UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA and the States of ARKANSAS, CALIFORNIA, DELAWARE, FLORIDA, HAWAII, ILLINOIS, INDIANA, LOUISIANA, MASSACHUSETTS, NEVADA, NEW HAMPSHIRE, NEW MEXICO, TENNESSEE, TEXAS, UTAH, and VIRGINIA, NEW YORK, MICHIGAN, GEORGIA and the DISTRICT OF COLUMBIA,	**CIVIL ACTION NO: 05-6609**
	HONORABLE JOHN R. PADOVA
Plaintiffs,	
	SECOND AMENDED COMPLAINT
ex rel.	**JURY TRIAL DEMANDED**
MARLENE SANDLER and SCOTT PARIS,	
Plaintiffs-Relators,	
v.	
WYETH PHARMACEUTICALS, INC. and PFIZER INC.	
Defendants.	

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INTRODUCTION

1. On behalf of the United States of America and the states of Arkansas, California, Delaware, Florida, Hawaii, Illinois, Indiana, Louisiana, Massachusetts, Nevada, New Hampshire, New Mexico, Tennessee, Texas, Utah, Virginia, New York, Michigan, Georgia and the District of Columbia (the "States"), and pursuant to the *qui tam* provisions of the Federal False Claims Act, 31 U.S.C. §§ 3729-3733 and the False Claims Acts of the States, Plaintiffs-Relators Marlene Sandler and Scott Paris file this *qui tam* Complaint against Defendant Wyeth Pharmaceuticals, Inc. ("Wyeth" of the "Company") and its successor in interest, Pfizer Inc. ("Pfizer").

2. This action concerns improper off-label marketing and other activities by Wyeth relating to an immunosuppressant drug called Rapamune (generic name sirolimus).

3. Defendant Wyeth placed transplant patients at risk and caused false claims to be submitted by:

- systematically engaging in illegal off-label marketing of Rapamune;
- furthering the unlawful off-label marketing of Rapamune through the transformation of ostensibly independent and unbiased educational and scientific programs, including physician continuing medical education ("CME") programs, into promotional vehicles for Rapamune; and
- unlawfully promoting Rapamune in violation of the Anti-Kickback Statute, 42 U.S.C. § 1320a-7b(b), as amended by the Patient Protection and Affordable Care Act ("PPACA"), Public Law No. 111-148, Sec. 6402(g), 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 Rapamune, including for off-label uses.

4. Kidney transplant patients are typically placed on immunosuppressant regimens for their entire lives after transplant to prevent kidney rejection, which may lead to illness and death of the graft and/or patient. Rapamune, originally owned and marketed by Wyeth (and now Pfizer), is one such prescription immunosuppressant drug. It was approved by the United States

Food and Drug Administration (FDA) in 1999 to prevent organ rejection in patients aged 13 years or older receiving renal (kidney) transplants. Rapamune costs between $8,000 to $20,000 a year per person.

5. Rapamune's package insert requires Rapamune to be administered as soon as possible following a kidney transplant operation (termed "*de novo* use" by the FDA) as part of a specific drug treatment regimen with cyclosporine (another immunosuppressive drug) and corticosteroids. In 2003, the FDA approved Rapamune for an additional dosing regimen limited to *de novo* kidney transplant patients – those patients placed on Rapamune, cyclosporine and steroids as soon as possible after transplant – who were at low to moderate immunologic risk. This dosing regimen allows *de novo* patients to remove the cyclosporine component 2-4 months after the kidney transplant, but this approval only extends to those patients in low to moderate risk groups.[1] Rapamune has never been approved for use in connection with other transplanted organs, such as liver, heart, lung, pancreas and islet cells nor in children under the age of 13. The FDA has not approved the safety and efficacy of Rapamune when other immunosuppressive drugs are given to the patient at the time of transplant and the patient is later switched or converted to Rapamune, a practice Wyeth refers to as "conversion." Indeed, the FDA even issued a warning against this practice in 2004.

6. Among the unapproved "off-label" uses of Rapamune that Wyeth markets or marketed are the following: (a) any use in liver transplant patients; (b) any use in lung transplant patients; (c) any use in heart transplant patients; (d) any use in pancreas or islet cell patients; (e) any non *de novo* use, including "conversion" protocols in kidney transplant patients who are currently on other treatment regimens; (f) any Rapamune treatment regimen in which

cyclosporine is withdrawn in high risk patients, such as African-American and pediatric patients; (g) any treatment regimen in which drugs other than cyclosporine and steroids are used with Rapamune; (h) any *de novo* use of Rapamune without cyclosporine; (i) any use in children under 13; (j) any use in high risk patients under the age of 18; and (k) any Rapamune regimens in which the corticosteroid component is discontinued.

