Thomas H. Bienert, Jr., State Bar No. 135311
tbienert@bmkattorneys.com
Ariana Seldman Hawbecker, State Bar No. 190506
ahawbecker@bmkattorneys.com
BIENERT, MILLER & KATZMAN, PLC
903 Calle Amanecer, Suite 350
San Clemente, California 92673
Tel: (949) 369-3700/Fax (949) 369-3701

Reuben A. Guttman *(admitted pro hac vice)*
rguttman@gelaw.com
Traci L. Buschner *(admitted pro hac vice)*
tbuschner@gelaw.com
David T. Fischer*(admitted pro hac vice)*
dfischer@gelaw.com
GRANT & EISENHOFER P.A.
1747 Pennsylvania Ave., NW, Suite 875
Washington, DC 20006
Tel: (202) 386-9500/Fax: (202) 386-9505

Jay W. Eisenhoffer *(admitted pro hac vice)*
jeisenhofer@gelaw.com
GRANT & EISENHOFER P.A.
485 Lexington Avenue, 29th Floor
New York, NY 10017
Tel: (646) 722-8500/Fax: (646) 722-8501

Attorneys for Plaintiff-Relator Beverly Brown

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA – WESTERN DIVISION

UNITED STATES OF AMERICA, the States of CALIFORNIA, COLORADO, CONNECTICUT, DELAWARE, FLORIDA, GEORGIA, HAWAII, ILLINOIS, INDIANA, LOUISIANA, MARYLAND, MASSACHUSETTS, MICHIGAN, MINNESOTA, MONTANA, NEVADA, NEW HAMPSHIRE, NEW JERSEY, NEW MEXICO, NEW YORK, NORTH CAROLINA, OKLAHOMA, RHODE ISLAND, TENNESSEE, TEXAS, VIRGINIA, WASHINGTON, WISCONSIN, the DISTRICT OF COLUMBIA, and the CITY OF CHICAGO,

Plaintiffs,

Case No. 10-cv-03165 GHK (SSx)

THIRD AMENDED COMPLAINT

DEMAND FOR JURY TRIAL

Ex rel.
BEVERLY BROWN,
Plaintiff-Relator,
v.
CELGENE CORPORATION,
Defendant.

TABLE OF CONTENTS

Page

I. INTRODUCTION

1. With sometimes no more than a narrow window of opportunity to make critical decisions about medical treatment, doctors and their patients must have honest information about treatment options including appropriate drug regimens. Patients ravaged by cancer, and often on the edge of life, have no choice but to trust that their healthcare providers and the pharmaceutical manufacturers are providing information based on solid evidence, and that independent scientists at the Food and Drug Administration ("FDA") have reviewed their drugs for safety and efficacy.

2. Cancer is a dread disease, still the second leading cause of death in the United States. In the last 30 years, new treatments have come on the market. Unfortunately, most of these potent treatments have toxic side effects and can be fatal themselves. Therefore, Congress carefully balanced the need to speed treatments to desperately ill patients with the need for reliable evidence that the benefits of new treatments outweighed their risks. Congress created the FDA to independently evaluate the safety and efficacy of each new drug, for each intended use, before a manufacturer could put it on the market in the United States. In 1992, it amended the Food Drug and Cosmetic Act ("FDCA") to create an accelerated approval process for drugs for which there was an urgent need. The FDA requires pharmaceutical manufacturers to develop adequate evidence to allow doctors and their patients to make informed decisions about the best treatment.

3. This case is about a large drug manufacturer, Celgene Corporation ("Celgene" or the "Company"), that deliberately chose to ignore this process and preyed on a vulnerable patient population. By marketing drugs to cancer patients and their doctors for unapproved purposes and paying kickbacks to physicians, Celgene compromised physicians' professional judgment so that they would make decisions not based solely on scientific evidence. Celgene put an old, highly toxic drug – Thalidomide, and later Revlimid, a related compound – on the market and sold them for all types of cancer without any of the research the FDA requires or the oversight it

provides. Celgene persevered with its unlawful marketing conduct even after receiving warning letters from the FDA in 1998 and 2000. Celgene's unlawful marketing endangered patients because it knowingly concealed the risks of venous thromboembolism and death associated with Thalomid use in cancer patients. When Celgene ultimately secured an indication for a treatment of multiple myeloma ("MM") with Thalomid, that approval was conditioned on the package insert containing a black box warning – the most serious warnings given out by the FDA – alerting doctors and patients of the risks of venous thromboembolism.

4. While this case is ultimately about the wrongful expenditure of government and private payor monies for prescriptions flowing from unlawful marketing schemes, Celgene's conduct compromised or potentially compromised medical care for countless cancer patients. Celgene racked up hundreds of millions of dollars a year in sales for purposes not approved by the FDA by pushing drugs to treat cancers even though there were well-known, evidence-based treatments that worked as well or better than Thalomid and its cousin, Revlimid. Celgene profited by persuading – and sometimes paying – doctors to substitute its untried remedies for treatments proven to be safe and effective in desperately ill patients. Celgene, a multi-billion dollar company, was built on profits derived from unlawful marketing.

5. Without any of the research or oversight the FDA requires, Celgene placed thalidomide, which caused horrific birth defects in the 1960's, back on the market for all kinds of cancer. The story begins in 1998, when Celgene secured from the FDA an indication that it never intended to use for a skin disease, erythema nodosum leprosum ("ENL"), associated with leprosy. There was no profit in treating a disease that affects less than a few hundred people a year in the United States. So Celgene never developed substantive marketing materials about ENL or trained its sales representatives to sell Thalomid to physicians who treat leprosy. Instead of marketing Thalomid for its limited ENL indication, Celgene violated explicit FDA regulations prohibiting misbranding including off-label marketing: Celgene flooded the country with sales representatives

under heavy pressure to sell Thalomid, and later Revlimid, to oncologists for whatever cancer they treated, blood cancers as well as solid tumors, on the basis of minimal evidence. As early as 1999, in its Annual Report to shareholders, Celgene announced that more than 90% of Thalomid prescriptions were for oncology, a purpose not approved by the FDA.

6. From the beginning, the FDA warned Celgene about these illegal off-label marketing efforts. Celgene received its FDA approval for ENL on July 16, 1998; 15 days later the FDA contacted Celgene "to discuss concerns about promotional materials containing uses of thalidomide other than those" approved by the FDA. Four months later, it sent Celgene a warning letter regarding its marketing, including a press release entitled "Celgene Announces Plans to Pursue Multiple Myeloma Indication for THALOMID." The FDA criticized Celgene for failing to present any information concerning "the significant, potentially fatal, risks associated with the use of thalidomide ...." On December 22, 1998, FDA staff met with Celgene executives and expressed "strong concern regarding Celgene's promotion of unapproved use of thalidomide, and its failure to fully state risks." On April 21, 2000, the FDA sent Celgene another warning letter because "Celgene [had] engaged in promotional activities that state or suggest that Thalomid is safe and effective for use in treating multiple myeloma." The FDA was particularly concerned about Celgene's conduct relating to Thalomid because "[p]erhaps more than for any other available drug, the need to provide and distribute thalidomide responsibly is essential to the public health." The FDA stated that:

> Celgene is demonstrating a continuing pattern and practice of violative behavior that evince its failure to comply with the conditions under which Thalomid was approved. Previous discussions with Celgene have not resulted in Celgene's compliance with the Act.

7. At the time the FDA issued this warning letter, investment analysts estimated that Celgene's sales were almost all off-label. For example, in 2000, U.S. Bancorp Piper Jaffery analyst Peter Ginsburg estimated that 90% of Thalomid's 1999 sales were for cancer. Celgene's sale of Thalomid continued to be overwhelmingly for

cancer. Bob Hugin, the then-CF of Celgene Corp., stated at the Lehman Brothers Global Health Care Conference on or about Mar. 31, 2005 that about 92% of Thalomid prescriptions were for cancer. Mr. Hugin boasted that Thalomid was the "financial engine" powering Celgene's growth, delivering the company's first full-year positive earnings in 2003.

8. Celgene's initial marketing efforts for Thalomid were tantamount to ongoing human experimentation. Because Celgene marketed the drug off-label, patients and their medical advisors were denied the appropriate warnings provided in a package insert when a product is used on-label. For example, by 2003, if not earlier, Celgene was aware that there was a serious risk of increased venous thromboembolism in multiple myeloma ("MM") patients taking Thalomid. Rather than disclose this deadly risk to doctors and their patients, Celgene trained its sales representatives to either conceal or downplay the risk.

9. In late 2005, Celgene secured an FDA indication for a derivative of Thalomid which it named Revlimid. The FDA approved a single, limited indication for Revlimid for a relatively uncommon subtype of the blood disorder, myelodysplastic syndrome ("MDS") (transfusion-dependent anemia due to low or intermediate risk MDS when associated with a deletion 5q cytogenic abnormality with or without additional cytogenic abnormalities), an early stage of cancer. As with Thalomid, Celgene proceeded to market Revlimid for a variety of cancers for which it had not obtained indications.

10. Revlimid proved to be a miracle drug for Celgene's revenue stream, because it was ten times more costly than Thalomid. Celgene began an aggressive campaign to switch Thalomid patients to Revlimid. In practical terms, this meant that a patient's – or his/her insurer's – monthly cost would rise from $2,000 per month to $10,000 per month. (To reduce the financial disincentive to switch, Celgene gradually raised the price of Thalomid to $5,000 per month.)

11. After years of flouting the Food Drug and Cosmetics Act's proscriptions against off-label marketing, in May 2006, Celgene finally obtained a new indication for Thalomid for the very limited purpose of treating newly diagnosed MM patients who had not undergone any other prior treatment. The indication also required that Thalomid be used in combination with another drug, dexamethasone. The approval required placement of a black box warning of increased risk of venous thromboembolism in MM patients. With this black box warning on the face of the Thalomid label, the Company could no longer conceal the increased and deadly risk of venous thromboembolism to, at least, MM patients.

12. One month later, in June 2006, Celgene secured another indication for Revlimid allowing it to market for a second narrow indication for MM taken in combination with dexamethasone, for patients who had received at least one prior therapy. Thus, in contrast to Thalomid, Revlimid was not approved for newly diagnosed MM patients. As of 2012, Celgene's drugs Thalomid and Revlimid had not received any indications for cancers other than MM and MDS. Yet, through continued off-label marketing, kickbacks and concealment of risks, Celgene was able to secure a revenue stream in the billions of dollars. This revenue stream exponentially exceeded the on-label market for Celgene's drugs. Celgene generated sales exceeding a hundred million dollars a year for Thalomid from 1998 through 2005, culminating in sales of approximately $389 million in 2005 alone. Revlimid sales in 2008 and 2009 totaled more than $1.7 billion and have continued to increase with more than a billion dollars in sales every year since then.

13. Because Thalomid and Revlimid cause severe birth defects, the FDA mandated that the Company implement a restricted distribution system requiring physicians to follow specific procedures before prescribing these drugs. In its effort to market Thalomid and Revlimid, the Company transformed a system required by the FDA to prevent birth defects into a system for reaching more doctors. Under the guise of assisting physicians with the FDA restrictions, Celgene dispatched more than 100

sales representatives across the country with purposefully misleading titles, including Immunology Specialist and Hematology Oncology Consultant, in order to gain access to doctors' offices and carry out Celgene's unlawful marketing objectives.

14. Despite being charged with implementing measures to prevent birth defects, Celgene's sales representatives were, and continue to be paid, bonuses based on off-label and on-label drug sales.

15. During relevant time periods, Celgene marketed Thalomid for at least 19 off-label uses and Revlimid for at least nine off-label uses.

16. During relevant time periods, there were other FDA approved treatments available for all of these diseases. Celgene's off-label marketing of Thalomid and Revlimid exposed patients to magnified risks of potentially fatal blood clots, potentially fatal skin conditions, severe nerve damage, decreased white blood cell counts, and other side effects.

17. Celgene caused false claims to be submitted in violation of the law for payment by federal and state agencies or programs, and by private insurers including those operating in the state of California by:

- systematically engaging in illegal off-label marketing of its drugs, Thalomid (generic name "thalidomide") and Revlimid (generic name "lenalidomide");

- furthering the unlawful off-label marketing of Thalomid and Revlimid through violations of continuing medical education ("CME") rules and regulations by directing and controlling the content of physician speaker programs that purported to be unbiased;

- unlawfully promoting Thalomid and Revlimid in violation of the Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b), and the Stark Law, 42 U.S.C. § 1395nn and 42 C.F.R. § 411.350 *et seq.*, by providing cash and other incentives to induce doctors to promote and prescribe these drugs, including for off-label uses; and

- unlawfully tampering with Revlimid prescriptions to deceive Medicare, Medicaid, and other government-funded programs into believing that off-label prescriptions were for on-label indications.

18. Celgene's illegal marketing of Thalomid and Revlimid caused federal, state and local government health care programs, as well as private insurers including those operating in the state of California, to pay for millions of prescriptions that never would have been submitted for reimbursement but for Celgene's activities. In addition to the federal healthcare dollars expended through Medicare and Medicaid, state governments spend money through Medicaid, as well as through their state workers' insurance plans. The City of Chicago expends municipal dollars to insure its own workers. Had federal, state, and city programs, including Medicare and Medicaid, as well as private insurers including those operating in the state of California, known that such prescriptions were induced by illicit incentives or illegal off-label marketing to physicians, they would not have reimbursed claims for Thalomid or Revlimid.

19. Relator discovered Celgene's wrongful conduct while she was employed by Celgene. She conducted her own investigations in furtherance of this action and disclosed her findings to the United States Government and the states prior to filing this action.

20. On behalf of the United States of America and on behalf of California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Illinois, Iowa, Indiana, Louisiana, Maryland, Massachusetts, Michigan, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Oklahoma, Rhode Island, Tennessee, Texas, Virginia, Washington, Wisconsin, the District of Columbia, and the City of Chicago, pursuant to the *qui tam* provisions of the federal False Claims Act , 31 U.S.C. § 3729 *et seq.*, and similar state law and municipal provisions, and the California Insurance Frauds Prevention Act, Cal. Ins. Code § 1871.7, Plaintiff or "Relator" Beverly Brown files this *qui tam* Complaint against Defendant Celgene Corporation.

II. JURISDICTION AND VENUE

21. Relator brings this action on behalf of herself and on behalf of the United States for violations of the False Claims Act, 31 U.S.C. §§ 3729-3733, and on behalf of California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Illinois, Iowa,

Indiana, Louisiana, Maryland, Massachusetts, Michigan, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Oklahoma, Rhode Island, Tennessee, Texas, Virginia, Washington, Wisconsin, the District of Columbia, and the City of Chicago for violations of their respective state false claims acts. Relator also brings this action pursuant to Cal. Ins. Code § 1871.7, the California Insurance Frauds Prevention Act.

22. This Court has federal subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1331 and 31 U.S.C. § 3732 and supplemental jurisdiction over the counts relating to the State False Claims Acts pursuant to 28 U.S.C. § 1367.

23. This Court has personal jurisdiction over the Defendant pursuant to 31 U.S.C. § 3732(a) because the Defendant can be found in and transacts business in this District. In addition, the acts prohibited by 31 U.S.C. § 3729 occurred in this District.

24. Venue is proper in this District pursuant to 31 U.S.C. § 3732(a) because Defendant transacts business in this District and numerous acts proscribed by 31 U.S.C. § 3729 occurred in this District.

25. There has been no public disclosure of the allegations herein. To the extent that there has been a public disclosure unknown to the Relator, she is the "original source" under 31 U.S.C. § 3730(e)(4) and similar state laws. Relator has direct and independent knowledge of the information on which the allegations are based and has voluntarily provided the information to the Government before filing this *qui tam* action based on that information. *See* 31 U.S.C. § 3730(e)(4).

III. PARTIES

26. Relator Beverly Brown was employed by Celgene from 2001 to 2011, working in Los Angeles, California and surrounding areas. Her job titles included S.T.E.P.S. (System for Thalidomide Education and Prescribing Safety) Field Coordinator, Immunology Specialist, and Hematology Oncology Consultant. Although Celgene bestowed upon her these science-related job titles, Relator was in truth a pharmaceutical sales representative who received a base salary and bonuses based on the

volume of both on-label and off-label sales of Thalomid and Revlimid in her sales district. Relator was a top performer, winning commendations from Celgene for her sales performance.

27. Defendant Celgene is a Delaware corporation, with its headquarters and principal place of business in Summit, New Jersey. Celgene holds itself out as a global biopharmaceutical company engaged in the business of discovery, development, manufacturing, marketing, and sales of prescription drugs and other products for the prevention, diagnosis, and treatment of diseases. Yet until at least 2005, almost all of Celgene's revenue was attributable to the use of its drugs for purposes not approved by the FDA. Thalomid and Revlimid generated $6.7 billion in sales revenues, with Thalomid generating $2.7 billion and Revlimid generating $4 billion. According to Company estimates (*see* Celgene Q4 2008 Earnings Call (Jan. 29, 2009)), as well as industry analysis (*see* Credit Suisse Analyst Report (Apr. 1, 2009)), Medicare and Medicaid paid for the majority of Thalomid and Revlimid prescriptions.

IV. STATUTORY AND REGULATORY PROVISIONS APPLICABLE TO DEFENDANT CELGENE'S FALSE CLAIMS ACT VIOLATIONS

A. Federal Government Health Programs

28. The federal and state governments are among the principal purchasers of Celgene's pharmaceutical products, primarily but not exclusively through their Medicaid and Medicare programs. Private insurers, including those operating in California, also pay for Celgene's pharmaceutical products.

29. Medicare is a federal government health program primarily benefiting the elderly and disabled that Congress created in 1965 when it adopted Title XVIII of the Social Security Act. Medicare is administered by the Centers for Medicare and Medicaid Services ("CMS").

30. There are four parts to Medicare: Medicare Part A (hospital insurance); Medicare Part B (medical insurance); Medicare Part C (Medicare Advantage, formerly known as Medicare + Choice); and Medicare Part D (prescription drug coverage that

was enacted as part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") and went into effect on January 1, 2006).

31. Medicare Part A generally pays for inpatient services for eligible beneficiaries in hospitals, hospices and skilled nursing facilities, as well as some home healthcare services. 42 U.S.C. §§ 1395e - 42 U.S.C. §§ 1395i-5. Prescription drugs are covered under Medicare Part A only if they are administered on an inpatient basis in a hospital or similar setting.

32. Medicare Part B covers some healthcare services and products not covered by Medicare Part A, generally on an outpatient basis. Doctor's visits and other services are covered by Part B. Medicare Part B also pays for some types of prescription drugs that are not administered in a hospital setting. 42 U.S.C. § 1395k(a); 42 U.S.C. § 1395x(s)(2); 42 C.F.R. § 405.517. These typically include drugs administered by a physician or other provider in an outpatient setting, including some anticancer drugs. 42 U.S.C. § 1395k(a); 42 U.S.C. § 1395x(s)(2); 42 C.F.R. § 405.517.

33. Medicare Part C, in effect, combines both Part A and Part B. Part C differs, however, because it is supplied through private insurance companies. Medicare beneficiaries have the option to receive their Medicare benefits through private health insurance plans, instead of through the original Medicare plan (Parts A and B). Originally, these programs were known as "Medicare+Choice" or "Part C" plans. Following the passage of the MMA – which created Part D – "Medicare+Choice" became known as "Medicare Advantage" ("MA") plans.

34. On January 1, 2006, Part D of the Medicare program began subsidizing optional drug coverage for all beneficiaries. This drug benefit covers drugs that are considered "covered outpatient drugs" under 42 U.S.C. § 1396r-8(k).

35. Congress created Medicaid at the same time it created Medicare in 1965 when Title XIX was added to the Social Security Act. Medicaid is a public assistance program that provides payment of medical expenses for primarily low-income patients. Funding for Medicaid is shared between the federal government and state governments.

The federal government also separately matches certain state expenses incurred in administering the Medicaid program. While specific Medicaid coverage guidelines vary from state to state, Medicaid's coverage is generally modeled after Medicare's coverage, except that Medicaid usually provides more expansive coverage than does Medicare.

36. Medicaid, since its beginning, generally has had broad coverage for prescription drugs, including self-administered drugs. Nearly every state has opted to include basic prescription drug coverage in its Medicaid plan.

37. Medicaid pays for services pursuant to plans developed by the states and approved by the U.S. Department of Health and Human Services ("HHS") through CMS. 42 U.S.C. §§ 1396a(a)-(b). After states pay doctors, hospitals, pharmacies, and other providers and suppliers of medical items and services according to rates the states establish, the federal government then pays each state a statutorily-established share of "the total amount expended ... as medical assistance under the State plan...." *See* 42 U.S.C. §§ 1396b(a)(1), 1396b(a)(1), and 1903(a)(1). This federal-to-state payment is known as federal financial participation ("FFP").

38. TRICARE is the healthcare system of the United States military, designed to maintain the health of active duty service personnel, provide healthcare during military operations, and offer health care to non-active duty beneficiaries, including dependents of active duty personnel and certain military retirees and their dependents. The program operates through various military-operated hospitals and clinics worldwide and is supplemented through contracts with civilian healthcare providers. Five managed care support contractors create networks of civilian healthcare providers.

39. Whereas TRICARE treats active duty military and their dependents, the Veterans Administration ("VA") provides healthcare and other benefits to military veterans through its nationwide network of hospitals and clinics.

40. The Federal Employees Health Benefits Program ("FEHBP") provides health insurance coverage for more than 8 million federal employees, retirees, and their dependents. FEHBP is a collection of individual healthcare plans such as the Blue Cross

and Blue Shield Association. FEHBP plans are managed by the Office of Personnel Management.

41. While each government-funded healthcare program establishes its own reimbursement criteria, none knowingly pays for medications that are not prescribed for a medically accepted indication or that are prescribed as a result of false or misleading information disseminated by pharmaceutical manufacturers to either payors or healthcare providers. In addition, none of the government-funded healthcare programs willingly pay for drugs that were prescribed as the result of the pharmaceutical manufacturer's unlawful inducements or unlawful marketing activities.

B. The False Claims Act

42. The Federal False Claims Act provides that any person who knowingly presents or causes another to present a false or fraudulent claim for payment or approval is liable for a civil penalty of up to $11,000 for each such claim, plus three times the amount of the damages sustained by the government. 31 U.S.C. §§ 3729(a)(1)(A), (B). Twenty-nine states, the District of Columbia, and the City of Chicago have enacted analogous false claims act statutes that apply to Medicaid fraud (the "State False Claims Acts").

C. FDA Regulations

43. The FDA regulates drugs based on the "intended uses" for such products. Before marketing and selling a prescription drug, a manufacturer must demonstrate to the FDA that the product is safe and effective for each intended use. 21 U.S.C. § 331(d); 21 U.S.C. §§ 355(a), 360b(a).

44. The FDA reviews pharmaceutical manufacturers' applications for new drugs to determine whether the drugs are safe and effective for each intended use. *See* 21 U.S.C. § 355.

45. Once a drug is approved for a particular use, doctors may legally prescribe the drug for any "non-indicated" or off-label purpose. Doctors may independently request information from drug manufacturers about such off-label uses. But with very

few exceptions, the FDA prohibits drug manufacturers from marketing or promoting drugs for uses, *i.e.*, indications, not explicitly approved by the FDA. As described above, "off-label marketing" refers to the marketing of an FDA-approved drug for uses that have not undergone FDA scrutiny and approval.

46. Under the statute, qualified medical professionals may provide purely scientific medical information for uses other than those approved by the FDA; all other presentations, promotions and marketing to physicians for uses other than those approved by the FDA are considered off-label marketing or "misbranding" proscribed by the Food, Drug and Cosmetics Act ("FDCA"). *See* 21 U.S.C. §§ 331(a)-(b), 352(a), (f). This includes any attempts by a pharmaceutical sales representative to initiate discussions with, or solicit questions from, physicians concerning off-label use.

47. Strong policy reasons exist for strict regulation of off-label marketing. Off-label promotion bypasses the FDA's strict review and approval process. It also removes the incentive to obtain definitive clinical study data showing the efficacy and safety of a product and, accordingly, the medical necessity for its use.

48. Pursuant to the FDCA, 21 U.S.C. § 301, *et seq.*, the FDA strictly regulates the content of direct-to-physician product promotion and drug labeling information used by pharmaceutical companies to market and sell FDA-approved prescription drugs.

49. FDA interprets "labeling" in its regulations broadly to include items that are "1) descriptive of a drug: 2) supplied by the manufacturer or its agents; and 3) intended for use by medical personnel." 21 C.F.R. § 202.1. The FDCA defines both misleading statements and the omission of material facts in a label or product labeling as "misbranding." 21 U.S.C. § 321(n). Labeling includes brochures, booklets, detailing pieces, literature, medical reprints, sound recordings, exhibits and audio visual material. 21 C.F.R. § 202.1 (l)(2).

50. The FDA regulations deem "advertising" to include any media-based activities that appear in magazines, newspapers, professional journals and on television, radio, and telephone communications systems. *See* 21 C.F.R. § 202.1(l)(1). Courts have

consistently held that oral statements made by a company's sales representative relating to a pharmaceutical product constitute commercial advertising or promotion. *See Abbott Labs. v. Mead Johnson & Co.*, 971 F.2d 6, 10 (7th Cir. 1992) (interpreting the Lanham Act).

51. Pharmaceutical promotional and marketing materials and presentations lacking in fair balance or that are otherwise false or misleading "misbrand" a drug in violation of the FDCA, 21 U.S.C. §§ 301, 321, 331, 352, 360b, 371; 21 C.F.R. §§ 202.1(e)(6), (e)(7); 21 C.F.R. § 1.21.

52. Such violations exist where promotional and marketing materials and presentations for an FDA approved drug:

- Minimize, understate, or misrepresent the risks, contra-indications, and complications associated with that drug;
- Overstate or misrepresent the risks, contra-indications, and complications associated with any competing drugs;
- Reference "off-label" uses of the drug — *i.e.*, those uses that have not been approved by the FDA — or expressly or implicitly promote uses and/or dosing regimens for which the drug is not indicated;
- Fail to reveal facts material in light of its representations or material with respect to consequences that may result from the use of the drug as recommended or suggested in the advertisement;
- Contain representations or suggestions, not approved or permitted in the labeling, that is not demonstrated by substantial evidence or substantial clinical experience;
- Present information from a study in a way that implies that the study represents larger or more general experience with the drug than it actually does;
- Use a quote or paraphrase out of context to convey a false or misleading idea; or
- Are otherwise false, misleading or lacking in fair balance in the presentation of information about the drug being marketed or about any competing drug.

See 21 C.F.R. §§ 202.1 (e)(4)(5)(6), (7).

53. Oral statements and written materials presented at industry-supported activities, including lectures and teleconferences, provide evidence of a product's intended use. If these statements or materials promote a use inconsistent with the product's FDA-approved labeling, it is misbranded as it fails to provide adequate directions for all intended uses.

D. Medicare and Medicaid Coverage Of Off-Label Prescriptions

54. By statute, Medicare and Medicaid can only reimburse claims for drugs if the drug is dispensed for a "medically accepted indication." *See e.g.*, 42 U.S.C. § 1369r-8(k). The law further provides a drug is dispensed for a "medically accepted indication" if it is for a use that the FDA has approved. *See, e.g., id.* Thus, normally, Medicare and Medicaid can only pay for pharmaceutical prescriptions if the doctor has prescribed the drug for a use that the FDA approved. This makes sense as the FDA comprehensively reviews pharmaceutical manufacturers' detailed applications for new drugs to determine whether the drugs are safe and effective for each intended use. *See* 21 U.S.C. § 355. Congress requires Medicare and Medicaid to only pay for prescription drugs that are safe and effective for their prescribed use.

55. There is an exception to Medicare and Medicaid's FDA approval requirement, however. The law also considers it a "medically accepted indication" - and thus permits Medicare and Medicaid to reimburse - if the prescribed use is "supported by citation" in one or more of several specified drug compendia. 42 U.S.C. § 1395x(t)(2)(B) and 42 U.S.C. § 1395w-102(2) (2007) (Medicare); 42 U.S.C. § 1396r-8(k)(6) and 42 U.S.C. § 1396r-8(g)(1)(B)(l) (Medicaid).

56. The drug compendia are privately owned, written and published indices of various pharmaceuticals products. For each product, a compendia includes information about the product's pharmacologic and pharmacokinetic properties (such as adverse effects, and drug interactions) and the FDA-approved indications for that drug. The

compendia also, however, includes information about studies of the product in diseases not approved by the FDA and not listed on the label (i.e., "off-label" uses).

57. Under Medicare Part B, until 2008, the statute listed only three compendia that CMS could consider: American Medical Association Drug Evaluations (AMA-DE), United States Pharmacopoeia Drug Information for the Health Professional (USP-DI), and American Hospital Formulary Service Drug Information (AHFS), 42 U.S.C. § 1395x. In 1994, the AMA and the U.S Pharmacopeial Convention agreed to combine the AMA-DE and the USP-DI into a single reference; they agreed to use the USP-DI name. In 1998, the USP-DI was sold to Thomson Healthcare, whose Micromedex subsidiary published DrugDex. Under the agreement with Thomson, the U.S Pharmacopeial Convention retained oversight of the USP-DI content until 2004 (when control transferred to Thomson) and Micromedex was responsible for product development, marketing and distribution. Publication of USP-DI ended in 2007.

58. When Part D came into effect in 2006, the statute allowed CMS to rely upon AHFS, USP-DI and DrugDex. 42 C.F.R. § 423.100.

59. Because two of the three original Part B statutory compendia had ceased publication, following its rule-making process, in 2008 CMS added National Comprehensive Cancer Network Drugs and Biologics Compendium (NCCN), and Clinical Pharmacology to the list of compendia (effective, June 5, and July 2, 2008 respectively) for both Part B and Part D and DrugDex for Part B (effective June 10, 2008).

