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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/739,180	04/24/2007	Thomas Kelleher	C062-02/03 US	8837

34103 7590 11/30/2010

Intellectual Property Department
Cubist Pharmaceuticals, Inc.
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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
11/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	11/739,180	KELLEHER ET AL.	
	Examiner	Art Unit	
	CHIH-MIN KAM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29,31-36,38-44,47-52,54-56 and 58-160* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-7 and 115* is/are allowed.

6)☒ Claim(s) *1,8-29,31-36,38-44,47-52,54-56,58-114 and 116-160* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 April 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-29, 31-36, 38-44, 47-52, 54-56 and 58-160 are pending.

Applicants' amendment filed September 22, 2010 is acknowledged. Claims 2, 3, 6, 8, 9, 11, 38, 47-52, 58, 59 and 61 have been amended, claims 46 and 57 have been cancelled, and new claims 64-160 have been added. Therefore, claims 1-29, 31-36, 38-44, 47-52, 54-56 and 58-160 are examined.

Withdrawn Claim Objections

2. The previous objection to claims 2-7, 31-36, 39-44, 47-52, 59 and 61-63 is withdrawn in view of applicants' amendment to the claims in the amendment filed September 22, 2010.

Withdrawn Claim Rejections - 35 USC § 102

3. The previous rejection of claims 8-29, 38, 46, 55-56, 58 and 60 under 35 U.S.C. 102(e) as being as anticipated by Baker *et al.* (US RE39,071 E) is withdrawn in view of applicants' amendment to the claims, applicants' cancellation of the claims, and applicants' response at pages 23-24 in the amendment filed September 22, 2010.

Withdrawn Claim Rejections - Obviousness Type Double Patenting

4. The previous rejection of claims 8-9, 46, 55, 57, 58 and 60 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-20, 26, 28 and 29 of U.S. Patent RE39,071 E is withdrawn in view of applicants' amendment to the claims, and applicants' cancellation of the claims in the amendment filed September 22, 2010.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 8-29, 31-36, 38-44, 47-52, 55-56, 58-114 and 116-160 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 8-29, 31-36, 38-44, 47-52, 55-56, 58-114 and 116-160 are indefinite because of the use of the term "impurities 1-14". The term cited renders the claim indefinite, it is not clear what these impurities are, and how they are defined. Claims 8-29, 31-36, 38-44, 47-52, 55-56, 59-61, 63-114 and 116-160 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claims from which they depend.

7. Claims 8-29, 31-36, 38-44, 47-52, 55-56, 95-113 and 116-160 are indefinite because of the use of the term "The composition" or "the composition", while the independent claim (i.e., claim 62) recites the term "Daptomycin", not "A composition".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1 and 54 are rejected under 35 U.S.C. 102(e) as anticipated by Baker *et al.* (US RE39,071 E, reissue of U.S. Patent 5,912,226, filed December 16, 1991).

Baker *et al.* teach an antibacterial composition comprising daptomycin (LY146032) obtained in substantially pure form, which refers to daptomycin that contains less than 2.5% of a combined total of anhydro-daptomycin and beta-isomer of daptomycin (column 8, lines 50-60; Examples 4 and 5; claim 1(g), 54), where daptomycin is purified by a procedure using Diaion HP-20 resin column, followed by HPLC and another HP-20 resin column (Examples 1-5). Baker *et al.* also teach the preparation of a pharmaceutical formulation comprising the purified daptomycin (LY146032) with pharmaceutical carriers or excipients (column 9, lines 47-59), and an antibiotic composition comprised of a combination of a compound of formula 1 (i.e., anhydro-A21978C; column 1, lines 14-21), a compound of formula 2 (isomer of A21978C) and a compound of formula 3 (the parent cyclic peptide of A21978C; LY146032) or pharmaceutically acceptable salts (Reissue: claim 18).

Response to Arguments

Applicants indicate that the purity of daptomycin in Baker can only be interpreted as defined by Baker, thus Baker can be interpreted to read that there is 97.5% of daptomycin over a daptomycin plus anhydro-daptomycin ("A") plus beta isomer daptomycin ("B") composition. The present application describes daptomycin purity relative to daptomycin plus anhydro-daptomycin (impurity No. 13) plus beta isomer daptomycin (impurity No. 8) plus 12 other impurities (impurities 1-7, 9-12 and 14) as described in Table 3 of the specification. Thus, Baker

uses a different purity and does not teach purity over the 14 daptomycin impurities. Applicants also indicate that Baker methods yield at best about 93% pure daptomycin measured under the current application while it yields 97.5% purity under its own teachings. Applicants further assert that evidence of inherency and/or notice of facts to support the inherency of the present claims have not been provided. Regarding product-by process claims, claims 11-29 have been amended to depend on claim 62 or claim 115, thus the basis for rejection is overcome. Therefore, Baker does not anticipate claims 1 and 54, the rejection under 35 U.S.C. 102 (e) should be withdrawn (pages 21-24 of the response).