7. Prior to Rapamune's launch in 1999 until at least the end of 2002, Wyeth management openly encouraged and directed their entire Rapamune sales force to promote Rapamune to physicians practicing heart, lung, liver, pancreas, and islet cell transplants even though the drug was not indicated for use as an immunosuppressant for patients receiving transplants of these solid organs (Wyeth termed this "extra-renal use").

8. Wyeth trained and encouraged its sales representatives to market Rapamune for uses outside those listed on the FDA-approved label and to misrepresent and withhold clinical information regarding the safety and efficacy of Rapamune. As a result of Wyeth's wrongdoing, patients were put at risk of serious physical and financial harm, including: the disruption or discontinuation of stable treatment regimens; increased costs associated with treating side effects caused or exacerbated by Rapamune; life-threatening side effects such as anemia, bone marrow suppression, inhibited wound-healing, proteinuria, blood clots, leukopenia, thrombocytopenia, liver failure, pulmonary dehiscence; and death.

9. A substantial portion of Rapamune prescriptions are paid for by Medicare, Medicaid, and other Government-funded health insurance programs. Prescriptions for uses other than those that are approved by the FDA or included in certain Government-approved drug compendia are not reimbursable under Medicaid. *See* 42 U.S.C. §§ 1396b(i)(10), 1396r-8(k)(6)

[1] Although the FDA has not approved a specific regimen of cyclosporine withdrawal for the high-risk group, the indication was modified in 2008 to state that high risk patients should stay on cyclosporine for at least twelve

(defining Medicaid drug coverage and "medically accepted indication"), 1396r-8(g)(1)(B)(i) (identifying compendia to be consulted); *see also United States ex rel. Franklin v. Parke-Davis* ("*Neurontin I*"), 147 F. Supp. 2d 39, 44-45 (D. Mass. 2001) (discussing reimbursement scheme). Wyeth's failure to fully disclose Rapamune's harmful side effects and limited efficacy, the Company's extensive illegal promotion of Rapamune for off-label uses, and its violations of CME regulations in manipulating physician speaker programs all illegally caused non-reimbursable claims to be submitted to (and to be paid by) the Government.

10. Through these proscribed activities, Wyeth increased the market for Rapamune, causing it to be prescribed when it should not have been. Claims for such prescriptions were submitted to and reimbursed by Medicare, Medicaid, and other Government-funded health insurance programs. Had the United States and the States known that such prescriptions were induced by illicit incentives or prescribed for off-label purposes they would not have reimbursed claims for this drug. Wyeth thereby caused false claims for payment to be submitted to Medicare, Medicaid, and other Government-funded health insurance programs. Wyeth's unlawful marketing schemes caused the submission of non-reimbursable claims to Medicare, Medicaid, and other Government-funded health insurance programs. The federal and state false claims acts provide redress for this conduct.

11. Wyeth knew that a substantial portion of Rapamune's cost would be borne by Government health programs, including Medicare and Medicaid. A January 22, 1999 Rapamune Marketing Plan, developed prior to Rapamune's launch, stated "[i]n 1997, Medicare covered 57% of kidney transplant procedures, while 38% was covered by commercial insurance companies." The Marketing Plan also noted that Medicare was a primary payer for End Stage

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months, and any subsequent withdrawal should be considered on a case by case basis.

Renal Disease ("ERSD") treatment, which may include immunosuppressant therapy (*i.e.*, Rapamune or its competitors). Later, a May 2005 PowerPoint presentation entitled, "Rapamune Diagnostic Report" by David Hartman of Wyeth's Global Market Research, noted that "[i]t is believed that around 60% of Rapamune patients pay for their treatments through Medicar (physician perceptions)." The 2005 Powerpoint also noted that "Medicare Part B covers patients for the first 36 months post transplant and will cover all transplant patients over 65" and that 19.4% of Rapamune sales are paid for by Medicaid.

12. Relators Sandler and Paris discovered these violations in 2004 and 2005, and conducted their own investigations in furtherance of a False Claims Act *qui tam* action. They bring this action on behalf of the United States and the States to recover damages for the false claims that have been and continue to be submitted.

