpected results exist.

Thus, while RLL and RPI were aware of the prosecution of the '633 patent during discovery in the Lipitor litigation, RLL and RPI only learned the truth about the mislabeled CSI data after discovery had closed and the parties were making final preparations for trial. Neither RLL, RPI, nor Pfizer presented any evidence at trial, nor made any arguments on appeal, regarding the obviousness of the '893 patent.

V. ARGUMENT

A. The Law Of *Res Judicata*

Pfizer's brief sets forth the general standard for *res judicata*. (D.I. 17 at 9-11). While there is some ambiguity as to whether Federal Circuit or Third Circuit law applies, there appears to be little difference between the standards applied by both Circuits. (*Id.* at 11). Under Federal Circuit law, *res judicata* bars a suit where there has been a judgment on the merits in a prior suit involving the same parties or their privies based on the same cause of action. *See In re Bose Corp.*, 476 F.3d 1331, 1335 (Fed. Cir. 2007) (citing *Parklane Hosiery Co. v. Shore*, 439 U.S. 322, 326 (1979)).

The Supreme Court has recognized that appropriate limitations must be placed on the doctrine of *res judicata*. Specifically, the Supreme Court has noted that, "*res judicata*

is no defense where between the time of the first judgment and the second there has been an intervening decision or a change in the law creating an altered situation." *State Farm Mut. Auto Ins. Co. v. Duel*, 324 U.S. 154, 162 (1945); *see also Bose*, 476 F.3d at 1335-36 (Federal Circuit applying *res judicata* only after assessing whether an intervening Supreme Court ruling prevented its application).

Courts have also refused to apply *res judicata* where an intervening change in the factual circumstances has occurred. *See Brown v. Felsen*, 442 U.S. 127, 132-34 (1979) (refusing to apply *res judicata* in view of intervening change in circumstances); *Mayer/Berkshire Corp v. Berkshire Fashions, Inc.*, 424 F.3d 1229, 1234 (Fed. Cir. 2005) (finding *res judicata* inapplicable based on evidence of "changed circumstances" following district court judgment); *Comm'r of Internal Revenue v. Thomas Flexible Coupling Co.*, 198 F.2d 350, 353 (3d Cir. 1952) (refusing to apply *res judicata* where "controlling facts" had changed); *see also Bose*, 476 F.3d at 1335-36 (applying *res judicata* only after assessing whether an intervening change in fact prevented its application).

Moreover, where the second proceeding involves a different cause of action and demand, as here, *res judicata* does not bar litigation of issues not actually litigated in the first proceeding. As stated by the Supreme Court:

> [W]here the second action between the same parties is upon a different cause or demand, the principle of *res judicata* is applied much more narrowly. In this situation, the judgment in the prior action operates as an estoppel, not as to matters which might have been litigated and determined, but 'only as to those matters in issue or points controverted, upon the determination of which the finding or verdict was rendered.' [citations omitted]. Since the cause of action involved in the second proceeding is not swallowed by the judgment in the prior suit, the parties

> are free to litigate points which were not at issue in the first proceeding, even though such points might have been tendered and decided at that time.

Comm'r of Internal Revenue v. Sunnen, 333 U.S. 591, 597-98 (1948). The Federal Circuit applies the same limitation on the doctrine of *res judicata*. *See Bose*, 476 F.3d at 1335 ("[A]pplication of res judicata is not applicable where 'it is apparent that all the questions of fact and law involved . . . [in the second proceeding] were not determined in the previous proceeding.") (quoting *Litton Indus., Inc. v. Litronix, Inc.*, 557 F.2d 709, 711 (C.C.P.A. 1978)); *Universal Overall Co. v. Stonecutter Mills Corp.*, 310 F.2d 952, 955-56 (C.C.P.A. 1962) (finding *res judicata* inapplicable where questions of fact and law involved in the second proceeding were not determined in the first proceeding).

B. *Res Judicata* Does Not Apply To Ranbaxy's Affirmative Defense And Counterclaim Of Invalidity Of The '893 Patent For Obviousness

1. The Supreme Court Has Dramatically Lowered The Obviousness Standard Since The Lipitor Litigation

At the time the Lipitor litigation was adjudicated by this Court, obviousness was governed by Federal Circuit precedent that rigidly required a "teaching, suggestion, or motivation" to modify a reference before it could be used to invalidate patent claims for obviousness. The Supreme Court, in the recent case of *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), explained that requirement as follows:

> Seeking to resolve the question of obviousness with more uniformity and consistency, the Court of Appeals for the Federal Circuit has employed an approach referred to by the parties as the "teaching, suggestion, or motivation" test (TSM test), under which a patent claim is only proved obvious if "some motivation or suggestion to combine the prior art teachings" can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art.

KSR, 127 S. Ct. at 1734 (citing *Al-Site Corp. v. VSI Int'l*, 174 F. 3d 1308, 1323-24 (Fed. Cir. 1999)).