60. The compendia portion of the Medicaid statute, by contrast, has been stable for the relevant time period. It originally limited the approved compendia to AHFS and the USP-DI. 42 U.S.C. § 1396r-8(g)(1)(B)(i). In 1997, Congress added DrugDex to the approved list of compendia that Medicaid programs could consider. Balanced Budget Agreement of 1997, Pub. L. 105-33 (amending 42 U.S.C. § 1396r-8(g)(1)(B)(i)).

61. Coverage of off-label drug use by TRICARE, the VA and other federal and state healthcare programs is similar to Medicare and Medicaid coverage. *See, e.g.*, TRICARE Policy Manual 6010.54-M, Chapter 8, Section 9.1.

62. From 1998 to the present day, Celgene marketed Thalomid for numerous uses not approved by the FDA including bladder cancer, breast cancer, brain cancer, cervical cancer, colorectal cancer, esophageal cancer, kaposi sarcoma, leukemia (including, but not limited to, chronic lymphocytic leukemia ("CLL")), lung cancer, lymphoma, melanoma, prostate cancer, pancreatic cancer, renal (i.e., kidney) cancer, thyroid cancer, new onset multiple myeloma (prior to the FDA's May 26, 2006 approval of Thalomid to treat one stage of this disease), multiple myeloma not in combination with the drug dexamethasone, ovarian cancer, and uterine cancer.

63. During the relevant time period, the compendia did not provide adequate support for using Thalomid to treat any of these diseases other than as approved by FDA. During relevant time periods, Celgene illegally "off-label" marketed Revlimid for brain cancer, leukemia (including, but not limited to, CLL), lymphoma, myelofibrosis, myelodysplastic syndromes (all types), new onset multiple myeloma (prior to the FDA's approval of Revlimid to treat an indication for this disease), multiple myeloma not in combination with the drug dexamethasone, prostate cancer, and stem-cell transplant maintenance therapy. As with Thalomid, the compendia do not provide support for using Revlimid to treat any of these medical conditions.

64. Accordingly, Medicare, Medicaid or other government healthcare programs should not pay for Thalomid and Revlimid prescriptions to treat these conditions because the indications were not "medically accepted." 42 U.S.C. § 1395x(t)(2)(B)(ii)(I).

65. Notwithstanding the lack of support in the drug compendia, Celgene attempted to influence the drug compendia. For example, Celgene paid 16 of the doctors who advised the NCCN compendium on multiple myeloma. Three of these sixteen – Dr.

Kenneth Anderson, Dr. Seema Singhal and Dr. Steven Treon – were also considered "core faculty" for the Speaker Corps series described herein.

E. The Medicare Fraud & Abuse/Anti-Kickback Statute

66. The Medicare Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b), which also applies to the state Medicaid programs, provides penalties for individuals or entities that knowingly and willfully offer, pay, solicit, or receive remuneration to induce the referral of business reimbursable under a federal health benefits program. The offense is a felony punishable by fines of up to $25,000 and imprisonment for up to 5 years.

67. In accordance with the Anti-Kickback Statute, Medicare regulations directly prohibit providers from receiving remuneration paid with the intent to induce referrals or business orders, including the prescription of pharmaceuticals. *See* 42 C.F.R. § 1001.952(f). Such remuneration is a kickback when paid to induce the writing of prescriptions. Kickbacks increase government-funded health benefit program expenses by causing medically unnecessary expenditures. Kickbacks also compromise a physician's judgment causing him/her to consciously or subconsciously select drug regimens based on his/her financial interest rather than the patient's medical need.

68. The Medicare Anti-Kickback Statute contains statutory exceptions and certain regulatory "safe harbors" that exclude certain types of conduct from the reach of the statute. *See* 42 U.S.C. § 1320a-7(b)(3). None of the statutory exceptions or regulatory safe harbors protects the Defendant's conduct in this case.

69. The Balanced Budget Act of 1997 added administrative civil penalties of $50,000 for each act violating the Anti-Kickback Statute, as well as an assessment of not more than three times the amount of remuneration offered, paid, solicited, or received, without regard to whether a portion of that amount was offered, paid, or received for a lawful purpose. *See* 42 U.S.C. § 1320a-740(7).

70. More recently, the Patient Protection and Affordable Care Act ("PPACA"), Public Law No. 111-148, Sec. 6402(g), amended the Medicare Anti-Kickback Statute to specifically allow violations of its "anti-kickback" provisions to be enforced under the

False Claims Act. The PPACA also amended the Social Security Act's "intent requirement" to make clear that violations of the Social Security Act's anti-kickback provisions, like violations of the False Claims Act, may occur even if an individual does not have "actual knowledge" or "specific intent to commit a violation." *Id.* at Sec. 6402(h).

71. As detailed below, Celgene's marketing of Thalomid and Revlimid repeatedly violated provisions of the Anti-Kickback Statute, which in turn violated the False Claims Act. Celgene's kickbacks and incentives induced physicians to prescribe Thalomid and Revlimid when they otherwise would not have, and many of those prescriptions were paid for by Medicare, Medicaid and other government funded health insurance programs as well as by private insurers, including those in California.

F. Stark Law - The Medicare/Medicaid Self-Referral Statute

72. The Medicare/Medicaid Self-Referral Statute, 42 U.S.C. § 1395nn, *et seq*., known as the "Stark" law, prohibits a pharmaceutical manufacturer from paying remuneration to physicians for referring Medicare and Medicaid patients to the manufacturer for certain "designated health services," including drug prescriptions, where the referring physician has a nonexempt "financial relationship" with that manufacturer. 42 U.S.C. §§ 1395nn(a)(1), (h)(6). The Stark law provides that the manufacturer shall not cause to be presented a Medicare or Medicaid claim for such prescriptions. Stark also prohibits payment of claims for prescriptions rendered in violation of its provisions. 42 U.S.C. §§ 1395nn(a)(1), (g)(1).

73. Celgene's marketing of Thalomid and Revlimid repeatedly violated the Stark law, which in turn violated the False Claims Act, because Celgene's unlawful payments and services to prescribing physicians induced those physicians to prescribe these drugs when they otherwise would not have done so. Many of those prescriptions were paid for by government funded health insurance programs.

G. The California Insurance Frauds Prevention Act

74. The California Insurance Frauds Prevention Act prohibits the knowing employment of "runners, cappers, steerers or other persons to procure clients or patients ... to perform or obtain services or benefits under a contract of insurance or that will be the basis for a claim against an insured individual or his or her insurer." Cal. Ins. Code § 1871.7(a). It also establishes liability for parties that violate "Section 549, 550, or 551 of the Penal Code…." Cal. Ins. Code § 1871.7(b).

75. California Penal Code § 549 makes it illegal for any firm or corporation to "solicit[], accept[],or refer[] any business to or from any individual or entity with the knowledge that, or with reckless disregard for whether" that individual or entity will present or cause to be presented any false or fraudulent claim for payment of a healthcare benefit.

76. California Penal Code § 550 makes it illegal for any firm or corporation to "[k]nowingly present or cause to be presented any false or fraudulent claim for the payment of a loss or injury, including payment of a loss or injury under a contract of insurance"; "[k]nowingly prepare, make, or subscribe any writing, with the intent to present or use it, or to allow it to be presented, in support of any false or fraudulent claim"; and "[k]nowingly make or cause to be made any false or fraudulent claim for payment of a health care benefit." Cal. Penal Code §§ 550 (a)(1), (5), and (6).

77. California Penal Code § 550 also makes it illegal for any firm or corporation knowingly to present, or to assist or conspire to "[p]resent or cause to be presented any written or oral statement as part of, or in support of or opposition to, a claim for payment or other benefit pursuant to an insurance policy, knowing that the statement contains any false or misleading information concerning any material fact": and to "[p]repare or make any written or oral statement that is intended to be presented to any insurer or any insurance claimant in connection with, or in support of or opposition to, any claim or payment or other benefit pursuant to an insurance policy,

knowing that the statement contains any false or misleading information concerning any material fact." Cal. Penal Code §§ 550 (b)(1), (2).

78. The legislative findings and declarations associated with the California Insurance Frauds Prevention Act make clear that the Legislature was concerned with healthcare fraud: "Health insurance fraud is a particular problem for health insurance policyholders. Although there are no precise figures, it is believed that fraudulent activities account for billions of dollars annually in added health care costs nationally. Health care fraud causes losses in premium dollars and increases health care costs unnecessarily." Cal. Ins. Code § 187l(h).

V. SPECIFIC ALLEGATIONS OF CELGENE'S FALSE CLAIMS

A. Celgene's Prescription Drugs Thalomid and Revlimid

1. Thalomid's FDA-Approved Uses and Restrictions

79. Initially, Celgene applied for, and in 1998 received, FDA approval for thalidomide, marketed by Celgene under the brand name Thalomid, for the treatment of ENL, a rare skin condition associated with leprosy. The drug was, and is, approved to treat "cutaneous manifestations of moderate to severe" ENL, as well as to prevent and suppress recurrences of ENL on human skin. ENL is an exceedingly uncommon skin condition that affects very few Americans each year. According to the Health Resources and Service Administration, a division of HHS, there were a mere 137 new cases of leprosy in America in 2006 and there were a total of 1,600 cases from 1998 through 2009. Thus, the number of patients suffering from moderate to severe ENL (most ENL is mild) – a subset of the total leprosy population – is quite small.

80. Celgene later applied for, and received in May 2006, FDA approval for Thalomid, when used in combination with the drug dexamethasone, for treatment of newly diagnosed MM. MM is a cancer of blood cells, like leukemia. An MM patient's plasma cells grow uncontrolled in the bone marrow, destroying the bone and eventually reaching the peripheral circulation. MM can cause patients to experience increased bleeding, increased rates of infection, kidney damage, bone disease, and death.

81. Thalomid is approved only in combination with another drug, dexamethasone, for patients who have newly diagnosed MM. Thalomid has never been approved as a solo or "monotherapy" treatment for MM. This means that Thalomid cannot be prescribed in conjunction with a drug other than dexamethasone or by itself to treat MM. In addition, Thalomid has never received FDA approval for treatment of patients with MM who have received any prior drug therapy.

82. From 1998 to the present day, however, Celgene marketed Thalomid for several other diseases, including:

i) bladder cancer;

ii) breast cancer;

iii) brain cancer;

iv) cervical cancer;

v) colorectal cancer;

vi) esophageal cancer;

vii) leukemia (including, but not limited to, chronic lymphocytic leukemia ("CLL"));

viii) lymphoma;

ix) melanoma;

x) prostate cancer;

xi) pancreatic cancer;

xii) renal (i.e., kidney) cancer;

xiii) thyroid cancer;

xiv) new onset multiple myeloma (prior to the FDA's May 26, 2006 approval of Thalomid to treat new onset (only) of this disease);

xv) multiple myeloma, not in combination with the drug dexamethasone;

xvi) myelodysplastic syndromes (MDS);

xvii) ovarian cancer; and

xviii) uterine cancer.

83. While the price of Thalomid varies by dose and duration, Thalomid prescriptions can cost as much as $24,000 per year per patient.

2. Revlimid's FDA-Approved Uses and Restrictions

84. Celgene sought and received on December 27, 2005, FDA approval for lenalidomide, marketed by Celgene under the brand name Revlimid, for an extremely narrow indication: the treatment of patients with transfusion-dependent anemia due to low or intermediate risk MDS only when associated with a deletion 5q cytogenic abnormality (*i.e.*, deletion of the long arm of chromosome 5) with or without additional cytogenic abnormalities. MDS refers to a group of blood disorders that prevents human bone marrow from producing healthy blood cells. This is largely a disease of older adults. Although MDS includes a range of subtypes, Revlimid is indicated only for the specific MDS-subtype of "low or intermediate risk" with "a deletion 5q cytogenic abnormality with or without additional cytogenic abnormalities." Stated differently, Revlimid is not indicated, and has never been indicated, for MDS patients (a) who do not have a deletion 5q cytogenic abnormality or (b) who have high risk MDS. Only about 20% to 30% of patients with MDS have a deletion 5q cytogenic abnormality. According to the Leukemia & Lymphoma Society, there are roughly 11,400 new cases of MDS (all types) each year, which equates to only 2,300 to 3,400 new cases of MDS with a deletion 5q cytogenic abnormality each year.

85. In June 2006, Celgene secured FDA approval for Revlimid when taken in combination with dexamethasone for MM patients who have received at least one prior therapy. Unlike Thalomid, Revlimid is not approved for newly diagnosed MM, but only for those who have already received another treatment other than Revlimid. Although the company has attempted to obtain approval for Revlimid to treat newly diagnosed MM, it has been unsuccessful. On or around June 21, 2012, Celgene was forced to withdraw its application in Europe to have Revlimid approved for use as initial therapy for newly diagnosed myeloma patients and elected to postpone any application for the

same to the FDA. Celgene's European application was withdrawn due to concerns raised by European regulators about the link between Revlimid and secondary cancers.

86. Despite Revlimid's very narrow indication, Celgene marketed and continues to market the drug for all types of MDS, as well as a host of other off-label uses, including:

i. brain cancer;

ii. leukemia (including, but not limited to, CLL);

iii. lymphoma;

iv. myelofibrosis;

v. multiple myeloma (prior to Revlimid receiving FDA approval to treat this disease under specified circumstances);

vi. multiple myeloma not in combination with the drug dexamethasone;

vii. newly-diagnosed multiple myeloma;

viii. prostate cancer; and

ix. stem-cell transplant maintenance therapy after stem cell transplant.

87. Revlimid is extremely expensive; prescriptions can cost as much as $120,000 per year per patient.

3. Safety Issue: FDA Warnings Concerning Potentially Fatal Side Effects of Thalomid and Revlimid

a. History of Thalomid

88. Thalidomide, which Celgene later marketed as Thalomid, was first manufactured in 1957 by Chemie Grünenthal, a German pharmaceutical company that hired several Nazi doctors and scientists. For example, it employed Martin Staemmler, a leading proponent of the Nazi "racial hygiene" program who, following Germany's invasion of Poland, worked with the SS on its population policy. He was Grünenthal's head of pathology at the time it sold thalidomide. Grünenthal also employed Otto Ambros, one of the four inventors of the nerve gas sarin. In 1948, Ambros was found guilty at Nuremberg of mass murder and enslavement and sentenced to eight years in

prison. Ambros was the chairman of Grünenthal's advisory committee at the time it developed thalidomide.

89. In 1958, thalidomide was used throughout Europe and Canada to treat morning sickness in pregnant women. By 1961, however, thalidomide had been identified as the cause of between 10,000 and 20,000 serious birth defects, including severely deformed, or all together missing, limbs. Thalidomide was not approved by the FDA during this period, but samples of thalidomide were blamed for at least 17 cases of severe birth defects in America.

90. Specifically in response to the horror stories concerning birth defects from thalidomide, in 1962 Congress passed the Kefauver Harris Amendment, which for the first time required pharmaceutical companies to demonstrate a drug's efficacy in addition to safety to the FDA in order to obtain approval to market any new drug in the United States. This legislation also required drug advertisements to disclose complete information about potential side effects to consumers.

91. More than thirty years later, in 1998 when the FDA approved thalidomide (now marketed as Thalomid) for treatment of ENL, the FDA required Celgene to take multiple precautions to prevent Thalomid from causing severe birth defects. In addition to requiring Celgene to place a black-box warning on Thalomid's product labeling, the FDA required Celgene to take the step of creating a distribution system to prevent fetal exposure to Thalomid.

92. Specifically, as a condition of FDA approval, Celgene created the "System for Thalidomide Education and Prescribing Safety" ("S.T.E.P.S."), which requires all Thalomid-prescribing physicians to register with Celgene. It also requires all prescribing physicians to counsel patients on the risks of sexual activity during Thalomid use. Before a physician can prescribe Thalomid, the physician must notify Celgene through an automated system that he or she has counseled the patients on the risks of birth defects; then a Thalomid prescription is authorized by Celgene.

93. As Revlimid is in the same class of drugs as Thalomid, it too can cause birth defects. The black box warning concerning risks of birth defects caused by Revlimid when taken during pregnancy recommends that all female patients of childbearing potential obtain two negative pregnancy tests before starting Revlimid and use two forms of contraception during and for four weeks after taking Revlimid. The black box warning for birth defects is as follows:

> **WARNING: FETAL RISK, HEMATOLOGIC TOXICITY, and DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM**
> **Do not use REVLIMID during pregnancy. Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is used during pregnancy, it may cause birth defects or death to a developing baby. In women of childbearing potential, obtain 2 negative pregnancy tests before starting REVLIMID® treatment. Women of childbearing potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment [see Warnings and Precautions (5.1), and Medication Guide (17)]. To avoid fetal exposure to lenalidomide, REVLIMID is only available under a restricted distribution program called "RevAssist®" (5.2). Information about the RevAssist program is available at www.REVLIMID.com or by calling the manufacturer's toll-free number 1-888-423-5436.**

94. When the FDA first approved Revlimid in December 2005, it mandated a distribution system similar to S.T.E.P.S. called RevAssist. Because of the S.T.E.P.S. and RevAssist programs, Celgene has detailed records regarding every Thalomid and Revlimid prescription including all of the prescriptions submitted to Medicare, Medicaid, TRICARE, the VA and other government payors. As explained in more detail below, Celgene ultimately manipulated the cumbersome nature of S.T.E.P.S. and RevAssist to cause Medicare, Medicaid, and other government funded programs to cover the high-cost of off-label Thalomid and Revlimid prescriptions.

b. Thalomid's and Revlimid's Black Box Warnings Concerning Venous Thromboembolism

95. Cancer patients, including those with MM, already have an increased risk of developing venous thromboembolism ("VTE"), which are blood clots that form within a vein. According to a 2005 article entitled *Deep Vein Thrombosis in Cancer: the*

scale of the problem and approaches to management published in the Annals of Oncology, VTE is found at autopsy in at least 50% of cancer patients. Annals of Oncology, 16(5): 696-701 (May 2005).

96. VTEs are called deep venous thrombosis ("DVT"s) when they form within the deep veins of the leg, the pelvic veins, or other veins. When the clots travel to the lungs, they are called pulmonary embolisms ("PE"s). PEs can compromise lung function and can be fatal. Short of death, VTEs may cause heart complications, ulcers, and vein damage which can permanently impair blood flow.

97. Both Thalomid and Revlimid exacerbate the risk of VTEs in cancer patients. After Thalomid received its MM indication in May 2006, the FDA required Celgene to add the following black-box warning:

> **The use of Thalomid® (thalidomide) in multiple myeloma results in an increased risk of venous thromboembolic events, such as deep venous thrombosis and pulmonary embolus. This risk increases significantly when thalidomide is used in combination with standard chemotherapeutic agents including dexamethasone. In one controlled trial, the rate of venous thromboembolic events was 22.5% in patients receiving thalidomide in combination with dexamethasone compared to 4.9% in patients receiving dexamethasone alone (p = 0.002). Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Preliminary data suggest that patients who are appropriate candidates may benefit from concurrent prophylactic anticoagulation or aspirin treatment.**

98. Revlimid carries a similar black-box warning concerning risk of VTEs in MM patients. The following is the FDA required black box warning for Revlimid concerning VTEs:

> **WARNING: FETAL RISK, HEMATOLOGIC TOXICITY, and DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM**
> **…**
> **Deep Vein Thrombosis and Pulmonary Embolism**
> **REVLIMID has demonstrated an increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with multiple myeloma who were treated with REVLIMID and dexamethasone therapy. Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. It is not known whether prophylactic anticoagulation or antiplatelet therapy prescribed in conjunction with REVLIMID may lessen the potential for venous thromboembolic events. The decision to take prophylactic**

measures should be done carefully after an assessment of an individual patient's underlying risk factors.

99. Because Thalomid was indicated solely for ENL from 1998 to 2006, Thalomid's product information did not carry a black-box warning specifically concerning VTEs in MM patients during that period. Moreover, because Thalomid and Revlimid are only FDA approved for MM and MDS, neither drug carries warnings concerning the potential risks of VTEs in other forms of cancer.

100. As a result, doctors that prescribed Thalomid for MM prior to its receiving an MM indication in 2006 were not specifically warned by the label of the risks of VTEs in MM patients taking Thalomid. Furthermore, at all relevant times, as discussed below, physicians prescribing Thalomid or Revlimid for cancers other than MM and for MDS were not, and are not, warned about the drugs' association with VTEs in various types of other cancers.

c. Thalomid's and Revlimid's Additional Safety Risks

101. In addition to the risk of potentially fatal blood clots, Thalomid and Revlimid can cause other serious side effects including hematologic toxicity, peripheral neuropathy, and Stevens-Johnson Syndrome. Revlimid can also cause new malignancies. Celgene's off-label marketing of Thalomid and Revlimid exposed patients to these risks.

102. Revlimid's package insert includes a black-box warning concerning hematologic toxicity − specifically neutropenia and thrombocytopenia. Patients with neutropenia have low white blood cell counts, which can seriously compromise their ability to fight off infections. Thrombocytopenia sufferers, by contrast, have low blood platelet levels, which can make it difficult for the blood to clot. Thrombocytopenia can cause patients to suffer hemorrhages, which can lead to death. The black box warns that patients taking Revlimid can suffer from these types of hematologic toxicity:

WARNING: FETAL RISK, HEMATOLOGIC TOXICITY, and DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

> **…Hematologic Toxicity (Neutropenia and Thrombocytopenia)**
> **REVLIMID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q myelodysplastic syndromes had to have a dose delay/reduction during the major study. Thirty-four percent of patients had to have a second dose delay/reduction. Grade 3 or 4 [on a scale of 1-4] hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy for del 5q myelodysplastic syndromes should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors [see Dosage and Administration (2.2)].**

103. Revlimid and Thalomid can also cause peripheral neuropathy (*i.e.*, nerve damage), which can be severe and potentially permanent. Finally, both drugs can cause Stevens-Johnson Syndrome, a painful and dangerous condition causing skin to necrose and peel off, as in a third-degree burn. Stevens-Johnson Syndrome can be fatal.

104. On April 8, 2011, the FDA issued a safety announcement concerning Revlimid's potential for causing new malignancies. The FDA announced that clinical trials conducted both within and outside the United States "found that patients treated with Revlimid (lenalidomide) may be at an increased risk of developing new types of cancer compared to patients who did not take the drug." The cancers associated with Revlimid and Thalomid use include acute myelogenous leukemia (AML) and B-cell lymphoma. In July of 2013, the FDA ordered Celgene to stop a Phase III clinical trial of Revlimid for chronic lymphocytic leukemia (CLL) in elderly patients because of an imbalance of deaths among study participants - 34 deaths in the Revlimid group compared to 18 deaths in the chlorambucil (a chemotherapeutic agent) group.

B. Celgene Engaged In a Wide Variety of Illegal Marketing Schemes To Promote Thalomid and Revlimid For Off-Label Use

1. Celgene Gave Its Staff Purposefully Misleading Titles

105. When Relator was hired at Celgene in April 2001 she was immediately directed by Celgene to commence marketing Thalomid to physicians for off-label uses.

To accomplish this task, Relator and other Celgene sales professionals were dispatched to physicians under false pretenses.

106. Celgene gave Relator the title "Immunology Specialist," which indicated to physicians that Relator was a medical professional, as opposed to a sales representative. Relator, however, has no formal medical training and never studied immunology. Nonetheless, Celgene required Relator to hold herself out as competent to educate physicians and other medical practitioners in immunology.

107. Celgene also gave Relator the title "S.T.E.P.S. Field Coordinator" – a reference to Thalomid's FDA-mandated education, recordkeeping, and distribution system – and dispatched her to medical practices under the guise of assisting physicians with the FDA-required S.T.E.P.S. program. In reality, Relator's and other sales representatives' purported assistance with S.T.E.P.S. was a "bait-and-switch." Celgene used the program as an additional opportunity to off-label market Thalomid to captive physicians who required help in complying with S.T.E.P.S.

108. More specifically, Celgene tasked Relator and the other 100-plus S.T.E.P.S. Field Coordinators across the country to physicians' offices where they instructed physicians on procedures for registering themselves and their patients with S.T.E.P.S. and the requirement to contact Celgene directly each time the physician wrote a Thalomid prescription. It was during these S.T.E.P.S. meetings with physicians that Relator marketed, at Celgene's direction, Thalomid for off-label uses.

109. In or about December 2004, Celgene changed Relator's title from Immunology Specialist to Hematology Oncology Consultant ("HOC"). Relator's job duties stayed exactly the same, but because Thalomid was being marketed for both hematologic malignancies and solid tumors, Celgene believed the HOC title more accurately reflected the message it intended its sales force to communicate to physicians. Again, while Relator has no formal medical training, Celgene required and continued to require her to hold herself out to physicians as learned in both hematology and oncology.

In reality, Relator was a sales representative and her compensation depended significantly upon her ability to market Thalomid and Revlimid to physicians.

2. Celgene Rewarded Its Sales Force For Their Off-Label Sales

110. Relator and other sales personnel were, and are, rewarded by Celgene for their off-label sales. Celgene's compensation and bonus structure incentivizes its sales force to meet or exceed certain benchmarks in drug sales. On March 23, 2003, Celgene distributed an internal memorandum to Relator and other Celgene sales professionals from Dwight D'Iorio, Celgene's then-National Executive Director of Sales, stating that Relator and her colleagues would have "the opportunity to earn additional bonus money with each additional sales level achieved," at a time when Thalomid was approved only for a single, rare indication related to leprosy.

111. Relator received Celgene stock options, cash bonuses, and vacations based on her off-label sales of Thalomid and Revlimid. In 2003, Relator was a member of the "Diamond Club" which, according to Celgene management, "represents the pinnacle of success at Celgene." Diamond Club members are "in the top 15% of performers" based on drug sales; they received a Movado watch enhanced with a diamond for each additional year the salesperson remains a Diamond Club member.

112. Celgene holds an annual "Chairman's Challenge," a bonus program that rewards sales personnel for gross on-label and off-label Thalomid and Revlimid sales and each salesperson's ability to exceed certain sales benchmarks. A March 2003 Chairman's Challenge announcement from Dwight D'Iorio states, "[a]s promised at the National Sales Meeting there will be an additional bonus opportunity if we achieve an even higher level of sales success."

113. Even when Celgene faced heightened scrutiny relating to its bonus structure, it pretended to curb its illegal practices but, in reality, continued them. At the 2005 National Sales Meeting, Celgene's Senior Vice President of Sales and Marketing, Francis Brown ("Brown") told Celgene's sales force that they would no longer be compensated for Thalomid sales. In 2005 Celgene anticipated FDA approval of

Revlimid and, according to Brown, the Company was worried that the FDA would question Thalomid's high volume of sales because Thalomid was then only approved for ENL. Brown said that Celgene intended to tell the FDA that Celgene's sales force was paid for administering the S.T.E.P.S. distribution system, not for Thalomid sales. This would indicate to the FDA that Celgene's sales force was not paid or incentivized to market Thalomid off-label. Brown also told Celgene sales personnel that not providing bonuses for off-label sales would show the FDA that sales representatives were not directed to off-label market. Brown said this would "protect" the sales representatives and Celgene would be able to show the FDA that the Company was not "out of line."

114. Despite these statements, Celgene did provide bonuses based on Thalomid sales in 2005.

115. In reality, Celgene had misbranded Thalomid for years and rewarded its sales force handsomely for their misbranded sales.

3. Celgene Was Aware Of The Serious Health Risks Caused By Thalomid And Revlimid But Trained Its Sales Force To Conceal The Facts

116. As explained above, Thalomid and Revlimid present a variety of serious risks to patients. Celgene was well aware of these risks but trained its sales force to conceal these risks from patients and doctors.

117. At the time Celgene promoted and marketed Thalomid and Revlimid off-label, and long before the FDA issued its black box warning about VTEs in 2006, the Company was aware of the elevated risks of VTE that these drugs posed to cancer patients. Celgene knew about trials showing an increased incidence of VTEs in cancer patients taking Thalomid and received reports from the Company's sales personnel that doctors were concerned about prescribing Thalomid to their cancer patients.

118. Shortly after Relator joined Celgene in 2001, she participated in a mandatory internal conference call with all of the Company's sales professionals and other employees. This training call was conducted by the pharmacists, Dr. and Dr. Long (a married couple), who were retained by the Company to discuss risks associated with

Thalomid. During this call, the Longs discussed the risks posed by Thalomid, but instructed the sales professionals to withhold this information and not mention the risks to doctors. The Celgene sales professionals were told that doctors would see the DVTs and PEs as side effects of MM in patients, and to address the issue by simply stating that people with MM have a greater chance of developing VTE, rather than warning the doctors that use of Thalomid by patients with MM would increase this risk. Relator was so concerned that immediately after this mandatory call ended, she talked to a fellow West Region sales representative who told her to not worry.

119. As concern grew about DVTs and PE's, Celgene addressed drug trials and doctors' concerns about Thalomid in education and training materials it distributed to its sales personnel, including a document entitled "Thromboembolism Backgrounder" distributed in 2004. In that document, which was sent directly to Relator by the Company, Celgene acknowledged that VTEs had been reported when thalidomide first began to be prescribed for MM, prostate cancer and other types of cancer, starting around 2000. In fact, as noted in the Backgrounder, "[b]ecause of a high incidence of this effect, some clinical trials with thalidomide were suspended."

120. The Backgrounder also discussed the results of a survey by the Canadian Coordinating Office for Health Technology Assessment, which published the results in January 2004:

> This report noted several studies where a high incidence of thromboembolism (15% to 50%) was reported. In a few trials, thromboembolism was reported in 5% to 10% of patients. … A study by Bowcock et al. (2002) reported thromboembolism in 7 of 23 patients (30%) who received thalidomide as a single agent.
>
> Several reports have described thromboembolism in patients who received thalidomide as part of treatment for prostate cancer. For example, in a study by Home et al. (2003), venous thromboembolism was reported in 0% of patients who received docetaxel alone, vs. 19% of patients who received docetaxel and thalidomide.

> VTE has also been reported in patients who received thalidomide as treatment for other cancer types, including renal cell carcinoma, myelodysplastic syndrome, and mantle cell lymphoma.