I. JURISDICTION AND VENUE

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

14. This Court has personal jurisdiction over Defendants pursuant to 31 U.S.C. §3732(a) because Defendants can be found in and transact business in this District. Additionally, this Court has personal jurisdiction over Defendants because acts prohibited by 31 U.S.C. §3729 occurred in this District. 31 U.S.C. §3732(a).

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

16. Relators' claims and this Second Amended Complaint are not based upon allegations or transactions which are the subject of a civil suit or an administrative civil money

penalty proceeding in which the Government is already a party, as enumerated in 31 U.S.C. § 3730(e)(3).[2]

17. To the extent that there has been a public disclosure unknown to the Relators, Relators are "original source[s]" and meet the requirements under 31 U.S.C. § 3730(e)(4)(B).[3]

II. PARTIES

18. Relator Marlene Sandler was employed by Wyeth until January 2008. Ms. Sandler was a Wyeth Transplant Account Manager ("TAM") until about March 2007. Ms. Sandler was a pharmaceutical sales representative for Wyeth (or its predecessors) for 26 years. She began her career in 1981 with Wyeth (then American Home Products, Inc.) as a general pharmaceutical sales representative. In 1984, she became a hospital sales representative for Wyeth and was responsible for selling a wide variety of prescription drugs to hospitals and hospital systems. In these positions, Ms. Sandler earned various sales awards and distinctions, ranking among the top 10 to 15% of representatives in her region for most of the years in which she was evaluated. In 1999, Jim Meyer, the head of Wyeth's Transplant Division, invited Ms. Sandler to become one of approximately 30 specialty transplant sales representatives. In 2004 and 2005, Relator Sandler served as a Rapamune Area Field Trainer. In this position, she was in charge of training some new representatives in the "field" (i.e. assisting them in learning to detail physicians). TAMs only market Rapamune, Wyeth's sole transplant drug. Ms. Sandler marketed Rapamune to eight transplant centers in Philadelphia, one in southern New Jersey, and one in Delaware, and has direct and independent knowledge of the false statements and claims that Wyeth caused to be submitted to the Government.

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[2] To the extent that conduct alleged in this Amended Complaint occurred prior to March 23, 2010, the prior versions of the False Claims Act are applicable (*i.e.*, 31 U.S.C. § 3730(e), as amended, October 27, 1986 and May 20, 2009).

[3] *Id.*

19. Relator Scott Paris was a Wyeth Transplant Account Manager from January 2002 until April 2005. Mr. Paris was responsible for marketing Rapamune to five transplant centers in New York City and Long Island, including Mount Sinai, Cornell University, and Stony Brook transplant centers. Mr. Paris has direct and independent knowledge of the false statements and claims that Wyeth caused to be submitted to the Government.

20. Defendant Wyeth is incorporated in Delaware. Its headquarters and principal place of business are in Collegeville, Pennsylvania. Wyeth engages in the business of manufacturing, marketing, and selling prescription drugs and other products for the prevention, diagnosis, and treatment of diseases throughout the United States and in many countries worldwide. According to Wyeth's Form 10-K filed with the Securities and Exchange Commission ("SEC") on February 27, 2009, Wyeth generated net revenue in excess of $22 billion for the fiscal year ending December 31, 2008.

21. Defendant Pfizer is headquartered in New York, with its principal place of business at 235 East 42nd Street, New York, New York. Pfizer is a research-based, global pharmaceutical company that develops, manufactures and markets prescription medicines for humans and animals, as well as consumer healthcare products. Pfizer operates in three primary business segments: the pharmaceutical segment, the consumer healthcare segment, and the animal health segment. Pfizer and Wyeth merged in October 2009 and Wyeth became a wholly-owned subsidiary of Pfizer. According to the terms of the Merger Agreement, Pfizer agreed to assume all the "property, rights, privileges, immunities, powers and franchises" of Wyeth, as well as assume the "debts, liabilities and duties" of Wyeth. According to Pfizer's Form 10-K filed with the SEC on February 27, 2009, Pfizer generated net revenue in excess of $48 billion in the fiscal year ending December 31, 2008. Pfizer has a sordid history with regard to compliance

with the False Claims Act. It is currently subject to its third corporate integrity agreement with the federal Government and in October 2009, Pfizer paid $2.3 billion to resolve marketing claims involving 11 drugs. Pfizer has been notorious for placing marketing goals ahead of reasoned medical decision-making and patient safety.