Applicants' response has been fully considered. Regarding claim 1(g) and claim 54, the arguments are not found persuasive because of the following reasons. Baker *et al.* teach an antibacterial composition comprising daptomycin (LY146032) obtained in substantially pure form, which refers to daptomycin that contains less than 2.5% of a combined total of anhydro-daptomycin and beta-isomer of daptomycin (column 8, lines 50-60; Examples 4 and 5). Since Baker *et al.* do not indicate other impurities besides anhydro-daptomycin and beta-isomer of daptomycin are contained in the daptomycin (LY146032) in substantially pure form, it reads that the daptomycin has more than 97.5% purity. While Baker implies that other degradants are present, but are not predominant in the pH range that optimizes the transpeptidation reactions, the reference does not indicate other degradants are present after the purification procedure (column 8, lines 45-49). While Baker's later work (U.S. Patent 4,874,843) shows undetermined impurities at least as great as 7%, and daptomycin has at best 93% purity, the '843 patent only use a single HP-20 resin column to purify daptomycin with a yield of 50-60% (Example 1-2), which is different from the purification procedure (i.e., Diaion HP-20 resin column, followed by

HPLC and another HP-20 resin column) used by Baker *et al.* in the US RE39,071 E (e.g., with a very low yield in Example 3). Thus, even Baker (U.S. Patent 4,874,843) shows undetermined impurities at least as great as 7%, and daptomycin has at best 93% purity, it does not mean that the daptomycin purified by Baker *et al.* in the US RE39,071 E has at best 93% purity since the purification procedures used by two patents are different. As shown in Example 2 of the present application, the purity level of the daptomycin was 91% using the purification method from the '843 patent, and the daptomycin sample was further confirmed to contain fourteen impurities (Example 10), which does not mean the daptomycin purified by Baker *et al.* in the US RE39,071 E would have at best 93% purity when a different purification procedure is used. The daptomycin purified by Baker *et al.* in the US RE39,071 E is obtained in substantially pure form that contains less than 2.5% of a combined total of anhydro-daptomycin and beta-isomer of daptomycin as taught by Baker *et al.* is not different from the claimed composition as indicated in claims 1(g) and 54 because the claimed substantially pure daptomycin has also >97% purity without indicating the existence of other 14 impuritites. Therefore, the rejection of claim 1(g) and claim 54 are maintained.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1 and 54 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-20, 26 and 28 of U.S. Patent RE39,071 E. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1 and 54 in the instant application disclose a composition comprising substantially pure daptomycin (i.e., >97% purity daptomycin). This is obvious variation in view of claims 18-20, 26 and 28 of the patent which disclose an antibiotic composition comprised of a combination of a compound of formula 1 (i.e., anhydro-daptomycin), a compound of formula 2 (i.e., beta-isomer of daptomycin) and a compound of formula 3 (i.e., daptomycin, A21978C), or pharmaceutically acceptable salts thereof, wherein the total amount of the compound of formula 1 and the compound of formula 2 or salts thereof, in the combination is less than 6 weight percent; or a pharmaceutical formulation comprising a combination of a compound of formula 1 (i.e., anhydro-daptomycin), a compound of formula 2 (i.e., beta-isomer of daptomycin) and a compound of formula 3 (i.e., daptomycin, A21978C), or pharmaceutically acceptable salts thereof, wherein the total amount of the compound of formula 1 and the compound of formula 2 or salts thereof, in the combination is less than 6 weight percent. Both claims of instant application and the patent are directed to a composition comprising substantially pure daptomycin (i.e., >97% purity daptomycin); or a pharmaceutical composition comprising the composition and a pharmaceutically acceptable carrier or excipient. Thus, claims 1 and 54 in present application and claims 18-20, 26 and 28 of the patent are obvious variations of a composition comprising substantially pure daptomycin (i.e., >97% purity daptomycin).

Response to Arguments

Applicants indicate that they reserve their right to file a terminal disclaimer upon an indication of allowance of these claims over Baker under 35 U.S.C. § 102(e) as requested above or to cancel such claims in a further amendment (page 24 of the response).

Applicants' response has been considered and the rejection is maintained.

Conclusion

10. Claims 1, 8-29, 31-36, 38-44, 47-52, 54-56, 58-114 and 116-160 are rejected; and claims 2-7 and 115 are free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

CMK

November 27, 2010