121. Celgene sold Thalomid in Australia through its business partner Pharmion Corporation ("Pharmion"). The labeling and other materials distributed by Celgene and Pharmion prior to 2005 in Australia recognized the VTE issue. For example, the January 2004 *Thalidomide Pharmion Information Brochure* stated that "[i]n malignant conditions … patients are predisposed to a hypercoaguable state" and that "[c]aution should be used when Thalomid is combined with chemotherapy, as venous thromboembolism is a potential complication …. An unexpectedly high risk of venous thromboembolism has been observed when Thalomid is combined with chemotherapy for newly diagnosed patients with myeloma." This same document also cites studies showing the potential for experiencing thrombotic events is particularly acute when Thalomid is used concomitant with vincristine, doxorubicin and dexamethasone.

122. Despite numerous studies showing increased risk of VTE in cancer patients taking thalidomide, Celgene told its sales professionals that there was no cause for alarm or need to warn doctors. In the Backgrounder, Celgene stated "The reasons for development of VTE with thalidomide use in cancer patients are not clearly understood." Celgene further stated that:

> Several reports have noted that thromboembolism is relatively uncommon when thalidomide is given as a single-agent therapy, and that the greatest incidence has come when thalidomide is used in combination with chemotherapy and/or corticosteroids.

123. In a section of the Backgrounder headed "Management," Celgene suggested that warfarin be proposed in conjunction with thalidomide to reduce the risk of VTE. The Backgrounder stated:

> Management of patients who have thromboembolic episodes in association with thalidomide use is similar to approaches described earlier in this program. Anticoagulation therapy (heparin, with or without warfarin) plus other approaches used in treatment of DVT and/or PE may be provided.

> When anticoagulant therapy is provided, DVT may not require discontinuance of thalidomide. Thalidomide has been resumed safely, in combination with warfarin, in patients who experienced thrombolic events.
>
> Some clinicians have provided warfarin prophylactically to cancer patients who are treated with thalidomide. The combined use of these agents may decrease the incidence of thromboembolism; however, this has yet to be established through controlled clinical trials.

124. In short, Celgene knew, but instructed its sales personnel not to warn doctors, about the increased risk of developing VTE in cancer patients taking thalidomide. If doctors raised this risk as an issue, Celgene trained its sales personnel to discount the risk and suggest that the doctors prescribe an anticoagulation therapy such as warfarin to purportedly decrease the risk of VTE. Celgene's training of its sales representatives to encourage warfarin use began as early as 2001 during the mandatory conference call with the Drs. Long discussed above.

125. Celgene also told its sales personnel to propose the use of baby aspirin if a doctor raised the issue of VTE. As purported support for that instruction, Celgene provided its sales personnel with copies of a summary of an article by Mohamad A. Hussein, titled "Thromboembolism Risk Reduction In Multiple Myeloma Patients Treated With Immunomodulatory Drug Combinations," which discussed the results of various trials. Celgene provided its sales personnel a summary of the Hussein article. (Celgene later hired Dr. Hussein.) In the summary, Celgene argued that aspirin reduced the incidence of VTE. The Hussein article concluded:

> Strategies to reduce the risk of VTE associated with thalidomide and lenalidomide combinations while maintaining activity should consider the prophylactic use of anti-coagulants. There are no randomized trials to favor one anticoagulation agent or regimen over another in this setting.

126. What Celgene did not tell its sales personnel was that the American Academy of Chest Physicians – in its contemporaneous (2004) Guidelines – states that

aspirin should not be used for VTE prophylaxis for any patient group (the Academy rates this recommendation 1A, its strongest rating). Nor did Celgene tell its sales personnel that the American College of Physicians (an association of internists) has never recognized aspirin as appropriate for thromboprophylaxis. Celgene also failed to provide an objective analysis of the various studies discussed in the Hussein article and to discuss any of the problems of those studies (such as their small size) or other problems (such as the failure to provide information on the number of patients or length of the trial).

127. Thus, Celgene directed its sales representatives to recommend that doctors couple Thalomid with aspirin as a way to reduce the risk of developing VTE. The Company suggested this multiple times including the 2001 mandatory conference call with the Drs. Long discussed above. This put patients' lives and health at risk.

128. At the time that Celgene was marketing Revlimid off-label, Celgene knew that the drug could cause other cancers, particularly in patients with newly-diagnosed MM. Clinical trials had demonstrated an increased risk of acute myelogenous leukemia, myelodysplastic syndromes, and Hodgkin's lymphoma. As with VTEs, rather than warning physicians about these risks, Celgene instructed Relator and others to withhold this information. Relator followed these instructions and cannot recall ever informing a single doctor about these risks. Moreover, Celgene's Director of Regulatory Affairs, William Woolever, often spoke at National Sales Meetings. During these meetings, he emphasized that sales representatives needed to disclose only risks in the label, and later, in the black box.

129. In May 2012, the FDA announced that information about this risk posed by Revlimid would be added to the drug's label.

4. Celgene Repeatedly Trained Relator and Other Sales Personnel To Market Thalomid and Revlimid Off-Label And Then Managed Them To Ensure That They Were Marketing Off-Label

130. From the day Relator began at Celgene in 2001, the company began training her to market Thalomid, and later Revlimid, off-label. The training continued

throughout her tenure at Celgene. The company's management also observed and approved of the off-label marketing.

a. Celgene Never Trained Its Sales Force To Market Thalomid On-Label

131. When Relator joined Celgene in April 2001, Thalomid was only approved for treatment of ENL; it did not receive an additional indication until a full five years later, in May 2006. Nevertheless, Celgene never provided Relator any information or training concerning Thalomid's use in ENL. Celgene never provided Relator with any studies, pamphlets, or educational materials of any sort concerning the sole disease for which Thalomid, at the time, was indicated. In her nearly twelve years at Celgene, Relator never met a physician who, to her knowledge, treated ENL. Furthermore, on average, a mere twelve new leprosy cases are treated in California each year, meaning ENL patients are virtually non-existent in Relator's sales territory.

132. When Relator first arrived at Celgene in 2001, she received some formal classroom training on Thalomid and the micro-environment. Significantly, Celgene provided her with a copy of a single patient case report by Dr. Bart Barlogie in which Thalomid was used to treat MM. At the time, the FDA had only approved Thalomid for the treatment of ENL. Celgene failed to train Relator about FDA rules and regulations prohibiting off-label marketing. In fact, her then-managers Deena Harding and Jeff Rowell told her that FDA limits on marketing only applied to large companies, like Merck.

133. Celgene never informed Relator about the 1998 FDA warning letters. Relator conducted her own research and asked about the FDA warnings during her second or third job interview with her future managers Dwight D'Iorio and Deena Harding. Ms. Harding told Relator that the April 21, 2000 warning letter was not important, maintaining that the conduct at issue was limited to one sales representative in the Pacific Northwest who failed to obtain a medical information request form.

134. After her classroom training ended, Relator was required to accompany Alana Torgelson, the fourth sales representative hired by Celgene, for a day. During this training ride-along, Relator witnessed Ms. Torgelson converse with a doctor regarding a patient suffering from renal cell cancer. The doctor asked Ms. Torgelson about the proper Thalomid dose to treat renal cell cancer. Ms. Torgelson told him "400 [mg] is what works" even though there is no evidence to support this dosage and there is no FDA approval for renal cell cancer.

135. Relator then accompanied Ms. Torgelson on additional visits, and watched her promote Thalomid to treat other solid tumor cancers including cervical cancer.

b. Celgene Trained Its Sales Force To Market Thalomid and Revlimid Off-Label at National Sales Meetings And By Bringing Relator and Other Sales Personnel To Corporate Headquarters

136. At national sales meetings and at intermittent visits to corporate headquarters, Celgene coached Relator and other sales personnel to market its products off-label. The company's management then observed and evaluated Relator and other sales personnel to ensure that they were implementing the off-label marketing plans.

137. For example, in 2004, at a Celgene National Sales Meeting at the Lacosta Resort and Spa in Carlsbad, California, Celgene provided its sales force with a written off-label marketing plan for Thalomid. In addition to Baer and Jackson, at that meeting, Larry Bishop, the West Region Sales Director, was present and provided the Celgene sales force with the "2004 Business Plan West Region (the 'Plan')." The Plan focused "solely on Thalomid," and instructed sales personnel to, *inter alia*, "[e]mphasize MM, MDS and targeted solid tumor activity[1] on every [sales] call." In other words, although Thalomid (a) was not approved for MM[2] at the time the memorandum was distributed,

[1] "[T]argeted solid tumor activity" refers to non-hematological cancers.

[2] As stated above, Thalomid did not receive FDA approval for MM until May 2006. Even in 2006, however, Thalomid received only a narrow indication: for treatment of newly diagnosed MM, and only when taken in combination with the agent dexamethasone.

(b) was and is not approved for MDS, and (c) was never approved for additional cancers, Celgene's senior management specifically directed Relator and her colleagues to market Thalomid for those diseases "on every call."

138. The 2004 Plan provides a "Market Analysis Summary" which reported that Celgene's West Region, through 2003, caused physicians to prescribe Thalomid to 230 brain cancer patients, 400 melanoma patients, 1000 MM patients, 730 MDS patients, 45 ovarian cancer patients, 250 prostate cancer patients, and 420 renal cell (i.e., kidney) cancer patients. Celgene's West Region was just one of Celgene's sales districts. The Plan also set "specific additional new patient goals, by malignancy."

139. The 2004 Plan encouraged Celgene sales representatives to use numerous off-label studies, journal articles and abstracts identified in the document when marketing Thalomid for off-label uses.

140. The Plan reiterated and memorialized management's previous (and continuing) directives to off-label market Thalomid. Relator's superiors, at times, referenced the Plan. In Relator's 2003 Performance Evaluation, completed in early 2004, Relator's then-district sales manager, Jeff Rowell ("Rowell"), instructed Relator to "Implement Larry Bishop's Regional Plan by targeting the selected tumors with the selected reference materials."

141. Relator successfully implemented the Plan. Every week, Celgene's national operations distributed spreadsheets summarizing Relator's and other sales representatives' sales data. Most of these sales report spreadsheets included a tab labeled "Indication and Duration Reports," which documented Relator's total Thalomid prescriptions for the current year as well as any "New [Thalomid] Patients" Relator successfully obtained. Each spreadsheet broke these figures down by total numbers of diagnosis and total Thalomid capsules prescribed. According to Relator's April 16, 2004 sales report, as of April 2004, Relator had successfully caused physicians to prescribe 11,116 Thalomid capsules for MM patients, 504 for renal cell cancer patients, 1,148 for MDS patients, 196 for melanoma patients, 168 for prostate cancer patients,

112 for ovarian cancer patients, and 3,080 for patients suffering from "Other" ailments. Strikingly, ENL – the only disease for which Thalomid was indicated, *i.e.*, FDA approved, until May 2006 – is not listed on any of these Celgene-generated spreadsheets.

142. Similarly, at the end of certain financial quarters, Celgene distributed spreadsheets to Relator and her colleagues that included a tab labeled "Indication Breakdown" and provided the "Total Business" for Thalomid in specific diseases. According to Celgene's spreadsheet for the first quarter of 2004, from the first quarter of 2003 through the first quarter of 2004, Celgene's West Region sales force successfully caused physicians to prescribe: 131,702 Thalomid capsules for MM patients, 13,608 for MDS patients, and 1,484 for prostate cancer patients, and a total of 190,342 capsules for all patients combined. Critically, this same spreadsheet indicates that zero physicians in the region prescribed Thalomid for ENL.

143. At national sales meetings, Celgene presented patients taking Thalomid for serious diseases that were outside Thalomid's label to attest to the drug's efficacy. These individuals were introduced to the sales force both informally and on-stage. Specifically, at the 2003 National Sales Meeting in West Palm Beach, a Celgene employee introduced a patient suffering from melanoma, who spoke about her success on Thalomid. Celgene also presented a patient taking Thalomid as a single agent for multiple myeloma at a National Sales Meeting. Following these patient presentations, a Celgene employee routinely closed the meeting by emphasizing the importance of providing off-label information to physicians so that similar patients could receive Thalomid therapy.

144. Celgene also routinely sent its sales force to the Company's headquarters in Summit, New Jersey to participate in off-label training sessions. For example, in or about 2004, Larry Bishop, who authored the 2004 marketing plan, conducted a "Phase II Training" to assist Celgene's sales force in marketing Thalomid for a number of off-label uses. Celgene required its entire sales force to attend this training. The Phase II Training materials discussed Thalomid use in the following cancers: prostate, ovarian,

melanoma, renal, colorectal, brain, pancreatic, bladder, esophageal, gastric, testicular, cervical, uterine, breast, and thyroid. Following the Phase II training session, Bishop circulated a number of off-label studies concerning these diseases to sales representatives for use in detailing physicians. Celgene routinely conducted mandatory training seminars similar to Bishop's Phase II Training at its headquarters in Summit, New Jersey.

c. Management Accompanied Relator and Other Sales Representatives on Sales Calls

145. Managers joined Relator and other sales representatives on their sales calls at least once every three months to ensure that sales representatives were effectively marketing Thalomid off-label. During Relator's first four months at Celgene, in or about July 2001, Relator's then-district sales manager, Deana Harding, accompanied Relator on a full day of sales calls. After those calls, Harding wrote in Relator's "Celgene Field Contact Report" that "I would like to hear you articulate the newly diagnosed [MM] data next time we are together; as well as the thought leaders [sic] dosing guidelines to move your MDs [doctors] forward." Similarly, in a 2002 report, Harding instructed Relator to "Brush up on your MDS and Figg data so that after Myeloma you have an alternative message." "Figg data" refers to a study concerning Thalomid use in prostate cancer. Relator memorized portions of the Figg study in an effort to promote Thalomid in prostate cancer.

146. Through discussions with fellow sales representatives, Relator has learned that Celgene began to off-label market Thalomid almost immediately upon receiving FDA approval. For instance, Linnie Burney, a fellow West Region sales representative told Relator that in or about 1999 or 2000, Jerome Zeldis, Celgene's then-Medical Director, accompanied Burney on a sales call to Dr. Joyce O'Shaughnessy, a preeminent breast cancer physician in Texas, in order to convince her to prescribe Thalomid to all of her breast cancer patients.

147. In Relator's 2003 performance evaluation, Relator's then-district sales manager, Jeff Rowell, commented on a ride-along with Relator, writing, "You are not afraid to seek to seek additional uses of Thalomid beyond Multiple Myeloma as evidenced by seeing you discuss data on MDS, Renal Cell Carcinoma, Prostate Cancer, Colorectal Cancer, Melanoma, and other tumor types [with physicians]."[3] Based on this and other performance measures, Rowell rated Relator's 2003 job performance "EE" for "Exceeds Expectations."

148. Moreover, Relator's managers conducted ride-alongs after Relator and other sales representatives secured "unsolicited" off-label medical information request forms signed by the physicians she called upon. When Relator returned with her manager, she asked the physician whether he or she had received the off-label information requested. As directed by Celgene, Relator often asked the physician for assurances that he or she would prescribe Thalomid for off-label use. This showed Relator's manager that she was securing off-label information requests, and succeeding in securing new prescriptions.

149. Similarly, as with Thalomid, Relator's managers continued to conduct routine "ride-alongs" to ensure that Relator and other sales staff effectively marketed Revlimid for off-label uses. In 2007, Relator's then-manager Shawn Gormish accompanied her on several ride-alongs. In one ride-along, they called upon Dr. Michael Steinberg at the City of Hope Hospital. At Gormish's direction, Relator suggested to the doctor that he prescribe Revlimid for his MM patients who had just

[3] As Harding's and Rowell's words plainly show, years before Celgene received approval for treatment of newly diagnosed MM, Celgene already considered Thalomid an MM medication. In a 2003 letter from Sol Barer to Relator, Barer warned of the competition that Thalomid could face for treatment of MM: "[o]ur commercial force will face competition: Velcade will be approved sometime this year for ***myeloma***. While we believe that it will be relegated to a salvage role and doesn't have the wealth of evidence Thalomid has[,] it is important to remember ***that we will for the first time have competition***." Thalomid did not receive an MM indication for more than three years after Barer's letter.

received a bone marrow transplant. During another sales call at the same hospital, Gormish instructed Relator to market Revlimid to Dr. Firoozeh Sahebi (who also worked for Kaiser) for newly diagnosed MM patients.

150. Celgene's highest level management, stationed in New Jersey, also conducted ride-alongs with Relator and other sales representatives. In 2001, Celgene's Vice President of Sales, Dwight D'Iorio, rode along with Relator. Moreover, Relator is aware that John Jackson, Celgene's former CEO, performed a ride-along with at least one representative, Jackie Qwon, a representative in the Rockville, Maryland area, in or about 2003 or 2004.

d. Celgene's Misbranding Was Directed By Company Management

151. Not only did the company's management, up to and including CEO John Jackson, observe the misbranding of Thalomid and Revlimid, the decision to market the product was made at the highest levels of the company.

152. For example, in its April 8, 2005 business review meeting with senior management the company discussed marketing its products to treat prostate cancer. None of Celgene's products have ever been approved by the FDA to treat prostate cancer. The company was certainly aware of this. In 2009, Bill Spruill, a Senior Regional Sales Director at Celgene, forwarded a 2005 email string regarding this meeting to Jeff Rowell, by then a national accounts management director. When Rowell noted that the company's "policy on destroying old information prevents you from still having this," Spruill responded "[d]ocument retention policy is for losers." Rowell then told Spruill:

> Think of how smart it is by the company, though. If anyone ever "whistle blows" with old proof either on email or printed, the company can fire them for cause for violating the Records Retention Policy … vs. firing them as "retaliation."

153. In his 2006 evaluation, Company management directed Vice President of Marketing, Mark Alles, "to develop and execute [Revlimid] [marketing] plans for Non 5q-MDS, CLL [chronic lymphocytic leukemia] and NHL [non-hodgkin lymphoma]."

The FDA has not approved Revlimid to treat any of these conditions. The instruction to develop a marketing plan for CLL is particularly troublesome. Celgene has long tried to develop evidence that Revlimid is effective to treat leukemia. Its unsuccessful efforts ended in 2013 when the FDA forced it to discontinue a late-stage large study of Revlimid in elderly CLL patients because patients taking the drug had a death rate nearly twice that of patients receiving chemotherapy.

5. Celgene Provided Its Sales Force With Marketing Materials Describing Off-Label Uses of Thalomid and Revlimid

154. Since 2001, Celgene deluged Relator and other sales representatives with marketing materials concerning a litany of diseases – primarily cancers – for which Thalomid and Revlimid were not FDA approved. Celgene designed these materials specifically to be used in sales calls.

155. Soon after Relator completed her formal training at Celgene, the Company provided her and her colleagues with copies of an abstract by Dr. William Figg and others that appeared in the July 2001 issue of Clinical Cancer Research. The objective of the study was to evaluate the response rates (tumor measurements and changes in PSA levels) associated with low-dose and high-dose thalidomide in patients with androgen-independent prostate cancer ("AIPC"). The results were, however, inconclusive. Only 50 patients were enrolled in the low-dose arm; and the high-dose arm was terminated due to the large number of individuals who could not tolerate the dose. There were 560 adverse events reported, ranging from constipation to fatigue, even suicide. About 30% of the patients had a decline of 40% or more in their PSA, but there was no control group. Relator, then a new hire, asked her then manager, Deena Harding, about the study and was told to use it when calling upon doctors who treated prostate cancer. Relator then used this abstract to promote the use of Thalomid for all forms of prostate cancer, not just AIPC. The FDA has never approved Thalomid to treat prostate cancer.

156. Relator's managers voiced their disapproval when she failed to use this study. For example, in or about 2004, Relator's then manager Jeff Rowell ("Rowell") accompanied her during a ride-along that included a visit to Dr. Karo Arzoo in Burbank, California. Rowell observed Relator talking to Dr. Arzoo about Thalomid and prostate cancer. When the conversation ended and Dr. Arzoo returned to an examination room to treat a patient, Rowell angrily confronted Relator in the doctor's office, demanding that she use the Figg study. They waited until Dr. Arzoo finished with the patient and then Relator – pursuant to her manager's demand – confronted Dr. Arzoo again and presented the Figg study.

157. Upon Revlimid's launch, Celgene provided Relator with "Revlimid Standard Letters" and a compilation of studies concerning off-label uses for Revlimid. These compilations, as later alleged in this Complaint, include studies concerning Revlimid's use for the off-label treatment of cancers including off-label combinations and or uses.

158. Subsequent to Revlimid's launch, Celgene provided Relator and other sales representatives information concerning Revlimid's use in non-indicated forms of MDS. For example, one document Celgene provided to Relator states "Field question/objection addressed: Doesn't Revlimid only work in those patients with a del5q abnormality" and provides study results that a sales representative can recite to a physician suggesting Revlimid's purported efficacy in MDS without a del5q deficiency. Celgene, its managers, and its documents routinely referred to "our MDS patients" in an effort to communicate that Revlimid should be used to treat all forms of MDS. Relator routinely probed physicians as to whether they treated general MDS, and then provided this information. Moreover, Relator memorized portions of a study in the New England Journal of Medicine that included partial findings concerning Revlimid's alleged efficacy in general MDS. Relator provided this information to physicians throughout her employment at Celgene.

159. Relator encountered resistance from doctors when she attempted to market Revlimid for use by all MDS patients as directed by the company's marketing plan. For example, in or about 2006, Relator's then-manager Shawn Gormish directed her to call upon Dr. Mark Kirschbaum at City of Hope Hospital and to use the probing question "do you have any non 5q deletion MDS patients?" Dr. Kirschbaum responded that he did not currently have any such patients. Nonetheless Relator attempted to market Revlimid for future non 5q deletion MDS patients. At that point, Dr. Kirschbaum answered, "Beverly, that is something I cannot help you with." Similarly, when Relator suggested to Dr. Mina in 2006 – at the Company's direction – that he use Revlimid to treat newly diagnosed MM patients, Dr. Mina refused, explaining that the FDA had not approved Revlimid to treat newly diagnosed MM patients. When Relator then suggested that he could use it alone – *i.e.*, not in combination with dexamethasone – to treat newly diagnosed MM patients, he told her that he could not do that as it would be unethical, the patient would not have had any prior treatments. Although these doctors did not respond to Celgene's misbranding, they were the exception.

6. Celgene Promoted Off-Label Uses of Thalomid and Revlimid Using Studies and Abstracts That Failed To Provided Scientific Support for the Off-Label Use

160. Celgene's national headquarters provided Relator and other sales personnel with stacks of studies so that she and others could detail physicians on off-label uses. In addition, Celgene routinely made false statements to physicians concerning Thalomid's and Revlimid's effectiveness in certain patient populations and withheld important safety information such as the risk of deep vein thrombosis described above. These representations constituted illegal misbranding because they were unsupported by FDA-approved prescribing information.

161. Celgene provided Relator with abstracts but not the complete studies to present to physicians. In many cases, the underlying studies were seriously flawed.

162. For example, shortly after Relator began working for Celgene in 2001, she attempted to market Thalomid for smoldering MM (i.e., early-stage, asymptomatic MM)

at the Ventura, California Hematology and Oncology Clinic. It is Relator's understanding that smoldering MM is never treated, since it is asymptomatic and treatment (which always has side effects) does not affect the course of the disease. Nevertheless, Relator provided physicians at the Ventura facility with a study given to her by Celgene to distribute to doctors in which a total of twelve patients were treated with Thalomid for smoldering MM. The head physician at the Ventura practice, Dr. Kelley, harshly scolded Relator for attempting to market Thalomid based on a woefully inadequate study.

163. In or about 2001, Celgene provided Relator with a binder of materials entitled "Colorectal Cancer." Curiously, Relator was never trained on colon cancer . When she asked her managers what she was to do with these materials, she was told by Deena Harding that they should be used to promote the use of Thalomid in patients with colorectal cancer. The FDA has never approved Thalomid to treat colon cancer.

164. In the binder, Celgene included selling points for Thalomid. For example, (1) a memorandum entitled "Use of Thalidomide in Combination Therapy with Irinotecan in the Treatment of Metastic Colorectal Cancer," (2) an August 2000 Lancet article by Dr. Rangasnamy Govindarajan and others titled "Effects of Thalomid on the Gastrointestinal Toxic Effects of Irinotecan (CPT-11)," and (3) an August 2000 memorandum titled "Thalidomide Reduces Side Effects of Chemotherapy for Colon Cancer," which presented the purported benefits of using thalidomide in combination with Irinotecan in colorectal cancer patients. In addition to noting a reduced overall incidence of diarrhea in patients given the combination therapy, the 2000 memorandum stated that "[a]necdotally, thalidomide as monotherapy has been noted to be associated with clinical improvement in a few patients with metastic colorectal carcinoma." However, the memorandum based its conclusion on small, preliminary studies. The Govindarajan study was, for example, a pilot clinical trial involving only nine patients of which eight completed the chemotherapy regimen. One required a dose reduction of thalidomide for somnolence. Of the remaining seven patients, only one had a complete

response. Another patient attained partial remission. Irinotecan is known to have activity in this disease, and the relative contribution of thalidomide is not clear. These results were far short of being sufficiently robust to support Thalomid treatment decisions. Subsequent small studies in 2003, 2006, and 2007 reported a lack of even radiographic response to thalidomide. The Company directed Relator and its sales force to use these materials to promote Thalomid to treat colorectal cancer. Nevertheless, from 2000 to today, there is no evidence that the drug benefits patients with colorectal carcinoma at any stage of disease, either alone or in combination with other agents.

165. Celgene's Medical Affairs department purchased prescribing data which allowed the company to target oncology specialists for off-label sales. Relator and other sales representatives used this information to prepare for their sales calls. For example, if Medical Affairs told Relator that a doctor treated colon cancer, Relator routinely used the materials in the "Colorectal Cancer" binder to market off-label. Medical Affairs assisted the sales force by specifying which abstracts, studies, and reports they should bring.

166. Continuing through at least 2011, Celgene provided to Relator and other sales representatives for distribution to physicians, studies concerning non-indicated Revlimid combinations for relapsed MM, such as use with Bortezomib and Melphalan. Additionally, as detailed below, the materials provided to Relator included studies concerning "Monotherapy with Revlimid," and "Newly Diagnosed [MM] and Revlimid."

167. Celgene provided Relator and her sales colleagues with a "Launch 2006 Reprint Cheat Sheet," that summarized the various abstracts and studies to be used in promoting Thalomid and Revlimid. These studies and abstracts failed, however, to provide legitimate scientific support for the proposed off-label uses.

168. For example, Celgene gave its sales representatives an article by Dr. Vincent Rajkumar, which was published in the December 2005 issue of *Blood.* Celgene directed sales representatives to use the article to "detail" physicians about the use of

Revlimid for newly diagnosed MM. This article, however, was suspect as Dr. Rajkumar received grant support from Celgene. Moreover, there were technical flaws in the underlying study.

169. The study purported to compare lenalidomide and dexamethasone to thalidomide and dexamethasone. Dr. Rajkumar suggested that the prior drug combination was more effective and less toxic than the latter in treating MM. The article, however, provided no information about the thalidomide group, such as the number of patients, trial period or treatment regimen. Without that information, physicians could not draw reliable conclusions about how lenalidomide compares to thalidomide. Nonetheless, Relator, at Celgene's direction, provided copies of this study to virtually every doctor she called upon.

170. Celgene also gave its sales representatives copies of what it represented was an article by Michael Wang and other authors, appearing in the December 2008 issue of *Blood*, for use in persuading physicians that Revlimid could be used in patients previously treated with Thalomid. Yet what appeared to be an article by independent authors was actually an advertisement. In addition, nine of the twelve authors (including four Celgene employees) received financial support from Celgene. Dr. Wang received honoraria from Celgene and research funding for this project. The studies discussed in the article were likewise funded by Celgene. The advertisement appeared to be a legitimate article in a respected journal; only if a reader happened to read a footnote in small type would the reader realize that this was not a peer-reviewed article but an advertisement paid for by Celgene.