III. STATUTORY AND REGULATORY PROVISIONS APPLICABLE TO WYETH'S FALSE CLAIMS ACT VIOLATIONS

A. FEDERAL GOVERNMENT HEALTH PROGRAMS

22. The federal, state and local Governments, through their Medicaid, Medicare, Tricare, Veteran's Administration and other Government healthcare payors, are among the principal purchasers of Wyeth's pharmaceutical products.

23. Medicare is a federal Government health program primarily benefiting the elderly 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").

24. 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 providing payment of medical expenses to 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.

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

26. Tricare is the health care system of the United States military, designed to maintain the health of active duty service personnel, provide health care during military operations, and offer health care to non-active duty beneficiaries, including dependents of active duty personnel and career military retirees and their dependents. The program operates through various military-operated hospitals and clinics worldwide and is supplemented through contracts with civilian health care providers. Tricare is a triple-option benefit program designed to give beneficiaries a choice between health maintenance organizations, preferred provider organizations and fee-for-service benefits. Five managed care support contractors create networks of civilian health care providers.

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

28. The Federal Employees Health Benefits Program ("FEHBP") provides health insurance coverage for more than eight (8) million federal employees, retirees, and their dependents. FEHBP is a collection of individual health care plans, including the Blue Cross and Blue Shield Association, Government Employees Hospital Association, and Rural Carrier Benefit Plan. FEHBP plans are managed by the Office of Personnel Management.

B. THE FALSE CLAIMS ACT AND THE MEDICARE FRAUD & ABUSE/ANTI-KICKBACK STATUTE

29. 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).[4] The states party to this Second Amended Complaint have enacted False Claims Act statutes that apply to Medicaid fraud and/or fraudulent health care claims submitted for payment by municipal funds.

30. 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.

31. The Balanced Budget Act of 1997 amended the Medicare Anti-Kickback Statute to include 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-7a(a).

32. 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 paid as a result of the volume or value of any referrals or business generated. *See* 42 C.F.R. § 1001.952(f).

33. Such remunerations are kickbacks when paid to induce or reward physicians' prescriptions. Kickbacks increase Government-funded health benefit program expenses by inducing medically unnecessary overutilization of prescription drugs and excessive reimbursements. Kickbacks also reduce a patient's healthcare choices, as physicians may

[4] To the extent conduct occurred in this Second Amended Complaint before May 2009, False Claims Act 31 U.S.C. § 3729 (a)(1) and (a)(2) are applicable.

prescribe drug products based on the physician's own financial interests rather than according to the patient's medical needs.

34. 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-7b(b)(3). None of the statutory exceptions or regulatory safe harbors protects Wyeth's conduct in this case.

35. Recently, the Patient Protection and Affordable Care Act ("PPACA"), Public Law No. 111-148, Sec. 6402(g), amended the Medicare Anti-Kickback Statute or "Social Security Act," 42 U.S.C. § 1320a-7b(b), 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).

36. As detailed below, Wyeth's marketing of Rapamune repeatedly violated provisions of the Anti-Kickback Statute, which in turn resulted in violations of the False Claims Act, because Wyeth's improper kickbacks and incentives induced physicians to prescribe Rapamune when they otherwise would not have and many of those prescriptions were paid for by Medicare, Medicaid and other Government-funded health insurance programs.

37. Knowingly paying kickbacks to physicians to induce them to prescribe a prescription drug on-label or off-label (or to influence physician prescriptions) for individuals who seek reimbursement for the drug from a federal Government health program or causing others to do so, while certifying compliance with the Medicare Anti-Kickback Statute (or while

causing another to so certify), or billing the Government as if in compliance with these laws, violates state and federal False Claims Acts.

C. STARK LAW - THE MEDICARE/MEDICAID SELF-REFERRAL STATUTE

38. 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 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. The Stark law also prohibits payment of claims for prescriptions rendered in violation of its provisions. 42 U.S.C. §1395nn(a)(1), (g)(1).

39. Knowingly paying physicians to induce them to prescribe a prescription drug on-label or off-label for individuals seeking reimbursement for the drug from a federal Government health program or causing others to do so, while certifying compliance with the Stark law (or while causing another to so certify), or billing the Government as if in compliance with these laws, violates state and federal False Claims Acts.