The Supreme Court held that application of the TSM test as a rigid and mandatory formula "is incompatible with [Supreme Court] precedents." *Id.* at 1741. The Supreme Court also declared that, "[t]he obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." *Id.*

In devising a less-rigid test for obviousness, the Supreme Court focused on its own precedent and declared that in an obviousness inquiry, "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *Id.* at 1740. The Supreme Court further clarified that while a conclusion of obviousness should be supported by some articulated reasoning with some rational underpinning, the analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 1741.

The Supreme Court in *KSR* also eliminated the prohibition against an "obvious-to-try" analysis, which was the prevailing (but erroneous) jurisprudence of the Federal Circuit at the time of the Lipitor litigation. As explained by the Supreme Court:

> 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.' [citation omitted]. 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.

Id. at 1742. The notion that a patent may be obvious for being "obvious to try," now formally endorsed by the Supreme Court, was previously rejected by this Court in the Lipitor litigation. *Pfizer, Inc. v Ranbaxy Labs. Ltd*, 405 F. Supp. 2d 495, 517 (D. Del. 2005) (finding Claim 6 of the '995 patent not invalid despite being "obvious to try").

These substantial changes in the law of obviousness have drastically and materially altered the obviousness analysis of the '893 patent since the Lipitor litigation. As the following analysis shows, this important intervening change in law should preclude the application of *res judicata* in the present case.

2. The Lowered Standard For Obviousness Has Materially Changed The Obviousness Analysis Of The '893 Patent

The relaxed standard of obviousness announced by the Supreme Court in *KSR* requires only that a court analyze whether the claims of the '893 patent cover anything more than the combination of elements, taught by available references, according to their known functions and properties. *KSR*, 127 S. Ct. at 1740. Under the previous legal constraints existing at the time of the Lipitor litigation, a reference such as the '559 publication had little value to render the '893 patent obvious absent additional evidence of a teaching, suggestion, or motivation to modify the compounds it disclosed. The new and lowered standard of obviousness set forth by *KSR*, however, materially alters the prior obviousness analysis of the '893 patent, in effect rendering it an entirely new and distinct cause of action.

Specifically, as confirmed in the prosecution of the European '893 counterpart application (the '633 patent), the '559 publication discloses compounds that have the same structural framework as those claimed in the '893 patent, and are taught to be useful

for the same indication, *i.e.*, lowering blood serum cholesterol. (*Compare* Attachment A ('559 publication) at P0267819-21, *with* D.I. 1 (Complaint), Ex. A ('893 patent) at col. 1). The '559 publication also discloses several compounds having the same R_1, R_2, R_4 and X substituents for Formula I as those of atorvastatin lactone in the '893 patent. (*Compare* Attachment A ('559 publication) at P0267821-23, P0267831, *with* D.I. 1 (Complaint), Ex. A ('893 patent) at col. 2, ll. 3-38, Table 1 (Compound 1), col. 10, ll. 40-44, Claims 1, 2, 3, 4 and 5). Indeed, the '559 publication and the '893 patent differ only in one substituent (the R_3 substituent), and the difference is clearly an obvious modification.

Under the prior test for obviousness, this trivial difference would preclude a finding that the '893 patent is obvious absent a specific teaching, suggestion or motivation to actually modify the R_3 substituent. However, where obtaining the same R_3 substituent merely represents selecting from a finite number of identified, predictable solutions available to one of ordinary skill in the art, as is the case here, obviousness under the *KSR* standard is easily found. *See KSR*, 127 S. Ct. at 1740-41. Moreover, obviousness can also be found where, as here, the claimed compound can be obtained by applying known chemical knowledge to select the proper R_3 substituent. *Id.*

Thus, under the lowered bar for obviousness pronounced by *KSR*, the obviousness analysis of the '893 patent has entirely changed and become much easier to establish. In view of the significant intervening change in law, *res judicata* should not prejudicially bar Ranbaxy from bringing this compelling, and heretofore unassertable, challenge to the validity of the '893 patent.

3. A Substantial Change In Fact Also Precludes Application Of *Res Judicata*

In addition to the substantial change in the law of obviousness, highly pertinent facts bearing on the obviousness of the '893 patent are different in the present Caduet case than they were in the Lipitor litigation. As discussed above, the '893 patent's European counterpart application (*i.e.*, the '633 patent) was initially rejected as *prima facie* obvious over the '559 publication. (Attachment B (Lipitor litigation trial exhibit DTX-331) at RA017527-28). Pfizer overcame that rejection by submitting data, misidentified as "COR" data, purportedly showing the unexpected activity of the '893 patent compounds over the '559 publication compounds. (Attachment B (Lipitor litigation trial exhibit DTX-331) at RA017520). Under U.S. obviousness law, such a showing of unexpected results may rebut a *prima facie* showing of obviousness. *See, e.g., United States v. Adams*, 383 U.S. 39, 50-52 (1966).

Consequently, the only facts available to Ranbaxy during discovery in the Lipitor litigation showed that Pfizer could rebut a *prima facie* obviousness challenge to the '893 patent with this "COR" data. Also, as mentioned above, even a *prima facie* showing of obviousness was itself a significant legal hurdle in view of the rigid TSM test. Thus, given this factual and legal context, Ranbaxy was unable to present a realistic obviousness case against the '893 patent in the Lipitor litigation.