CLINICAL TRIALS AND OBSERVATIONS

Lenalidomide plus dexamethasone is more effective than dexamethasone alone in patients with relapsed or refractory multiple myeloma regardless of prior thalidomide exposure

Michael Wang,[1] Meletios A. Dimopoulos,[2] Christine Chen,[3] M. Teresa Cibeira,[4] Michel Attal,[5] Andrew Spencer,[6] S. Vincent Rajkumar,[7] Zhinuan Yu,[8] Marta Olesnyckyj,[8] Jerome B. Zeldis,[8] Robert D. Knight,[8] and Donna M. Weber[1]

[1]Department of Lymphoma and Myeloma, M. D. Anderson Cancer Center, Houston, TX; [2]Department of Clinical Therapeutics, University of Athens School of Medicine, Athens, Greece; [3]Department of Medicine, Princess Margaret Hospital, Toronto, ON; [4]Hematology Department, Institute of Hematology and Oncology, Hospital Clinic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain; [5]Division of Hematology, Centre Hospitalier Universitè de Purpan, Toulouse, France; [6]Department of Malignant Hematology and Stem Cell Transplantation Service, The Alfred Hospital, Melbourne, Australia; [7]Mayo Clinic Cancer Center, Rochester, MN; and [8]Celgene, Summit, NJ

This analysis assessed the efficacy and safety of lenalidomide + dexamethasone in patients with relapsed or refractory multiple myeloma (MM) previously treated with thalidomide. Of 704 patients, 39% were thalidomide exposed. Thalidomide-exposed patients had more prior lines of therapy and longer duration of myeloma than thalidomide-naive patients. Lenalidomide + dexamethasone led to higher overall response rate (ORR), longer time to progression (TTP), and progression-free survival (PFS) versus placebo + dexamethasone despite prior thalidomide exposure. Among lenalidomide + dexamethasone-treated patients, ORR was higher in thalidomide-naive versus thalidomide-exposed patients ($P = .04$), with longer median TTP ($P = .04$) and PFS ($P = .02$). Likewise for dexamethasone alone-treated patients ($P = .03$ for ORR, $P = .03$ for TTP, $P = .06$ for PFS). Prior thalidomide did not affect survival in lenalidomide + dexamethasone-treated patients (36.1 vs 33.3 months, $P > .05$). Thalidomide-naive and thalidomide-exposed patients had similar toxicities. Lenalidomide + dexamethasone resulted in higher rates of venous thromboembolism, myelosuppression, and infections versus placebo + dexamethasone, independent of prior thalidomide exposure. Lenalidomide + dexamethasone was superior to placebo + dexamethasone, independent of prior thalidomide exposure. Although prior thalidomide may have contributed to inferior TTP and PFS compared with thalidomide-naive patients, these parameters remained superior compared with placebo + dexamethasone; similar benefits compared with placebo + dexamethasone were not evident for thalidomide-exposed patients in terms of overall survival. Studies were registered at http://www.clinicaltrials.gov under NCT00056160 and NCT00424047. (Blood. 2008;112:4445-4451)

Introduction

Despite advances in the treatment of multiple myeloma (MM), a disease characterized by the accumulation of clonal plasma cells in the bone marrow, the disease remains incurable. With the advent of novel therapies, the median survival of relapsed patients has been improved from about 1 to 2 years after relapse.[1] It is estimated that about 20 000 people (11 000 men and 9 000 women) will be diagnosed with MM, and 11 000 will die because of the disease in the United States in 2008.[2] Patients relapsing after 2000 had a median survival of 24 months, which was a clear improvement compared with those relapsing before 2000, indicating the benefit of new treatment options.[3] Nevertheless, novel agents and their rational combinations are needed. In the mid-1990s, a new class of immunomodulatory drugs was designed and synthesized using the structural backbone of thalidomide as the template. The intention was to create analogs with enhanced efficacy and reduced toxicity relative to their parent compound.[4,5] Lenalidomide (Revlimid; Celgene, Summit, NJ) is an oral derivative of thalidomide that has proven activity against MM in preclinical and clinical studies.[6-10] Whereas the immunomodulatory effects and in vivo antitumor activity of lenalidomide are similar to thalidomide, improved potency (evidenced by a greater ability to stimulate T-cell proliferation, interleukin-2 and interferon-γ production, and to inhibit tumor cell growth) and reduced toxicity (reduced somnolence, constipation, and peripheral neuropathy; no evidence of teratogenicity or mutagenesis in preclinical models) favor lenalidomide.[4,11,12] However, it must be noted that myelosuppression, not commonly observed with thalidomide, is often observed with lenalidomide.[4,12] Recently, lenalidomide plus dexamethasone was shown to be also highly active in newly diagnosed MM, leading to durable responses and a low progression rate and mortality.[13] In 2 prospective, randomized, double-blind, placebo-controlled phase 3 clinical trials (MM-009 and MM-010), it was shown that lenalidomide plus dexamethasone induced significantly higher rates of overall response (OR) and complete response (CR), as well as longer time to progression (TTP), and overall survival (OS), compared with placebo plus dexamethasone in patients with relapsed or refractory MM.[14,15]

Since lenalidomide is a derivative of thalidomide, there has been concern about possible resistance to lenalidomide in patients who had relapsed after, or who were refractory to, treatment with thalidomide. Preliminary data from early phase 1 and 2 trials

Submitted February 22, 2008; accepted July 25, 2008. Prepublished online as *Blood* First Edition paper, September 17, 2008; DOI 10.1182/blood-2008-02-141614.

Presented in part at the 42nd Annual Meeting of the American Society of Clinical Oncology, Atlanta, GA, June 4, 2006[16]; the 48th Annual Meeting of the American Society of Hematology, Orlando, FL, December 10, 2006[17]; and the XIth International Myeloma Workshop, Kos Island, Greece, June 26, 2007.[21]

The publication costs of this article were defrayed in part by page charge payment. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734.

171. Rather than presenting a new study, the Wang advertisement merely analyzes a subset of data obtained from two prior studies conducted by Celgene. The authors look at only selected data and results from those prior studies and conclude (from preliminary data in early phase 1 and phase 2 trials) that Revlimid alone and in combination with dexamethasone produced a response in patients who had previously received thalidomide. The subgroups analyzed by Wang, however, number as few as ten or fifteen patients – numbers that are too small to provide meaningful results. Indeed, the advertisement noted that the analysis "is a post hoc analysis, performed without pre-specified power calculation or adjustment for multiplicity, and is therefore considered exploratory in nature." Moreover, the data also demonstrated that a patient who was

first treated with thalidomide is not likely to do as well on Revlimid as a patient previously treated with another drug. At Celgene's direction, Relator and her colleagues provided copies of this study to doctors.

A complete, full-sized, full-length copy of this advertisement is attached as Exhibit 1.

172. Celgene regularly gave its sales professionals materials from ASCO meetings that discussed off-label uses of Revlimid and Thalomid for use in marketing the Company's drugs. For example, Celgene distributed a document titled "Renal Cell Carcinoma Express Report" from the 38th Annual Meeting of the American Society of Clinical Oncology (ASCO) in 2002 to be used by Relator and others to promote the use of thalidomide for renal cell carcinoma. The material consisted largely of an editorial by Dr. Howard Burris and a summary of presentations by Dr. Robert Amato and Dr. Sandy Srinivas.

173. In addition, the material describes two studies that are too small to be meaningful. The first is the initial phase of a study involving only 15 patients treated with thalidomide and IL-2. After 12 weeks eight patients demonstrated a positive response while in seven patients the disease progressed. There was no discussion of adverse events.

174. The second study involved only 14 patients, randomized to two groups receiving different doses of thalidomide. All seven patients in the high dose group required dose reduction because of toxicity, and two patients developed DVTs. There was no information on disease responses; the "disease stabilization" rate was 46%, which could be consistent with the natural progress of renal cell carcinoma. Nevertheless, the summary concluded that "thalidomide, either as single-agent or in combination with immunotherapy, often achieves disease stabilization in this otherwise progressive carcinoma." The studies – small, lacking important information, and otherwise incomplete – even taken together, provide no meaningful support for this sweeping conclusion.

175. Another document Celgene provided to Relator purportedly supporting the use of Thalomid to treat renal cell carcinoma was a study by Dr. Danai Daliani and others, supported by Celgene, published in the August 2002 issue of *Lancet*. The article reported on a pilot study involving only 20 patients. Only two patients showed any response at all to thalidomide treatment; furthermore, the disease progressed in all 20 patients. Dr. Daliani reviewed the results of various small studies (some of which found a response, others of which did not) and concluded that "[t]ogether, our data show some antitumor activity of thalidomide in heavily pretreated patients with [metastatic] RCC and warrant evaluation of the role of thalidomide in RCC patients in controlled, randomized trials." Even though the studies in the Daliani material were small, preliminary, showed that thalidomide had serious toxicities, and were not intended to provide a basis for treating patients, Celgene told Relator and other sales professionals to use the study to promote the use of Thalomid for renal cell carcinoma. Relator, at the Company's instruction, used this article to market Thalomid to treat renal cell cancer, including to Dr. Mukund Shah in 2005 at the Antelope Valley Cancer Center. The FDA has never approved Thalomid to treat renal cell carcinoma.

176. In short, the articles and studies used by Celgene to market Thalomid and Revlimid off-label lacked sufficient information or indicia of reliability to enable physicians to make objective and informed decisions about prescribing Thalomid or Revlimid.

7. Celgene Trained Its Sales Personnel To "Probe" Physicians In Order to Induce Discussions of Off-Label Thalomid and Revlimid Uses

177. The use of probing questions to prompt a dialogue about the off-label use of Celgene's drugs was a hallmark of Celgene's marketing schemes. For example, Celgene directed Relator to ask physicians if they treated patients who suffered from a number of cancers and other diseases so that Relator could segue into Thalomid's use for these off-label purposes. For instance, Celgene managers directed Relator to ask physicians, "Do you treat any [off-label disease] patients?" If a physician responded

"yes," Relator was told to highlight studies that purportedly showed strong data supporting Thalomid's use for the off-label indication. A 2002 Celgene Field Contact Report written by Relator's then-district sales manager, Deanna Harding, directed Relator to "[i]dentify your goal before walking into the office and establish an appropriate probe question to get you into a discussion."

178. The materials Celgene provided to Relator also described the following "Potential Probes" to use with doctors in promoting the off-label use of Thalomid in combination with Irinotecan in colorectal cancer patients: "What are your biggest concerns for treating colorectal pts [patients]?"; "Where do you see Thalomid fitting into your treatment regimen?"; and "How do you feel about combining an immunomodulator's agent with a cytotoxic agent?"

179. Other training materials suggested questions to pose to doctors in order to prompt a discussion of the use of Thalidomide to treat kidney cancer. For example, Celgene materials stated:

> Dr. Smith, do you have any renal cell patients that have failed IL-2? … Thalidomide and its analogs overcome drug resistance of human multiple myeloma cells to conventional therapy. … This is why thalidomide is being tried in over 10 clinical trials in the U.S. for renal cell cancer.

180. The use of probing questions was a technique not limited to the off-label marketing of Thalomid. For example, an April 27, 2010 email from Andrew Odenwald, a district sales manager, provides questions that sales representatives should ask doctors about Cutaneous T cell lymphoma ("CTCL"), a class of non-Hodgkin's lymphoma, which is a type of cancer of the immune system. The FDA has never approved Revlimid to treat Cutaneous T cell lymphoma. In his email, Odenwald attached "CTCL target lists, CTCL profiling tool[s], and the Cross Functional meeting slides" and said the "critical questions" to ask doctors were:

1. How many patients with CTCL are you currently treating?
2. How many new patients with CTCL do you see per year?
3. Are these patients referred by a dermatologist?

8. To Provide Cover For The Company, Celgene Directed Its Sales Force to Secure Off-Label Medical Request Forms

181. Celgene used "medical information request forms" to memorialize physician requests for off-label information. A physician's unsolicited or voluntary request directly to the company for such information generally is not considered evidence of company's intent to misbrand or off-label market a drug. However, Celgene subverted the "medical information request" process by requiring its sales force to verbally discuss off-label uses of its drugs during visits with physicians and then ask physicians to request materials from Celgene, using "medical information request" forms. The forms, which were completed by sales representatives and signed by physicians, were designed to make it appear that a physician's request for off-label information from Celgene's medical services department was entirely voluntary and unsolicited. Celgene started this practice early. At Relator's second job interview, Deena Harding attributed the FDA's April 21, 2000 warning letter to a sales representative's failure to obtain a medical request form. Thus, even before Relator was officially hired, her supervisor-to-be stressed the importance of papering the files by soliciting "unsolicited" request forms.

182. Complying with Celgene's directives, Relator routinely encouraged physicians to order off-label information from Celgene's medical services department during her sales pitches. If the physician agreed, Relator commonly completed the form for the physician and then asked the physician to sign. Relator sent the signed medical information request forms to Celgene's headquarters in Summit, New Jersey, which in turn sent the information to the physician.

183. Celgene put intense pressure on Relator and other sales personnel to secure as many medical information request forms as possible. Relator's 2003 Performance Evaluation directed Relator to "obtain a signed Medical Services Request form on each call." The push to obtain these medical information request forms is illustrated in Chad Saward's Monthly Activity report for September 2002. He writes, under the heading

"Accomplishments" that he "submitted nearly 30 Med Request Forms" and under "Goals" he wrote "submit a Med. Info Request form for nearly every call." (In this same monthly activity report he notes, under the heading "message," that "I discussed colorectal, prostate, renal cell carcinoma, melanoma, MDS and MM. This month I am going back to the basics with a MM focus." At this time, the FDA had approved Thalomid to treat none of these conditions and only approved it in 2006 for a subset of MM.)

184. Relator and other sales representatives who failed to secure sufficient numbers of these medical information request forms were routinely admonished by their superiors while those that obtained large numbers were praised. At almost every national sales meeting, a member of Celgene's marketing department stood and commended the Celgene regional sales force that secured the greatest number of medical information request forms during the previous year. Some of Celgene's highest level management, including Sol J. Barer (Celgene's Chief Operating Officer from March 1994 to May 1, 2006; Chairman and Chief Executive Officer from May 2006 until June 2010; Executive Chairman from June 2010 until December 2010; and Non-Executive Chairman from January 2011 until June 2011), who were present at these meetings, joined in applauding the regional team that secured the most off-label request forms.

185. If a sales representative's total submitted medical request forms was low, however, then the representative would be confronted by his/her manager. It was expected that each sales representative would obtain at least 30 such requests a month. The pressure to obtain these forms was so great that the Relator is aware of at least one person – Chad Saward – that was caught forging doctor's signatures. Mr. Saward was later promoted by Celgene.

186. As with Thalomid, Relator's managers pressured her and other sales representatives to persuade physicians to sign medical request forms for off-label uses of Revlimid. When Revlimid was launched in December 2005, it was approved solely for treatment of transfusion-dependent anemia due to low or intermediate risk MDS

associated with a deletion 5q cytogenic abnormality.[4] As previously alleged, deletion 5q cytogenic abnormality is relatively uncommon, as only 20% to 30% of MDS patients suffer from the condition. Nevertheless, Celgene immediately began directing Relator and other sales representatives to market the drug off-label for all types of MDS, including high risk MDS, and MDS without the deletion 5q cytogenic abnormality. As part of this marketing effort, Relator and other sales personnel routinely secured these medical request forms for general MDS.

187. Celgene's directive to circumvent the "medical information request" process was intended to further the Company's goal of unlawfully increasing its sales of Thalomid and Revlimid, as well as to provide needed but superficial "cover" should regulators learn that the Company had unlawfully distributed materials outside the drugs' labeling.

9. Celgene Directed Its Sales Force To "Push The Dose" With Thalomid

188. Thalomid is more expensive as the dose increases. Accordingly, Celgene directed sales representatives, including Relator, to encourage physicians to prescribe high doses of Thalomid, and sales representatives received larger bonuses for higher dosages. Celgene's marketing strategy focused on those diseases for which patients in studies were given very high doses of Thalomid. For example, Celgene's managers directed Relator to target physicians who treated renal cell (*i.e.*, kidney) cancer, because there existed published studies where renal cell cancer patients were treated with up to 1200mg of Thalomid per day (1200mg is a very high dose of Thalomid). Allison Tozer, a Medical Information Specialist at Celgene's headquarters in New Jersey, provided Relator with stacks of these and other studies to distribute directly to physicians. Celgene directed Relator to detail physicians concerning these studies and related off-label uses of Thalomid.

[4] To this day, Revlimid is still not FDA-approved for any other type of MDS.

189. Relator also targeted physicians that treated glioblastoma (*i.e.*, brain cancer) patients, because there were studies that used extremely high Thalomid dosage levels in treatment. In an effort to target these physicians, Celgene's national sales operations provided Relator and other sales representatives with lists of physicians in their areas that prescribed Temodar, a popular brain cancer medication. Celgene directed its sales representatives to persuade these doctors to use Thalomid to treat brain cancers.

190. Notwithstanding Celgene's efforts to target brain and kidney cancer specialists, Relator and other representatives often encountered resistance from physicians related to "pushing the dose," because many patients cannot tolerate high doses of Thalomid. Elevated doses can cause VTE, peripheral neuropathy, neutropenia, and constipation.

191. In May 2002, for example, Dr. Devitt objected to Chad Saward's efforts to push the dose. According to Saward's notes in his May 2002 Monthly Activity report, Dr. Devitt had "10 MM and 10 MDS patients" but "she was not aware of any evidence to support increasing the dose [and therefore Saward] share[d] the Barlogie Benchmark analysis" with Dr. Devitt. He was referring to "Extended Survival in Advanced and Refractory Multiple Myeloma after Single-Agent Thalidomide: Identification of Prognostic Factors in a Phase 2 Study of 169 Patients," authored by Dr. Bart Barlogie and others in the 2001 edition of *Blood*. At this time, Thalomid was not approved by the FDA to treat any form of MM or MDS. (Saward's report for May 2002 also stated that his "message has been MM and MDS"). Later that year, in his December Monthly Activity report, Saward continued to describe his efforts to push the dose. Under goals, he wrote "increase my average dose in December vs November."

10. Celgene Provided Relator and Other Sales Personnel With "Training" Materials Describing Off-Label Uses, Most of Which Failed to Provide Scientific Support For the Off-Label Use

192. Celgene routinely provided Relator and other sales personnel with materials purportedly for "training" and/or "education" that provided detailed information regarding off-label uses of Thalomid or Revlimid. Relator's managers instructed her,

and other sales representatives, to use these materials despite their designation, to market to physicians.

193. For example, in 2001 Celgene provided Relator and other sales personnel with "training" materials to be used to promote the use of Thalomid in patients with renal cell (kidney) cancer. These materials, purportedly authored or assembled by Hank Schwarz, a Clinical Science Liaison, stated that:

> Thalomid appears to have anti-angiogenic benefits. Since kidney cancer is very vascular and attracts blood vessels, anti-angiogenic therapy is the next frontier in the battle against kidney cancer.

194. The training materials provided by Celgene to its sales force provided the following summaries of ongoing trials about Thalomid:

> Despite employing a low dose of thalidomide, we observed encouraging responses in patients with renal cell carcinoma. In 18 patients treated for renal carcinoma, three showed partial responses to thalidomide and 13 showed stable disease, three of them for more than 3 months.
>
> * * *
>
> Our findings suggest that thalidomide may be useful in the management of advanced renal cell carcinoma and possibly of symptomatic benefit in other solid malignancies.

195. There is no clear published evidence of clinical benefits of thalidomide in renal cell carcinoma at any stage of disease, either alone or in combination with other therapies. Early studies used duration of stable disease as an endpoint. This endpoint is not meaningful in a disease which can have long indolent periods. A negative study in 2006 led authors to conclude that the risks of thalidomide outweigh potential benefits, and publications subsequently recommended against use of thalidomide in this disease.

196. Relator was never trained on renal cell cancer. When she asked what she was to do with these materials, she was told by her managers to give the studies to doctors, which she – like other sales representatives – did.

197. The below chart summarizes some of the studies that the company provided Relator, all of which related to one or more uses of Thalomid or Revlimid that were not

approved by the FDA at the time the study or abstract was written and distributed. In some cases, Celgene sent the Relator dozens of copies of studies stamped "do not distribute."

Study or Abstract Title	**Study or Abstract Author(s)**	**Publication**
Myelosuppresion Associated With Novel Therapies in Patients With Multiple Myeloma: Consensus Statement of the IMF Nurse Leadership Board	Miceli, *et al.*	*Clinical Journal of Oncology Nursing.* June 2008, Supplement to 12(3)
Thromboembolic Events Associated With Novel Therapies in Patients With Multiple Myeloma: Consensus Statement of the IMF Nurse Leadership Board	Rome, *et al.*	*Clinical Journal of Oncology Nursing.* June 2008, Supplement to 12(3)
Peripheral Neuropathy Associated With Novel Therapies in Patients With Multiple Myeloma: Consensus Statement of the IMF Nurse Leadership Board	Tariman, *et al.*	*Clinical Journal of Oncology Nursing.* June 2008, Supplement to 12(3)
Gastrointestinal Side Effects Associated With Novel Therapies in Patients With Multiple Myeloma: Consensus Statement of the IMF Nurse Leadership Board	Smith, *et al.*	*Clinical Journal of Oncology Nursing.* June 2008, Supplement to 12(3)
Steroid-Associated Side Effects in Patients With Multiple Myeloma: Consensus Statement of the IMF Nurse Leadership Board	Faiman, *et al.*	*Clinical Journal of Oncology Nursing.* June 2008, Supplement to 12(3)
Stem Cell Mobilization with Cyclophosphamide Overcomes the Suppressive Effect of Lenalidomide Therapy on Stem Cell Collection in Multiple Myeloma	Mark, *et al.*	*Biology of Blood and Marrow Transplantation.* 2008; 14(7)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Lenalidomide: Targeted Anemia Therapy for Myelodysplastic Syndromes	List, *et al.*	*Cancer Control.* 2006; 13 (Supplement)
Relationship of Treatment-Related Cytopenias and Response to Lenalidomide in Patients With Lower-Risk Myelodysplastic Syndromes	Sekeres, *et al.*	*Journal of Clinical Oncology.* 2008; 26(36)
Lenalidomide plus Dexamethasone for Relapsed or Refractory Multiple Myeloma	Dimopoulous, *et al.*	*New England Journal of Medicine.* 2007; 357(21)
Lenalidomide plus Dexamethasone Is More Effective than Dexamethasone Alone in Patients with Relapsed or Refractory Multiple Myeloma Regardless of Prior Thalidomide Exposure	Wang, *et al.*	*Blood.* 2008; 112(12)
Multiple Myeloma	Kyle, *et al.*	*New England Journal of Medicine.* 2004; 351(18)
Advances in Oral Therapy for Multiple Myeloma	Morgan, *et al.*	*Lancet Oncology.* 2006; 7
Advances in Oral Therapy in the Treatment of Multiple Myeloma	Doss	*Clinical Journal of Oncology Nursing.* 2006; 10(4)
Superiority of Thalidomide and Dexamethasone Over Vincristine-Doxorubicin-Dexamethasone (VAD) as Primary Therapy in Preparation for Autologous Transplantation for Multiple Myeloma	Cavo, *et al.*	*Blood.* 2005; 106(1)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Phase III Clinical Trial of Thalidomide Plus Dexamethasone Compared With Dexamethasone Alone in Newly Diagnosed Multiple Myeloma: A Clinical Trial Coordinated by the Eastern Cooperative Oncology Group	Rajkumar, *et al.*	*Journal of Clinical Oncology*. 2006; 24(3)
Oral Melphalan and Prednisone Chemotherapy Plus Thalidomide Compared with Melphalan and Prednisone Alone in Elderly Patients With Multiple Myeloma: Randomized Controlled Trial	Palumbo, et al.	*The Lancet*. 2006; 367
Maintenance Therapy with Thalidomide Improves Survival in Patients with Multiple Myeloma	Attal, *et al.*	*Blood*. 2006; 108(10)
Combination Therapy with Lenalidomide plus Dexamethasone (Rev/Dex) for Newly Diagnosed Myeloma	Rajkumar, *et al.*	*Blood*. 2005;106(13)
Lenalidomide and Pegylated Liposomal Doxorubicin-Based Chemotherapy for Relapsed or Refractory Multiple Myeloma: Safety and Efficacy	Baz, *et al.*	*Annals of Oncology*. September 2006
A Randomized Phase 2 Study of Lenalidomide Therapy for Patients with Relapsed or Relapsed and Refractory Multiple Myeloma	Richardson, *et al.*	*Blood*. 2006; 108(10)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Prevention of Pulmonary Embolism and Deep Vein Thrombosis with Low Dose Aspirin: Pulmonary Embolism Prevention (PEP) Trial	Rodgers	*The Lancet*. 2000; 355
Management of Thalidomide Toxicity	Ghobrial, *et al.*	*The Journal of Supportive Oncology*. 2003; 1(3)
Deep Vein Thrombosis in Patients with Multiple Myeloma Treated with Thalidomide and Chemotherapy: Effects of Prophylactic and Therapeutic Anticoagulation	Zangari, *et al.*	*British Journal of Haernatology*. 2004; 126(5)
The Role of Aspirin in the Prevention of Thrombotic Complications of Thalidomide and Anthracycline-Based Chemotherapy for Multiple Myeloma	Baz, *et al.*	*Mayo Clinic Proceedings*. 2005; 80(12)
Thromboembolism risk reduction in multiple myeloma patients treated with immunomodulatory drug combinations	Hussein	*Thrombosis & Hemostasis*. 2006; 95(6)
A Phase 2 Study of Bortezomib in Relapsed, Refractory Myeloma	Richardson, *et al.*	*New England Journal of Medicine*. 2003; 348
Bortezomib Therapy Alone and in Combination with Dexamethasone for Previously Untreated Symptomatic Multiple Myeloma	Jagannath, *et al.*	*British Journal of Haematology*. 2005; 129(6)
PAD Combination Therapy (PS-341/bortezomib, doxorubicin and dexmethasone) for Previously Untreated Patients with Multiple Myeloma	Oakervee, *et al.*	*British Journal of Haematology*. 2005; 129(6)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Bortezomib or High-Dose Dexamethasone for Relapsed Multiple Myeloma	Richardson, *et al.*	*New England Journal of Medicine.* 2005; 352(24)
Clinical Factors Predictive of Outcome with Bortezomib in Patients with Relapsed, Refractory Multiple Myeloma	Richardson, *et al.*	*Blood.* 2005; 106(9)
Bortezomib plus Dexamethasone as Induction Treatment Prior to Autologous Stem Cell Transplantation in Patients with Newly Diagnosed Multiple Myeloma: Results of an IFM Phase II Study	Harousseau, *et al.*	*Haematologica.* 2006; 91(11)
Thalidomide - A Revival Story	Raje, *et al.*	*New England Journal of Medicine.* 1999; 341(21)
Antitumor Activity of Thalidomide in Refractory Multiple Myeloma	Singhal, *et al.*	*New England Journal of Medicine.* 1999; 341(21)
Extended Survival in Advanced and Refractory Multiple Myeloma after Single-Agent Thalidomide: Identification of Prognostic Factors in a Phase 2 Study of 169 Patients	Barlogie, *et al.*	*Blood.* 2001; 98(2)
First-line Therapy with Thalidomide and Dexamethasone in Preparation for Autologous Stem Cell Transplantation for Multiple Myeloma.	Cavo, *et al.*	*Haematologica.* 2004; 89(7)

Study or Abstract Title	Study or Abstract Author(s)	Publication
A Pilot Study of Thalidomide in Patients with Progressive Metastatic Renal Cell Carcinoma	Daliani, *et al.*	*Cancer.* 2002; 95(4)
Temozolomide Plus Thalidomide in Patients With Advanced Melanoma: Results of a Dose-Finding Trial	Hwu, *et al.*	*Journal of Clinical Oncology.* 2002; 20(11)
Thalidomide for the Treatment of patients with MDS	Strupp, *et al.*	*Leukemia.* 2002; 16(1)
A Randomized Phase II Trial of Thalidomide, an Angiogenesis Inhibitor, in Patients with Androgen-independent Prostate Cancer	Figg, *et al.*	*Clinical Cancer Research.* 2001; 7.
Thalidomide Produces Transfusion Independence in Long-standing Refractory Anemias of Patients with Myelodisplastic Syndromes	Raza, *et al.*	*Blood.* 2001; 98(4)
Colorectal and Anal Cancers	Pazdur, *et al.*	*Cancer Management: A Multidisciplinary Approach*
Renal Cell Carcinoma Express Report: Encouraging Preliminary Results from Thalidomide in Renal Cell Carcinoma		*38th Annual Meeting of the American Society of Clinical Oncology* (ASCO) May 16-21, 2002
Compendia-Based Drug Bulletin	N/A	*Compendia-Based Drug Bulletin.* 2006; 15(2)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Thalidomide and its Analogs Overcome Drug Resistance of Human Multiple Myeloma Cells to Conventional Therapy	Hideshima, *et al.*	*Blood.* 2000; 96(8)
Apoptotic Signaling Induced by Immunomodulatory Thalidomide Analogs in Human Multiple Myeloma Cells: Therapeutic Implications	Mitsiades, *et al.*	*Blood.* 2002; 99(12)
Thalidomide Selectively Modulates the Density of Cell Surface Molecules Involved in the Adhesion Cascade	Geitz, *et al.*	*Immunopharmacology*. 1996; 31.
Adherence of Multiple Myeloma Cells to Bone Marrow Stromal Cells Upregulates Vascular Endothelial Growth Factor Secretion: Therapeutic Applications	Gupta, *et al.*	*Leukemia.* 2001; 15.
Immunomodulatory Analogs of Thalidomide Inhibit Growth of Hs Sultan Cells and Angiogenesis in Vivo	Lentzsch, *et al.*	*Leukemia.* 2003; 17.
Thalidomide and Immunomodulatory Derivatives Augment Natural Killer Cell Cytoxicity in Multiple Myeloma	Davies, *et al.*	*Blood.* 2001; 98(1)
Initial Stages of Tumor Cell-Induced Angiogenesis: Evaluation Via Skin Window Chambers in Rodent Models	Li, *et al.*	*Journal of the National Cancer Institute.* 2000; 92(2)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Clinical Application of Antiangiogenic Therapy: Microvessel Density, What It Does and Doesn't Tell Us	Hlatky, *et al.*	*Journal of the National Cancer Institute.* 2002; 94(12)
Impact of Lenalidomide Therapy on Stem Cell Mobilization and Engraftment Post-peripheral Blood Stem Cell Transplantation in Patients with Newly Diagnosed Myeloma	Kumar, *et al.*	*Leukemia.* 2007; 21
Melphalan and Prednisone plus Thalidomide versus Melphalan and Prednisone Alone or Reduced-intensity Autologous Stem Cell Transplantation in Elderly Patients with Multiple Myeloma (IFM 99-06): a Randomized Trial	Facon, *et al.*	*Lancet.* 2007; 370
Lenalidomide plus Dexamethasone (Rev/Dex) in Newly Diagnosed Myeloma: Response to Therapy, Time to Progression, and Survival	Lacy, *et al.*	*Blood.* 2006; 108(11)
Oral Revlimid plus Melphalan and Prednisone (R-MP) for Newly Diagnosed Multiple Myeloma: Results of a Multicenter Phase I/II Study	Palumbo, *et al.*	*Blood.* 2006; 108(11)
Melphalan (M), prednisone (P) and lenalidomide ® combination (MPR) for newly diagnosed multiple myeloma patients who are not candidates for stem cell transplantation	Roy, *et al.*	*Blood.* 2006; 108(11)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Lenalidomide plus High-dose Dexamethasone Provides Improved Overall Survival Compared to High-Dose Dexamethasone Alone for Relapsed or Refractory Multiple Myeloma (MM): Results of 2 Phase II Studies (MM-009, MM-010) and Subgroup Analysis of Patients with Impaired Renal Function	Weber, *et al.*	*Blood.* 2006; 108(11)
Lenalidomide in Combination with Dexamethasone is more Effective than Dexamethasone at First Relapse in Relapsed Multiple Myeloma	Stadtmauer, *et al.*	*Blood.* 2006; 108(11)
Lenalidomide (L) in Combination with Dexamethasone (D) Significantly Improves Time to Progression (TTP) in Non-stem Cell Transplant Patients (pts) with Relapsed or Refractory (rel/ref) in Multiple Myeloma (MM): Analysis from MM-009 and MM-010 Randomized Phase III Clinical Trials	Chanan-Khan, *et al.*	*Blood.* 2006; 108(11)
Lenalidomide overcomes poor prognosis conferred by deletion of chromosome 13 and t(4;14) in multiple myeloma: MM016 trial	Bahlis, *et al.*	*Blood.* 2006; 108(11)
Phase III trial of lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone in newly diagnosed multiple myeloma (E4A03): A trial coordinated by the Eastern Cooperative Oncology Group	Rajkumar, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Pharmacokinetics of lenalidomide in subjects with various degrees of renal function	Chen, *et al.*	Abstract
A Randomized Phase 2 study of Lenalidomide Therapy for Patients with Relapsed or Relapsed and Refractory Multiple Myeloma	Richardson, *et al.*	*Blood.* 2006; 108(10)
Doxil (D), vincristine (V), Reduced Frequency Dexamethasone (d) and Revlimid DVd-R) a Phase I/II Trial in Advanced Relapsed/refractory Multiple Myeloma (Rmm) Patients	Hussein, *et al.*	Abstract
Symposium on Oncology Practice: Hematological Malignancies - The Myelodysplastic Syndromes: Diagnosis and Treatment	Steensma, *et al.*	*Mayo Clinic Proceedings.* 2006; 81(1)
A phase II trial of lenalidomide for patients with AL amyloidosis	Sanchorawala, *et al.*	Abstract
Skin reactions associated with oral Revlimid (lenalidomide) in AL amyloidosis (ALA); Patient teaching encouraging prompt reporting, and clinical assessment and management of skin reactions can impact patient outcomes	Finn, *et al.*	*Oncology Nursing Forum.* 2006; 33(2)
Lenalidomide has activity in a phase II trial in patients with primary systemic amyloidosis	Dispenzieri, *et al.*	Abstract
Reversal of myelofibrosis in a patient	Besa, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
A phase I trial of CC-5013, a potent thalidomide analog, in patients with recurrent high-grade gliomas and other refractory CNS malignancies	Fine, *et al.*	Abstract
Lenalidomide (L) induces high response rates with molecular remission in patients (pts) with relapsed (rel) or refractory (ref) chronic lymphocytic leukemia (CLL)	Miller, *et al.*	Abstract
Antileukemic activity of lenalidomide (L) (Revlimid) in patients (pts) with relapsed (REL) or refractory (REF) chronic lymphocytic leukemia (CLL)	Chanan-Khan, *et al.*	Abstract
Prednisone (P) Prophylaxis Decreases Incidence and Severity of Lenalidomide (L) Induced Flare Reaction (flr) in Patients with Relapse (rel) or Refractory (ref) Chronic Lymphocytic Leukemia	Musial, *et al.*	Abstract
Clinical Characteristics and Management Strategy of Revlimid-Induced Tumor Flare Reaction in Patients with CLL	Miller, *et al.*	*Oncology Nursing Forum.* 2006; 33(2)
Results of Phase II Study of Lenalidomide (L) (Revlimid) in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia (CLL)	Chanan-Khan, *et al.*	*Blood.* 2005; 106(11)
Lenalidomide in Patients with Cutaneous T-cell Lymphoma. Preliminary Data of Phase II Trial	Querfeld, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Results of Phase I Study of CO-5013 for the Treatment of Multiple Myeloma (MM) Patients who Relapse after High-Dose Chemotherapy (HDCT)	Zangari, *et al.*	Abstract
A Multi-Center, Randomized, Phase 2 Study to Evaluate the Efficacy and Safety of 2 CDC-5013 Dose Regimens When Used Alone or in Combination with Dexamethasone (Dex) for the Treatment of Relapsed or Refractory Multiple Myeloma (MM)	Richardson, *et al.*	Abstract
Revlimid 25 mg (REV 25) x 20 Versus 50 mg (REV 50) x 10 g 28 Days with Bridging of 5 mg x 10 Versus 10 mg x 5 as Post-Transplant Salvage Therapy for Multiple Myeloma (MM)	Zangari, *et al.*	Abstract
A Multicenter, Single-arm, Open-label Study to Evaluate the Efficacy and Safety of Single-agent Lenalidomide in Patients with Relapsed and Refractory Multiple Myeloma; Preliminary Results	Richardson, *et al.*	Abstract
Doxil (D), Vincristine (V), Reduced Frequency Dexamethasone (d) and Revlimid [DVd-R]) Results in a High Response Rate in Patients with Refractory Multiple Myeloma (RMM)	Baz, *et al.*	*Blood*. 2005; 106(11)

