

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LUPIN LTD. and LUPIN PHARMACEUTICALS INC.

Petitioners,

v.

HORIZON THERAPEUTICS, LLC.

Patent Owner.

IPR2017-01159

**PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,254,278
PURSUANT TO §§ 35 U.S.C. 311-319 AND 37 C.F.R. § 42**

Mail Stop PATENT BOARD
Patent Trial and Appeal Board
United States Patent and Trademark Office
PO Box 1450
Alexandria, Virginia 22313-1450

Dr. Gregory Enns
April 23, 2018
Exhibit No. 1026
Megan F. Alvarez
RPR, CSR No. 12470

LUPIN EX. 1026

TABLE OF CONTENTS

	<u>Page</u>
I. INTRODUCTION.....	1
II. SUMMARY OF THE '278 PATENT AND ITS PROSECUTION HISTORY.....	2
A. Independent Claims	2
B. Prosecution History.....	5
III. BACKGROUND ON THE UREA CYCLE, UCDS, AND NITROGEN SCAVENGING DRUGS	5
IV. GROUNDS FOR STANDING (37 C.F.R. § 42.104(a))	8
V. PAYMENT OF FEES (37 C.F.R. § 42.103).....	8
VI. MANDATORY NOTICES (37 C.F.R. § 42.8).....	8
A. Real Parties-in-Interest.....	8
B. Related Matters	8
C. Lead and Backup Counsel (37 C.F.R. § 42.8(b)(3)) and Service Information (37 C.F.R. § 42.8(b)(4))	9
VII. PERSON OF ORDINARY SKILL IN THE ART	10
VIII. CLAIM CONSTRUCTION	10
IX. STATEMENT OF THE PRECISE RELIEF REQUESTED AND THE REASONS THEREFORE (37 C.F.R. §§ 42.22(a) and 42.104(b)).....	13
A. Ground 1: Claims 1-3 are Unpatentable as Obvious Over the '859 Publication..	14
1. Overview of Prior Art Applied in Ground 1	14
2. Independent Claim 1	17
3. Dependent Claims 2 and 3	21
4. Lack of Secondary Considerations	21
B. Ground 2: Claims 4-7 and 12-15 are Unpatentable as Obvious Over <i>Blau, Simell,</i> and the '859 Publication.....	24
1. Overview of Prior Art Applied in Ground 2.....	24
2. Motivation to Combine Applied Prior Art.....	25
3. Lack of Secondary Considerations	27
4. Independent Claim 4	27
(a) Preamble	27
(b) Claim 4, Part (a).....	31
(c) Claim 4, Part (b).....	32
(d) Claim 4, Part (c).....	34
(e) Claim 4, Wherein Clause	36
5. Independent Claim 12.....	38
(a) Preamble	38
(b) Claim 12, Parts (a) and (b).....	40

(c)	Claim 12, Part (c).....	40
(d)	Claim 12, Part (d).....	41
6.	Dependent Claims 5 and 13	42
7.	Dependent Claims 6, 7, 14 and 15	43
C.	Ground 3: Claims 8-11 are Unpatentable as Obvious in View <i>Blau, Simell</i> , the '859 <i>Publication</i> , and the <i>Brusilow '979 Patent</i>	44
1.	Overview of Prior Art Applied in Ground 3	44
2.	Motivation to Combine Applied Prior Art.....	45
3.	Lack of Secondary Considerations	46
4.	Independent Claim 8	46
(a)	Preamble and Parts (a)-(c) of Independent Claim 8.....	46
(b)	Wherein Clause of Claim 8.....	46
5.	Dependent Claim 9	48
6.	Dependent Claims 10 and 11	48
X.	CONCLUSION	49

