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PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Calderari, et al.

Serial No.: **11/186,311**

Filing Date: **July 21, 2005**

Title: **LIQUID PHARMACEUTICAL FORMULATIONS OF PALONOSETRON**

Art Unit: **1614**

Examiner: **Gembeh, Shirley V.**

STATUTORY DECLARATION OF DANIELE BONADEO, M. Chem. Pharm.
37 C.F.R. §§ 131 and 132

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

I, Daniele Bonadeo, hereby give this declaration under 37 C.F.R. §§ 131 and 132:

1) My name is Daniele Bonadeo.

2) I make this declaration based on my own personal knowledge, information, and belief. I am competent to testify concerning the matters set forth herein.

3) I am Deputy Director, Head of Corporate Technical Affairs, Manufacturing Operations, for Helsinn Healthcare SA ("Helsinn"), the assignee of the above-referenced patent application.

4) I am also an inventor for this application.

5) This patent application is based on the discovery of liquid formulations of palonosetron hydrochloride with improved stability. The formulations can be stored for prolonged

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on February 16, 2007

Clark G. Sullivan, Reg. No. 36,942

Dr. Reddy's Laboratories, Ltd., et al.
v.
Helsinn Healthcare S.A., et al.
U.S. Patent No. 9,173,942

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periods of time in a variety of conditions without significant degradation or loss of potency, and thus are considered pharmaceutically stable.

6) The formulations were developed by myself and others at Helsinn in the late 1990s, and were completed sometime before March 24, 1999.

7) We filed U.S.S.N. 60/444,351, which was our first patent application based on these formulations, on January 30, 2003. We filed PCT application No. PCT/EP04/000888 on January 30, 2004, claiming priority to the '351 application. We filed U.S.S.N. 11/186,311 on July 21, 2005, claiming priority to the US '351 and PCT '888 applications. Finally, we filed three continuation applications -- U.S.S.N. 11/388,268 (the '268 application), U.S.S.N. 11/388,269 (the '269 application), and U.S.S.N. 11/388,270 (the '270 application), on March 4, 2006, claiming priority to the US '311 application, the US '351 application, and the PCT '888 application.

8) Each of the foregoing applications contains the following example of an injectable formulation of palonosetron hydrochloride:

EXAMPLE 4: FORMULATION I

Ingredient	mg/mL
Palonosetron Hydrochloride	0.05
Mannitol	41.5
EDTA	0.5
Trisodium citrate	3.7
Citric acid	1.56
WFJ	1.0
Sodium hydroxide solution and/or hydrochloric acid solution	pH 5.0 ± 0.5

9) For ease of reference, I will refer to this formulation as the Example 4 formulation.

10) The Example 4 formulation was developed sometime before March 24, 1999, by myself and others at Helsinn Healthcare, and transmitted to a contract manufacturer for Helsinn, Oread Laboratories in Palo Alto California ("Oread"), for the production of commercial scale batches of palonosetron hydrochloride.

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11) A copy of the master batch record developed by Oread for the formulation is contained in Exhibit A hereto.

12) The master batch record describes the Example 4 formulation on page 2 of 22. As can be seen, the batch record has an effective date of March 24, 1999, and thus makes clear that we had developed the formulation before this date.

13) I am familiar with the work of Macciocchi et al. that is described in WO 2004/045615 (the "Macciocchi application"), and the work of Baroni et al. that is described in WO 2004/073714 (the "Baroni application"). With the exception of Dr. Macciocchi, who recently passed away, the inventors for those patent applications are close colleagues of mine who also work at Helsinn or, in the case of Dr. Baroni, recently retired from Helsinn.

14) The Macciocchi and Baroni PCT applications were filed on November 6, 2003 and February 18, 2004, respectively, which is more than four years after we first invented the Example 4 formulation.

15) At least some of the clinical studies described in the Macciocchi and Baroni applications used the Example 4 formulation.

16) Any description in the Macciocchi and Baroni applications of palonosetron formulations having a pH between 4 and 6, palonosetron concentrations between 0.01 and 5.0 mg/ml, or the use of mannitol or a chelating agent in liquid palonosetron formulations, was derived from the Example 4 formulation that we presented to Drs. Macciocchi and Baroni for use by them in their clinical programs.

17) All of the formulation development work described in the foregoing paragraphs was performed in Switzerland, which to my knowledge has been a member of the World Trade Organization (WTO) since July 1, 1995, and the United States.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, further, that these statements were made with the knowledge that willful false statements and the like so made are punishable

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by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code. I declare under penalty of perjury that the foregoing is true and correct.

Dated: February 13, 2007

Daniele Bonadeo

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Exhibit A

Gilead, Palo Alto, CA

Product: Palonosetron HCl Intravenous Injection, 0.05 mg/mL, Bulk	Formulation No.: FD77A-009	PID No.: 75941	MBR No.: D77B001.00
	Client FID No.: N/A		Lot No.: 17373

Effective Date: MAR 24 1999 Supersedes: Original

Scale: 30 Liters

Master Record Approvals

E. Marambay	3/17/99	[signature]	3/17/99	[signature]	
Prepared By	Date	Sterile Manufacturing	Date	Client	
[signature]	3-17-99	[signature]	18 Mar '99	[signature]	
Formulation Development	Date	Quality Assurance	Date	Client Corporate Quality	

Client Lot No.:

Theoretical Lot Size: 30 Liters

Date Compounding Started:

5,660 Units, 5.3 mL/Vial

Date Filtration Completed:

Manufacturing Site:

Batch Record Issued By: [signature]
Documentation

Completed Batch Record Reviewed By: [signature]
Sterile Manufacturing

Completed Batch Record Reviewed By: [signature]
Quality Assurance

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