#### UNITED STATES DISTRICT COURT CENTRAL DISTRICT OF CALIFORNIA WESTERN DIVISION

### BRISTOL-MYERS SQUIBB COMPANY,

Plaintiff/Counter-Defendant,

v.

GENENTECH, INC., and CITY OF HOPE

Defendants/Counter-Plaintiffs.

ELI LILLY AND COMPANY and IMCLONE SYSTEMS LLC,

DOCKE<sup>-</sup>

Δ

Plaintiffs/Counter-Defendants,

v.

GENENTECH, INC. and CITY OF HOPE, Defendants/Counter-Plaintiffs. Case No. 2:13-cv-05400-MRP-JEM

## CONFIDENTIAL

# EXPERT REPORT OF CARLO M. CROCE, M.D.

Case No. 2:13-cv-07248-MRP-JEM

Mylan v. Genentech IPR2016-00710

Find authenticated court documents without watermarks at <u>docketalarm.com</u>.

# **TABLE OF CONTENTS**

		<u>P</u>	age	
I.	INTRODUCTION			
II.	PROFESSIONAL EXPERIENCE AND QUALIFICATIONS1			
III.	PRIOR TESTIMONY4			
IV.	COMPENSATION			
V.	MATERIALS CONSIDERED			
VI.	QUESTIONS PRESENTED			
VII.	SUMMARY OF OPINION			
VIII.	RELE	VANT LAW	8	
	A.	35 U.S.C. § 112—Written Description and Enablement	8	
IX.	THE PERSON OF ORDINARY SKILL IN THE ART10			
Х.	THE MEANING OF THE CLAIMS OF THE CABILLY II AND III PATENTS 11			
XI.	OPINION			
	A.	The State of the Art of Antibody Production in 1983 Was Focused on Approaches that Did Not Involve Recombinant DNA	14	
	B.	Many Working In the Field In 1983 Were Using Hybridoma Technology to Make Monoclonal Antibodies, Including Human Ones	17	
	C.	Although My Laboratory Worked at the Intersection of Molecular Biology, Immunology and Medicine, We Did Not Envisage Making Antibodies Recombinantly	23	
	D.	The Cabilly II and Cabilly III Patents Adequately Describe How to Make a Recombinant Human Antibody that Binds to a Known or Desired Antigen	26	
		1. The Cabilly II and Cabilly III Patents Adequately Disclose Sour for Obtaining the DNA Sequences of an Antibody Capable of Binding a Known or Desired Antigen	27	

		2. The Cabilly II and Cabilly III Patents Sufficiently Describe How to Isolate the mRNA Encoding a Human Antibody that Binds to a Known Antigen
		3. The Cabilly II and Cabilly III Patents Sufficiently Describe How to Isolate the mRNA Encoding a Human Antibody that Binds to a Desired Antigen
		4. Phage Display, PCR, and Recombinant Mouse Technology Are Not Required to Make a Recombinant Human Antibody That Binds to a Known or Desired Antigen
	E.	The Cabilly II and Cabilly III Patent Show Possession of How to Make a Recombinant Human Antibody that Contains the DNA Sequence of an Antibody that Binds to a Known or Desired Antigen
	F.	The Cabilly II and Cabilly III Patents Adequately Describe and Enable How to Make a Recombinant Antibody Having a Variable Region
	G.	The Cabilly II and Cabilly III Patents Adequately Describe and Enable How to Make the Full Scope of Recombinant Antibodies
XII.	CON	LUSION

### I. INTRODUCTION

1. I submit this expert report, pursuant to Federal Rule of Civil Procedure 26(a)(2), on behalf of the defendants, Genentech, Inc. and City of Hope. I expect to testify at trial concerning the matters set forth in this report.

2. If called to testify, I may also explain principles and terminology referred and alluded to in this report as well as the documents referenced herein. I have not prepared at this time any exhibits that I expect to use to illustrate or summarize my testimony at trial.

3. However, I expect to refer to some or all of the information set forth below, and I will prepare any exhibits in accordance with the Court's orders. I also reserve the right to modify, amend and/or supplement the opinions expressed herein – particularly in response to any additional information cited by or opinions offered on behalf of Lilly or BMS.

#### II. PROFESSIONAL EXPERIENCE AND QUALIFICATIONS

4. I am the John W. Wolfe Chair in Human Cancer Genetics; Professor and Chairman of the Department of Molecular Virology, Immunology and Medical Genetics; Professor of Medicine; and Director of the Institute of Genetics and of the Human Cancer Genetics Program at Ohio State University in Columbus, OH.

5. My expertise is in the field of genetic mechanisms implicated in the pathogenesis of human cancer. Research performed in my laboratory has resulted in several significant scientific discoveries, including: a) demonstrating the juxtaposition of the human immunoglobulin genes to the *myc* oncogene and the deregulation of *myc* in Burkitt's lymphoma; and b) the discovery of the ALL1 gene (involved in acute leukemias) and the TLC 1 gene (associated with T-cell leukemias). My laboratory was

Find authenticated court documents without watermarks at docketalarm.com.

also the first to clone and characterize the Bc12 gene which is involved in follicular lymphoma and many other malignancies.

6. My research also focuses on the early events involved in the pathogenesis of lung, nasopharyngeal, head and neck, esophageal, gastro-intestinal and breast cancers. Recently, my laboratory discovered the involvement of microRNA genes in human cancer.

7. I received my M.D. degree, *summa cum laude*, from the University of Rome in 1969. I joined the faculty of the Wistar Institute in Philadelphia, Pennsylvania in 1970 and became a Professor in 1976. From 1980 to 1991, I was an Institute Professor and Associate Director at the Wistar Institute, and from 1980 to 1988 I was the Wistar Professor of Human Genetics at the University of Pennsylvania School of Medicine.

8. From 1988 to 1991, I also held the following positions at Temple University: a) Professor in the Departments of Pathology and Medicine at the School of Medicine; b) Chairman of the Graduate Program in Molecular Biology and Genetics, at the School of Medicine; and c) Director of the Fels Institute for Cancer Research and Molecular Biology.

9. From 1991-2004, I was the Director of the Kimmel Cancer Institute/Kimmel Cancer Center, and the Pugh Professor within and Chairman of the Department of Microbiology/Immunology at Jefferson Medical College of the Thomas Jefferson University, Philadelphia, Pennsylvania.

During the span of my career I have received over 20 awards from various institutions and foundations for cancer research, including: a) the Outstanding
Investigator Award, from the National Cancer Institute of the National Institutes of

# 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.