40. Wyeth's conduct repeatedly violated the Stark law, which in turn resulted in violations of the False Claims Act, because Wyeth's unlawful payments and services to prescribing physicians induced (and still induces) those physicians to prescribe Rapamune when they otherwise would not have done so. Many of those prescriptions were paid for by Government funded health insurance programs.

D. FDCA AND FDA REGULATIONS

41. The Food and Drug Administration ("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).

42. The FDA reviews pharmaceutical manufacturers' applications for new drugs to determine whether the drugs' intended uses are safe and effective. *See* 21 U.S.C. § 355. Once a drug is approved for a particular use, doctors are free to prescribe the drug for "non-indicated" or off-label purposes. While doctors may independently request information from drug manufacturers about such off-label uses, with very few exceptions, the FDA prohibits drug manufacturers from marketing or promoting drugs for uses, *i.e.* "indications," not approved by the FDA. As described above, "off-label" refers to the marketing of an FDA-approved drug for uses that have not undergone FDA review and approval, *i.e.*, for purposes not approved by the FDA.

43. While purely scientific or educational programs are permissible, sales and marketing presentations, promotions, or marketing to physicians for uses other than those approved by the FDA are considered off-label marketing or "misbranding" proscribed by the FDA. *See* 21 U.S.C. §§ 331(a)-(b), 352(a), (f). Additional proscribed marketing activity includes any attempts by a pharmaceutical sales representatives to solicit discussions with physicians concerning off-label use.

44. Strong policy reasons exist for strict regulation of off-label marketing. Off-label promotion bypasses the FDA's strict review and approval process and 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.

45. Pursuant to the Food, Drug and Cosmetics Act ("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.

46. The 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 failure to reveal material facts in a label or product labeling as "misbranding." 21 U.S.C. § 321(n). Labeling includes, among other things, brochures, booklets, detailing pieces, literature, reprints, sound recordings, exhibits and audio visual material. 21 C.F.R. § 202.1 (l)(2).

47. FDA regulations deem "advertising" to include advertisements in published journals, magazines, newspapers and other periodicals, and broadcast through media such as television, radio, and telephone communications systems. *See* 21 C.F.R. § 202.1(I)(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).

48. 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.

49. Such violations exist where promotional marketing materials and presentations (*i.e.*, advertisements) for an FDA approved drug, among other things:

- Minimize, understate, or misrepresent the side effects, contraindications and/or effectiveness of the drug;
- Overstate or misrepresent the side effects, contraindications, and/or effectiveness of competing drugs;

- Expressly or implicitly promote uses, dosages or combination usage of the drug that are not contained in the FDA approved labeling (*i.e.*, off-label uses);

- Fail to reveal material facts 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 the drug is better, more effective, useful in a broader range of conditions or patients, safer, or has fewer, or less incidence of, or less serious side effects or contraindications than 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; and/or

- Are otherwise false, misleading or lacking in fair balance in the presentation of information about the drug being marketed or any competing drug.

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

50. 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, the drug is misbranded, as the statements and materials fail to provide adequate directions for all intended uses.

V. SPECIFIC ALLEGATIONS OF WYETH'S FALSE CLAIMS

A. WYETH'S PRESCRIPTION DRUG RAPAMUNE

1. Rapamune's FDA-Approved Uses And Restrictions

51. Rapamune is the brand name for sirolimus, an immunosuppressant marketed by Wyeth that was first approved by the FDA on September 15, 1999 as an "adjunct drug" for "the

prophylaxis of organ rejection in patients receiving renal transplants." *See* FDA Approval Letter dated September 15, 1999. As an adjunct drug, Rapamune was approved for use only in conjunction with other immunosuppressive drugs (specifically, cyclosporine plus corticosteroids or "steroids") that must be administered together to form the patient's treatment regimen. These drugs in combination (Rapamune, cyclosporine and steroids) are intended to affect a kidney transplant recipient's immune system in such a way to prevent the body from attacking and rejecting the transplanted kidney. As an adjunct drug in the stated combination, Rapamune was approved for use for adult kidney transplant patients. To this day, the safety and efficacy of Rapamune's use in combination with other drugs, except cyclosporine and steroids, has never been demonstrated.