Study or Abstract Title	Study or Abstract Author(s)	Publication
A Phase 1 Trial of Lenalidomide (REVLIMID) with Bortezomil (VELCADE) in Relapsed and Refractory Multiple Myeloma	Richardson, *et al.*	*Blood.* 2005; 106(11)
Evaluating Oral Lenalidomide (Revlimid) and Dexamethasone versus Placebo and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma	Dimopoulous, *et al.*	Abstract
Study of Lenalidomide plus Dexamethasone versus Dexamethasone Alone in Relapsed or Refractory Multiple Myeloma (MM): Results of a Phase 3 Study (MM-010)	Dimopoulous, *et al.*	Abstract
A Multicenter Phase I/II Trial Evaluating the Safety and Efficacy of Lenalidomide (Revlimid, CC-5013) in Combination with Doxorubicin and Dexamethasone (RAD) in Patients with Relapsed or Refractory Multiple Myeloma	Gerecke, *et al.*	*Blood.* 2005; 106(11)
Lenalidomide (Revlimid), in Combination with Cyclophosphamide and Dexamethasone (CRD) Is an Effective Regimen for Heavily Pre-Treated Myeloma Patients.	Davies, *et al.*	Abstract
BiRD (Biaxin/Revlimid/Dexamethasone) Combination Therapy (Rx) Results in High Complete Remissions (CR) and Overall Responses in Myeloma (MM) with Poor Prognostic Features	Niesvizky, *et al.*	*Blood.* 2005; 106(11)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Clarithromycin, Lenalidomide and Dexamethasone Combination Therapy as Primary Treatment of Multiple Myeloma	Niesvizky, *et al.*	Abstract
Oral Lenalidomide plus Melphalan and Prednisone (R-MP) for Newly Diagnosed Multiple Myeloma	Palumbo, *et al.*	Abstract
High Incidence of Thrombotic Events Observed in Patients Receiving Lenalidomide (L) + Dexamethasone (D) (LD) as First-line Therapy for Multiple Myeloma (MM) without Aspirin (ASA) Prophylaxis	Zonder, *et al.*	Abstract
Lenalidomide plus High-dose Dexamethasone Provides Improved Overall Survival Compared to High-dose Dexamethasone Alone for Relapsed or Refractory Multiple Myeloma (MM): Results of a North American Phase III Study (MM-009)	Weber, *et al.*	Abstract
Lenalidomide (Revlimid) in Combination with Dexamethasone (DEX) is more Effective than DEX alone in Patients with Relapsed or Refractory Multiple Myeloma Who Have Received Prior Thalidomide Therapy	Blade, *et al.*	Abstract
Increased Risk of Thrombosis with Lenalidomide in Combination with Dexamethasone and Erythropoietin	Niesvizky, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Comparison of Lenalidomide in Combination with Dexamethasone to Dexamethasone Alone in Patients Who Have Received Prior Thalidomide in Relapsed or Refractory Multiple Myeloma	Wang, *et al.*	Abstract
Lenalidomide (Len) in Combination with Dexamethasone (Dex) is more Effective than Dex Alone at first Relapse and Provides Better Outcomes when Used Early Rather than as Later Salvage Therapy in Relapsed Multiple Myeloma (MM)	Stadtmauer, *et al.*	Abstract
Lenalidomide (Revlimid) Combination with Dexamethasone (DEX) is more Effective than DEX alone in Patients with Relapsed or Refractory Multiple Myeloma and Independent of Number of Previous Treatments	Dimopoulous, *et al.*	Abstract
Results of the MDS-002 and -003 International Phase II studies Evaluating Lenalidomide (CC-5013; Revlimid) in the Treatment of Transfusion-dependent (TD) Patients with Myelodysplastic Syndrome (MDS)	List, *et al.*	Abstract
Lenalidomide (CC-5013; Revlimid)-induced Red Blood Cell (RBC) Transfusion-independence (TI) Response in Low-/Int 1-risk Patients with Myelodysplastic Syndromes (MDS): Results of the Multicenter MDS 002 Study	Razal, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Phase II Study of Lenalidomide (CC-5013) for Patients with Myelofibrosis	Verstovsek, *et al.*	Abstract
Reversal of Myelofibrosis in a Patient with Low-risk Myelofibrostic Syndrome on Revlimid Therapy	Besa, *et al.*	*Blood.* 2005; 106(11)
Preliminary Results from Two-phase II Studies of Lenalidomide Monotherapy in Relapsed/refractory Non-Hodgkin's' Lymphoma	Wiernik, *et al.*	Abstract
Preliminary Results from a Phase II Study of Lenalidomide Monotherapy in Relapsed or Refractory Aggressive Non-Hodgkin's Lymphoma	Wiernik, *et al.*	Abstract
Phase II Study of CC-5013 in Patients (pts) with Metastatic Renal Cell Cancer (MRCC)	Rawat, *et al.*	Abstract
Phase II Study of CC-6013 in Patients with Renal Cell Cancer	Amato, *et al.*	Abstract
Tolerability of the Novel Oral Thalidomide Analog CC-6013 Demonstrating Extensive Immune Activation and Clinical Response	Sharma, *et al.*	Abstract
Doxil (D), Vincristine (V), Reduced Frequency Dexamethasone (d) and Revlimid (R) (DVd-R) Rests in a High Response Rate in Patients with Refractory Multiple Myeloma (RMM)	Baz, *et al.*	*Blood.* 2005; 106(11)

Study or Abstract Title	Study or Abstract Author(s)	Publication
Increased Risk of Thrombosis with Lenalidomide in Combination with Dexamethasone and Erythropoletin	Niesvizky, *et al.*	Abstract
Clarithromyein, Lenalidomide and Dexamethasone Combination Therapy as Primary Treatment of Multiple Myeloma	Niesvizky, *et al.*	Abstract
Lenalidomide in the Context of Complex Karyotype or Interrupted Treatment: Case Reviews of Del(5q)MDS Patients with Unexpected Responses	Giagounidis, *et al.*	*Annals of Hematology*. 2007; 86
BiRD (Biaxin [clarithromycin]/Revlimid [lenalidomide]/dexamethasone) Combination Therapy Results in High Complete- and Overall-response Rates in Treatment-naïve Symptomatic Multiple Myeloma	Niesvizky, *et al.*	*Blood*. 2008; 111(3)
A Prognostic Score for Patients with Lower Risk Myelodysplastic Syndrome	Garcia-Manero, *et al.*	*Leukemia*. 2007; 21
Treatment of Newly Diagnosed Multiple Myeloma Based on Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART): Consensus Statement	Dispenzieri, *et al.*	

Study or Abstract Title	Study or Abstract Author(s)	Publication
Randomized Trial of Lenalidomide plus High-dose Dexamethasone versus Lenalidomide plus Low-dose Dexamethasone in Newly Diagnosed Myeloma (E4A03), a Trial Coordinated by the Eastern Cooperative Oncology Group: Analysis of Response, Survival, and Outcome with Stem Cell Transplantation	Rajkumar, *et al.*	Abstract
A Randomized Southwest Oncology Group Study Comparing Dexamethasone (D) to Lenalidomide + Dexamethasone (LD) as Treatment of Newly-diagnosed Multiple Myeloma (NDMM): Impact of Cytogenetic Abnormalities on Efficacy of LD, and Updated Study Results	Zonder, *et al.*	Abstract
Final Analysis of MM-014: Single-agent Lenalidomide in Patients with Relapsed or Refractory Multiple Myeloma	Hussein, *et al.*	Abstract
Bortezomib, Pegylated-lyposomal-doxorubicin and Dexamethasone (PAD) as Induction Therapy Prior to Reduced Intensity Autologous Stem Cell Transplant (ASCT) Followed by Lenalidomide and Prednisone (LP) as Consolidation and Lenalidomide Alone as Maintenance	Palumbo, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Safety and Efficacy of Lenalidomide (Len), Bortezomib (Bz), and Dexamethasone (Dex) in Patients (pts) with Newly Diagnosed Multiple Myeloma (MM): A Phase I/II Study	Richardson, *et al.*	Abstract
Prolonged Overall Survival with Lenalidomide Plus Dexamethasone Compared with Dexamethasone Alone in Patients with Relapsed or Refractory Multiple Myeloma. Session Type: Oral Session	Weber, *et al.*	*Blood.* 2007; 110(11)
Clinical Management of Myelodysplastic Syndromes With Interstitial Deletion of Chromosome 5q	Nimer	*Journal of Clinical Oncology.* 2006; 24(18)
Long-term Follow-up on Overall Survival from the MM-009 and MM-010 Phase III Trials of Lenalidomide plus Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma	Dimopoulous, *et al.*	*Leukemia.* 2009; 23
Phase II Study of Lenalidomide in Transfusion - Dependent, Low-and Intermediate-1 Risk Myelodysplastic Syndrome with Karyotypes Other Than Deletion 5q	Raza, *et al.*	*Blood.* 2008; 1(111)
Lenalidomide in the Myelodysplastic Syndrome with Chromosome 5q Deletion	List, *et al.*	*New England Journal of Medicine.* 2006; 355

Study or Abstract Title	Study or Abstract Author(s)	Publication
Safety and Efficacy of Single-agent Lenalidomide in Patients with Relapsed and Refractory Multiple Myeloma [abstract]	Richardson, *et al.*	*Blood.* 2009; 114(4)
Safety and Efficacy of Single-agent Lenalidomide in Patients with Relapsed and Refractory Multiple Myeloma	Richardson, *et al.*	*Blood.* 2009; 114(4)
Most Common Medical Information Requests (Listed in order by disease state)		N/A
Materials that are Allowed to Be Given Out at Congresses and Conventions 12/4	N/A	
IS Educational Information Summary - June 2003		
Managing Patients With Low-Risk MDS	Sekeres, *et al.*	*Clinical Roundtable Monograph.* July 2006
Treatment Options for Low-Risk MDS	Sekeres	*Clinical Advances in Hematology & Oncology.* 2006; 4(7), Supp. 16
Treating Patients with Low-Risk MDS: Nurses' Perspective	Cosgrove, *et al.*	*Clinical Advances in Hematology & Oncology.* 2006; 4(7), Supp. 16
Combination Therapy with CC-5013 (lenalidomide; Revlimid) plus Dexamethasone (Rev/Dex) for Newly Diagnosed Myeloma (MM)	Rajkumar, *et al.*	

Study or Abstract Title	Study or Abstract Author(s)	Publication
Myelodysplastic Syndromes - Coping with Ineffective Hemtopoiesis	Cazzola, *et al.*	*New England Journal of Medicine.* 2005; 352 (6)
Impact of Risk Stratification on Outcome among Patients with Multiple Myeloma Receiving Initial Therapy with Lenalidomide and Dexamethasone	Kapoor, *et al.*	*Blood.* 2009; 114(3)
The Efficacy of Thalidomide and Irinotecan in Metastatic Colorectal Carcinoma (phase II study)	Govindarajan, *et al.*	Abstract
Clinical and Pharmacokinetic Study of Thalidomide in Patients with Advanced Refractory Metastatic Colorectal Cancer	Dal Lago, *et al.*	Abstract
Effect of Thalidomide on Gastrointestinal Toxic Effects of Irinotecan	Govindarajan, *et al.*	Abstract
Irinotecan/Thalidomide in Metastatic Colorectal Cancer	Govindarajan	*Oncology.* 2002; Supplement
Thalidomide Alone and in Combination for Previously Untreated Myeloma	Weber, *et al.*	Abstract
Hypothyroidism in Patients with Multiple Myeloma Following Treatment with Thalidomide	Badros, *et al.*	*American Journal of Medicine.* 2002; 112
Biaxin, Low-dose Thalidomide, and Dexamethasone [BLT-D] are Highly Active in Waldenstrom's Macroglobulinemia and Multiple Myeloma	Coleman, *et al.*	Abstract

Study or Abstract Title	Study or Abstract Author(s)	Publication
Salvage Therapy with Thalidomide for Patients with Relapsed/refractory Multiple Myeloma	Tosi, *et al.*	Abstract
Low Dose Thalidomide and Dexamethasone Are as Effective as Oral Melphalan and Prednisone in Refractory and Relapsed Myeloma Patients	Palumbo, *et al.*	Abstract
Thalidomide with Dexamethasone for Resistant Multiple Myeloma	Weber, *et al.*	Abstract

198. At Celgene's direction, Relator and other Celgene sales representatives frequently used these materials to market Thalomid and Revlimid for uses not approved by the FDA. For example, in 2008 and 2009, physicians complained that they were not able to collect stem cells after using Revlimid. Celgene's management suggested that Relator and other sales representatives use the article entitled "Stem Cell Mobilization with Cyclophosphamide Overcomes the Suppressive Effect of Lenalidomide Therapy on Stem Cell Collection in Multiple Myeloma" on every call in which the physician complained or pushed back due to issues related to collection of stem cells.

199. When doctors did not use Revlimid because of its toxicity, Relator and other sales representatives used the article titled "Relationship of Treatment-Related Cytopenias and Response to Lenalidomide in Patients With Lower-Risk Myelodysplastic Syndromes."

11. Celgene Manipulated Continuing Medical Education Programs To Off-Label Market Thalomid And Revlimid

200. To further its off-label marketing of Thalomid and Revlimid, Celgene utilized multiple continuing medical education ("CME") programs led by speakers paid by Celgene to tout the benefits of using Thalomid and Revlimid for non-indicated diseases. In order to encourage physicians to prescribe Thalomid for off-label uses,

Celgene required Relator and other sales representatives to bring CME programs to physicians' practices in their areas.

201. For example, in or about 2004, Celgene provided educational grants for various CME programs concerning Thalomid treatment in MM, MDS, and renal cell carcinoma, among other diseases (at the time, Thalomid was only approved to treat ENL). These CMEs consisted of speakers paid by Celgene to promote Thalomid's off-label uses. In or about 2003 or 2004, Dr. Howard A. Burris, III ("Burris") gave Celgene-sponsored speeches concerning "Recent Developments and Future Directions in the Treatment of Renal Cell Carcinoma." At the time, Burris was both a paid Celgene consultant and a member of Celgene's Speakers Bureau.

202. Celgene pressured Relator and other sales representatives to bring Burris and other CME presenters to medical practices to encourage off-label Thalomid use. In 2001, Deena Harding, Relator's manager, told her that these programs would result in additional sales. Relator, along with her managers Deena Harding and Jeff Rowell, also chose the speakers based on the number of Thalomid (or, later, Revlimid) prescriptions that they wrote or based upon a belief that the speaker would write more prescriptions once he/she was paid to present a CME. For example, Relator knows that Dr. Robert Vescic began writing substantially more prescriptions for Thalomid after Dawn Devore, another sales representative, hired him to present a CME. Ms. Devore told Relator that following the CME, "all he wrote" were Celgene prescriptions.

203. Relator kept "Oncology Profiling Notes" which tracked her experiences at various physicians' practices where she promoted Thalomid. In one set of Relator's notes from 2004 (*i.e.*, while Thalomid was still indicated solely for ENL), Relator described how she considered bringing Dr. Burris to one medical practice, Kaiser Woodland Hills, to present a renal cell cancer CME, but decided to conduct a CME concerning Thalomid for MM instead, since that practice treated a greater number of MM patients. Relator's note read: "Met with CME coordinator to bring Dr. Bargolie to Kaiser Woodland Hills for the morning tumor boards . . . I originally planned on Dr.

Burris for renal cell, but Woodland Hills has more MM." Following the CME, Relator observed an increase in Thalomid prescriptions written for MM at Kaiser Woodland Hills. She saw a similar increase following a CME at Kaiser Panorama City.

204. Celgene was well aware that CME programs were an effective way to promote its products for off-label uses. For example, Chad Saward wrote a May 26, 2006 email stating that "[o]bviously, if Revlimid gets approval [to treat MM], you will not be able to discuss the role of Revlimid in Newly Dx'd patients, so having a CME accredited resource that discuss all options for Newly Dx'd [diagnosed] patients will be very valuable." Four days later, on May 30, 2006, Lindsay Luke forwarded Saward's email to other managers, praising Saward's message as a "super initiative" and "a good way to be sure the field is aware of the wide array of educational offerings."

205. Celgene urged its sales representatives to promote CME's, rather than promotional programs. Celgene told sales representatives that a doctor could talk about an off-label use during a CME, but could not do so during a promotional program. Celgene paid presenting physicians to discuss CME's off-label uses. If the doctor did not, he would be confronted by someone from Celgene. For example, in late 2006 or early 2007, another sales representative in the West Region, Lisette Lopatic, used Dr. Mark Kirschbaum to present a CME at Hoag Hospital in Orange County. She confronted him after he failed to mention in a CME the use of Revlimid to treat non 5q deletion MDS patients (Revlimid is only approved by the FDA to treat low- or intermediate risk MDS that is associated with a deletion 5q abnormality). When this was discussed during a conference call of West Region sales representatives, Ms. Lopatic noted that she learned to do this after learning that Shawn Gormish – their manager – had done the same thing when he chased down a doctor following a CME at UCLA. Because Dr. Kirschbaum was in her territory, Relator also discussed this incident with him.

12. Relator And Other Sales Representatives Were Required To Conduct Training Sessions Concerning Thalomid's Off-Label Uses

206. Despite Relator's lack of formal medical training, she and other Celgene sales representatives were required to present information to fellow sales personnel concerning Thalomid's use in various off-label diseases. Celgene required that these presentations not only convey medical information, but that they include strategies for encouraging physicians to prescribe for the off-label uses.

207. In or about 2003, two of Relator's fellow sales representatives, Alana Torgelson and Suzanna Zalutko, conducted training on Thalomid's use in colorectal cancer. The colorectal cancer training materials provided "Selling points of Thalomid use" in colorectal cancer, as well as "Potential Probes" for physicians, including "What is your treatment regimen for [colorectal cancer] [patients]?" Another of Relator's colleagues, Hank Schwarz, conducted a "Kidney Cancer" training session in or about 2004, which included similar hypothetical "probe" questions. In or about 2003 or 2004, Relator conducted a training session concerning Thalomid's use in prostate cancer. Relator felt uncomfortable giving this presentation, as she had no formal medical training, let alone training concerning prostate cancer.

13. Celgene Provided Thalomid and Revlimid To Patients To Treat Off-Label Diseases

208. Under the guise of giving away free drugs, Celgene provided Thalomid and Revlimid to patients suffering from the cancers and other diseases that the drugs were not approved by the FDA to treat, in order to get Medicare and Medicaid patients on its desired therapy just prior to enrolling in a government health care plan.

209. Celgene provides free Revlimid and Thalomid prescriptions to patients suffering from the cancers and other diseases that the drugs were not approved by the FDA to treat and who are not insured under Medicare Part D but who are eligible for the program.

210. To secure this customer base, Celgene supplies these patients with free Revlimid and Thalomid prescriptions. *See* Celgene Patient Support, http://www.celgenepatientsupport.com/ (stating that a "Celgene Patient Support® Specialist" can "[h]elp you apply for the Celgene free medication program"). Once these patients became eligible for Medicare or Medicaid, they continued to use Thalomid or Revlimid that they previously obtained for free, with the result that those programs paid for the costs of using these drugs for unapproved uses. Celgene possesses records relating to these free prescriptions and accordingly is aware of the resulting false claims submitted to Medicare.

C. Sales Representatives Encouraged Physicians to Switch Patients From Thalomid To Revlimid Regardless Of Whether The Patients Were Stable

211. Since Revlimid is considerably more expensive than Thalomid ($10,000 per month for Revlimid, compared to up to $2,000 per month for Thalomid), Celgene pressured Relator and other sales personnel to move all patients on Thalomid to Revlimid, even though the products have different indications. (Celgene tried to make the cost increase less unpalatable by increasing the price of Thalomid.) This practice, which serves no medical purpose, places patients at risk of potentially fatal VTE and peripheral neuropathy, among other serious ailments. Furthermore, this practice causes federal, state, and city governments to expend significant, additional funds to cover the far higher cost of Revlimid. And as explained in more detail below, Celgene provided free Revlimid prescriptions to patients that it hopes will soon enroll in a government health program. Since Revlimid is far more expensive than Thalomid, these free prescriptions were intended to induce patients to switch from Thalomid to Revlimid – prescriptions that were ultimately paid for by Medicare and other government-funded insurance.

212. In a February 11, 2008 email from Shawn Tomasello, Celgene's Vice President of Sales, Tomasello refers to the need to "crack" physicians who have

prescribed Thalomid but not Revlimid. In the February 2008 email, Tomasello circulated a list of physicians who have prescribed Thalomid but not Revlimid and wrote "Let's get a plan together on what we need to convert these docs . . . I am sure there are nuances for some that we will not crack but other should be ready for 'cracking.'"

213. Similarly, Celgene held, and continues to hold, "Rev/Dex" contests, which award the sales representatives and sales teams that successfully move the most MM patients from Thalomid to Revlimid. A November 7, 2008 email from Tomasello to Celgene's sales force and sales and marketing departments stated, "Looks like Atlantic Central is leading the way in quarterly standings with an average of 6.10 patients converting from Thalomid MM to Revlimid MM . . . Keep up the great work with our customers!" Representatives who are successful in converting physicians from Thalomid to Revlimid earned points that could be exchanged for gifts, including airline tickets, vacations, clothing, appliances, and jewelry. In 2009, Relator used her Rev/Dex contest points to purchase airfare.

214. Celgene trained Relator and other sales representatives to move physicians from Thalomid to Revlimid. Relator participated in Phase III training at Celgene's corporate headquarters in New Jersey from June 26 through June 29, 2007. During this training, she and the other sales representatives were required to "[i]dentify 10 prescribers that have written Thalomid MM but not Revlimid MM," and then list "tactics you will employ with these prescribers" and "probing questions you might ask."

215. Celgene tracked these conversions and presented the results to its sale force. For example, at its April 13-14, 2010 West Region Cross Functional Meeting, the company presented data for each representative's conversion. Relator accomplished 73 conversions between April 2009 and March 2010 and her "% Rev Conversions" was "26.0%."

216. Doctors were often reluctant to switch MM patients from Thalomid to Revlimid as the drugs were in the same class. For example, Drs. Anthony Stein and David Snyder at City of Hope Hospital told Relator that "it's the same drug" while

another doctor told her "under the microscope, it's the same drug." Thus, in order for Celgene to accomplish its goal of switching patients from Thalomid to Revlimid, it was forced to misbrand Revlimid. For example, during the Phase III Training Celgene directed Relator to make unsubstantiated claims concerning the supposed superiority of Revlimid to Thalomid. While there are no head-to-head trials comparing Revlimid's versus Thalomid's efficacy in, for instance, MM patients, Celgene specifically instructed Relator to make claims to physicians that Revlimid is a more effective medication for the disease. Relator was also instructed to claim that Revlimid had fewer side effects than Thalomid and that it was more potent. These representations constituted unlawful misbranding since they were not supported by Revlimid's FDA-approved labeling.

217. In an effort to begin convincing physicians to switch their patients from Thalomid to Revlimid, Celgene marketed Revlimid to physicians in this fashion prior to receiving FDA approval for the drug.

D. Celgene Manipulated the FDA Mandated Patient Protection Programs to Market Its Products Off-Label

1. Celgene Created a Position, the Patient Support Coordinator, to Assist Patients in obtaining Government Funding for these Drugs

218. In 2006, Celgene created the Patient Support Coordinator program (the "PSC").[5] The PSC provides "reimbursement assistance" to patients prescribed Thalomid, Revlimid and other Celgene drugs. Sales representatives, such as Relator, informed physicians about the PSC anticipating that the physicians will then refer their patients to the program. The program includes individuals called Patient Support Specialists ("PSSs") who assist patients in enrolling in Medicare or Medicaid and help patients receive reimbursement from government-funded insurance. The primary PSS responsible for Relator's sales district was Samuel Vasquez ("Vasquez"). The PSC has

[5] Celgene later changed PSC's name to "Celgene Patient Support."

caused Medicare and Medicaid to pay for a greater number of off-label Thalomid and Revlimid prescriptions.

219. Celgene sales representatives touted the PSC to physicians in order to encourage them to prescribe Thalomid and Revlimid. Moreover, at the Celgene National Sales meeting in 2009 in Scottsdale, Arizona, sales representatives were told to encourage physicians to enroll as many patients as possible in the PSC. A prime example of Celgene's efforts with the PSC is contained in a November 17, 2009 email sent by Katherine Stultz ("Stultz") – Celgene Director of Patient Support and Reimbursement Services – to Celgene's national sales force in which Stultz directs Celgene's sales force to distribute PSC materials concerning Medicare enrollment to physicians. Specifically, Stultz writes the following:

> Next week each of you will receive an auto shipment of the "**Reminder Medicare Part D enrollment cards**" . . . Please utilize these cards to remind your office this is the only time of year to enroll patients in Medicare Part D . . . Most important – these cards are a trigger to come to our team for assistance if they or their patients have questions about coverage of a Celgene product in any Medicare Part D plan.

(emphasis in original).

220. Celgene's efforts have been very successful. A September 28, 2009 email from Vasquez states that "there is a rise in the number of cases I am currently handling . . . due to the Patient Support initiative to enroll patients into Medicare Part D." Vasquez's email includes a chart showing Thalomid and Revlimid patients for whom Vasquez is assisting with Medicare and Medicaid enrollment. Prior to the Patient Support initiative, roughly one-third of Revlimid and Thalomid takers were enrolled in the PSC.

