MYLAN PHARMACEUTICALS INC.,

Petitioner,

v.

BAUSCH HEALTH IRELAND LIMITED,

Patent Owner.

Case IPR2022-00722 U.S. Patent No. 7,041,786

PATENT OWNER'S RESPONSE



Case IPR2022-00722 U.S. Patent No. 7,041,786

Table of Contents

I.	Intro	oduction				
II.	Scope and Content of the Art					
	A.	The Gastrointestinal Tract and Chronic Constipation				
	B.	Naturally Occurring Guanylate Cyclase-C Agonist Peptides				
		1. Uroguanylin and its topoisomerism problem	9			
		2. Guanylin	12			
		3. Heat-stable enterotoxins	13			
		4. Relative activity of naturally occurring guanylate cyclase-C agonist peptides	15			
	C.	Development of Therapeutic Peptides Was Unpredictable				
	D.	Development of GCC Agonists				
III.	The Invention of Plecanatide					
	A.	U.S. Patent No. 7,041,786				
	B.	The Person of Ordinary Skill in the Art				
IV.	Ground 1: Claim 1 Would Not Have Been Obvious Over Currie and Li					
	A.	Absent Hindsight, a POSA Would Not Have Selected Human Uroguanylin as a Lead Compound				
		1. Human uroguanylin's interconverting topoisomers made it an unattractive option for further development	29			
		2. Heat-stable enterotoxins were a far more attractive option	33			
	В.	Even Accepting Human Uroguanylin as a Lead Compound, a POSA Would Not Have Been Motivated to Substitute Asp ³ with				



Case IPR2022-00722 U.S. Patent No. 7,041,786

		ny Expectation of Yielding a Peptide with Improved38			
1.	would	ing in the art suggested substituting Asp ³ for Glu ³ d have addressed human uroguanylin's conversion			
2.	Nothing in the art suggested that substituting Asp ³ for Glu ³ would have reasonably been expected to improve the resulting peptide's activity				
	a.	A POSA seeking to improve human uroguanylin's activity would not have made a "conservative substitution"			
	b.	The art taught that Asp ² and Asp ³ were required, and a POSA would not have replaced either amino acid with an expectation of maintaining activity45			
		i. Li did not suggest Glu as an obvious substitution at position 3 of human uroguanylin			
		ii. Contemporaneously with Li, the art taught the importance of Asp³ to human uroguanylin's activity			
		iii. By January 2002, the art had confirmed the perceived importance of retaining Asp ² and Asp ³			
	c.	A POSA would not have expected that substituting Asp ³ for Glu ³ would result in a peptide that was protonated longer than human uroguanylin or had improved activity			
	d.	Aspartimide formation would not have motivated substituting Asp ³ for Glu ³ 56			



Case IPR2022-00722 U.S. Patent No. 7,041,786

	3.	Unexpected Superior Results Underscore the Lack of any Reasonable Expectation of Success and Reinforce the			
		Non	obviousness of Plecanatide	57	
		a.	Unexpected stabilization against interconversion	58	
		b.	Unexpectedly superior potency	60	
		c.	Unexpectedly superior heat stability	64	
		d.	Unexpectedly superior binding affinity	66	
V.			Claims 2-6 Would Not Have Been Obvious Over sed on Currie and Li	67	
VI	Conclusion			67	



TABLE OF AUTHORITIES

Page(s) **Federal Cases** *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat.* Litig., Daiichi Sankyo Co. v. Matrix Lab'ys, Ltd., Eli Lilly & Co. v. Zenith Goldline Pharms., Inc., Hybritech Inc. v. Monoclonal Antibodies, Inc., InfoBionic, Inc. v. Braemer Mfg., LLC, IPR2015-01704, Paper 11 (PTAB Feb. 16, 2016)......42 Kinetic Techs., Inc. v. Skywork Sols., Inc., In re Kubin, 561 F.3d 1351 (Fed. Cir. 2009)44 Mintz v. Dietz & Watson, Inc., 679 F.3d 1372 (Fed. Cir. 2012)57 Otsuka Pharm. Co. v. Sandoz, Inc., Rohm & Haas Co. v. Brotech Corp., 127 F.3d 1089 (Fed. Cir. 1997)42 Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.,



DOCKET

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.

