

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANDOZ INC.,
Petitioner,

v.

PHARMACYCLICS LLC,
Patent Owner.

Case IPR2019-00865
U.S. Patent No. 9,795,604

PATENT OWNER'S RESPONSE

TABLE OF CONTENTS

I.	Introduction.....	1
II.	The Patented Invention	4
III.	The Clinical Efficacy Limitations Must Be Given Patentable Weight	5
A.	Legal Standard.....	6
B.	The Efficacy Limitations Here “Demand Efficacy” as Shown by the Claims and the Intrinsic Record	8
C.	The Clinical Efficacy Limitations Are Not an Inherent or Intended Result	12
D.	Once Given Patentable Weight, There Is Little Dispute as to Construction	15
IV.	Claims 6-8, 29-31, 44-46, and 51-53 Are Not Unpatentable at Least Because of their Claimed Clinical Efficacies	16
V.	Claims 4, 13, and 15 (and claims depending therefrom), Directed to Treatment of Specific Patient Populations, Are Not Anticipated by the '085 Publication	20
VI.	Claims 4, 13, and 15 (and claims depending therefrom), Directed to Treatment of Specific Patient Populations, Are Not Obvious.....	22
A.	Ground 2: The '085 Publication in View of a POSA's Knowledge.....	22
1.	The '085 Publication would not have motivated a POSA to treat steroid-resistant/refractory cGVHD with ibrutinib	22
2.	Petitioner ignores the requirement for a reasonable expectation of success	24
3.	A POSA would not have reasonably expected success based on the limited disclosure of the '085 Publication	25
B.	Ground 3: The '085 Publication in View of Shimabukuro- Vornhagen and Herman	28

1.	None of the asserted references contain any <i>in vitro</i> , preclinical, or clinical data for ibrutinib in cGVHD	30
2.	Shimabukuro-Vornhagen would not have given rise to a reasonable expectation of success.....	31
a.	The role of B cells in cGVHD pathogenesis was complex and poorly understood	31
b.	Rituximab and ibrutinib are fundamentally different drugs.....	33
c.	Drugs targeting both B and T cells presented safety concerns in cGVHD patients	36
d.	Steroid-resistant/refractory cGVHD patients were notoriously difficult to treat and rituximab studies were met with skepticism	38
3.	Herman’s disclosures regarding cytokines would not have given rise to a reasonable expectation of success	41
C.	Ground 4: The ’085 Publication, Shimabukuro-Vornhagen, and Uckun	44
1.	Like the ’085 Publication and Shimabukuro-Vornhagen, Uckun does not contain any <i>in vitro</i> , preclinical, or clinical data for ibrutinib in cGVHD	45
2.	Mouse models cannot establish a reasonable expectation of success for treating steroid-resistant/refractory cGVHD patients	45
3.	Petitioner improperly conflates aGVHD with cGVHD and prophylaxis with treatment.....	46
4.	LFM-A13 had not been shown to prevent or treat aGVHD	48
VII.	Claims 24, 28, 35, 39, 43, 50, and 55 Are Neither Anticipated nor Obvious at Least Because of Their 420 mg Daily Dose	50

VIII.	Claim 1 Is Not Unpatentable, Thus All Challenged Claims Are Not Unpatentable	52
A.	Ground 1 Fails as to Claim 1 Because the '085 Publication Does Not Enable Treatment of cGVHD with Ibrutinib	53
B.	Grounds 2-4 Fail as to Claim 1 Because No Reference, Alone or in Combination, Provides a Motivation to Treat cGVHD with Ibrutinib with a Reasonable Expectation of Success	56
IX.	The Objective Indicia Compel a Finding of Nonobviousness	57
A.	There Is a Strong Nexus Between the Challenged Claims and the Objective Indicia of Nonobviousness	57
B.	Substantial Industry Acclaim, Including from Petitioner's Expert, Demonstrates Nonobviousness.....	58
C.	The Claimed Methods Satisfied a Long-felt, Unmet Need.....	61
D.	Failures of Others Negate Any Expectation of Success	63
E.	Ibrutinib Is Unexpectedly Effective in Treating cGVHD	65
X.	Constitutional Challenge under <i>Arthrex</i>	66

TABLE OF AUTHORITIES

	Page(s)
Federal Cases	
<i>Allergan Sales LLC v. Sandoz, Inc.</i> , 935 F.3d 1370 (Fed. Cir. 2019)	<i>passim</i>
<i>Allergan, Inc. v. Sandoz, Inc.</i> , 726 F.3d 1286 (Fed. Cir. 2013)	7, 8, 12
<i>Arthrex, Inc. v. Smith & Nephew Inc.</i> , 941 F.3d 1320 (Fed. Cir. 2019)	66
<i>Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.</i> , 246 F.3d 1368 (Fed. Cir. 2001)	12, 13, 14
<i>Connell v. Sears, Roebuck & Co.</i> , 722 F.2d 1542 (Fed. Cir. 1983)	21
<i>In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.</i> , 676 F.3d 1063 (Fed. Cir. 2012)	63
<i>Eli Lilly & Co. v. Teva Parenteral Meds., Inc.</i> , 845 F.3d 1357 (Fed. Cir. 2017)	51, 52
<i>Endo Pharm. Inc. v. Depomed, Inc.</i> , IPR2014-00654, Paper 69 (PTAB Sept. 21, 2015).....	59
<i>Ferring B.V. v. Watson Labs, Inc.</i> , 764 F.3d 1401 (Fed. Cir. 2014)	63
<i>Ferrum Ferro Capital, LLC v. Allergan Sales, LLC</i> , IPR2015-00858, Paper 10 (PTAB Sept. 31, 2015).....	7
<i>Galderma Labs., L.P. v. Tolmar, Inc.</i> , 737 F.3d 731 (Fed. Cir. 2013)	52
<i>Gambro Lundia AB v. Baxter Healthcare Corp.</i> , 110 F.3d 1573 (Fed. Cir. 1997)	59

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.