221. The Patient Support Specialists were acutely aware which prescriptions were being paid by Medicare, Medicaid and other government payors since this was their job. Celgene passed on this information to its sales force in an effort to generate additional sales, including its off-label sales. As a result of Celgene's introduction of the

Patient Support Specialists, it possessed detailed information regarding prescriptions submitted to Medicare, Medicaid and other government payors. Thus, Celgene knew of, for example, the Revlimid prescriptions submitted to Medicare that were prescribed by Dr. Leland Green on January 10, 2007; Dr. David Leibowitz on December 26, 2006 and on January 18, 2007; Dr. Jeffery Wolf on January 15, 2007 and on January 31, 2007; Dr. Veena Charu on January 16, 2007 and on May 2, 2007; Dr. Samar Shihabi on February 1, 2007; Dr. Michael Kosmo on March 6, 2007; Dr. Howard Chen on March 7, 2007; Dr. John Kailath on March 8, 2007; Dr. Jason Salgnick on March 14, 2007; Dr. John Gunnel on March 12, 2007; Dr. David Bodkin on March 23, 2007; Dr. Patrick Sheeny on April 6, 2007 and on May 30, 3007; Dr. Jeffery Shinoda on April 11, 2007; Dr. Jonathan Blitzer on April 17, 2007; Dr. John Siebel on April 16, 2007; Dr. William Read on April 23, 2007; Dr. Salomon Hamburg on April 26, 2007; Dr. Michelle Rooney on April 26, 2007; Dr. Madhu Jodhani on May 1, 2007; Dr. Kathleen Turner-Hubbard on May 14, 2007 and on May 30, 2007 and on June 27, 2007; Dr. John Clune on May 16, 2007; Dr. Marilyn Norton on June 5, 2007; Dr. Lynn Bemiller on June 18, 2007; Dr. Anna Ganeles on June 28, 2007; Dr. Robert Klein on June 22, 2007; Dr. Jareed Manscor on July 2, 2007; and Dr. Harry Menco on July 12, 2007.

2. Celgene Manipulates RevAssist To Cause Medicare And Medicaid To Pay For Off-Label Revlimid Prescriptions

222. As previously alleged, due to the high risk of birth defects with Thalomid and Revlimid, the FDA requires Celgene to implement strict distribution systems for each drug. Revlimid prescribers must comply with the RevAssist system, which operates in the following manner.

223. First, the physician uses RevAssist software (loaded onto a computer via CD and accessible online) to create a Patient-Physician Agreement Form ("PPAF"). The PPAF has a patient information page, where the physician selects the patient's "Diagnosis" from a "drop-down" menu of ICD-9 codes, which are three-to-five digit

codes indicating the disease for which a patient is receiving Revlimid. This is a one-time process for each new Revlimid patient.

224. The physician then completes either an online or telephone survey confirming that the patient has been counseled about the risk of birth defects and the need to use protection if engaging in sex while taking Revlimid. After completing the survey, the physician receives an authorization number from Celgene that allows him or her to write the prescription. A physician must complete this survey every time he or she writes a prescription. Physicians may only write a prescription for a one-month or less supply of Revlimid, and may not include any refills. Thus, if a patient takes Revlimid long-term, the physician must write a new prescription every month.

225. Once the physician writes a prescription, RevAssist requires the physician to complete a dedicated RevAssist prescription form. This form can be generated through RevAssist software, faxed to the physician from Celgene, or downloaded from Celgene's website. The form has a blank field for the "Patient's Diagnosis Code (ICD-9 Code)."

226. The physician is then required to submit the prescription to a "specialty pharmacy" that is specifically licensed to supply Revlimid. When the specialty pharmacy receives the prescription form, the pharmacist must contact Celgene and confirm the physician's authorization code.

227. In or about 2006, shortly after Revlimid's launch, Relator's manager, Gormish, directed Relator and other sales representatives to "change the [ICD 9] codes" on Revlimid prescriptions that were written for off-label indications to reflect that the prescriptions were for on-label uses. At the 2009 national sales meeting in Scottsdale, Arizona, during a "district break-out session," the manager of the West Region's PSC, Tom Girrardi, directed the West Region sales representatives to change the codes on physicians' Revlimid prescriptions.

228. Relator refused to take part in the scheme. In October 2008, Relator wrote a letter to Celgene stating that she understood changing ICD-9 codes was unlawful.

Moreover, Relator participated as a third party in a deposition brought by a former Celgene sales representative who claimed unlawful discharge in the summer of 2009. During the deposition, Relator reiterated her position concerning changing ICD-9 codes.[6]

229. Since Relator stalwartly refused to participate in Celgene's unlawful code-changing practice, she never inquired as to how she could change physicians' prescription forms. Nevertheless, from 2006 through 2011, Relator has observed activities within Celgene that suggest the various ways Celgene personnel accomplish this task.

230. Without FDA approval, Celgene modified its RevAssist program under the guise of "assisting" physicians with RevAssist's cumbersome process. Under RevAssist, Celgene provides physicians with a specific RevAssist prescription form. But Celgene allows at least one specialty pharmacy, PharmaCare Specialty Pharmacy ("PharmaCare"), to create its own prescription form for physicians who write Revlimid prescriptions. This new prescription form requires the physician to check one of two boxes that include a corresponding on-label ICD-9 code for either MDS or MM. The physician can also check a box for "Other" which is adjacent to a blank line.

[6] In response to her opposition to Celgene's violations outlined in this Complaint, Relator, for the first time in her career at Celgene, received poor performance reviews. For instance, during the week of March 6, 2010, Gormish provided Relator with her 2009 performance evaluation, which stated that Relator "needs improvement." When Relator inquired about the basis for her poor performance review, Gormish provided very little explanation. Furthermore, Relator asked Gormish for her current "ranking" among Celgene's sales force. Gormish was initially unable to provide Relator her current ranking, instead telling her that her rank fell somewhere between 80 and 100 out of 102 total sales representatives. On March 10, 2010, Gormish forwarded to Relator an email from a member of Celgene's West Region that stated that Relator was then-currently ranked 98th ranked (out of 102) sales representatives within the Company. According to Relator, this sales rank is incorrect, as she out-performed many of her peers within the Company.

231. The PharmaCare prescription form is laid out in this manner to encourage physicians to check a box that corresponds to an on-label ICD-9 code, even if the prescription is off-label. Moreover, Relator believes that PharmaCare specialty pharmacists may "doctor" prescriptions where the "Other" box is checked, and fill in an on-label ICD-9 code. These prescription forms are then submitted to Medicare, Medicaid, other government payors, or private insurers including those in California. Relator and her fellow sales representatives have received intense pressure from Gormish to encourage physicians to send all prescriptions to PharmaCare, which distributes this alternate prescription form.

232. Similarly, Relator learned that shortly before a patient's prescription ends, PharmaCare may be sending physicians pre-prepared prescription forms that merely require the physician to sign for a patient's refill. These forms contain on-label ICD-9 codes, which most physicians will not bother to change.

233. Relator is also aware that Greater Sacramento Specialty Pharmacy engaged in similar practices, including code manipulation, as PharmaCare. Other RevAssist specialty pharmacies include Walgreens Specialty Pharmacy, Caremark Connect, Aetna Specialty Pharmacy, McKesson Specialty Pharmacy, BioScrip Pharmacy, US Bioservices, Medco Special Care Pharmacy, Medmark Pharmacy, Advanced Care Scripts, and Axium Healthcare Pharmacy, Inc.

234. Additionally, Relator is aware of at least one practice in the Los Angeles area that has had its Revlimid prescriptions for prostate cancer patients changed to on-label, MDS ICD-9 codes. Specifically, the Compassionate Oncology Medical Group in Los Angeles, run by Dr. Bob Liebowitz, predominately treats prostate cancer patients. Celgene's records indicate that Dr. Liebowitz is one of the highest-volume prescribers of Revlimid for MDS. Dr. Liebowitz's off-label Revlimid prescriptions have, in fact, been unlawfully altered.

E. Celgene Pays Kickbacks To Physicians To Prescribe Thalomid and Revlimid And To Encourage Other Physicians To Prescribe The Drugs

235. The federal Medicare Anti-Kickback Statute makes it unlawful to pay remuneration in any form to induce the generation of business reimbursable by Medicare, Medicaid, or any other government-funded insurance program. Celgene nonetheless made kickbacks a key part of its strategy to induce Thalomid and Revlimid prescriptions.

236. Celgene's marketing strategy also included the allocation of substantial resources to educate physicians and other health care professionals about off-label uses of Thalomid and Revlimid. The 2004 Business Plan – West Region authored by Larry Bishop and described in detail above, recognized that "[w]e can't sell clinicians on Thalomid, because most don't have an indication. What we really do is make sure that those who have the targeted patient population appreciate the product mechanism of action, know its possible clinical effect, and know how to prescribe it." It therefore instructed the sales force to "utilize speaker programs, grant request funds and entertainment budgets strategically for the education required to assure that patients and physicians understand the value of Thalomid therapy" and prescribe Thalomid. Celgene did this.

237. Celgene repeatedly hired doctors to promote off-label uses of Thalomid and Revlimid at conferences attended by practicing physicians. For example, as set forth in Monica Blackstone's letter to Dr. Fine, Celgene paid Dr. Fine to speak at the 2004 American Society of Clinical Oncology (ASCO) meeting about "THALOMID/REVLIMID's clinical developments and new approaches as a potential therapy in gliobastomas" (brain cancers). Ms. Blackstone's letter, written on or about May 26, 2004, also requested Dr. Fine's tax identification number so that Celgene could pay him to promote this off-label use to other doctors attending the ASCO meeting. Then, as now, neither of Celgene's products were approved by the FDA to treat

gliobastomas. In 2004 and 2005, Celgene also hired Dr. Gordon to speak at ASCO on using Thalomid to treat renal cell cancer; Dr. Whu to speak at ASCO on Thalomid to treat metastic malignant melanoma; Dr. Attal to speak at the American Society of Hematology (ASH) national meeting regarding Thalomid maintenance; and Dr. Palumbo to speak about using Thalomid and Revlimid to treat newly diagnosed multiple myeloma.

238. Immediately after Revlimid's launch, Relator and other sales representatives began receiving intense pressure to find physicians Celgene could pay to promote Revlimid. Celgene sales representatives were required to take these physicians to other medical practices where the physicians could promote Revlimid use. Celgene's payments to physicians for the talks constitute illegal kickbacks meant to directly and/or indirectly encourage the writing of Revlimid prescriptions.

239. Celgene designates certain physicians as "Thought Leaders." A Thought Leader is an experienced, respected physician who writes a high volume of Revlimid prescriptions. After Celgene designates a physician as a Thought Leader, the Thought Leader is connected with a company called Envision, which trains the Thought Leaders to give presentations, and facilitates Thought Leader programs. Celgene refers to the programs as "Envision Programs." Envision Programs can take nearly any form. More specifically, an Envision Program can be a one-on-one, in-office conversation between a Thought Leader and another physician or a breakfast, lunch or dinner presentation either within or outside of a physician's practice. Physicians are paid from $1,600 to $4,000 for each Envision Program he or she conducts. Certain physicians were paid even more. For example, Relator is aware of a Dr. Berenson in California who receives upwards of $10,000 to conduct Envision Programs. As part of Celgene's Envision speaker training, Celgene and Envision developed written material, including PowerPoint presentations and slides, for use by physicians at speaker's programs. Celgene encouraged its sales force to provide the materials to speakers who lectured on the off-label uses of Thalomid

and Revlimid. Celgene devoted substantial resources to these Envision Programs. For example, its budget for just Envision programs in 2004 was $910,500.

240. From 2006 through 2009, Relator was required to facilitate 15 or 16 Envision Programs per year. Within Relator's sales district, total Envision Program goals are generally to exceed 150 programs per year. Tellingly, Celgene strongly encouraged Relator and other sales representatives to hold Envision Programs at physicians practices where Celgene can get the most bang for its buck. Multiple emails from Relator's manager ordered Relator and her fellow sales representatives to "target" physicians who are high Dacogen (a competitor MDS drug) and Velcade (a competitor MM drug) prescribers in an effort to convert those physicians to Revlimid.[7]

241. For instance, an August 31, 2009 email from Relator's then-district sales manager, Shawn Gormish, to Relator and other sales representatives stated that sales representatives should focus on "opportunities in high Velcade or Dacogen accounts" and to "capitalize on ROI" (i.e., return on investment). For 2009, Celgene's budget for Envision Programs was $5 million. In 2008, Relator alone facilitated more than $45,000 in Envision Programs.

242. Celgene routinely set timetables for representatives to exhaust their speaker budgets, so as to ensure that representatives were devoting enough time and money to this key component of Celgene off-label message and kickback plans. Relator and other sales representatives were praised for holding high numbers of Envision Programs and were penalized for failing to meet certain quotas. In Relator's 2006 Performance Evaluation, Gormish praised Relator for developing Thought Leaders and utilizing Envision Programs, writing "You developed the following advocates: Dr. George

[7] Dacogen is FDA-approved for treatment all types of MDS, while Velcade is indicated for *all* types of MM. As stated throughout the Complaint, Revlimid is indicated *solely* for low to intermediate risk MDS with deletion 5q cytogenic abnormality, and previously treated MM. By encouraging sales representatives to target Dacogen and Velcade prescribers and market Revlimid as a competitor drug, Celgene further caused its sales representatives to off-label market Revlimid.

Somlo and Dr. Amrita Krishnan, both attended MM speaker training and Dr. Somlo also attended the MDS advisory board . . . Bev, I am especially proud of this effort . . . [T]he envision programs worked for you." Relator was similarly praised in her 2008 Performance Evaluation: "[O]f particular note of Business management is your ability to use your envision promotional programs which you have completed 16 envision programs . . . In 2009, continue to analyze your business needs and place your envision programs."

243. An August 25, 2008 email from Gormish praised Relator and two other sales representatives who had "planned or executed the most" Envision Programs. The email continues by encouraging other sales representatives to do more programs: "Per the guidance on our last Conference call, I would like everyone to end up with at least 16, those who have 12 or more, please keep planning and executing where your territory needs . . . The district average per territory, should at least [sic] 16 programs per HOC. That would place the great Hollywood district at 160 for the year."

244. Celgene also violated the anti-kickback statute by unlawfully promoting Revlimid through its "Speaker Corps" speaker's series. Celgene engaged numerous speakers who frequently spoke on predetermined topics areas such as "Recent Developments and Future Directions in the Treatment of Multiple Myeloma," or "The Role of Revlimid (lenalidomide) in Multiple Myeloma." The doctors engaged as speakers for Celgene spoke frequently, often multiple times a day, and received generous compensation from Celgene for their often limited speaking engagements. Celgene's most active Revlimid speakers, many considered "core faculty" for the Speaker Corps series include: Steven T. Rosen, MD, Kenneth Anderson, MD, Bart Barlogie, MD, PhD, James R. Berenson, MD, Gregory Berk, MD, Ivan Borrello, MD Asher Chanan-Khan, MD, Raman K. Desikan, MD, Philip Greipp, MD, Mohamad A. Hussein, MD, Sundar Jagannath, MD, Robert A. Kyle, MD, Alan List, MD, Sangar Lonial, MD, Jayesh Mehta, MD, Nikhil Munshi, MD, Prabhjit Purewal, MD, Azra Raza, MD, Paul Richardson, MD, Eric K. Rowinsky, MD, David S. Siegel, MD, PhD, Seema

Singhal, MD, Gordon Srkalovic, MD, PhD, Stefano Tarantolo, MD, Steven Treon, MD, MA, PhD, Robert A. Vescio, MD, and Thomas Witzig, MD.

245. Several of these speakers were engaged multiple times by Relator or other speakers in Relator's district. For example, Dr. James R. Berenson was engaged to speak 22 times between May 2009 and April 2010. Quite often, Dr. Berenson spoke multiple times in one day giving the same speech for the same Celgene sales representative. Another speaker, Dr. Azra Raza was listed as – and paid for – giving four speeches for the same representative on the same day.

246. Celgene analyzed its "investment" in speakers both formally and informally. Sales representatives also paid close attention the prescribing of doctors who spoke and doctors who attended the speaker programs. For example, as described above, Dr. Robert Vescic began writing substantially more prescriptions for Thalomid after Celgene began paying him to speak.

247. Celgene also analyzed sales data relating to its speakers at a corporate level. For example, a 2009 PowerPoint on its "Speakers Bureau" includes slides describing it "Return on Investment Analysis" and its efforts to "quantify any additional revenue of speaker bureau programs." Celgene's also evaluated its sales force, in part, based upon the increase in prescriptions written by paid speakers. In Dawn DeVore's 2009 evaluation, she is praised for development of "Dr. Berenson as a speaker and advocate for Celgene. You may not notice the rise in his TRXs [total prescriptions] in MM for his trial. However, the TRXs in the district took a dramatic upswing for new patient starts in November and December. This aided greatly in the district making its goal."

248. All of Celgene's payments to physicians to speak were intended, at least in part, to induce them to write additional prescriptions for Celgene's products. Robert Pearl, the executive director and CEO of the Permanente Medical Group, Kaiser Permanente, recently wrote in the *Wall Street Journal* that financial relationships between pharmaceutical and medical device companies and physicians "are formed under the guise of advancing education and innovation. But they are really part of a

thinly veiled promotional strategy designed to increase sales, particularly for expensive products with high profit margins." Celgene's payments described above likewise were part of its marketing plans to increase the number of prescriptions written for its products by paying doctors to prescribe Thalomid and Revlimid.

249. In addition to paying doctors under the guise of speaker programs, Celgene made payments to doctors who could have an even broader impact on the market for honest medical information. Celgene worked to get the drug compendia to treat favorably Thalomid and Revlimid and so has made payments to the doctors advising the compendia. For example, of the 30 doctors used by the National Comprehensive Cancer Network (NCCN) compendia to prepare its section on Multiple Myeloma, 16 had received money from Celgene. Three of these 16 – Dr. Kenneth Anderson, Dr. Seema Singhal and Dr. Steven Treon – were also considered "core faculty" for the Speaker Corps series as described above.

F. Celgene Directly Targets Federal And State Healthcare Dollars

250. Throughout Relator's tenure at Celgene, she and other sales representatives have been immersed in educational materials concerning government insurance programs. In or about 2006, Celgene sent Relator a booklet entitled "Reimbursement in the Oncology Market." The booklet contains a section entitled "Key Payers for Chemotherapeutic Drugs," that states "[b]ecause the average age of a multiple myeloma patient is 65 or greater, Medicare is the primary payer for most patients and is therefore essential to Celgene's business." The booklet continues with a discussion of, *inter alia*, Medicare and Medicaid.

251. Moreover, due to the high cost of Thalomid and Revlimid, Celgene knew it could raise the volume of Thalomid and Revlimid prescriptions by assuring doctors that government programs could mitigate the costs of the drugs. For example, in or about 2006, Celgene provided Relator with a DVD entitled "Medicare Part D and Beyond: Facilitating Patient Access to Novel Therapeutics in Oncology." Celgene directed Relator and other sales personnel to provide this DVD to physicians to help them better

understand how Medicare could pay for Thalomid and Revlimid. Similarly, in 2008, Relator was praised by Gormish for her "thorough understanding of Reimbursement for Medicare [P]art D," which she was able to effectively communicate to physicians.

252. As suggested above, a large percentage of Revlimid and Thalomid prescriptions are paid for by Medicare. As Celgene's President and Chief Operating Officer, Robert J. Hugin, stated on January 29, 2009 Earnings Conference Call, a majority of [Revlimid] patients are most likely Medicare." Similarly, an April 1, 2009, Credit Suisse analyst report states that "Medicare . . . patients account for the lion's share of [Celgene's] revenue."

1. Celgene Targeted Veterans Administrations And TRICARE

253. In addition to directly targeting Medicare and Medicaid dollars, Celgene targeted Veterans Administration patients. A 2007 Company newsletter titled, "What's Up In Summit?" (a reference to Celgene's headquarters in Summit, New Jersey) provides "Tips for Working a VA" for sales representatives who are "having trouble meeting with [their] VA Hematologists/Oncologists."

254. Indeed, Relator promoted Thalomid and Revlimid for off-label uses at the North Hills VA in North Los Angeles County, CA.

255. In or about 2004, Relator learned that the North Hills VA treated many MM patients, but with VAD, a combination of generic chemotherapy drugs.[8] Around that time, Celgene informed Relator that TRICARE offered a minimal $5 co-pay on the otherwise expensive Thalomid (some TRICARE beneficiaries can be treated at VA facilities). Relator, however, experienced great difficulties gaining access to physicians at this VA, notwithstanding that she had informed physicians of patients' mere $5 co-pay for their Thalomid prescriptions. Accordingly, at a 2004 Diamond Club Meeting, Relator approached then-COO, Barer, concerning her difficulties persuading VA physicians to prescribe Thalomid for MM. Barer agreed with Relator that it was an

[8] In 2004, Thalomid was not indicated for MM.

interesting problem, and then allowed other sales representatives to interject and offer their strategies for penetrating VAs. Barer told Relator that he would have to contemplate the issue and see if he could come up with any solutions.

256. Celgene's marketing to TRICARE and VA physicians was successful. As a result of Celgene's RevAssist and S.T.E.P.S. programs and its Patient Support Specialists, Celgene possesses detailed records of the false claims paid by the VA and TRICARE including but certainly not limited to TRICARE prescriptions of Revlimid written by Dr. John Wilkinson on April 3, 2007; Dr. David Bodkin on April 1, 2007; Dr. David Campbell on May 7, 2007; Dr. Ram Lanchandani on May 11, 2007; Dr. Jareed Manscor on May 15, 2007; Dr. John Kailath on May 29, 2007; Dr. Nanda Miswas on June 25, 2007; Dr. Carolyn Wild on July 10, 2007 and on August 14, 2007; Dr. Peter Wittlinger on August 13, 2007; Dr. Dennis Hillard on August 27, 2007; Dr. Veena Charu on September 4, 2007; Dr. Kai Zu on November 1, 2007; and Dr. Phillip Dreisbach on November 14, 2007.

2. Celgene Targeted Private Payors, Including Insurers In California

257. In addition to directly targeting Medicare and Medicaid dollars and VA and TRICARE funds, Celgene also targeted private insurers, including those in California. Because private insurers were viewed as critical to the success of Revlimid and Thalomid, Celgene targeted private insurers including, but not limited to, Kaiser Permanente, United Healthcare, Healthnet, HMSA, Excellus, Highmark, Horizon, Coventry, WellCare, Aetna, Cigna, and MemberHealth.

258. For example, as early as 1999, Celgene began targeting private insurers in California. Alana Mintzer's business plan for the second quarter of 1999, for example, stated that she would "focus and identify all the key players within Kaiser and the major Managed Care Groups to seek approval and reimbursement." Kaiser refers to Kaiser Permanente, one of the nation's largest not-for-profit health plans, that provides health

insurance to more than 9.1 million people, almost 7 million of whom are located in California. Kaiser is headquartered in Oakland, Calif.

259. In 2004, as Celgene began to prepare to "launch" Revlimid, it targeted Kaiser by assigning Alana S. Torgelson, by than a Corporate Account Manager, to as she wrote in a July 12, 2004 email, "work[ ] the account at a national level." At the same time, the company's Government Affairs, Corporate Account Management, Sales Operations and Customer Care Center departments were preparing a Thalomid "Multiple Myeloma Launch Plan." As part of that plan, Celgene decided to "[i]nclude Kaiser KOLs [key opinion leaders] on Celgene Roadmaps and speaker programs" and "[i]nclude Kaiser KOLs in Ad Boards in all disease states." In other words, in order to get Kaiser physicians to prescribe Thalomid, it was going to pay key doctors at Kaiser. This launch plan also described the Company's efforts to influence doctors at PacifiCare Health Systems, Cigna and Aetna.

260. Celgene's targeting of Kaiser was successful. In the first two months of 2006, Celgene held 18 "in-services" at Kaiser, and Celgene became a "Vendor" for Kaiser Permanente. As explained in Celgene's Government Affairs operations report for the week of February 13, 2006, this was important as it allowed Kaiser's orders to be placed directly with Celgene and ensured that "Revlimid will be covered in all plans with a branded co-pay …."

261. As set forth in Celgene's Managed Care team 2008 business plan, the company attempted to have these insurers pay for its products by blanketing them with speaker programs, continuing education programs, and clinical presentations designed to educate these insurers about, among other things, Revlimid indications.

262. Through Celgene's targeting efforts, Kaiser Permanente went on to become a key account bringing in $33 million in revenue a year to Celgene by 2009. As explained by Sam Wissa, a national account manager, in a April 19, 2010 email, this $33 million in yearly sales "blows away the Rev volume of all of England" and is starting to "look a lot like the volume of the entire VA in the US."

COUNT ONE
Federal False Claims Act, 31 U.S.C. § 3729(a)(1)(A)[9]

263. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

264. This is a claim for treble damages and civil penalties under the False Claims Act, 31 U.S.C. § 3729(a)(1).

265. By virtue of the conduct described above, Defendant knowingly caused to be presented to Medicaid, Medicare, and other Government funded health insurance programs false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

266. The United States, unaware of the falsity or fraudulent nature of the claims that Defendant caused, paid for claims that otherwise would not have been allowed.

267. By reason of these payments, the United States has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWO
Federal False Claims Act, 31 U.S.C. § 3729(a)(1)(B)[10]

268. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

269. This is a claim for treble damages and civil penalties under the False Claims Act, 31 U.S.C. § 3729(a)(1)(B).

270. By virtue of the conduct described above, Defendant knowingly caused to be made or used false records or statements that caused false claims to be paid or approved by the United States Government.

---

[9] To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *.e.g.*, 31 U.S.C. § 3729(a)(1).

[10] To the extent wrongdoing occurred prior to May 20, 2009, this Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *.e.g.*, 31 U.S.C. § 3729(a)(2).

271. The United States, unaware of the falsity or fraudulent nature of the claims that Defendant caused, paid for claims that otherwise would not have been allowed.

272. By reason of these payments, the United States has been damaged, and continues to be damaged, in a substantial amount.

COUNT THREE
California False Claims Act., Cal. Gov't Code § 12651 *et seq*.

273. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

274. This is a claim for treble damages and civil penalties under the California False Claims Act. Cal. Gov't Code § 12651 *et seq*.

275. By virtue of conduct described above, Defendant knowingly caused to be presented to the California Medicaid Program (i.e., Medi-Cal) false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

276. The California Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

277. By reason of these payments, the California Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT FOUR
California Insurance Frauds Prevention Act, Cal. Ins. Code § 1871.7

278. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

279. This is a claim for treble damages and civil penalties under the California Insurance Frauds Prevention Act, Cal. Ins. Code § 1871.7.

280. By virtue of the conduct described above, Defendant caused to be presented, or knowingly assisted or conspired in presenting or causing to be presented, to the insurers in the State of California fraudulent claims that were induced by

payments of kickbacks to physicians, in violation of Penal Code § 550(b)(1), among other provisions.

281. Moreover, by virtue of the conduct described above, Defendant knowingly caused to be made fraudulent bills intended to be presented to the insurers in connection with, or in support of, claims for the payment of compensation under contracts of insurance knowing that the statements contained false or misleading information concerning material facts, in violation of Penal Code § 550(b)(2), among other provisions.

282. By virtue of the kickbacks, misrepresentations, and submissions of non-reimbursable claims described above, Defendant knowingly presented or caused to be presented false or fraudulent claims for the payment of a loss or injury, including payment of a loss or injury under a contract of insurance; prepared, made, and subscribed writings, with the intent to present or use them, or to allow them to be presented, in support of false or fraudulent claims; and made or caused to be made false or fraudulent claims for payment of a health care benefit in violation of Penal Code § 550 (a)(1), (5), and (6), among other provisions.

283. By virtue of the conduct described above, Defendant caused false claims to be submitted to insurance companies for the payment of health care benefits. Had the private insurance companies known that prescriptions for Defendant's drugs were written because physicians had been paid kickbacks by Defendant to do so, and/or that Defendant had made statements containing false or misleading information concerning material facts these companies would not have provided reimbursement for these prescriptions.

284. By virtue of the conduct described above, Defendant's conduct represents the inducement of health care benefits through a pattern and practice of fraudulent conduct and constitutes false claims within the meaning of Cal. Ins. Code § 1871.7(b) and Sections 549 & 550(a)(6) of the California Penal Code, among other provisions.

285. By reason of these payments, insurers have been damaged, and continue to be damaged, in a substantial amount.

COUNT FIVE
Colorado Medicaid False Claims Act, Colo. Rev. Stat. § 25.5-4-303.5, *et seq*.

286. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

287. This is a claim for treble damages and civil penalties under the Colorado Medicaid False Claims Act, Colo. Rev. Stat. § 25.5-4-303.5, *et seq.*

288. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Colorado Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

289. Moreover by virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendant conspired to commit violations of the Colorado False Claims Act.

290. The Colorado Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

291. By reason of these payments, the Colorado Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT SIX
Connecticut False Claims Act, Conn. Gen. Stat. § 17b-301b *et seq.*

292. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

293. This is a claim for treble damages and civil penalties under the Connecticut False Claims Act, Conn. Gen. Stat. § 17b-301b, *et seq*.

294. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Delaware Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid.

295. The Connecticut Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

296. By reason of these payments, the Connecticut Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT SEVEN
Delaware False Claims Act, Del. Code Ann. Tit. 6, § 1201 *et seq*.

297. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

298. This is a claim for treble damages and civil penalties under the Delaware False Claims Act. Del Code Ann. tit. 6, § 1201 *et seq.*

299. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Delaware Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid.

300. The Delaware Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

301. By reason of these payments, the Delaware Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT EIGHT
Florida False Claims Act, Fla. Stat. Ann. § 68.081 *et seq*.

302. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

303. This is a claim for treble damages and civil penalties under the Florida False - Claims Act. Fla. Stat. Ann. § 68.081 *et seq*.

304. By virtue of, the conduct described above, Defendant knowingly caused to be presented to the Florida Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

305. The Florida Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

306. By reason of these payments, the Florida Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT NINE
Georgia False Medicaid Claims Act, O.C.G.A. § 49-4-168 *et seq*.

307. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

308. This is a claim for treble damages and civil penalties under the Georgia False Medicaid Claims Act, O.C.G.A. § 49-4-168 *et seq*.