Only after discovery had closed and the parties were preparing for trial did Pfizer acknowledge that the "COR" data it submitted in the '633 application was actually "CSI" data from CSI screen 124. (Lipitor litigation D.I. 191). This revelation was significant because the accuracy and reliability of Warner-Lambert's CSI data was vigorously debated by the parties and experts at the trial in the Lipitor litigation. (*See, e.g.*, Lipitor

litigation D.I. 292 (Ranbaxy's Opening Post-Trial Brief) at 40; *see generally* Lipitor litigation D.I. 289, 308 and 310). Moreover, unaware that the data was actually from the CSI test, Ranbaxy was foreclosed from properly comparing this data with Warner-Lambert's other CSI test data to assess the credibility of Pfizer's unexpected results argument. This inability was especially prejudicial, as a comparison of this data with Warner-Lambert's other CSI data reveals that no unexpected results exist. (*See, e.g.*, Lipitor litigation trial exhibit DTX-3347). Thus, not only was the data purportedly showing unexpected results incorrectly identified, it also does not show unexpected results when compared to the entirety of Warner-Lambert's CSI data.

However, despite Pfizer revealing on the verge of trial that its unexpected results argument was specious, Ranbaxy still could not have made a persuasive obviousness case against the '893 patent in view of the rigid TSM obviousness test. Thus, Ranbaxy presented no obviousness challenge to the '893 patent in the Lipitor litigation.

Now, however, the TSM constraint has been removed from the obviousness inquiry, and Ranbaxy is finally aware of, and has the ability to take discovery of, the new facts concerning unexpected results. Thus, a compelling obviousness challenge to the '893 patent is now available to Ranbaxy.

Viewed in the light most favorable to Ranbaxy, the changes in law and fact discussed above preclude application of *res judicata* to Ranbaxy's Affirmative Defense and Counterclaim of obviousness of the '893 patent. *See Green v. Fund Asset Mgmt., L.P.*, 245 F.3d 214, 220 (3d Cir. 2001) (facts and inferences to be drawn from the pleadings must be viewed in the light most favorable to the non-moving party).

C. Collateral Estoppel Does Not Apply to Ranbaxy's Affirmative Defense And Counterclaim Of Obviousness

Pfizer argues that Ranbaxy's invalidity Affirmative Defense and Counterclaim of obviousness should also be precluded on collateral estoppel grounds. (D.I. 17 at 15 n.6). However, as with *res judicata*, collateral estoppel does not apply where, as here, significant intervening changes in law and fact have occurred since the prior litigation. *See Sunnen*, 333 U.S. at 599-600 (collateral estoppel "must be confined to situations where . . . the controlling facts and applicable legal rules remain unchanged."). As the Federal Circuit has recognized:

> Courts have crafted an exception to the collateral estoppel principle when there has been a change in the applicable law between the time of the original decision and the subsequent litigation in which collateral estoppel is invoked.

Bingaman v. Dep't of the Treasury, 127 F.3d 1431, 1437 (Fed. Cir. 1997) ("In this case, there was a significant change in the governing principles of law between the time of the original *Peek* decision and the time this case came before the Board."); *see Wilson v. Turnage*, 791 F.2d 151, 157 (Fed. Cir. 1986); *Texaco, Inc v. United States*, 579 F.2d 614, 617 (Ct. Cl. 1978) ("Without doubt, the intervening decision of the Supreme Court in the *Waterman* case on the identical issue litigated previously in this court, qualifies as a change in the legal atmosphere, which renders the bar of collateral estoppel inapplicable here."); *Hawksbill Sea Turtle v. Fed. Emergency Mgmt. Agency*, 126 F.3d 461, 477 (3d Cir. 1997) ("Collateral estoppel applies only when the same issues decided in the past action arise again in the present context . . . so that when significant new facts grow out of a continuing course of conduct the issues in a successive suit may fail to constitute the same 'issue' so as to merit preclusive effect."); *see also* Restatement (Second) of Judgments § 28 (1982) (stating that re-litigation of an issue is not precluded where the

"issue is one of law and . . . a new determination is warranted in order to take account of an intervening change in the applicable legal context . . . .").

Moreover, because the issue of obviousness of the '893 patent was not determined in the prior Lipitor litigation, and certainly not under the legal and factual circumstances now present, collateral estoppel, like *res judicata*, does not apply. *See Mayer/Berkshire*, 424 F.3d at 1234 (quoting *Litton Indus., Inc. v. Litronix, Inc.*, 557 F.2d 709, 711 (C.C.P.A. 1978)); *Universal Overall*, 310 F.2d at 955-56.

Thus, Pfizer's argument that collateral estoppel applies to Ranbaxy's Affirmative Defense and Counterclaim of obviousness of the '893 patent fails.

