

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PAR PHARMACEUTICAL, INC.,
Petitioner,

v.

HYPERION THERAPEUTICS, INC.,
Patent Owner.

Case IPR2015-01117
Patent 8,642,012

PETITIONER'S REPLY TO PATENT OWNER'S RESPONSE

Mail Stop "PATENT BOARD"
Patent Trial and Appeal Board
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Table of Contents

INTRODUCTION	1
ARGUMENT	2
I. PATENT OWNER'S REBUTTAL ARGUMENTS ARE WITHOUT MERIT.....	2
A. Petitioner's Construction of "About 60%" Is the Broadest Reasonable Construction.	2
B. There Was No "Consensus" in the Prior Art that PAA Completely Converts to UPAGN.....	5
C. The Prior Art Teaches Incomplete Conversion.....	6
1. A POSA reading <i>Brusilow '91</i> Would Recognize That It Does Not Teach Complete Conversion.....	7
2. A POSA Reading <i>Shiple</i> Would Recognize That It Does Not Teach Complete Conversion.....	10
D. Patent Owner Ignores Or Mischaracterizes Any Prior Art Showing Incomplete Conversion As "Confusing," Or "Discredited."	11
1. Patent Owner Failed To Show That Posas Regard <i>Sherwin '19</i> As Confusing, Discredited, Or To Be Ignored.	12
2. Patent Owner Failed To Show That Posas Regard <i>Comte As</i> Confusing, Discredited, Or To Be Ignored.....	15
E. Patent Owner Fails to Recognize <i>Brusilow '91</i> Teaches Dose Adjustment Based on UPAGN.....	17
F. Patent Owner Ignores Clear Motivation to Combine.....	19
II. PETITIONER'S RELIANCE ON CERTAIN PRIOR ART TEACHINGS REMAINS UNREBUTTED.....	21
A. Patent Owner Does Not Refute the Teachings of <i>Fernandes</i> , the '647 patent, <i>Kasumov</i> or the '979 patent, as Applied in Instituted Grounds 2, 3 Or 4.....	21
B. Patent Owner Does Not Refute that A Person of Ordinary Skill in the Art Would Have Considered Residual Enzyme Activity in View of <i>Fernandes</i>	22

C. Patent Owner Does Not Refute that the '647 Patent Teaches the Use of a Ratio of UPAGN to Creatinine to Target an Output for UPAGN.22

D. Patent Owner Does Not Refute that *Kasumov* and the '979 Patent Disclose the PAA Prodrug HPN-100.....23

III. PATENT OWNER FAILED TO PROVIDE ANY EVIDENCE OF SECONDARY CONSIDERATIONS.23

IV. CONCLUSION.....24

INTRODUCTION

The '012 patent claims are directed to methods for determining an effective dosage of a PAA prodrug to treat a urea cycle disorder in a patient, which involves measuring the patient's UPAGN output, and then calculating the effective dosage based on a mean conversion of PAA prodrug to UPAGN of about 60%. It is undisputed that it was well known in the art prior to the filing of the '012 patent, that (1) PAA prodrugs were used to treat UCDs, (2) UPAGN is a direct measure of waste nitrogen clearance provided by a PAA prodrug, and (3) effective dose of PAA prodrug based on a target UPAGN could be calculated. The central dispute, therefore, is whether the prior art teaches or suggests the use of *about 60%* mean conversion of PAA prodrug to UPAGN. The answer is undoubtedly yes.

Indeed, the prior art including *Brusilow '91*, *Sherwin '19*, *Comte*, *Kasumov*, and *Simell* – discloses conversions of PAA or PAA prodrugs to UPAGN ranging from 51% to 90%. Patent Owner attempts to skirt these disclosures by positing, without any evidence from a POSA, that the prior art taught that PAA or PAA prodrugs are completely or nearly completely converted to UPAGN. The calculations and results included in the references cited by Petitioner, however, show actual conversion values falling within the range of “about 60%” as recited in

the '012 patent claims. Therefore, Patent Owner's teaching away arguments must fail.

For these reasons, and for the reasons discussed in the Petition, Dr. Sondheimer's declaration, and below, Petitioner respectfully submits that the Board should find each of the '012 patent claims unpatentable as obvious over the prior art.

ARGUMENT

I. PATENT OWNER'S REBUTTAL ARGUMENTS ARE WITHOUT MERIT.

Patent Owner's Response presents a very limited rebuttal to the instituted grounds of review. Without the aid of a qualified expert to provide it with a POSA's point of view, Patent Owner: misinterprets the claim term "about 60%"; misunderstands the prior art, such as *Brusilow '91*; and misreads what the prior art as a whole disclosed to a POSA as of 2008.

A. Petitioner's Construction of "About 60%" Is the Broadest Reasonable Construction.

Petitioner's construction for "about 60%" (i.e., encompassing the range 53-67%) is soundly based on and supported by Dr. Sondheimer's expert declaration and testimony, as well as numerous citations to intrinsic evidence. (Petition, Paper No. 2 ("Pet.") at 10-11; Ex. 1002 at ¶ 27; Ex. 2012 at 58:22-23; Ex. 1001 at 31:32-35; Ex. 1021 at 682-683.) Patent Owner, on the other hand, concludes, without

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.