

***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***

Applicant: Horst OLSCHESKI et al.  
Title: TREPASTINIL ADMINISTRATION BY  
INHALATION  
Appl. No.: 12/591,200  
Filing Date: 11/12/2009  
Examiner: Sarah Elizabeth Townsley  
Art Unit: 1629  
Confirmation Number: 4093

SUBSTANTIVE SUBMISSION UNDER 37 C.F.R. § 1.114

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Commissioner:

This paper responds to the outstanding Final Office Action dated October 10, 2014, the Advisory Action dated February 27, 2015 and the Notice of Panel Decision from Pre-Appeal Brief Review mailed May 8, 2015, while following the response filed January 12, 2015 and the Notice of Appeal filed March 9, 2015. A Request for Continued Examination including petition for a five month extension of time accompanies this paper.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this document. **Remarks** begin on page 5 of this document.

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1-17. (Canceled)

18. (Previously Presented) A method of treating pulmonary hypertension comprising:  
administering by inhalation to a human in need thereof a therapeutically effective single event dose of an inhalable formulation with a pulsed ultrasonic nebulizer, wherein said therapeutically effective single event dose comprises from 15  $\mu\text{g}$  to 90  $\mu\text{g}$  of treprostinil or a pharmaceutically acceptable salt thereof, said therapeutically effective single event dose is inhaled in 18 or less breaths by the human.

19.-24. (Canceled)

25. (Previously Presented) The method of claim 18, wherein the single event dose contains from 15  $\mu\text{g}$  to 60  $\mu\text{g}$  of treprostinil or a pharmaceutically acceptable salt thereof.

26-27. (Canceled)

28. (Previously Presented) The method of claim 18, wherein said administering does not significantly disrupt gas exchange in said human.

29. (Previously Presented) The method of claim 18, wherein said administering does not significantly affect heart rate of said human.

30. (Previously Presented) The method of claim 18, wherein said administering does not significantly affect systemic arterial pressure and systemic arterial resistance of said human.

31. (Canceled)
32. (Previously Presented) The method of claim 18, wherein said administering of said therapeutically effective single event dose is performed in 5 or less breaths.
33. (Previously Presented) The method of claim 18, wherein said human receives several therapeutically effective single event doses per day.
34. (Previously Presented) The method of claim 27, wherein the concentration of said treprostinil or a pharmaceutically acceptable salt thereof in the aerosolable solution is 600 µg/ml.
35. (Previously Presented) The method of claim 18, wherein the single event dose is administered in 5 minutes or less.
36. (Previously Presented) The method of claim 27, wherein the single event dose is administered in 5 minutes or less.
37. (Previously Presented) The method of claim 34, wherein the single event dose is administered in 5 minutes or less.
38. (Previously Presented) The method of claim 18, wherein said therapeutically effective single event dose is inhaled in 12 or less breaths by the human.
39. (Previously Presented) The method of claim 27, wherein said therapeutically effective single event dose is inhaled in 12 or less breaths by the human.
40. (Previously Presented) The method of claim 34, wherein said therapeutically effective single event dose is inhaled in 12 or less breaths by the human.
41. (New) A method of treating pulmonary hypertension comprising: administering by inhalation to a human in need thereof a therapeutically effective single event dose of an inhalable formulation with a pulsed ultrasonic nebulizer having a concentration of said treprostinil or a pharmaceutically acceptable salt thereof from 500 µg/ml to 2000 µg/ml, wherein said therapeutically effective single event dose comprises from

15  $\mu\text{g}$  to 90  $\mu\text{g}$  of treprostinil, or its acid derivative, or a pharmaceutically acceptable salt thereof, said therapeutically effective single event dose being inhaled in 18 or less breaths by the human.

42. (New) A method of treating pulmonary hypertension comprising: administering by inhalation to a human in need thereof a therapeutically effective single event dose of an inhalable formulation with a pulsed ultrasonic nebulizer having a concentration of said treprostinil or a pharmaceutically acceptable salt thereof of 600  $\mu\text{g}/\text{ml}$ , wherein said therapeutically effective single event dose comprises from 15  $\mu\text{g}$  to 90  $\mu\text{g}$  of treprostinil, or its acid derivative, or a pharmaceutically acceptable salt thereof, said therapeutically effective single event dose being inhaled in 18 or less breaths by the human.

43. (New) The method of claim 18, wherein the pulsed ultrasonic nebulizer comprises an opto-acoustical trigger for timing inspiration by the human to coincide with generation of an aerosol pulse produced by the pulsed ultrasonic nebulizer.

44. (New) The method of claim 41, wherein the pulsed ultrasonic nebulizer comprises an opto-acoustical trigger for timing inspiration by the human to coincide with generation of an aerosol pulse produced by the pulsed ultrasonic nebulizer.

45. (New) The method of claim 42, wherein the pulsed ultrasonic nebulizer comprises an opto-acoustical trigger for timing inspiration by the human to coincide with generation of an aerosol pulse produced by the pulsed ultrasonic nebulizer.

46. (New) The method of claim 18, wherein said administering results in pulmonary vasodilation in the human for longer than 3 hours.

REMARKS

Applicants respectfully request reconsideration and allowance of the present application.

CLAIMS STATUS

Applicants have added new claims 41-46. Support for the new claims may be found in throughout the specification as filed including, in examined claims 18 and 27 as well as in paragraph [0094] for claim 41; in examined claim 18 as well as in paragraphs [0070], [0075] and [0078] for claim 42; in paragraph [0078] for claims 43-45; in paragraphs [0093]-[0094] for claim 46. No new matter has been added.

Applicants have canceled claim 27, without prejudice or disclaimer.

After the amendment, pending claims include a) examined claims 18, 25, 28-30 and 32-40 and b) new claims 41-46.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a)

Claims 18, 25, 27-30 and 32-40 stand rejected as obvious over Chaudry (US 2004/0265238) in view of Cewers (USPN 6,357,671). Applicants respectfully traverse.

The PTO failed to establish a *prima facie* case of obviousness at least because of the reasons discussed below.

**1) The cited references do not teach or suggest the dosage recited in claim 18**

Chaudry generically encompasses a number of drugs and inhalation devices, creating an enormous number of drug-device dosing possibilities. The only specific guidance provided by Chaudry in relation to treprostinil dosing is found in prophetic example 4, reproduced here in its entirety:

“Example 4  
[0097]  
5 Treprostinil sodium 0.1-10.0 mg/ml Sodium Chloride 2.0-10.0 mg/ml Sodium

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