52. On April 11, 2003, the FDA issued new approved dosing instructions for Rapamune. The FDA 2003 dosing instructions recommend that the cyclosporine component be withdrawn after 2-4 months in low to moderate immunological risk patients. Under this dosing regimen, patients must be treated initially (*i.e.*, *de novo*) with Rapamune, cyclosporine and corticosteroids, but the cyclosporine component is discontinued after 2-4 months of treatment. Cyclosporine should be withdrawn because, although it works with Rapamune to suppress a patient's immune system, the two drugs in combination greatly increase nephrotoxicity (poisoning of the patient's kidneys). The withdrawal of cyclosporine is only FDA-approved for the treatment of low to moderate immunological risk patients. This withdrawal protocol is not approved for high-risk transplant recipients, including African-American patients, whose immune systems require a different dosing regimen. Patients displaying other high immunological risk factors include patients with certain types of organ rejection, dialysis-dependent patients, patients with elevated serum creatinine levels, re-transplant patients, multi-

organ transplant patients, or patients with a high panel of reactive antibodies. Rapamune is also not approved to be used *de novo* without cyclosporine (*i.e.*, a regimen in which Rapamune is introduced after a kidney transplant).

53. Rapamune is only approved for use in treatment as soon as possible following the kidney transplant procedure, termed "*de novo* use" by the FDA. The FDA has not approved Rapamune to be introduced to a patient's treatment regimen months or years after the transplant operation, a practice Wyeth refers to (among other terms) as "conversion." On July 20, 2004 the FDA issued a "conversion warning" in which it specifically noted that the safety and efficacy of conversion from calcineurin inhibitors to Rapamune in the maintenance renal (kidney) transplant population had not been established, and that higher rates of serious adverse events, such as acute rejection, graft loss and death occurred when converting patients from other treatment regimens to Rapamune. The FDA required this language to be added to Rapamune's package insert. On May 2, 2007, Rapamune's package insert was further updated to include a "Precaution" concerning conversion to Rapamune, which stated:

> In a study evaluating conversion from calcineurin inhibitors to sirolimus in maintenance renal transplant patients 6-120 months post-transplant, increased urinary protein excretion was commonly observed from 6 through 24 months after conversion to Rapamune. In general, those patients with the greatest amount of urinary protein excretion prior to sirolimus conversion were those whose protein excretion increased the most after conversion. New onset of nephritic proteinuria was also reported. In some patients, reduction in the degree of urinary protein excretion was observed following discontinuation of sirolimus. Periodic quantitative monitoring of urinary protein excretion is recommended. The safety and efficacy of conversion from calcineurin inhibitors to Rapamune in maintenance renal transplant population has not been established.

See May 2, 2007 Package Insert, pg. 26. This precaution warns of a serious side effect called proteinuria (protein in urine), which demonstrates serious damage to the kidney graft. Later on

October 17 2007, Rapamune's package insert added precautions about the use of Rapamune in "conversion," which included study data showing "a 5-fold increase in the reports of tuberculosis."

54. Rapamune has never been FDA-approved for use in preventing organ rejection in patients receiving transplants of organs other than kidneys.

55. Rapamune has never been approved for use by children under the age of 13, nor has it been approved for patients under the age of 18 who are considered at high-immunological risk.

56. Rapamune has never been approved for *de novo* use without cyclosporine and steroids. By at least 2007, the "Warnings and Precautions" section of Rapamune's package insert was modified to warn against Rapamune's "*de novo* use without cyclosporine." Specifically, Rapamune's package insert at section 5.12 states:

> The safety and efficacy of *de novo* use of Rapamune without cyclosporine is not established in renal transplant patients. In a multicenter clinical study, *de novo* renal transplant patients treated with Rapamune, myclophenolate mofetil (MMF), steroids and an IL-2 receptor antagonist had significantly higher acute rejection rates and numerically higher death rates compared to patients treated with cyclosporine, MMF, steroids, and IL-2 receptor anatagonist. A benefit, in terms of better renal function, was not apparent in the treatment arm with *de novo* use of Rapamune without cyclosporine. These findings were also observed in a similar treatment group of another clinical trial.

57. Depending on the dosage required by the patient and the stage of the patient's recovery, Rapamune prescriptions average per patient anywhere from $8,000 to $20,000 per year. Because immunosuppression therapy is a life-long course of treatment, once started on Rapamune, patients must take the drug consistently for as long as they have their transplanted kidney.

58. Thousands of patients are on a life-long course of treatment with Rapamune. In 2004 alone, 45,000 patients were taking Rapamune. According to the Wyeth Annual Reports, Rapamune sales have increased exponentially, from $169.8 million in 2003 to $364.8 million in 2007.

