

On Behalf Of:

Noven Pharmaceuticals, Inc.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

**NOVEN PHARMACEUTICALS, INC.,
Petitioner**

v.

**NOVARTIS AG AND LTS LOHMANN THERAPIE-SYSTEME AG,
Patent Owners**

Inter Partes Review No.: 2014-00549

U.S. Patent 6,316,023

REPLY DECLARATION OF AGIS KYDONIEUS, PH.D.

TABLE OF CONTENTS

	<u>Page</u>
I. QUALIFICATIONS.....	1
II. INFORMATION CONSIDERED.....	1
III. SUMMARY	3
IV. PERSON OF ORDINARY SKILL IN THE ART	6
V. CLAIM CONSTRUCTION.....	7
VI. A POSA WOULD HAVE ANALYZED THE STRUCTURE OF RIVASTIGMINE AND DETERMINED THAT RIVASTIGMINE IS SUSCEPTIBLE TO OXIDATIVE DEGRADATION, WITHOUT NEEDING TO CONDUCT TESTING TO REACH THIS CONCLUSION.....	10
VII. DR. KLIBANOV MISCHARACTERIZES THE PRIOR ART AND MY OPINIONS REGARDING THE PRIOR ART.....	14
A. Dr. Klibanov Mischaracterizes Enz (Exhibit 1002).....	15
B. Dr. Klibanov Mischaracterizes Rosin (Exhibit 1008).	15
C. Dr. Klibanov Mischaracterizes Elmalem (Exhibit 1009).	24
D. Dr. Klibanov Mischaracterizes Sasaki (Exhibit 1005).	34
VIII. A POSA WOULD HAVE BEEN MOTIVATED TO COMBINE THE TEACHINGS OF THE PRIOR ART TO ADDRESS THE EXPECTED SUSCEPTIBILITY OF RIVASTIGMINE TO OXIDATIVE DEGRADATION BY ADDING AN ANTIOXIDANT.	43
A. A POSA Would Not Draw a Distinction Between Enz, Rosin and Elmalem Based on Modes of Drug Administration.	44
B. A POSA Would Have Considered Prior Art Regarding RA ₇ (Rosin and Elmalem) as Relevant to Rivastigmine.	47
C. A POSA Would Have Been Motivated to Combine Enz and Ebert.	48
IX. ROSIN (EXHIBIT 1008) WOULD HAVE BEEN UNDERSTOOD BY A POSA TO CLAIM RIVASTIGMINE.....	49

X. A POSA WOULD HAVE HAD A REASONABLE EXPECTATION THAT ADDING AN ANTIOXIDANT WOULD SUCESSFULLY REDUCE OR ELIMINATE OXIDATIVE DEGRADATION OF RIVASTIGMINE..... 50

XI. THE INVENTOR’S EXPERIENCE SUPPORTS MY ANALYSIS..... 53

APPENDICIES

APPENDIX A: Sasaki (Exhibit 1005) Working Examples Calculation

APPENDIX B: Calculation of Antioxidant Weight Percentage for Elmalem (Exhibit 1009)

I, Agis Kydonieus, Ph.D., declare and state as follows:

I. QUALIFICATIONS

1. I previously submitted a Declarations in IPR2014-00549 (Exhibit 1010) setting forth my background and credentials. My curriculum vitae (Exhibit 1023) sets forth my education and experience in further detail, and I further explained my background during my January 13, 2015 deposition (Exhibit 1030 at 107:2-109:13).

II. INFORMATION CONSIDERED

2. In forming the opinions set forth herein, I have considered the documents and exhibits referenced by Patent Owners and those referenced by Dr. Klibanov in his declaration (Exhibit 2012). I have also relied on my own experiences and knowledge, and have also considered the documents referenced in my initial declaration (Exhibit 1010) and those I mentioned during my deposition (Exhibit 1030).

3. I have also considered the documents discussed herein, which include the following:

- The Board's institution Decision for IPR2014-00549 (Paper 10).
- The transcript for the *Novartis v Noven* trial that was held December 1-3, 2014. (Exhibits 1026-1028.)

- Internal Novartis memorandum written by Dr. Tiemessen, N0272228-29. (Exhibit 1033.)
- Internal Novartis e-mail communication from Dr. Tiemessen to O. Garinot, N0272563. (Exhibit 1034.)
- [REDACTED] Meeting minutes of the LTS-Sandoz (Novartis) working group, N0317247-64. (Exhibit 1035.)
- Excerpts of the confidential transcript of the October 17-18, 2012 deposition of Dr. Henricus L.G.M. Tiemessen. (Exhibit 1036.)
- Morrison and Boyd, 2nd Ed. 1992. (Exhibit 1038.)
- PDR Medical Dictionary, 1st Ed. 1995. (Exhibit 1039.)
- CRC Handbook of Chemistry and Physics. (Exhibit 1040.)
- U.S. Patent 7,683,205. (Exhibit 1041.)
- U.S. Patent 8,324,429. (Exhibit 1042.)
- Toronto Research Chemicals Inc. web page. (Exhibit 1044.)
- David Shamah, *Alzheimer Drug Pioneer to Get Israel Prize, Professor Weinstock-Rosin, who developed Exelon, will be recognized for her work on Israel Independence Day*, TIMES OF ISRAEL, Mar. 4, 2014. (Exhibit 1045.)
- Textbook of Polymer Science, Chapter 9 (Billmeyer, 2d ed. 1971). (Exhibit 1046.)

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.