List of Exhibits

Ex. No.	Description
Ex. 1001	U.S. Patent No. 9,254,278 to Scharschmidt <i>et al.</i> (“’278 Patent”)
Ex. 1002	Declaration of Keith Vaux, M.D.
Ex. 1003	U.S. Patent No. 9,326,966 to Scharschmidt <i>et al.</i> (“’966 Patent”)
Ex. 1004	Brusilow, <i>et al.</i> , <i>Treatment of Episodic Hyperammonemia in Children with Inborn Errors of Urea Synthesis</i> , 310 <i>The New England Journal of Medicine</i> , 1630-1634 (1984). (“ <i>Brusilow ’84</i> ”).
Ex. 1005	Simell, <i>et al.</i> , <i>Waste Nitrogen Excretion Via Amino Acid Acylation: Benzoate and Phenylacetate in Lysinuric Protein Intolerance</i> , 20 <i>Pediatric Research</i> , 1117-1121 (1986). (“ <i>Simell</i> ”).
Ex. 1006	Blau, Duran, Blaskovics, Gibson (editors), <i>Physician’s Guide to the Laboratory Diagnosis of Metabolic Diseases</i> , 261-276 (2d ed. 1996). (“ <i>Blau</i> ”).
Ex. 1007	U.S. Patent Publication No. 2010/0008859, filed January 7, 2009, published January 14, 2010. (<i>the “’859 Publication</i> ”).
Ex. 1008	Scientific Discussion for Ammonaps, EMEA 2005, available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000219/WC500024748.pdf . (“ <i>Scientific Discussion</i> ”).
Ex. 1009	Dixon, <i>et al.</i> , <i>Intercurrent Illness in Inborn Errors of Intermediary Metabolism</i> , 67 <i>Archives of Disease in Childhood</i> , 1387-1391 (1992). (“ <i>Dixon</i> ”).
Ex. 1010	UMass Memorial Laboratories, Lab Updates, February 2007, Measurement of Ammonia in Blood
Ex. 1011	Brusilow, <i>Phenylacetylglutamine May Replace Urea as a Vehicle for Waste Nitrogen Excretion</i> , 29 <i>Pediatric Research</i> , 147-150 (1991). (“ <i>Brusilow ’91</i> ”).

Ex. 1012	Yajima, <i>et al.</i> , <i>Diurnal Fluctuation of Blood Ammonia Levels in Adult-Type Citrullinemia</i> , 137 <i>Tohoku J. Exp. Med.</i> , 213-220 (1982). (“Yajima”).
Ex. 1013	Batshaw, <i>et al.</i> , <i>Treatment of Carbamyl Phosphate Synthetase Deficiency with Keto Analogues of Essential Amino Acids</i> , 292 <i>The New England J. Medicine</i> , 1085-1090 (1975). (“Batshaw”).
Ex. 1014	Kasumov, <i>et al.</i> , <i>New Secondary Metabolites of Phenylbutyrate in Humans and Rats</i> , 32 <i>Drug Metabolism and Disposition</i> , 10-19 (2004). (“Kasumov”).
Ex. 1015	Barsotti, <i>Measurement of Ammonia in Blood</i> , 138 <i>J Pediatrics</i> , S11- S20 (2001). (“Barsotti”).
Ex. 1016	Berry, <i>et al.</i> , <i>Long-term management of patients with urea cycle disorders</i> , <i>Journal of Pediatrics</i> , Vol. 138, No. 1, S56–S61 (2001). (“Berry”).
Ex. 1017	Levin, <i>et al.</i> , <i>Hyperammonaemia A Variant Type of Deficiency of Liver Ornithine Transcarbamylase</i> , <i>Arch. Dis. Childh.</i> , 1964, 44. 162 (1968).
Ex. 1018	Prosecution History of U.S. Patent No. 8,404,215.
Ex. 1019	Excerpt from <i>Stedman’s Medical Dictionary</i> (Lippincott Williams & Wilkins 2006).
Ex. 1020	Buphenyl [®] label, <i>Physician’s Desk Reference</i> , 60 th ed. (2006) at 3327-28.
Ex. 1021	Ammonul [®] label, <i>Physician’s Desk Reference</i> , 60 th ed. (2006) at 3323-26.
Ex. 1022	Prosecution History of U.S. Patent No. 9,254,278.
Ex. 1023	<i>Curriculum vitae</i> of Keith Vaux, M.D.
Ex. 1024	U.S. Patent No. 5,968,979 (“ <i>Brusilow ’979 Patent</i> ”).
Ex. 1025	Prosecution History of U.S. Patent No. 9,326,966.

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.