309. By virtue of, the conduct described above, Defendant knowingly caused to be presented to the Georgia Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

310. The Georgia Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

311. By reason of these payments, the Georgia Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TEN
Hawaii False Claims Act, Haw. Rev. Stat. § 661-22 *et seq*.

312. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

313. This is a claim for treble damages and civil penalties under the Hawaii False Claims Act. Haw. Rev. Stat. § 661-22 *et seq.*

314. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Hawaii Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

315. The Hawaii Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

316. By reason of these payments, the Hawaii Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT ELEVEN
Illinois Whistleblower Reward and Protection Act,
740 III. Comp. Stat. 175/1 *et seq*.

317. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

318. This is a claim for treble damages and civil penalties under the Illinois Whistleblower Reward and Protection Act. 740 111. Comp. Stat. 175/1 *et seq.*

319. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Illinois Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

320. The Illinois Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

321. By reason of these payments, the Illinois Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWELVE
Indiana False Claims and Whistleblower Protection Act,
Indiana Code § 5-11-5.5

322. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

323. This is a claim for treble damages and civil penalties under the Indiana False Claims and Whistleblower Protection Act, Indiana Code § 5-11-5.5.

324. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Indiana Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

325. The Indiana Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

326. By reason of these payments, the Indiana Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT THIRTEEN
Maryland False Health Claims Act of 2010, Md. Code Ann. § 2-601 *et seq*.

327. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

328. This is a claim for treble damages and civil penalties under the Maryland False Health Claims Act, Md. Code Ann. § 2-601 *et seq.*

329. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Maryland Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

330. Moreover by virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendant conspired to commit violations of the Maryland False Health Claims Act.

331. The Maryland Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

332. By reason of these payments, the Maryland Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT FOURTEEN
Louisiana Medical Assistance Programs Integrity Law,
La. Rev. Stat. Ann. § 46:439.1 *et seq*.

333. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

334. This is a claim for treble damages and civil penalties under the Louisiana Medical Assistance Programs Integrity Law. La. Rev. Stat. Ann. § 46:439.1 *et seq.*

335. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Louisiana Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off label uses of Thalomid and Revlimid.

336. The Louisiana Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

337. By reason of these payments, the Louisiana Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT FIFTEEN
Massachusetts False Claims Act, Mass. Ann. Laws Ch. 12, § 5(A)-(0)

338. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

339. This is a claim for treble damages and civil penalties under the Massachusetts False Claims Act. Mass. Ann. Laws ch. 12, § 5(A)-(0).

340. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Massachusetts Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

341. The Massachusetts Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

342. By reason of these payments, the Massachusetts Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT SIXTEEN
Michigan Medicaid False Claims Act, MCLS § 400.601 *et seq*.

343. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

344. This is a claim for treble damages and civil penalties under the Michigan Medicaid False Claims Act, MCLS § 400.601 *et seq*.

345. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Michigan Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

346. The Michigan Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

347. By reason of these payments, the Michigan Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT SEVENTEEN
Minnesota False Claims Act Minn. State Minn. Stat. § 15C.01 *et seq*.

348. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

349. This is a claim for treble damages and civil penalties under the Minnesota False Claims Act Minn. Stat. § 15C.01 *et seq.*

350. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Minnesota Medicaid Program false or fraudulent claims

for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

351. Moreover by virtue of the conduct described above, Defendant conspired to commit violations of the Minnesota False Claims Act.

352. The Minnesota Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by the Defendant, paid for claims that otherwise would not have been allowed.

353. By reason of these payments, the Minnesota Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT EIGHTEEN
Montana False Claims Act, Mont. Code Anno § 17-8-401 *et seq.*

354. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

355. This is a claim for treble damages and civil penalties under the Montana False Claims Act. Mont. Code Anno. § 17-8-401 *et seq*.

356. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Montana Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

357. The Montana Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

358. By reason of these payments, the Montana Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT NINETEEN
Nevada False Claims Act, Nev. Rev. Stat. § 357.010 *et seq.*

359. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

360. This is a claim for treble damages and civil penalties under the Nevada False Claims Act. Nev. Rev. Stat. § 357.010 *et seq.*

361. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Nevada Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

362. The Nevada Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

363. By reason of these payments, the Nevada Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY
New Hampshire Medicaid Fraud and False Claims,
N.H. Rev. Stat. Ann. § 167:61 *et seq.*

364. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

365. This is a claim for treble damages and civil penalties under the New Hampshire Medicaid Fraud and False Claims Law, N.H. Rev. Stat. Ann. § 167:61, *et seq.*

366. By virtue of the conduct described above, Defendant knowingly caused to be presented to the New Hampshire Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

367. The New Hampshire Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

368. By reason of these payments, the New Hampshire Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-ONE
New Jersey False Claims Act, N.J. Stat. § 2A:32C-1 *et seq.*

369. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

370. This is a claim for treble damages and civil penalties under the New Jersey False Claims Act. N.J. Stat. § 2A:32C-1 *et seq*.

371. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the New Jersey Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

372. The New Jersey Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

373. By reason of these payments, the New Jersey Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-TWO
New Mexico Medicaid False Claims Act, N.M. Stat. Ann. § 27-14-1 *et seq.*

374. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

375. This is a claim for treble damages and civil penalties under the New Mexico Medicaid False Claims Act. N.M. Stat. Ann. § 27-14-1 *et seq.*

376. By virtue of the conduct described above, Defendant knowingly caused to be presented to the New Mexico Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

377. The New Mexico Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

378. By reason of these payments, the New Mexico Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-THREE
New York False Claims Act, N.Y. CLS St. Fin. § 186 *et seq.*

379. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

380. This is a claim for treble damages and civil penalties under the New York False Claims Act, N.Y. CLS St. Fin. § 186 *et seq.*

381. By virtue of the conduct described above, Defendant knowingly caused to be presented to the New York Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

382. The New York Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

383. By reason of these payments, the New York Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-FOUR
North Carolina False Claims Act, N.C. Gen. Stat. § 1-605 *et seq*.

384. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

385. This is a claim for treble damages and civil penalties under the North Carolina False Claims Act, N.C. Gen. Stat. § 1-605 *et seq*.

386. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the North Carolina Medicaid program for false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

387. The North Carolina Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

388. By reason of these payments, the North Carolina Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-FIVE
Oklahoma Medicaid False Claims Act, 63 Okl. St. §5053 *et seq*.

389. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

390. This is a claim for treble damages and civil penalties under the Oklahoma Medicaid False Claims Act. 63 Okl. St. § 5053 *et seq.*

391. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Oklahoma Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

392. The Oklahoma Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

393. By reason of these payments, the Oklahoma Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-SIX
Rhode Island False Claims Act, R.I. Gen. Laws §9-1.1-1 *et seq*.

394. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

395. This is a claim for treble damages and civil penalties under the Rhode Island False Claims Act. R.I. Gen. Laws § 9-1.1-1 *et seq*.

396. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Rhode Island Medicaid Program false or fraudulent

claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

397. The Rhode Island Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

398. By reason of these payments, the Rhode Island Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-SEVEN
Tennessee Medicaid False Claims Act, Tenn. Code Ann. § 71-5-181 *et seq*.
and Tennessee False Claims Act, Tenn. Code Ann. § 4-18-101 *et seq*.

399. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

400. This is a claim for treble damages and civil penalties under the Tennessee Medicaid False Claims Act, and the Tennessee False Claims Act. Tenn. Code Ann. § 71-5-181 *et seq*.; Tenn. Code Ann. § 4-18-101 *et seq*.

401. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Tennessee Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

402. The Tennessee Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

403. By reason of these payments, the Tennessee Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-EIGHT
Texas Medicaid Fraud Prevention Act,
Tex. Hum. Res. Code Ann. § 36.001 *et seq*.

404. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

405. This is a claim for treble damages and civil penalties under the Texas Medicaid Fraud Prevention Act. Tex. Hum. Res. Code Ann. § 36.001 *et seq*.

406. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Texas Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

407. The Texas Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

408. By reason of these payments, the Texas Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT TWENTY-NINE
Virginia Fraud Against Taxpayers Act, Va. Code Ann. §8.01-216 *et seq*.

409. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

410. This is a claim for treble damages and civil penalties under the Virginia Fraud Against Taxpayers Act. Va. Code Ann. §8.01-21.6 *et seq.*

411. By virtue of the conduct described above, Defendant knowingly caused to be presented to the Virginia Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

412. The Virginia Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

413. By reason of these payments, the Virginia Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT THIRTY
Washington Medicaid Fraud False Claims Act,
Rev. Code Wash. § 48.80.010 *et seq*.

414. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

415. This is a claim for treble damages and civil penalties under the Washington Medicaid Fraud False Claims Act, Rev. Code Wash. § 48.80.010 *et seq*.

416. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Washington Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

417. Moreover by virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendant conspired to commit violations of the Washington Medicaid Fraud False Claims Act.

418. The Washington Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

419. By reason of these payments, the Washington Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT THIRTY-ONE
Wisconsin False Claims Act, Wis. Stat. § 20.931 *et seq*.

420. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

421. This is a claim for treble damages and civil penalties under the Wisconsin False Claims Act. Wis. Stat. § 20.931 *et seq*.

422. By virtue of the conduct described above, Defendant knowingly presented or caused to be presented to the Wisconsin Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, using, or causing to be made or used a false record or statement.

423. The Wisconsin Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

424. By reason of these payments, the Wisconsin Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT THIRTY-TWO
District of Columbia False Claims Act, D.C. Code § 2-308.03 *et seq.*

425. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

426. This is a claim for treble damages and civil penalties under the District of Columbia False Claims Act. D.C. Code § 2-308.03 *et seq*.

427. By virtue of the conduct described above, Defendant knowingly caused to be presented to the District of Columbia Medicaid Program false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

428. The District of Columbia Medicaid Program, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

429. By reason of these payments, the District of Columbia Medicaid Program has been damaged, and continues to be damaged, in a substantial amount.

COUNT THIRTY-THREE
City of Chicago False Claims Act, Chicago Mun. Code Chapter 1-22 *et seq*.

430. Relator re-alleges and incorporates by reference the allegations contained in the preceding paragraphs of this Complaint.

431. This is a claim for treble damages and civil penalties under the City of Chicago False Claims Act, Chicago Municipal Code Chapter 1-22, *et seq.*

432. By virtue of the conduct described above, Defendant knowingly caused to be presented to the City of Chicago false or fraudulent claims for the improper payment or approval of prescriptions for off-label uses of Thalomid and Revlimid.

433. The City of Chicago, unaware of the falsity or fraudulent nature of the claims caused by Defendant, paid for claims that otherwise would not have been allowed.

434. By reason of these payments, the City of Chicago has been damaged, and continues to be damaged, in a substantial amount.

WHEREFORE, Relator requests that judgment be entered against Defendant, ordering that:

(i) Defendant ceases and desists from violating the False Claims Act, 31 U.S.C. § 3729, *et seq*., the State False Claims Acts, and the California Insurance Frauds Prevention Act;

(ii) Defendant pays not less than $5,500 and not more than $11,000 for each violation of 31 U.S.C. § 3729, plus three times the amount of damages the United States has sustained because of Defendant's actions, plus the appropriate amount to the States under similar provisions of the state false claims acts;

(iii) Defendant pays $10,000 for each and every fraudulent claim Defendant presented or caused to be presented to an insurance company, plus three times the amount of damages the insurance companies sustained because of Defendant's actions pursuant to the California Insurance Frauds Prevention Act;

(iv) The Relator be awarded the maximum "relator's share" allowed pursuant to 31 U.S.C. § 3730(d) and similar provisions of the state false claims acts and the California Insurance Frauds Prevention Act;

(v) The Relator be awarded all costs of this action, including attorneys' fees and costs pursuant to 31 U.S.C. § 3730(d) and similar provisions of the State False Claims Acts the California Insurance Frauds Prevention Act;

(vi) Defendant be enjoined from concealing, removing, encumbering or disposing of assets which may be required to pay the civil monetary penalties imposed by the Court;

(vii) Defendant disgorges all sums by which it has been enriched unjustly by its wrongful conduct; and

(viii) The United States, the States, and the Relator recover such other relief as the Court deems just and proper.

Dated: February 5, 2014

GRANT & EISENHOFER P.A

By: _____

Reuben A. Guttman
Traci L. Buschner
David T. Fischer
Jay W. Eisenhofer
Attorneys for Plaintiff – Relator
BEVERLY BROWN

REQUEST FOR TRIAL BY JURY

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, Relator hereby demands a trial by jury.

Dated: February 5, 2014

GRANT & EISENHOFER P.A

By: _____

Reuben A. Guttman
Traci L. Buschner
David T. Fischer
Jay W. Eisenhofer
Attorneys for Plaintiff – Relator
BEVERLY BROWN

EXHIBIT

"1"

blood

2008 112: 4445-4451
Prepublished online September 17, 2008;
doi:10.1182/blood-2008-02-141614

Lenalidomide plus dexamethasone is more effective than dexamethasone alone in patients with relapsed or refractory multiple myeloma regardless of prior thalidomide exposure

Michael Wang, Meletios A. Dimopoulos, Christine Chen, M. Teresa Cibeira, Michel Attal, Andrew Spencer, S. Vincent Rajkumar, Zhinuan Yu, Marta Olesnyckyj, Jerome B. Zeldis, Robert D. Knight and Donna M. Weber

Blood (print ISSN 0006-4971, online ISSN 1528-0020), is published weekly by the American Society of Hematology, 2021 L St, NW, Suite 900, Washington DC 20036.

Lenalidomide plus dexamethasone is more effective than dexamethasone alone in patients with relapsed or refractory multiple myeloma regardless of prior thalidomide exposure

Michael Wang,[1] Meletios A. Dimopoulos,[2] Christine Chen,[3] M. Teresa Cibeira,[4] Michel Attal,[5] Andrew Spencer,[6] S. Vincent Rajkumar,[7] Zhinuan Yu,[8] Marta Olesnyckyj,[8] Jerome B. Zeldis,[8] Robert D. Knight,[8] and Donna M. Weber[1]

[1]Department of Lymphoma and Myeloma, M. D. Anderson Cancer Center, Houston, TX; [2]Department of Clinical Therapeutics, University of Athens School of Medicine, Athens, Greece; [3]Department of Medicine, Princess Margaret Hospital, Toronto, ON; [4]Hematology Department, Institute of Hematology and Oncology, Hospital Clinic, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Barcelona, Spain; [5]Division of Hematology, Centre Hospitalier Université de Purpan, Toulouse, France; [6]Department of Malignant Hematology and Stem Cell Transplantation Service, The Alfred Hospital, Melbourne, Australia; [7]Mayo Clinic Cancer Center, Rochester, MN; and [8]Celgene, Summit, NJ

This analysis assessed the efficacy and safety of lenalidomide + dexamethasone in patients with relapsed or refractory multiple myeloma (MM) previously treated with thalidomide. Of 704 patients, 39% were thalidomide exposed. Thalidomide-exposed patients had more prior lines of therapy and longer duration of myeloma than thalidomide-naive patients. Lenalidomide + dexamethasone led to higher overall response rate (ORR), longer time to progression (TTP), and progression-free survival (PFS) versus placebo + dexamethasone despite prior thalidomide exposure. Among lenalidomide + dexamethasone-treated patients, ORR was higher in thalidomide-naive versus thalidomide-exposed patients ($P = .04$), with longer median TTP ($P = .04$) and PFS ($P = .02$). Likewise for dexamethasone alone-treated patients ($P = .03$ for ORR, $P = .03$ for TTP, $P = .06$ for PFS). Prior thalidomide did not affect survival in lenalidomide + dexamethasone-treated patients (36.1 vs 33.3 months, $P > .05$). Thalidomide-naive and thalidomide-exposed patients had similar toxicities. Lenalidomide + dexamethasone resulted in higher rates of venous thromboembolism, myelosuppression, and infections versus placebo + dexamethasone, independent of prior thalidomide exposure. Lenalidomide + dexamethasone was superior to placebo + dexamethasone, independent of prior thalidomide exposure. Although prior thalidomide may have contributed to inferior TTP and PFS compared with thalidomide-naive patients, these parameters remained superior compared with placebo + dexamethasone; similar benefits compared with placebo + dexamethasone were not evident for thalidomide-exposed patients in terms of overall survival. Studies were registered at http://www.clinicaltrials.gov under NCT00056160 and NCT00424047. (Blood. 2008;112:4445-4451)

Introduction

Despite advances in the treatment of multiple myeloma (MM), a disease characterized by the accumulation of clonal plasma cells in the bone marrow, the disease remains incurable. With the advent of novel therapies, the median survival of relapsed patients has been improved from about 1 to 2 years after relapse.[1] It is estimated that about 20 000 people (11 000 men and 9 000 women) will be diagnosed with MM, and 11 000 will die because of the disease in the United States in 2008.[2] Patients relapsing after 2000 had a median survival of 24 months, which was a clear improvement compared with those relapsing before 2000, indicating the benefit of new treatment options.[3] Nevertheless, novel agents and their rational combinations are needed. In the mid-1990s, a new class of immunomodulatory drugs was designed and synthesized using the structural backbone of thalidomide as the template. The intention was to create analogs with enhanced efficacy and reduced toxicity relative to their parent compound.[4,5] Lenalidomide (Revlimid; Celgene, Summit, NJ) is an oral derivative of thalidomide that has proven activity against MM in preclinical and clinical studies.[6-10] Whereas the immunomodulatory effects and in vivo antitumor activity of lenalidomide are similar to thalidomide, improved potency (evidenced by a greater ability to stimulate T-cell proliferation, interleukin-2 and interferon-γ production, and to inhibit tumor cell growth) and reduced toxicity (reduced somnolence, constipation, and peripheral neuropathy; no evidence of teratogenicity or mutagenesis in preclinical models) favor lenalidomide.[4,11,12] However, it must be noted that myelosuppression, not commonly observed with thalidomide, is often observed with lenalidomide.[4,12] Recently, lenalidomide plus dexamethasone was shown to be also highly active in newly diagnosed MM, leading to durable responses and a low progression rate and mortality.[13] In 2 prospective, randomized, double-blind, placebo-controlled phase 3 clinical trials (MM-009 and MM-010), it was shown that lenalidomide plus dexamethasone induced significantly higher rates of overall response (OR) and complete response (CR), as well as longer time to progression (TTP), and overall survival (OS), compared with placebo plus dexamethasone in patients with relapsed or refractory MM.[14,15]

Since lenalidomide is a derivative of thalidomide, there has been concern about possible resistance to lenalidomide in patients who had relapsed after, or who were refractory to, treatment with thalidomide. Preliminary data from early phase 1 and 2 trials

Submitted February 22, 2008; accepted July 25, 2008. Prepublished online as *Blood* First Edition paper, September 17, 2008; DOI 10.1182/blood-2008-02-141614.

Presented in part at the 42nd Annual Meeting of the American Society of Clinical Oncology, Atlanta, GA, June 4, 2006[19]; the 48th Annual Meeting of the American Society of Hematology, Orlando, FL, December 10, 2006[20]; and the XIth International Myeloma Workshop, Kas Island, Greece, June 26, 2007.[21]

The publication costs of this article were defrayed in part by page charge payment. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734.

suggested that lenalidomide alone and combined with dexamethasone produced a response in patients who had received prior thalidomide.[9,10] The present prospective subgroup analysis of data pooled from the MM-009 and MM-010 phase 3 clinical trials assessed the efficacy of lenalidomide plus dexamethasone in patients with prior thalidomide exposure.

Methods

We evaluated data from 704 patients included in the MM-009 and MM-010 trials who had relapsed or refractory MM and were not resistant to dexamethasone. This is a secondary analysis of pooled data from 2 primary trials. Patients enrolled in these trials gave written informed consent in accordance with the Declaration of Helsinki, and an ethics committee at each study site (M. D. Anderson Cancer Center, University of Athens, Princess Margaret Hospital, University of Barcelona, Université de Purpan, Alfred Hospital, Mayo Clinic) approved the protocol. Patients were randomized to receive either oral lenalidomide (25 mg/day for 21 days, every 28-day cycle) plus dexamethasone (40 mg on days 1-4, 9-12, and 17-20 every 28-day cycle for 4 cycles, after the 4th cycle on days 1-4), or placebo plus an identical schedule of dexamethasone. Prophylactic anticoagulation was not recommended for the patients enrolled in the 2 trials. Patients who were dexamethasone resistant to more than 200 mg dexamethasone in a month were excluded from the 2 trials. We identified 274 patients (39%) who had received prior thalidomide treatment and 430 patients (61%) who had not been previously treated with this agent.

The present analysis is a posthoc analysis, performed without prespecified power calculation or adjustment for multiplicity, and is therefore considered exploratory in nature. For this analysis, patients with prior exposure to thalidomide were further categorized, according to their response to thalidomide, into the following 3 subgroups: (1) thalidomide-sensitive (T1) patients with best response of stable disease (SD) or better, who never progressed while on thalidomide; (2) thalidomide-relapsed (T2) patients with best response of SD or better, who progressed while on thalidomide; and (3) thalidomide-refractory (T3) patients who had progressed while on thalidomide and never responded to prior thalidomide treatment. Patients in T1 did not progress while on thalidomide treatment, but discontinued thalidomide treatment for other reasons, such as toxicity or stem cell transplantation. For the 41 patients from the thalidomide-exposed group not included in T1, T2, or T3, response to prior thalidomide was not evaluable or was unknown.

As previously reported,[14,15] toxicity was graded according to the National Cancer Institute Common Toxicity Criteria version 2 (http://ctep.cancer.gov/reporting/ctc archive.html). Response to treatment was assessed according to European Group for Blood and Marrow Transplantation criteria[16] and the International Myeloma Working Group uniform response criteria,[17] which define the following responses: CR: no M-protein detectable by immunofixation in the serum and urine, disappearance of any soft tissue plasmacytomas, and 5% or less plasma cells in the bone marrow; very good partial response (VGPR): 90% or more reduction in serum M-protein and urine M-protein level less than 100 mg per 24 hours; and partial response (PR): 50% or more reduction of serum M-protein and reduction in 24-hour urinary M-protein by 90% or more or less than 200 mg per 24 hours. Progressive disease was defined by any of the following: a 25% or more increase from baseline serum or urinary M-protein, which must also be an absolute increase of at least 500 mg/dL in serum or 200 mg per 24 hours in urine; new or increased size of bone lesions or plasmacytomas; or development of hypercalcemia (serum calcium > 2.875 mM [11.5 mg/dL]). TTP was measured from randomization to the date of the first assessment showing disease progression. Patients who died or discontinued the study without evidence of disease progression were censored at the last evaluation for assessment of TTP. Progression-free survival (PFS) was measured from randomization to the date of the first assessment showing disease progression or death during treatment, whichever occurred first. Patients who were alive and discontinued the study without evidence of disease progression were censored at the last evaluation for assessment of PFS.

OS was calculated as the time from randomization until death from any cause, or censored at the last follow-up visit. Follow-up data on OS were obtained up to January 2007, for a median follow-up duration of 31.3 months. Data on OR, TTP, and PFS were assessed up to unblinding, which occurred in June 2005 for study MM-009 and August 2005 for study MM-010, for a median follow-up duration of 17.5 months. Differences in OR rates between treatment groups were analyzed using continuity-corrected Pearson chi square tests. Time-to-event variables with censoring, including TTP, PFS, OS, and response duration, were estimated by Kaplan-Meier methods. Two-sided log-rank tests were used to compare survivorship functions between treatment groups for TTP, PFS, OS, and response duration.

Results

Patient characteristics

The prior thalidomide-exposed patients and thalidomide-naive patients were similar with regard to age; β_2-microglobulin, hemoglobin, serum M-protein, and creatinine levels; and history of previous transplantation (Table 1). Patients previously treated with thalidomide had significantly more prior lines of therapy ($P < .05$) and a longer time since diagnosis ($P < .05$) compared with patients who were thalidomide naive (Table 1). The thalidomide-exposed patients were also more likely to have received prior dexamethasone (86%) compared with the thalidomide-naive group (62%) ($P < .001$). Although numbers were small, a nonsignificant trend was observed for prior bortezomib treatment (10% vs 7%). Within the lenalidomide plus dexamethasone treatment group, patients previously treated with thalidomide had a lower absolute neutrophil count ($P < .05$) compared with patients who were thalidomide naive (Table 1).

Outcomes

For patients treated with lenalidomide plus dexamethasone, the OR rate was higher in the thalidomide-naive than in the thalidomide-exposed group of patients (65% vs 54%, $P = .04$; Table 2), but response duration was not different (median of 16.2 months vs 13.4 months, $P = .41$; Table 2). The same difference in OR rate was seen for patients treated with dexamethasone alone (28% vs 14%, respectively; $P = .003$). In T2 and T3 subgroups, despite the small sample sizes and therefore limited statistical power, treatment with lenalidomide plus dexamethasone resulted in a significantly higher OR rate than dexamethasone alone ($P < .05$; Tables 2,3). Even the group categorized as being refractory to thalidomide (T3) benefited from lenalidomide plus dexamethasone treatment with a higher OR rate compared with dexamethasone alone ($P = .042$; Table 3).

Treatment with lenalidomide plus dexamethasone led to a longer duration of response than treatment with dexamethasone alone in thalidomide-naive patients and in those who had received prior thalidomide ($P < .01$ for both comparisons; Table 2). Duration of response was similar among patients in these thalidomide-relapsed (T2) and thalidomide-refractory (T3) subgroups treated with lenalidomide plus dexamethasone (T2 vs T3: $P = .88$),

Lenalidomide plus dexamethasone was significantly more effective than dexamethasone alone in prolonging TTP and PFS in all subgroups (Tables 2,3; Figure 1). The group categorized as being refractory to thalidomide (T3) benefited from treatment with lenalidomide plus dexamethasone, with prolonged TTP and

Table 1. Characteristics of study patients (N = 704)

	No prior exposure to thalidomide, n = 430		Prior exposure to thalidomide, n = 274	
Characteristic	**Len/Dex, n = 226**	**Placebo/Dex, n = 204**	**Len/Dex, n = 127**	**Placebo/Dex, n = 147**
Median age, y	64	64	63	62
Median prior lines of therapy, no.	2‡	2§	3‡	3§
Median time since diagnosis, y	2.8‡	2.9§	4‡	4.3§
Median baseline ECOG score	1	1	0	1
Mean β_2-microglobulin, mg/L (SD)	4.1 (2.7)	4.2 (3.1)	4.8 (4.6)	4.0 (2.6)
Mean hemoglobin, g/L (SD)	1.16 (0.17)	1.18 (0.18)	1.18 (0.21)	1.17 (0.19)
Mean serum M-protein, g/dL (SD)	2.6 (1.6)	2.6 (1.7)	2.6 (1.9)	2.7 (1.6)
Mean ANC-PS, $\times 10^9$/L (SD)	3.4 (1.8)‡	3.5 (1.7)	2.9 (1.3)‡	3.2 (1.6)
Mean creatinine, μM (SD)	1.0 (0.4)	1.0 (0.4)	1.1 (0.4)	1.0 (0.4)
Previous transplantation(s), %				
0	42	46	39	39
1	46	41	52	49
2	11	13	9	12
Prior dexamethasone, %	65	59	89	84
Prior bortezomib, %	7	6	9	10
Prior vincristine, %	61	58	51	52
MM disease status, %				
1	5	4	4	4
2	29	31	33	33
3	66	65	63	63
Median duration of prior thalidomide treatment, mo*	N/A	N/A	10	10
Median time since last thalidomide exposure, mo†	N/A	N/A	7	5

ANC-PS indicates absolute neutrophil count–phosphotidyl serine; Dex, dexamethasone; ECOG, Eastern Cooperative Oncology Group; Len, lenalidomide; MM, multiple myeloma; N/A, not applicable; NS, not significant; SD, standard deviation.

*Data missing for 3 patients receiving lenalidomide plus dexamethasone and 2 patients receiving dexamethasone alone.

†Data missing for 2 patients receiving lenalidomide plus dexamethasone and 2 patients receiving dexamethasone alone.

‡*P* value less than .05 for patients receiving lenalidomide plus dexamethasone is for comparison between no prior exposure vs prior exposure to thalidomide, based on Fisher exact test, without adjustment for multiplicity.

§*P* value less than .05 for patients receiving dexamethasone alone is for comparison between no prior exposure vs prior exposure to thalidomide, based on Fisher exact test, without adjustment for multiplicity.

PFS compared with dexamethasone alone ($P < .05$; Table 3). For patients treated with lenalidomide plus dexamethasone, TTP and PFS were longer in the thalidomide-naive patients compared with the thalidomide-exposed patients (median of 13.9 vs 8.4 months, $P = .004$ for TTP; median of 13.2 months vs 8.4 months, $P = .02$ for PFS; Table 2). There were no differences in TTP or PFS between the thalidomide-relapsed and the thalidomide-refractory subgroups (Table 3). Results were similar for patients treated with dexamethasone alone (Table 2).

Per protocol, patients treated with dexamethasone alone could receive lenalidomide-based therapy following disease progression or

Table 2. Outcomes in thalidomide-naive and thalidomide-exposed patients

	No prior exposure to thalidomide			Prior exposure to thalidomide		
	Len/Dex, n = 226	**Placebo/Dex, n = 204**	***P****	**Len/Dex, n = 127**	**Placebo/Dex, n = 147**	***P****
Response, %						
Complete response	19.0†	2.5		7.9†	1.4	
Very good partial response	19.5	4.4		13.4	0.7	
Partial response	26.1	20.6		32.3	12.2	
Overall response	64.6†	27.5‡	< .001§	53.5†	14.3‡	< .001§
Median response duration, mo (95% CI)	16.2 (12.1 to NE)	7.9 (5.1 to 11.9)	.003‖	13.4 (8.5 to NE)	5.1 (3.2 to 11.8)	.004‖
(responders only)	(n = 146)	(n = 56)		(n = 68)	(n = 21)	
Median TTP, mo (95% CI)	13.9 (11.1 to 18.5)†	4.7 (4.7 to 5.6)‡	< .001‖	8.4 (6.7 to 11.1)†	4.6 (3.7 to 4.7)‡	< .001‖
% Progressed	43.4	77.0		59.8	79.6	
Median PFS, mo (95% CI)	13.2 (10.2 to 15.3)†	4.7 (4.6 to 5.4)	< .001‖	8.4 (6.5 to 10.3)†	4.6 (3.7 to 4.7)	< .001‖
% Progressed/died	48.2	80.4		62.2	80.3	
Median overall survival, mo (95% CI)	36.1 (32.8 to NE)	32.0 (26.4 to NE)	.04‖	33.3 (25.8 to NE)	28.7 (20.6 to 36.8)	NS (*P* = .23)
% Died	39.8	49.5		48.8	53.7	

All comparisons without adjustment for multiplicity.