D. Public Policy Favors Precluding The Application Of *Res Judicata* And/Or Collateral Estoppel

The Supreme Court has repeatedly emphasized the vital public interest in resolving the validity of patents so that the public may be free to practice ideas that are in the public domain. *See, e.g., Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 100 (1993) (recognizing the "importance to the public at large of resolving questions of patent validity"); *Blonder-Tongue Labs., Inc. v. University of Ill. Found.*, 402 U.S. 313, 349-350 (1971) (describing the Court's "consistent view" that "the holder of a patent should not be insulated from the assertion of defenses and thus allowed to exact royalties for the use of an idea that is not in fact patentable or that is beyond the scope of the patent monopoly granted"); *Edward Katzinger Co. v. Chicago Metallic Mfg. Co.*, 329 U.S. 394, 400 (1947) (noting the "necessity of protecting our competitive economy by keeping open the way for interested persons to challenge the validity of patents which might be shown to be invalid").

Because "[i]t is the public interest which is dominant in the patent system," the Supreme Court has recognized that *res judicata* should be limited where it may adversely effect the public interest in the patent system. *See Mercoid Corp. v. Mid-Continent Inv Co.*, 320 U.S. 661, 665, 669-70 (1944) (refusing to apply *res judicata* to patent misuse claims that could have been brought in an earlier litigation because of the strong public interest in patents). These vital public interest concerns are thwarted by the prejudicial application of *res judicata* or collateral estoppel in the current case.

Specifically, the obviousness challenge Ranbaxy now asserts could not have been brought in the Lipitor litigation. Through no fault of Ranbaxy's, the law governing obviousness was much stricter during the Lipitor litigation, and Pfizer withheld critical information that bore directly on the obviousness analysis. Thus, not only are the legal elements for showing obviousness different in this case than they were in the Lipitor litigation, the facts to which those new elements are applied are different as well. Consequently, Ranbaxy's obviousness claim in the Caduet litigation is an entirely new and distinct cause of action than it was in the Lipitor litigation.

Based on these unique circumstances, the jurisprudential policies behind *res judicata* and collateral estoppel are not applicable to the current dispute. First, allowing Ranbaxy to litigate the single issue of obviousness is not piecemeal litigation, as this obviousness challenge could not have been asserted previously. Second, the interests of finality inherent in *res judicata* and collateral estoppel are not served where the law and facts have significantly changed and the obviousness of the '893 patent is ripe for adjudication. *See Brown*, 442 U.S. at 132-34 (refusing to apply *res judicata* where its interests are not served).

Additionally, affording the prior judgment preclusive effect on the issue of obviousness, which was not litigated, undermines the strong public interest in having only valid patents in force. The public's right to have the '893 patent's validity challenged by Ranbaxy should not be unfairly restrained. Thus, the Court should not apply *res judicata* or collateral estoppel on the issue of obviousness of the '893 patent in this case.

E. Pfizer's Request For Entry Of Judgment On Infringement Should Be Denied

Pfizer also asks this Court to enter a judgment that Ranbaxy infringes the '893 patent based on collateral estoppel. While Ranbaxy does not contest infringement of the '893 patent in the present case, Ranbaxy does contest validity for the reasons discussed above. Entry of a judgment of infringement is inappropriate while validity is in dispute as a party "can incur no liability for 'infringement' of invalid claims." *Shelcore, Inc. v. Durham Indus. Inc.*, 745 F.2d 621, 628 (Fed. Cir. 1984) (citing *Richdel, Inc. v. Sunspool Corp.*, 714 F.2d 1573, 1580 (Fed. Cir. 1983) ("[t]he claim being invalid there is nothing to be infringed")). Accordingly, the Court should deny Pfizer's request to enter a judgment of infringement against Ranbaxy at this time.

VI. CONCLUSION

For the foregoing reasons, Ranbaxy respectfully requests that the Court deny Pfizer's Motion.

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Dated: May 31, 2007

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

I hereby certify that on May 31, 2007, I caused to be served by hand delivery the foregoing document and electronically filed the same with the Clerk of Court using CM/ECF which will send notification of such filing(s) to the following:

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC, PFIZER PHARMACEUTICALS, LLC, PFIZER LIMITED, C.P. PHARMACEUTICALS INTERNATIONAL C.V., PFIZER IRELAND PHARMACEUTICALS, WARNER-LAMBERT COMPANY, WARNER-LAMBERT COMPANY, LLC and WARNER-LAMBERT EXPORT LTD,	)	
Plaintiffs/Counterdefendants,	)	C.A. No. 07-138-JJF
v.	)	
RANBAXY LABORATORIES LIMITED, and RANBAXY INC.,	)	
Defendants/Counterclaimants.	)	

[PROPOSED] ORDER DENYING PFIZER'S MOTION TO DISMISS AND FOR PARTIAL JUDGMENT ON THE PLEADINGS PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 12(c)

This matter, having come before the Court upon Pfizer's Motion to Dismiss and for Partial Judgment on the Pleadings Pursuant to Federal Rule of Civil Procedure 12(c), and the Court having considered the submissions of the parties, IT IS HEREBY ORDERED that:

Pfizer's Motion to Dismiss and for Partial Judgment on the Pleadings Pursuant to Federal Rule of Civil Procedure 12(c), is DENIED.

