Filed on behalf of Patent Owners Genentech, Inc. and City of Hope by:

David L. Cavanaugh	Adam R. Brausa	Jeffrey P. Kushan
Reg. No. 36,476	Reg. No. 60,287	Reg. No. 43,401
Heather M. Petruzzi	Daralyn J. Durie	Peter S. Choi
Reg. No. 71,270	Pro Hac Vice Application	Reg. No. 54,033
Robert J. Gunther, Jr.	Pending	Sidley Austin LLP
Pro Hac Vice Application	Durie Tangri LLP	1501 K Street, N.W.
Pending	217 Leidesdorff Street	Washington, D.C.
Wilmer Cutler Pickering	San Francisco, CA 94111	20005
Hale and Dorr LLP		
1875 Pennsylvania Ave., NW		

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANOFI-AVENTIS U.S. LLC AND REGENERON PHARMACEUTICALS, INC., Petitioners

V.

GENENTECH, INC. AND CITY OF HOPE Patent Owners

Case IPR2015-01624 Patent 6,331,415

EXPERT DECLARATION OF JOHN FIDDES, PH.D.



Washington, DC 20006

MERCK v. GENENTECH

TABLE OF CONTENTS

			Page
I.	INT	RODUCTION AND BACKGROUND	1
	A.	Qualifications And Experience	2
	B.	Compensation	4
	C.	Prior Expert Testimony	4
II.	LEC	GAL PRINCIPLES ON OBVIOUSNESS	4
III.	BAC	CKGROUND OF THE TECHNOLOGY	7
	A.	Genes, Proteins And Antibodies	7
	B.	Antibody Production Techniques As Of April 1983	16
	C.	Use of Recombinant Gene Expression To Produce Proteins	18
		1. Basic principles of recombinant gene expression	18
		2. As of April 1983, Only a Small Number of Monomeric Eukaryotic Proteins Had Been Produced Recombinantly	20
	D.	As of April 1983, Insulin Was The Only Multimeric Eukaryotic Protein Which Had Been Produced Recombinantly	
	E.	In May 1981 (When Bujard Was Filed), The Speculative Possibility Of Using Recombinant Techniques To Produce Antibodies Was Highly Uncertain And Unpredictable	37
	F.	Research Involving Antibodies And Recombinant Gene Expression Between May 1981 And April 1983 Confirmed The Uncertainty And Unpredictability Of Whether Antibodies Could Be Produced Recombinantly	
	G.	As Of April 1983, Highly Acclaimed Scientists Were Still Uncertain Whether It Was Even Possible To Make Antibodies Using Recombinant Techniques	46



Case No. IPR2015-01624 Declaration of John Fiddes, Ph.D.

	H.		ombinantly	49
	I.		Of April 1983, Nobody Had Produced A Multimeric aryotic Protein Recombinantly In A Single Host Cell	49
IV.			IMS UNDER CONSIDERATION AND THEIR ET ATION	53
	A.	The	Cabilly '415 Patent	53
	B.	Sum	mary Of Contested Claims.	54
	C.	The	Person Of Ordinary Skill In The Art.	56
V.	OPI	NIONS	S REGARDING THE ASSERTED PRIOR ART	57
	A.	Buja	rd	58
		1.	What is the focus of the Bujard reference?	58
		2.	Do the references to "multimers" and "one or more structura genes" in Bujard suggest the use of the co-expression of multiple, distinct eukaryotic genes of interest in a single hos cell?	st
		3.	Do the references to multiple "stop codons" in Bujard sugge the use of the strong promoter/terminator system for the expression of multiple, distinct genes in a single host cell?	
		4.	Does Bujard "at least suggest the coexpression of the heavy light chains" of an immunoglobulin in a "single host cell," a the Board found?	ıs
		5.	Does Bujard "teach away from the production of light chains one culture and heavy chains in another, to be combined chemically at a stage after their harvest and isolation," as Dr Foote argues?	ſ .
		6.	Does the statement in Bujard that the "proteins may be preparated as a single unit or as individual subunits and then joined	arec



Case No. IPR2015-01624 Declaration of John Fiddes, Ph.D.

		together in appropriate ways" suggest in vivo assembly of a multimeric protein in a single host cell, as Dr. Foote argues?.	84
	7.	Do you agree with the Board's finding that Bujard is "more specific and robust" than the Axel reference?	86
B.	Riggs	& Itakura	88
	1.	What is the focus of the Riggs & Itakura reference?	88
	2.	Does the Riggs & Itakura reference address the "same probler as Bujard and would the skilled artisan have had "good reason to combine these two references in April 1983?	n"
	3.	Would inferences gleaned from Riggs & Itakura have provide the person of ordinary skill with the motivation to "selectively apply the teachings of Bujard to the specific production of immunoglobulins" by means of co-expressing both the heavy and light chain in a single host cell?	/
	4.	Do you agree with Dr. Foote's opinion and the Board's preliminary finding that Bujard in combination with Riggs & Itakura renders the claimed invention of the Cabilly '415 pate obvious?	
C.	South	nern	00
	1.	What is the focus of the Southern reference?	00
	2.	Do you agree with Dr. Foote's opinion that the skilled artisan would have been motivated to combine Bujard and Southern because "both have as a goal the expression of genes of intere in a single transformed host cell, whether by using one (Bujar or two (Southern) vectors"?	est ed)
	3.	Would inferences gleaned from Southern have provided the person of ordinary skill with the motivation to "selectively apply the teachings of Bujard to the specific production of immunoglobulins" by means of co-expressing both the heavy and light chain in a single host cell?	



Case No. IPR2015-01624 Declaration of John Fiddes, Ph.D.

1.	Do you agree with Dr. Foote's opinion and the Board's	
	preliminary finding that Bujard in combination with South	ern
	renders the claimed invention of the Cabilly '415 patent	
	obvious?	111



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.