CI indicates confidence interval; Dex, dexamethasone; Len, lenalidomide; NE, not estimable; NS, not significant; PFS, progression-free survival; and TTP, time to progression.

**P* value is for comparison between lenalidomide plus dexamethasone versus dexamethasone alone.

†*P* value less than .05 for patients receiving lenalidomide plus dexamethasone is for comparison between no prior versus prior exposure to thalidomide.

‡*P* value less than .05 for patients receiving dexamethasone alone is for comparison between no prior versus prior exposure to thalidomide.

§Probability from continuity-corrected Pearson chi square tests.

‖Based on 2-sided log-rank tests for differences in survival distributions.

Table 3. Outcomes in subgroups of thalidomide-exposed patients

	T1: Sensitive,* n = 124			T2: Relapsed,* n = 65			T3: Refractory,* n = 44		
	Len/Dex, n = 54	Placebo/Dex, n = 70	P†	Len/Dex, n = 31	Placebo/Dex, n = 34	P†	Len/Dex, n = 20	Placebo/Dex, n = 24	P†
Response, %									
Complete response	11.1	1.4		6.5	2.9		5.0	0.0	
Very good partial response	13.0	1.4		12.9	2.9		20.0	0.0	
Partial response	40.7	14.3		22.6	0.0		25.0	20.8	
Overall response	64.8	17.1	< .001‡	41.9	5.9	< .001‡	50.0	20.8	.042‡
Median response duration, mo (95% CI)	13.4 (7.0 to NE)	3.2 (2.3 to NE)	.009§	8.8 (5.3 to NE)	NE (8.6 to NE)	NS (P = .77)	NE (6.0 to NE)	11.8 (5.1 to 12.5)	NS (P = .22)
(Responders only)	(n = 35)	(n = 12)		(n = 13)	(n = 2)		(n = 10)	(n = 5)	
Median TTP, mo (95% CI)	9.3 (5.6 to 18.0)	4.6 (3.9 to 4.7)	< .001§	7.8 (5.6 to 12.1)	3.7 (2.8 to 6.5)	.002§	7.2 (6.0 to NE)	3.7 (2.1 to 8.4)	.007§
% Progressed	57.4	80.0		71.0	85.3		55.0	83.3	
Median PFS, mo (95% CI)	9.3 (5.6 to 18.0)	4.6 (3.9 to 4.7)	< .001§	7.8 (5.2 to 11.1)	3.7 (2.8 to 6.5)	.002§	7.0 (4.9 to 16.9)	3.7 (2.1 to 8.4)	.013§
% Progressed/died	57.4	80.0		74.2	88.2		60.0	83.3	

All comparisons without adjustment or multiplicity.

CI indicates confidence interval; Dex, dexamethasone; Len, lenalidomide; NE, not estimable; NS, not significant; PFS, progression-free survival; and TTP, time to progression.

*Thalidomide-exposed subgroups (T1-T3) based on their best response to, and final outcome after, prior thalidomide therapy (see "Methods").

†*P* value is for comparison between lenalidomide plus dexamethasone versus dexamethasone alone.

‡Probability from continuity-corrected Pearson chi square tests.

§Based on 2-sided log-rank tests for differences in survival distributions.

unblinding of the study (164 patients crossed over). Nevertheless, OS was significantly longer for thalidomide-naive patients originally assigned lenalidomide plus dexamethasone than for those given dexamethasone alone ($P = .04$; Table 2). For thalidomide-exposed patients, there was a trend toward a longer OS in the originally assigned lenalidomide plus dexamethasone group, although it was not statistically significant ($P = .23$; Table 2), possibly due to the smaller sample sizes of the subgroups and the confounding factors in OS analysis including crossover and other treatment options after patients discontinued the original assigned treatment. For patients receiving lenalidomide plus dexamethasone, there was no significant difference in OS between thalidomide-naive and thalidomide-exposed patients (median of 36.1 vs 33.3, $P = .20$).

Twelve patients, whose only prior treatment was thalidomide, received lenalidomide plus dexamethasone with their only prior treatment being thalidomide. Of these, 10 (83%) responded to lenalidomide plus dexamethasone, with a CR/VGPR rate of 42%, and a median TTP of 13.6 months. For the 22 patients whose responses to prior thalidomide therapy were not evaluable and were therefore not included in the T1, T2, or T3 subgroups, 46% responded (≥ PR) to lenalidomide plus dexamethasone with a median TTP of 8.5 months, and median PFS of 8.5 months.

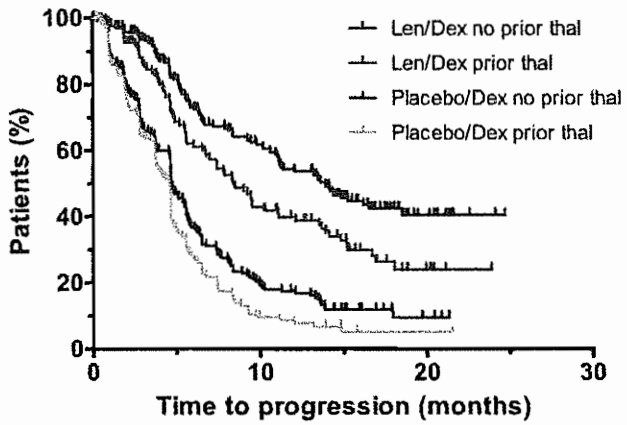

Figure 1. Kaplan-Meier plots of the time to progression in the lenalidomide plus dexamethasone and dexamethasone alone groups for patients with or without prior thalidomide exposure. The estimate of time to progression for the intent-to-treat population of the lenalidomide plus dexamethasone and dexamethasone alone groups. Len/Dex indicates lenalidomide plus dexamethasone; Dex, dexamethasone; and thal, thalidomide.

Adverse events

In thalidomide-naive patients, grade 3 or 4 deep vein thrombosis or pulmonary embolism (DVT/PE) was more common in patients treated with lenalidomide plus dexamethasone than in those who had received dexamethasone alone (10% vs 4%, $P < .05$; Table 4). In thalidomide-exposed patients, the incidences of grade 3 or 4 DVT/PE were 15% and 3% for those treated with lenalidomide plus dexamethasone and those on dexamethasone alone, respectively ($P < .05$; Table 4). Among patients treated with lenalidomide plus dexamethasone, DVT/PE rates (all grade 3 or 4) were similar, irrespective of the presence or absence of prior thalidomide treatment (15% vs 10%, respectively; $P = .17$; Table 4).

Anticoagulation usually involves prophylactic low-molecular-weight heparin (either low dose or full dose), or warfarin orally with the targeted INR range between 2 and 3. Antithrombotic prophylaxis is usually with oral aspirin. We do not have data to support the choices of anticoagulation. Our data suggest to use prophylactic therapeutic anticoagulation in thalidomide-exposed patients receiving lenalidomide plus dexamethasone rather than not to use any forms of anticoagulation.

The frequencies of grade 3 or 4 neutropenia and thrombocytopenia were higher for patients receiving lenalidomide plus dexamethasone than for those receiving dexamethasone alone, irrespective of prior thalidomide treatment (Table 4).

In thalidomide-naive patients, the occurrence of grade 3 or 4 neutropenia was 32% with lenalidomide plus dexamethasone, higher than that of dexamethasone alone (4%, $P < .05$). In

Table 4. Occurrence of grade 3 or 4 adverse events in thalidomide-naive and thalidomide-exposed patients

	No prior exposure to thalidomide, %		Prior exposure to thalidomide, %	
Adverse event	Len/Dex, n = 226	Placebo/Dex, n = 204	Len/Dex, n = 127	Placebo/Dex, n = 147
DVT/PE	9.7*	4.4*	15.0*	2.7*
Neutropenia	32.3*	4.4*	40.9*	2.1*
Thrombocytopenia	10.6	5.4	17.3*	7.5*
Anemia	10.2	5.4	11.8	6.9
Febrile neutropenia	2.7*	0.0*	1.6	0
Infection	15.5*	7.4*	14.2	8.9
Fatigue	8.0	3.9	3.9	6.2
Gastrointestinal	5.3	2.0	2.4	1.4
Peripheral neuropathy	0.4	0.5	3.1	0.7

All comparisons without adjustment for multiplicity. *P* value more than .05 for all adverse events for the comparison between no prior exposure versus prior exposure to thalidomide in patients receiving lenalidomide plus dexamethasone.

Dex indicates dexamethasone; DVT, deep-vein thrombosis; Len, lenalidomide; NS, not significant; PE, pulmonary embolism.

*P value less than .05 based on comparison between Len/Dex versus Dex using Fisher exact test.

thalidomide-exposed patients, the frequency of grade 3 or 4 neutropenia was 41% with lenalidomide plus dexamethasone, higher than that of dexamethasone alone (2%, $P < .05$). In patients treated with lenalidomide plus dexamethasone, the frequency of grade 3 or 4 neutropenia was not significantly different between thalidomide-naive and thalidomide-exposed patients (32% vs 41%, $P > .05$).

In thalidomide-naive patients, the rate of febrile neutropenia was 3% with lenalidomide plus dexamethasone, much higher than that of dexamethasone alone (0%). In thalidomide-exposed patients, similar differences exist (2% vs 0%). Therefore, lenalidomide plus dexamethasone was associated with higher frequencies of febrile neutropenia either in thalidomide-naive patients or thalidomide-exposed patients.

In thalidomide-naive patients, the rate of grade 3 or 4 nonneutropenic infections was 16% with lenalidomide plus dexamethasone, higher than that with dexamethasone alone (7%, $P < .05$). However, similar differences between lenalidomide plus dexamethasone and dexamethasone alone in the thalidomide-exposed group of patients did not reach statistical difference (14% vs 9%, $P > .05$).

In patients treated with lenalidomide plus dexamethasone, the frequencies of grade 3 or 4 anemia were similar for those with and without prior thalidomide exposure ($P > .05$ for all; Table 4).

In thalidomide-naive patients, the occurrence of grade 3 or 4 thrombocytopenia was 11% with lenalidomide plus dexamethasone, similar to that of dexamethasone alone (5%, $P > .05$). In thalidomide-exposed patients, the frequency of grade 3 or 4 thrombocytopenia was 17% with lenalidomide plus dexamethasone, much higher than that of dexamethasone alone (8%, $P < .05$). This was likely to be due to a combination of the myelosuppression by lenalidomide plus dexamethasone and/or the impact of a greater number of prior lines of therapy and longer duration from of disease on the marrow. (Table 1).

In thalidomide-naive patients, the rate of grade 3 or 4 neuropathy was 0.4% with lenalidomide plus dexamethasone, similar to that with dexamethasone alone (0.5%, $P > .05$). However, in thalidomide-exposed patients, the rate of grade 3 or 4 neuropathy tended to be higher (3%) in patients treated with lenalidomide plus dexamethasone, but was not significantly different from that noted in patients treated with dexamethasone alone (1%, $P = .06$, Table 4). This trend could be due to the addition of lenalidomide to therapy in patients with prior thalidomide exposure or to the greater number of prior lines of therapy and longer duration of disease prior to protocol entry (Table 1).

Dosing

In patients who received prior thalidomide treatment and in those who were thalidomide naive, the median daily doses were 25 mg lenalidomide or placebo, and 40 mg dexamethasone in both the lenalidomide plus dexamethasone and dexamethasone alone groups. In thalidomide-naive patients and those who had received prior thalidomide treatment, dose reductions were more common in those treated with lenalidomide plus dexamethasone compared with dexamethasone alone. Prior thalidomide treatment did not influence the number of patients needing a dose reduction (Table 5).

Discussion

Results from this posthoc subgroup analysis of data pooled from the phase 3 randomized clinical trials, MM-009 and MM-010, showed that lenalidomide plus dexamethasone was more effective than dexamethasone alone in the treatment of patients with relapsed or refractory MM, irrespective of prior thalidomide exposure. Furthermore, lenalidomide plus dexamethasone was active in patients who had relapsed on or had never previously responded to thalidomide.

Preliminary results have shown that lenalidomide plus dexamethasone at first relapse resulted in a higher OR rate (65% vs 58%) and

Table 5. Dose reductions in thalidomide-naive and thalidomide-exposed patients

	No prior exposure to thalidomide		Prior exposure to thalidomide	
	Len/Dex, n = 226	Placebo/Dex, n = 204	Len/Dex, n = 127	Placebo/Dex, n = 147
Median dose, mg/d				
Lenalidomide or placebo	25	25	25	25
Dexamethasone	40	40	40	40
Patients with 1 or more dose reduction, no. (%)				
Lenalidomide or placebo	80 (35.4)	27 (13.2)	49 (38.6)	11 (7.5)
Dexamethasone	66 (29.2)	31 (15.2)	35 (27.6)	23 (15.8)

Dex indicates dexamethasone; and Len, lenalidomide.

a longer median TTP (16.4 vs 9.5 months) than when the treatment was used later, after multiple relapses.[18] Patients in the prior thalidomide groups (T1-T3) were generally treated later after diagnosis (ie, in a later phase of the disease) and had received more prior therapies compared with patients not previously treated with thalidomide. It is interesting to note that in the small number of patients who received lenalidomide plus dexamethasone as second-line therapy, immediately after thalidomide treatment, the combination resulted in an OR (83% for the 12 patients) much higher than lenalidomide plus dexamethasone used later in the treatment, after other additional therapies. This further supports the significant role of lenalidomide plus dexamethasone as second-line treatment, regardless of prior exposure to thalidomide.

Despite receiving more prior therapies and a longer duration of disease since diagnosis, 54% of patients with prior thalidomide exposure responded to lenalidomide plus dexamethasone treatment. Furthermore, our subgroup analysis demonstrated that even in the truly thalidomide-refractory subgroup of patients, 50% responded to lenalidomide plus dexamethasone, with 5% achieving CR. To our knowledge, these are the highest response rates reported in patients who were resistant to thalidomide.

As reported in the primary studies, a superior OR rate, TTP, and PFS after lenalidomide plus dexamethasone treatment compared with dexamethasone alone was observed, regardless of the number of prior therapies or prior exposure to thalidomide.[14,15] In the present analysis, the longest TTP and PFS were observed among patients without prior thalidomide exposure who received lenalidomide plus dexamethasone. However, all the thalidomide-exposed subgroups, including those relapsed on or who were refractory to thalidomide, also benefited significantly from lenalidomide plus dexamethasone treatment. It is worth noting that the more favorable efficacy results for thalidomide-naive patients compared with thalidomide-exposed patients were not only observed in the lenalidomide plus dexamethasone group, but also in the dexamethasone alone group. Moreover, the lower efficacy of lenalidomide plus dexamethasone in thalidomide-exposed patients is likely because this is a more heavily pretreated group in general. These results indicate that although there might be some degree of cross-resistance between thalidomide and lenalidomide, there are still benefits for all patients regardless of prior thalidomide exposure.

There was a higher incidence of DVT for the thalidomide-exposed patients who were treated with lenalidomide and dexamethasone. We believe that all these patients should receive prophylactic anticoagulation. Anticoagulation usually involves prophylactic low-molecular-weight heparin (either low dose or full dose), or warfarin orally with the targeted INR range between 2 and 3. We do not have data from these 2 trials to support the choices of anticoagulation or antithrombotic therapy. Our data suggest to use prophylactic therapeutic anticoagulation in thalidomide-exposed patients receiving lenalidomide plus dexamethasone or antithrombotic therapy rather than not to use any forms of anticoagulation or antithrombotic therapy. Currently, for patients with prior history of DVT/PE, we use full anticoagulation as described in "Adverse events" with either full-dose low-molecular-weight heparin or warfarin with a targeted INR between 2 and 3. For patients receiving lenalidomide plus dexamethasone without prior history of DVT/PE, with or without prior history of thalidomide exposure, we use antithrombotic medications such as aspirin.

In either thalidomide-naive or thalidomide-exposed patients with myeloma, there were higher rates of neutropenia with lenalidomide plus dexamethasone compared with that of dexamethasone alone. These significantly higher rates of neutropenia were translated into higher frequencies of neutropenia fevers and severe nonneutropenia infections with lenalidomide plus dexamethasone therapy than with dexamethasone alone.

The incidence of peripheral neuropathy was low in both groups of patients with and without prior thalidomide exposure, but a trend toward a higher incidence of peripheral neuropathy was observed in thalidomide-exposed patients treated with lenalidomide plus dexamethasone. These results indicate that toxicities may be increased in patients receiving lenalidomide plus dexamethasone after prior thalidomide exposure. However, it must be noted that the thalidomide-exposed patients were more heavily pretreated than the thalidomide-naive patients.

In conclusion, our secondary analysis of data pooled from two phase 3 trials showed that treatment with lenalidomide plus dexamethasone was superior to dexamethasone alone in relapsed or refractory MM patients with or without prior thalidomide exposure. Prior thalidomide might have contributed to inferior TTP and PFS, without affecting OS in patients treated with lenalidomide + dexamethasone or dexamethasone alone.

Acknowledgments

The authors thank Dr Raymond Alexanian for his input in the analysis and the preparation of the paper.

The MM-009 and MM-010 studies were funded by Celgene Corporation, Summit, NJ; editorial support for the preparation of this paper was also funded by Celgene.

Authorship

Contribution: M.W., M.A.D., C.C., M.T.C., M.A., A.S., S.V.R., and D.M.W. enrolled patients; Z.Y. and M.O. analyzed results and made the figures; M.W., M.A.D., C.C., M.T.C., M.A., A.S., S.V.R., Z.Y., M.O., J.B.Z., R.D.K., and D.M.W. wrote the paper; the authors were fully responsible for content and editorial decisions for this paper.

Conflict-of-interest disclosure: M.W. received honoraria from Celgene and received research funding for this project from Celgene; M.A.D. received honoraria from Celgene; C.C. received honoraria and has done consultant work for Celgene; M.T.C. received honoraria for lectures from Janssen-Cilag and Pharmion; Z.Y., M.O., J.B.Z., and R.D.K. are employees of Celgene; D.M.W. received grant support and lecture fees from Celgene. All other authors declare no competing financial interests.

Correspondence: Michael Wang, M. D. Anderson Cancer Center, Department of Lymphoma/Myeloma, 1515 Holcombe Blvd, Unit 429, Houston, TX 77030; e-mail: miwang@mdanderson.org.

References

1. Kumar SK, Rajkumar SV, Dispenzieri A, et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood. 2008;111:2516-2520.
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71-96.
3. Kumar SK, Rajkumar SV, Dispenzieri A, et al. Improved survival in multiple myeloma and the impact of novel therapies. Blood. 2008;111:2516-2520.
4. Knight R. IMiDs: a novel class of immunomodulators. Semin Oncol. 2005;32(suppl 5):S24-S30.
5. Bartlett JB, Dredge K, Dalgleish AG. The evolution of thalidomide and its IMiD derivatives as anticancer agents. Nat Rev Cancer. 2004;4:314-322.
6. Corral LG, Haslett PA, Muller GW, et al. Differential cytokine modulation and T cell activation by two distinct classes of thalidomide analogues that

are potent inhibitors of TNF-alpha. J Immunol. 1999;163:380-386.

7. Hideshima T, Chauhan D, Shima Y, et al. Thalidomide and its analogs overcome drug resistance of human multiple myeloma cells to conventional therapy. Blood. 2000;96:2943-2950.
8. Mitsiades N, Mitsiades CS, Poulaki V, et al. Apoptotic signaling induced by immunomodulatory thalidomide analogs in human multiple myeloma cells: therapeutic implications. Blood. 2002;99: 4525-4530.
9. Richardson PG, Schlossman RL, Weller E, et al. Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma. Blood. 2002; 100:3063-3067.
10. Richardson PG, Blood E, Mitsiades CS, et al. A randomized phase 2 study of lenalidomide therapy for patients with relapsed or relapsed and refractory multiple myeloma. Blood. 2006;108: 3458-3464.
11. Anderson KC. Lenalidomide and thalidomide: mechanisms of action: similarities and differences. Semin Hematol. 2005;42(suppl 4):S3-S8.
12. Kumar S, Rajkumar SV. Thalidomide and lenalidomide in the treatment of multiple myeloma. Eur J Cancer. 2006;42:1612-1622.
13. Lacy MQ, Gertz MA, Dispenzieri A, et al. Long-term results of response to therapy, time to progression, and survival with lenalidomide plus dexamethasone in newly diagnosed myeloma. Mayo Clin Proc. 2007;82:1179-1184.
14. Weber DM, Chen C, Niesvizky R, et al. Lenalidomide plus dexamethasone for relapsed multiple myeloma in North America. N Engl J Med. 2007; 357:2133-2142.
15. Dimopoulos M, Spencer A, Attal M, et al. Lenalidomide plus dexamethasone for relapsed or refractory multiple myeloma. N Engl J Med. 2007; 357:2123-2132.
16. Bladé J, Samson D, Reece D, et al. Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haemopoietic stem cell transplantation. Myeloma Subcommittee of the EBMT. European Group for Blood and Marrow Transplant. Br J Haematol. 1998;102:1115-1123.
17. Durie BG, Harousseau JL, Miguel JS, et al. International Myeloma Working Group: International uniform response criteria for multiple myeloma. Leukemia. 2006;20:1467-1473.
18. Stadtmauer E, Weber D, Dimopoulos M, et al. Lenalidomide in combination with dexamethasone is more effective than dexamethasone at first relapse in relapsed multiple myeloma. Blood. 2006;108: Abstract 3552.
19. Wang M, Knight R, Dimopoulos M, et al. Comparison of lenalidomide in combination with dexamethasone to dexamethasone alone in patients who have received prior thalidomide in relapsed or refractory multiple myeloma. J Clin Oncol. 2006; 24: Abstract 7522.
20. Wang M, Knight R, Dimopoulos M, et al. Lenalidomide in combination with dexamethasone was more effective than dexamethasone in patients who have received prior thalidomide for relapsed or refractory multiple myeloma. Blood. 2006;108: Abstract 3553.
21. Wang M, Knight R, Dimopoulos M, et al. Effect of Lea/Der in MM despite thal resistance. Haematologica. 2007;92: Abstract PO-662.

On February 5, 2014, I hereby certify that a copy of Plaintiff-Relator's Third Amended Complaint (file-stamped) and Exhibit 1 pursuant to the Federal False Claims Act will be served promptly on the following after Plaintiff-Relator's Counsel receives a file-stamped copy of the Third Amended Complaint and Exhibit 1 from the Clerk's office and in accordance with Fed. R. Civ. P. 4.

David T. Fischer
Attorney for Plaintiff – Relator
BEVERLY BROWN

SERVICE LIST

Attorney General Eric H. Holder
United States Department of Justice
950 Pennsylvania Avenue., NW
Washington, DC 20530
(202) 514-2001

Ms. Joyce R. Branda
Deputy Director
c/o Jamie A. Yavelberg
William E. Olson
Commercial Litigation Branch Civil Fraud
U.S. Department of Justice
601 D Street, NW
Washington, DC 20530
(202) 307-0231/(202) 616-3085 (fax)

Attorney General Kamala D. Harris
Office of the Attorney General
1300 "I" Street
Sacramento, CA 94244-2550
(916) 445-9555

André Birotte, Jr.
United States Attorney
c/o Howard Daniels
Assistant United States Attorney
Central District of California
312 North Spring Street, Suite 1200
Los Angeles, CA 90012
(213) 894-6947

Attorney General George Jepsen
Office of the Attorney General
State of Connecticut
55 Elm Street
Hartford, CT 06106
(860) 808-5318/(860) 808-5387 (fax)
attorney.general@po.state.ct.us

John Fisher, Deputy Attorney General
Bureau of Medi-Cal Fraud and Elder Abuse
Office of the Attorney General
California Department of Justice
1455 Frazee Road, Suite 315
San Diego, CA 92108

Attorney General Pam Bondi
Office of the Attorney General
State of Florida,The Capitol PL-01
Tallahassee, FL 32399-1050
(850) 414-3300/(487) 487-9475 (fax)

Attorney General Joseph R. Biden, III
Carvel State Office Building
820 North French Street
Wilmington, DE 19801
(302) 577-8400/(302) 577-2496 (fax)
Attorney.General@State.DE.US

Attorney General Sam Olens
Office of the Attorney General
40 Capitol Square, SW
Atlanta, GA 30334
(404) 656-3300/(404) 657-8733 (fax)

Jeff Atwater, Chief Financial Officer
Division of Legal Services
Florida Department of Financial Services
200 East Gaines Street
Tallahassee, FL 32399
(850) 513-3110/(850) 413-7460 (fax)

Susana A. Mendoza, City Clerk
City of Chicago
121 North LaSalle Street, Room 107
Chicago, IL 60602
(312) 742-5375
cityclerk@cityofchicago.org

Attorney General David M. Louie
Office of the Attorney General
425 Queen Street
Honolulu, HI 96813
(808) 586-1500/(808) 586-1239 (fax)

Attorney General Lisa Madigan
Chicago Main Office
100 West Randolph Street
Chicago, IL 60601
(312) 814-3000/(312) 814-3806 (fax)

Stephen R. Patton, Corporation Counsel
City of Chicago, Law Department
121 North LaSalle Street, Room 600
Chicago, IL 60602
(312) 744-0200/(312) 744-8538 (fax)

David Thomas
Inspector General of Indiana
315 West Ohio Street, Room 104
Indianapolis, IN 46202
(317) 232-3850

Attorney General Greg Zoeller
Office of the Indiana Attorney General
Indiana Government Center South
302 West Washington Street, 5th Floor
Indianapolis, IN 46204
(317) 232-6201/(317) 232-7979 (fax)
constituent@atg.in.gov

Attorney General Martha Coakley
Office of the Attorney General
One Ashburton Place
Boston, MA 02108
(617) 727-2200/(617) 727-3251 (fax)

Attorney General James Caldwell
1885 North 3rd Street
Baton Rouge, LA 70802
(225) 326-6705/(225) 326-6793 (fax)
AdminInfo@ag.state.la.us

Attorney General Tim Fox
Department of Justice
215 North Sanders Street
Helena, MT 59620
(406) 461-1264

Attorney General Bill Schuette
Michigan Department of Attorney General
Lansing Office
G. Mennen Williams Building, 7th Floor
525 West Ottawa Street
Lansing, MI 48909
(517) 373-1110/(517) 373-3042
miag@michigan.gov

Attorney General Joseph A. Foster
33 Capitol Street
Concord, NH 03301
(603) 271-3658/(603) 271-2110 (fax)

Attorney General Catherine Cortez Masto
Office of the Attorney General
100 North Carson Street
Carson City, NV 89701-4717
(775) 684-1100/(775) 684-1108 (fax)

Attorney General Gary King
408 Galisteo Street
Santa Fe, NM 87501
(505) 827-6000/(505) 827-5826 (fax)

Attorney General John Jay Hoffman
Office of the Attorney General
25 Market Street
Trenton, NJ 08625-0080
(609) 292-4925/(609) 292-3508 (fax)

Attorney General Roy Cooper
North Carolina Department of Justice
Legal Services Department
9001 Mail Service Center
Raleigh, NC 27699-9901
(919) 716-6400/(919) 716-6750 (fax)

Attorney General Eric Schneiderman
Office of the Attorney General
The Capitol, 2nd Floor
Albany, NY 12224-0341
(800) 771-7755
serveAG@oag.state.ny.us

Attorney General Peter Kilmartin
Office of the Attorney General
150 South Main Street
Providence, RI 02903
(401) 274-4400

Attorney General Scott Pruitt
313 NE 21st Street
Oklahoma City, OK 73105
(405) 521-3921

Attorney General Greg Abbott
c/o Kerry Ascher
Christen Nedwick
Office of the Attorney General
300 W. 15th Street
Austin, TX 78701
(512) 463-2100
greg.abbott@oag.state.tx.us
Kerry.ascher@texasattorneygeneral.gov
Christen.nedwick@texasattorneygeneral.gov

Attorney General Robert E. Cooper, Jr.
Office of the Attorney General
Cordell Hull Building, Ground Floor
425 Fifth Avenue North
Nashville, TN 37243-3400
(615) 741-3491

Attorney General Irvin Nathan
John A. Wilson Building
1350 PA Ave, NW, Suite 409
Washington, DC 20009
(202) 727-3400/(202) 347-8922 (fax)

Attorney General Kenneth T. Cuccinelli
Office of the Attorney General
900 East Main Street
Richmond, VA 23219
(804) 786-2071

Attorney General John Suthers
Office of the Attorney General
Ralph L. Carr Colorado Judicial Center
1300 Broadway, 10th Floor
Denver, CO 80203
(720) 508-6000

Attorney General J. B. Van Hollen
Wisconsin Department of Justice
Risser Justice Center
17 West Main Street
Madison, WI 53703
(608) 266-1221/(608) 267-2779 (fax)

Attorney General Lori Swanson
Office of the Attorney General
1400 Bremer Tower
445 Minnesota Street
St. Paul, MN 55101

Attorney General Bob Ferguson
Office of the Attorney General
Medicaid Fraud Control Unit
2425 Bristol Ct. SW
P.O. Box 40114
Olympia, WA 98504

California Insurance Commissioner
Attn: Darrel Woo
300 Capitol Mall, Suite 1700
Sacramento, CA 95814
916-492-3500/916-445-5280 (fax)

Attorney General Douglas F. Gansler
Office of the Attorney General
200 St. Paul Place
Baltimore, MD 21202
(410) 576-6300

Los Angeles District Attorney
Jackie Lacey, District Attorney
210 West Temple Street
Los Angeles, CA 90012
(213) 974-3501