Dated:_____

_____
Honorable Joseph J. Farnan, Jr.

EXHIBIT A

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 179 559**
A2

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 85306382.4

(22) Date of filing: 09.09.85

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A 61 K 31/40

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10.12.84 US 679676

(43) Date of publication of application:
30.04.86 Bulletin 86/18

(84) Designated Contracting States:
AT BE CH DE FR GB IT LI LU NL SE

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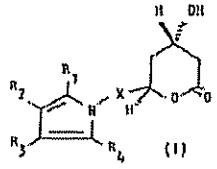
(54) Trans-6-[2-(substituted pyrrol-1-yl)alkyl]-pyran-2-one inhibitors of cholesterol synthesis.

(57) 6-[2-(Substituted-pyrrol-1-yl)alkyl]pyran-2-ones of formula I



(I)

and the corresponding ring-opened hydroxy-acids derived therefrom are potent inhibitors of the enzyme 3-hydroxy-3-methylglutarylcoenzyme A reductase (HMG-CoA reductase), and are thus useful hypolipidemic and hypocholesterolemic agents. Pharmaceutical compositions containing such compounds, and a method of preparing the compounds are also disclosed.

EP 0 179 559 A2

Croydon Printing Company Ltd

0179559

TRANS-6-[2-(SUBSTITUTEDPYRROL-1-YL)ALKYL]-PYRAN-2-ONE INHIBITORS OF CHOLESTEROL SYNTHESIS

The present invention is related to compounds and pharmaceutical compositions useful as hypocholesterolemic and hypolipidemic agents. More particularly, this invention concerns certain trans-6-[2-(substitutedpyrrol-1-yl)alkyl]-2-ones and the corresponding ring-opened acids derived therefrom which are potent inhibitors of the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase), pharmaceutical composition containing such compounds, and a method of lowering blood serum cholesterol levels employing such pharmaceutical compositions.

High levels of blood cholesterol and blood lipids are conditions which are involved in the onset of arteriosclerosis. It is well known that inhibitors of HMG-CoA reductase are effective in lowering the level of blood plasma cholesterol, especially low density lipoprotein cholesterol (LDL-C), in man (cf. M. S. Brown and J. L. Goldstein, New England Journal of Medicine (1981), 305, No. 9, 515-517). It has now been established that lowering LDL-C levels affords protection from coronary heart disease (cf. Journal of the American Medical Association (1984) 251, No. 3, 351-374).

Moreover, it is known that certain derivatives of mevalonic acid (3,5-dihydroxy-3-methylpentanoic acid) and the corresponding ring-closed lactone form, mevalonolactone, inhibit the biosynthesis of cholesterol (cf. F. M. Singer et al., Proc. Soc. Exper. Biol. Med. (1959), 102, 270) and F. H. Hulcher, Arch. Biochem. Biophys. (1971), 146, 422.

United States Patents 3,983,140; 4,049,495 and 4,137,322 disclose the fermentative production of a natural product, now called compactin, having an inhibitory effect on cholesterol biosynthesis. Compactin has been shown to have a complex structure which includes a mevalonolactone moiety (Brown et al., J. Chem. Soc. Perkin I, (1976), 1165.

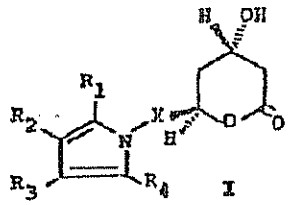
United States Patent 4,255,444 to Oka et al. 0179359 discloses several synthetic derivatives of mevalonolactone having antilipidemic activity.

United States Patents 4,198,425 and 4,262,813 to Mitsue et al. disclose aralkyl derivatives of mevalonolactone which are useful in the treatment of hyperlipidemia.

United States Patent 4,375,475 to Willard et al. discloses certain substituted 4-hydroxytetrahydropyran-2-ones which, in the 4(R)-trans stereoisomeric form, are inhibitors of cholesterol biosynthesis.

In accordance with the present invention, there are provided certain trans-6-[2-(substitutedpyrrol-1-yl)-alkyl]pyran-2-ones and the corresponding ring-opened hydroxy-acids derived therefrom which are potent inhibitors of cholesterol biosynthesis by virtue of their ability to inhibit the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA reductase).