2. FDA Warnings Concerning Fatal Side Effects Of Rapamune

59. The FDA does not prohibit a physician from using Rapamune in an off-label application if the physician makes an independent determination that off-label use of a prescription drug is in the best interests of the patient. FDA regulations, however, categorically proscribe pharmaceutical companies from marketing their drugs to physicians for off-label uses. To the extent a manufacturer learns about reported cases of severe side effects that are associated with off-label uses of a prescription drug, the FDA requires the manufacturer to issue warning letters to physicians and other health care providers.

60. On April 24, 2002, the FDA issued a "black box warning" (the most aggressive warning it can issue short of recall) regarding Rapamune's off-label use for preventing organ rejection following liver transplants. The FDA required Wyeth to change its product labeling and to send letters to health care providers that warned of increased fatality rates when Rapamune was used off-label for liver transplants. The black box warning states in part:

> The use of sirolimus in combination with tacrolimus was associated with excess mortality graft loss in a study in *de novo* liver transplant recipients. Many of these patients had evidence of infection at or near the time of death. In this and another study in *de novo* liver transplant recipients, the use of sirolimus in combination with cyclosporine or tacrolimus was associated with an increase in HAT [hepatic artery thrombosis].

61. On May 2, 2002, the FDA added an adverse event warning regarding the association of Rapamune with interstitial lung disease (fluid in the lungs of unknown origin) which resolves with the discontinuation or dose reduction of Rapamune, as well as an adverse

event warning regarding abnormal healing following transplant surgery, including wound dehiscence (meaning a separation of the surgical wound).

62. On February 13, 2003, the FDA required Wyeth to update its black box warning by sending a second letter to health care providers that reported increased fatalities when Rapamune was used in off-label treatment programs in *de novo* lung transplant recipients. The updated warning states:

> Cases of bronchial anastomotic dehiscence, most fatal, have been reported in *de novo* lung transplant patients when Rapamune has been used as part of an immunosuppressive regimen. The safety and efficacy of Rapamune (sirolimus) have not been established in liver or lung transplant patients and therefore, such use is not recommended.

63. The FDA's black box warnings on the use of Rapamune in liver and lung transplant recipients remain in effect today, as well as the warnings regarding interstitial lung disease and wound dehiscence. Similarly, the warnings regarding conversion discussed above remain today. The cyclosporine withdrawal protocol has never been approved for high immunological risk patients.

B. WYETH MARKETED RAPAMUNE FOR A VARIETY OF USES, COMBINATIONS AND DOSING REGIMENS NOT WITHIN THE DRUG'S PACKAGE INSERT

1. Wyeth Trained And Encouraged Representatives To Aggressively Market Rapamune Off-Label In Transplants Of Non-Approved Solid Organs

64. Even before Rapamune was approved in 1999, Wyeth began to build its sales force to market the drug to transplant physicians and transplant centers (*i.e.*, large hospitals or research centers). Rapamune's sales representatives, equaling about 40 across the United States, are called Transplant Account Managers ("TAMs") and only market the drug Rapamune.

65. As part of its nationwide scheme to obtain Rapamune prescriptions for extra-renal use, Wyeth tracked Rapamune prescription sales for kidney and other solid organs. For example,

a Rapamune performance and market research analysis document dated June 2001 contained a comprehensive competitive analysis for Rapamune, which included an examination of the market share Rapamune commanded for solid organ transplants, as well as on-label and off-label prescriptions of Rapamune for kidney transplant patients. Wyeth continued to gather data on extra-renal prescription sales at least through 2005.

66. Wyeth also tracked Rapamune sales by territory, region and hospital in order to calculate bonuses for its Rapamune sales force, including TAMs and Transplant Area Directors (TADs). These reports included, *inter alia*, total Rapamune sales and market share for all uses of Rapamune, including extra-renal use and other off-label kidney uses. While the bonus plans changed throughout the years, TAMs were incentivized through bonuses from 1999 to at least 2006 to garner off-label sales of Rapamune, including for extra-renal and off-label kidney uses. Specifically, during these years, at least some component of TAM bonuses were derived from total Rapamune sales. Wyeth did not exclude Rapamune sales that were for off-label uses, including extra-renal uses, from the total sales figures when determining bonuses.

