IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Giorgio CALDERARI et al.	Group Art Unit: 1628
Application No.: 13/901,830	Examiner: Shirley V. GEMBEH
Filed: May 24, 2013	
For: LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSETRON	Confirmation No.: 3806

SUPPLEMENTAL AMENDMENT AND RESPONSE TO OFFICE ACTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TROUTMAN SANDERS
Customer Number 06980

Dear Sir:

In further response to the Office Action mailed November 22, 2013, please enter the following amendments and consider the following remarks.

A REPLACEMENT CLAIM SET begins on page 2.

REMARKS begin on page 4.

REPLACEMENT CLAIM SET

1-25. (Canceled)

26. (New) A formulation comprising a pharmaceutical sterile aqueous intravenous solution, wherein said pharmaceutical sterile aqueous intravenous solution comprises:

palonosetron hydrochloride or another pharmaceutically acceptable salt of palonosetron at a concentration of 0.05 mg/mL based on the weight of the palonosetron free base; and

from about 10 mg/mL to about 80 mg/mL mannitol;

wherein the pharmaceutical sterile aqueous intravenous solution has a pH of 4.0 to 6.0.

27. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises palonosetron hydrochloride or another pharmaceutically acceptable salt of palonosetron is in an amount of 0.25 mg.

28. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises from about 20 mg/mL to about 60 mg/mL mannitol.

29. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises from about 40 mg/mL to about 45 mg/mL mannitol.

30. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises 41.5 mg/mL mannitol.

31. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises a chelating agent.

32. (New) The formulation of claim 31, wherein said chelating agent is EDTA.

33. (New) The formulation of claim 32, wherein said pharmaceutical sterile aqueous intravenous solution comprises from about 0.3 mg/mL to about 0.7 mg/mL EDTA.

34. (New) The formulation of claim 32, wherein said pharmaceutical sterile aqueous intravenous solution comprises 0.5 mg/mL EDTA.

35. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution has a pH of 5.0 ± 0.5.

36. (New) The formulation of claim 26, wherein said pharmaceutical sterile aqueous intravenous solution comprises a citrate buffer.

37. (New) A formulation comprising a pharmaceutical sterile aqueous intravenous solution, wherein said pharmaceutical sterile aqueous intravenous solution comprises:

palonosetron hydrochloride or another pharmaceutically acceptable salt of palonosetron at a concentration of 0.05 mg/mL based on the weight of the palonosetron free base;

from about 10 mg/mL to about 80 mg/mL mannitol; and

from about 0.3 mg/mL to about 0.7 mg/mL EDTA.

38. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution comprises palonosetron hydrochloride or another pharmaceutically acceptable salt of palonosetron is in an amount of 0.25 mg.

39. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution has a pH of 4.0 to 6.0.

40. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution has a pH of 5.0 ± 0.5.

41. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution comprises from about 20 mg/mL to about 60 mg/mL mannitol.

42. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution comprises from about 40 mg/mL to about 45 mg/mL mannitol.

43. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution comprises 41.5 mg/mL mannitol and 0.5 mg/mL EDTA.

44. (New) The formulation of claim 37, wherein said pharmaceutical sterile aqueous intravenous solution comprises a citrate buffer.

REMARKS

Status of Claims

Upon entry of this Supplemental Amendment, claims 26-44 will be pending in this application. Claims 1-9 were previously canceled and claims 10-25 are canceled herein, all without prejudice or disclaimer. New claims 26-44 are added by this amendment. Support for the new claims can be found throughout the specification of the priority application (U.S. Provisional Application No. 60/444,351), for instance at:

- page 2, lines 4-6;
- page 5, line 3 to page 6, line 2;
- page 6, line 16 to page 7, line 1;
- page 7, line 29 to page 8, line 8;
- page 8 lines 14-25;
- page 8, line 26 to page 9, line 23;
- page 10, lines 9-25; and
- Examples 1-3.

No new matter is added by this amendment.

Status of Application

On February 21, 2014, Applicants filed a timely and complete response to the Office Action mailed November 22, 2013. On April 17, 2014, Applicants requested a three-month suspension of prosecution to consider the strategic direction of this application relative to Applicants' other pending applications. On August 25, 2014, Applicants requested an additional three-month suspension to continue such consideration. Applicants hereby request that prosecution of this application be resumed and examination extended to include new claims 26-44 presented herein.

The remarks presented in the Response filed February 21, 2014, regarding the patentability of claims 10-18 remain in full force and are incorporated herein by reference. In the

pages that follow, Applicants provide reasons why the previous obviousness rejection of claims 10-18 does not apply to new claims 26-44.

Rejection Under 35 U.S.C. § 103

In the Office Action mailed November 22, 2103, the Office rejected claims 10-18 under pre-AIA[1] 35 U.S.C. § 103 as obvious over U.S. Patent No. 5,202,333 to Berger et al. ("Berger") in view of Barton "Citric Buffer Calculation" (2000) ("Barton") and U.S. Patent No. 6,284,749 to Castillo et al. ("Castillo"), and further in view of U.S. Patent No. 5,854,270 to Gambhir ("Gambhir") as evidenced by Matsumoto et al. "Manual for Practical Pharmacy" (1989) ("Matsumoto"). Office Action at pp. 3-8. For the reasons discussed below, Applicants respectfully traverse this rejection with respect to new claims 26-44.

A. The Concentration of Palonosetron Hydrochloride Recited in Claims 26-44 Would Not Have Been Obvious

Applicants have prosecuted several applications in the same family as this application, including U.S. Patent No. 8,598,219 ("the '219 patent"), which is the parent of this application. Like the claims of the '219 patent, claims 26-44 recite a specific concentration of palonosetron hydrochloride of 0.05 mg/mL based on the weight of its free base. The Office has already acknowledged that Berger is directed toward much higher concentrations of 10 to 100 mg/mL and thus, would have led the POSITA away from using the claimed concentration in intravenous formulations. *See* Interview Summary dated October 11, 2013 in the '219 file history.

Specifically, the Office stated, in distinguishing the 0.05 mg/mL (*i.e.*, 0.25 mg/5 mL) palonosetron hydrochloride concentration recited in the '219 claims, that Berger describes "high concentrations." The Office supported that conclusion by referencing Berger's Example 13,

[1] As discussed in the Response filed February 21, 2014, Applicants believe that this case should be examined under post-AIA 35 U.S.C. § 103 because it claims priority to an application that presented a claim having a priority date after March 16, 2013. *See also* the "Choice of Law" section of the Preliminary Amendment filed May 24, 2013. Nevertheless, Applicants do not believe that the choice of law has any bearing on the patentability of the claims.

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