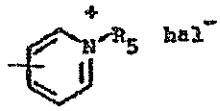
In particular, in its broadest chemical compound aspect, the present invention provides compounds of structural formula I



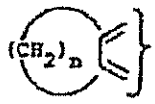
I

wherein X is $-CH_2-$, $-CH_2CH_2-$, or $-CH(CH_3)CH_2-$. R_1 is 1-naphthyl; 2-naphthyl; cyclohexyl; norbornenyl; phenyl; phenyl substituted by fluorine, chlorine, hydroxy, trifluoromethyl, alkyl of from one to four carbon atoms, alkoxy of from one to four carbon

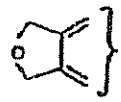
atoms, or alkanoyloxy of from two to eight carbon atoms; 2-, 3-, or 4-pyridinyl; 2-, 3-, or 4-pyridinyl-N-oxide; or



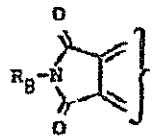
where R_5 is alkyl of from one to four carbon atoms and hal^- is chloride, bromide, or iodide. R_2 and R_3 are independently hydrogen; chlorine; bromine; cyano; trifluoromethyl; phenyl; alkyl of from one to four carbon atoms; carboalkoxy of from two to eight carbon atoms; $-CH_2OR_6$ where R_6 is hydrogen, alkanoyl of from one to six carbon atoms, or where R_2 and R_3 are $-CH_2OCONHR_7$ where R_7 is alkyl of from one to six carbon atoms, phenyl, or phenyl substituted with chlorine, bromine, or alkyl of from one to four carbon atoms. R_2 and R_3 may also, when taken together with the carbon atoms to which they are attached, form a ring denoted by



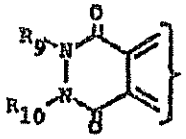
where n is three or four; a ring denoted by



a ring denoted by



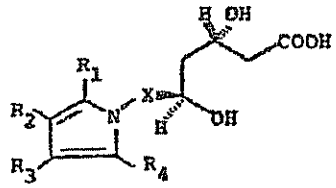
where R_8 is hydrogen, alkyl of from one to six carbon atoms, phenyl, or benzyl; or a ring denoted by



where R_9 and R_{10} are hydrogen, alkyl of from one to four carbon atoms, or benzyl.

R_4 is alkyl of from one to four carbon atoms, cyclopropyl, cyclobutyl, or trifluoromethyl.

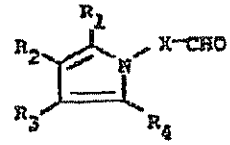
Also contemplated as falling within this aspect of the invention are the corresponding dihydroxy-acid compounds of formula II corresponding to the opened form of the lactone ring of compounds of formula I



II

where X, R_1, R_2, R_3, and R_4 are as defined above, and the pharmaceutically acceptable salts thereof, all of the compounds being in the trans racemate of the tetrahydropyran moiety.

In another aspect of the present invention, there is provided a method of preparing compounds of formula I above by (a) first reacting a substituted [(pyrrol-1-yl)-alkyl]aldehyde compound of formula III



III

where X, R_1, R_2, R_3, and R_4 are as defined above, with the alkali metal salt of the dianion of methyl acetoacetate to form a compound of structural formula IV

trans-Ethyl 5-(4-Fluorophenyl)-2-(1-methylethyl)-4-phenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxylate.

trans-6-[2-[1-(4-Fluorophenyl)-4,5,6,7-tetrahydro-3-methyl-2H-isoindol-2-yl]ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-4-(4-Fluorophenyl)-2-methyl-6-(1-methylethyl)-5-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione.

trans-6-[2-[1-(4-Fluorophenyl)-5,6-dihydro-3-(1-methylethyl)pyrrolo[3,4-c]pyrrol-2(4H)-yl]ethyl]-tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-6-[2-[1-(4-Fluorophenyl)-5,6-dihydro-5-methyl-3-(1-methylethyl)pyrrolo[3,4-c]pyrrol-2(4H)-yl]-ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-6-[2-[3-Chloro-5-(4-fluorophenyl)-2-(1-methylethyl)-4-phenyl-1H-pyrrol-1-yl]ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-6-[2-[2-(4-Fluorophenyl)-5-(1-methylethyl)-3,4-diphenyl-1H-pyrrol-1-yl]ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

Particularly preferred compounds in accordance with the present invention are:

trans-6-[2-[3,4-Dichloro-2-(4-fluorophenyl)-5-(1-methylethyl)-1H-pyrrol-1-yl]ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-6-[2-[3,4-Dibromo-2-(4-fluorophenyl)-5-(1-methylethyl)-1H-pyrrol-1-yl]ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-6-[2-[2-(4-Fluorophenyl)-5-(trifluoromethyl)-1H-pyrrol-1-yl)ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

trans-Dimethyl 2-(4-Fluorophenyl)-5-(1-methylethyl)-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3,4-dicarboxylate.

trans-6-[2-[2-(4-Fluorophenyl-5-methyl-1H-pyrrol-1-yl)ethyl]tetrahydro-4-hydroxy-2H-pyran-2-one.

EXHIBIT B

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COPY

Datum/Date: 04/12/91

Zeichen/Ref./Réf.	Anmeldung Nr./Application No./Demande n°./Patent No./Patent No./Brevet n°.
PD-3514	87107847.3-2101-0247633

Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire
WARNER-LAMBERT COMPANY

COMMUNICATION REGARDING THE EXPIRY OF THE TIME LIMIT WITHIN WHICH NOTICE OF OPPOSITION MAY BE FILED

You are hereby informed that on expiry of the nine-month time limit from the publication of the mention of the grant of European Patent No 0247633 no notice of opposition had reached the files.

The entry in the Register of European Patents will be automatically generated by the electronic data processing system.

LAUSENMEYER J J
Formalities Officer
Tel. No. (089) 2399-8013

Newton
EXHIBIT NO. 331
KWP 4-21-04

EPO Form 2050 04.91 7066060 30/11/91

RA017395

DEFENDANTS' TRIAL EXHIBIT 331 CV 03-209 JJF

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Registered Letter

European Patent Office
Erhardtstr. 27

8000 München 2

Your Ref.:	Our Ref.:	Telephone	Freiburg,
	Ma/Am	(49)-761-5182525	10/12/1989

European Patent Application No. 87 107 847.3-2101
Applicant: Warner-Lambert Company
Our Ref: PD-3514

To the Communication of April 20, 1989:

1.) Following the interview of July 29, 1989 applicants submit data clearly demonstrating a superior effect of compounds showing the substitution pattern of the present invention in the 3- and 4-positions of the pyrazole ring. It should be noted that both tested compounds are at least by the factor 10 more effective than the compounds according to EP-A-179 559. This effect is unexpected and was not to be foreseen.

Applicants generally accept the Examining Division's arguments saying that a person skilled in the art would expect that the pyrazole ring was susceptible to further substitutions at the 3 and 4 position including other carboxy derivatives ... without leading to a significant change in qualitative properties. In the present case, however, it can be shown that the substitution of the pyrazole-ring according to the claims is much more effective than it could be expected from the prior art.

It is therefore requested, that the Examining Division reconsider its concerns and acknowledge the inventive step in view of Article 56 EPC.

2.) Claims 3, 4 and 5 correspond to the compounds of Examples 1, 3 and 4. The nomenclature seems to be consistent with the usual IUPAC-rules. The nomenclature of Example 2 is different because it describes a ring-opened heptanoic-acid derivative as disclosed on page 2, line 7 of the original specification.

In case the Examining Division wishes a uniformly amended nomenclature throughout the application, applicants are of course willing to follow appropriate suggestions. With respect to claim 2, however, applicants do not believe that amendments will be required.

3.) Applicants further do not believe that the special reaction conditions set out as being preferred on page 10 of the original description should be inserted into present claim 8.

The conditions of steps a) to d) are well known and may be varied depending on the reactants used. Since for example the reduction conditions using trialkylboranes belong to the basic knowledge of a chemist, it is not believed that the preferred temperature range mentioned on page 10 of the description should be added to claim 8. The word inert, which of course is not a contradiction in connection with the term "polar solvent" has been used to demonstrate that the solvent remains unchanged and does not participate in the reactions.

4.) A short statement concerning reference (A) has been inserted in line 24, page 3 of the description. The amended page 3 is attached to this paper.

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3

The Examining Division is respectfully requested to reconsider the present case and to step forward granting a patent. In case this is not possible, it is requested to grant an interview to the undersigned representative in order to be able to discuss the present invention in more detail.

Ivo Mansmann

(General Authorization
No. 14435)

Encl. New page 3
Comparison Data

To examiner
Case 3
10.89 CK

United States Patent 4,255,444 to Oka et al. discloses several synthetic derivatives of mevalonolactone having antilipidemic activity.

United States Patents 4,198,425 and 4,262,013 to Mitsue et al. disclose aralkyl derivatives of mevalonolactone which are useful in the treatment of hyperlipidemia.

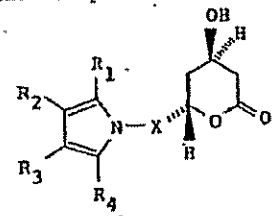
United States Patent 4,375,475 to Willard et al. discloses certain substituted 4-hydroxytetrahydropyran-2-ones which, in the 4(R)-trans-stereoisomeric form, are inhibitors of cholesterol biosynthesis.

Published PCT application WO 84/02131 discloses certain indole analogs and derivatives of mevalonolactone having utility as hypolipoproteinemic and antiatherosclerotic agents.

In accordance with the present invention, there are provided certain trans-6-[2-(3- or 4-carboxamido-substituted pyrrol-1-yl)alkyl]-4-hydroxypyran-2-ones and the corresponding ring-opened hydroxy-acids derived therefrom which are potent inhibitors of cholesterol biosynthesis by virtue of their ability to inhibit the enzyme 3-hydroxy- 3-methylglutaryl coenzyme A reductase (HMG-CoA reductase).

EP-A-179 559 describes Trans-6-[2-(substituted pyrrol-1-yl)-alkyl]-pyran-2-one derivatives as inhibitors of cholesterol synthesis. The pyrrol-ring may carry a variety of substituents, especially in the 3- and 4-position of the pyrrole-ring. The specification; however, does not mention the 3- or 4-carboxamido-substituion, which makes the compounds surprisingly more active.

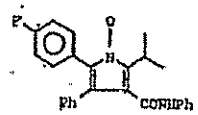
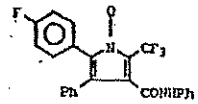
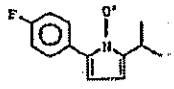
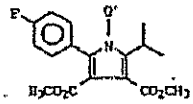
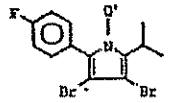
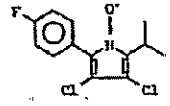
In particular, in its broadest aspect the present invention provides compounds of structural formula I



(I),

wherein X is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$ or $-CH_2CH(CH_3)-$.

33

COMPARISON DATA	COR-TEST IC_{50} in M
EP-A-247633	
	1.00×10^{-9}
	1.15×10^{-9}
EP-A-179559	
	4.57×10^{-7}
	1.60×10^{-7}
	7.58×10^{-8}
	7.43×10^{-8}

Q = CH_2CH_2-CH(OH)-CH_2-CH(OH)-CH_2COONa

Q' = -CH_2CH_2-CH(OH)-CH_2-CH(OH)-CH_2COOH

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Datum/Date: 20.04.89

Aktenzeichen/Ref. No.: EP-3514
Anmeldung Nr./Application No./Demande n°/Patent No./Patent No./Brevet n°: 87107847.2 - 2301
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire: BAUER-KAUBER COMPANY

Please give the complete application number in all communications

Communication pursuant to Article 96(2) and Rule 51(2) EPC

The /further/ examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.
You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 78(3) and 83(2) and (4) EPC.

Amendments to the description, claims and drawings are to be filed where appropriate within the said period in three copies on separate sheets (Rule 36(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).

Marc Gettins

Primary examiner
for the Examining Division

Enclosures: 3 page/s reasons (Form 2044/2906)

Registered letter

Telephone numbers:
Primary examiner (substantive examination): (089) 2399-2721
Formalities officer (formalities including extension of time limits): (089) 2399-2727
Examiners' clerk (other matters): (089) 2399-2711

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Communication despatched, EXRE and statistical data record
17.4.89 Ries

RA017526

Ergänzung zum Bescheid vom 20.04.89
Supplement to the communication of
Complément de la notification du

Blatt 1
Sheet 1
Feuille 1

Anmeldungs-Nr.:
Application No.: 87 107 847.3
Demande n°:

21

The examination is being carried out on the following application documents (description, claims and, where appropriate, drawings):

☒ the application documents as published

☐ description, pages ..... as published
description, pages ..... filed with your letter of .....
description, pages ..... filed with your letter of .....
description, pages ..... filed with your letter of .....

☐ claims, Nos. ..... as published
claims, Nos. ..... filed with your letter of .....
claims, Nos. ..... filed with your letter of .....
claims, Nos. ..... filed with your letter of .....

☐ drawings, sheet/fig. ..... as published
drawings, sheet/fig. ..... filed with your letter of .....
drawings, sheet/fig. ..... filed with your letter of .....
drawings, sheet/fig. ..... filed with your letter of .....

☐ with the amendments, suggested in your letter of ....., to the description/ the claims/ the drawings

1. Of the documents cited in the European Search Report the most pertinent is:

(A) EP-A-0 179 559.

2. The claimed matter differs structurally from (A) in that one of R^2 and R^3 must be an amide group. Consequently, the novelty of the claimed matter can be recognised (Article 54 EPC).

3. In the light of the most relevant prior art (A) the problem underlying the invention was the provision of further 6(pyrrol-1-yl) alkyl pyran-2-one inhibitors of cholesterol synthesis. From (A) it is clear that the 3 and 4 positions of the pyrazole ring can be substituted by a wide variety of substituents, including esters - Claim 1, column 58, line 26

.../...

without leading to a loss of the said pharmaceutical properties. The man skilled in the art would expect that the pyrazole was susceptible to further substitutions at the 3 and 4 position including other carboxy derivatives such as amides, without leading to a significant change in qualitative properties. The claimed matter therefore appears to represent an obvious solution to the said problem.

An inventive step could be acknowledged if the Applicant can demonstrate that an alternative problem has been solved e.g. the making available of further inhibitors of cholesterol synthesis which are surprisingly more effective than those of the closest prior art. As per T181/82 OJ 9/1984, p.401 any comparative tests must be carried out against the structurally closest prior art (A).

4. The nomenclature used in Claims 3, 4 and 5 is considered to be unclear (Article 84 EPC). The term "...-N,4-diphenyl ...-3-carboxamide" should be rewritten along the lines of Example 2 on page 13, i.e. "...4-phenyl...3-[(phenylamino)-carbonyl]".

5. Claim 8 (b) does not include all of the essential features needed to define that particular part of the process (Article 84 EPC and Guidelines C-III, 4.4). Reference should be made in Claim 8(b) to the need to cool to a temperature between 0°C and -78°C and while the description (page 6, lines 12-17) refers to an inert solvent the said claim refers to a polar solvent.

6. Reference should be made to (A) as relevant prior art (Rule 27(1)(c) EPC).

7. Where appropriate the above points also apply to the claims

.../...

for the Contracting States AT, GR and ES.

8. The description should be brought into conformity with any amended claims. All amendments must meet the requirements of Article 123(2) EPC.