67. In order to secure Rapamune sales for transplants of organs other than kidneys, Wyeth mangers required TAMs to prepare and submit to TADs annual business plans outlining their efforts to increase Rapamune sales. These business plans were distributed to other Transplant Account Managers as models and for use in discussion and training. The business plans were also submitted and reviewed by upper level Wyeth executives and managers in its sales and medical divisions, such as Wyeth's National Director of Transplant Sales (Jim Meyer from 1999 to 2003 and Joseph McCafferty after 2003); Executive Director of Marketing of Rapamune, Larry Bauer; and Rapamune Marketing Product Manager, Ron Notvest. Wyeth's National Directors of Sales, Messrs. Meyer and McCafferty, routinely provided comments to the

business plans of Rapamune's sales force, including the business plans of Relators Sandler and Paris. Mr. McCafferty distributed the business plans of TAMs as models to the entire Rapamune sales force to highlight marketing activities that he believed served as models or "best practices" for TAMs. Some of what Wyeth considered to be the best business plans were presented at Rapamune national sales meetings, also called national Plan of Action ("POA") meetings, which were attended by Rapamune's marketing, sales and medical managers and high-level executives including Mr. Gino Germano, Wyeth's Executive Vice President and General Manager. Relator Sandler attended national POA meetings in which business plans discussing marketing Rapamune for extra-renal use were presented to Wyeth's top executives and managers.

68. From 1999 through at least the end of 2002, Wyeth management encouraged TAMs to include in their business plans explicit and aggressive efforts to market Rapamune off-label to transplant centers and physicians for transplants of solid organs other than kidneys. TAM Kim Owen's 2001 business plan announced as a chief goal "to attain some usage of Rapamune in the *de novo*, cadaveric liver population and increase the overall comfort level of the drug amongst liver surgeons." The business plan called for TAM Owen to plan "consistent, weekly meetings" with the liver transplant program director at a transplant center. In late 2003, TAM Owen was promoted to District Manager of Wyeth's Pharma Group.

69. Following management directives, Relator Sandler's 2001 business plan, submitted to and approved by her supervisor and shared with other Transplant Account Managers, included a strategy to increase sales at a certain liver transplant department.

70. TAM Marilyn Moore, who marketed Rapamune in Virginia and other states, outlined key points regarding her various accounts in April of 2000, in which she listed figures for not only kidney transplants, but also liver, pancreas, heart and lung transplants for each

hospital. She commented in her reports on various transplant physicians who are Wyeth "advocates," but who use Rapamune more for liver, heart and lung transplants as opposed to kidney transplants.

71. TAM Joanne Crowley's reports are very similar to those of Marilyn Moore. Ms. Crowley's Rapamune sales territory covered Boston, Massachusetts. In Ms. Crowley's 2001 business plan, she described each hospital in her market with an accounting of the number of transplants it did of the various solid organs, including kidney, heart, liver, lung and pancreas. In this business plan, Ms. Crowley frequently described the liver programs and/or liver protocols in her various hospitals and identified pediatric and liver transplant surgeons as "key personnel." Under product performance, Ms. Crowley pointed out that the hospitals are using Rapamune for bone marrow and islet cell transplants (*i.e.*, pancreas), and recommended giving the hospitals liver studies as a way to generate business.

72. Wyeth managers also required TAMS to submit weekly, bi-monthly and monthly reports so that managers could track each TAM's progress in marketing Rapamune and suggest changes or additions in strategy when necessary. In "business briefs" generated by Relator Sandler, she frequently discussed how her physicians were implementing Rapamune in off-organ protocols, such as lung, heart and liver. For example, on March 24, 2002, Relator Sandler reported that after a Wyeth Medical Science Liaison ("MSL" or Transplant Science Liaison, "TSL") presented Rapamune data to the heart and liver transplant teams at HUP (Hospital at the University of Pennsylvania) and Temple University, the physicians began to write Rapamune prescriptions for these patients.[5]

[5] Wyeth used the scientific and medical divisions of the Company to assist in the marketing of Rapamune for off-label uses. As described more fully below, this conduct was proscribed by Wyeth's own written policies.

73. On July 26, 2002, Relator Sandler reported that Dr. Roy Bloom was now a "sirolimus consultant" to the liver and cardiovascular teams at HUP. In other similar business briefs, Relator Sandler reported on the treatment preferences of various liver transplant surgeons and discussed the numbers of liver transplants they performed each year. Relator Sandler's business briefs also recounted her numerous efforts to detail heart and lung transplant teams at various hospitals in her territory about the off-label use of Rapamune for these patients. Rapamune has never been approved as an immunosuppressant treatment for patients receiving anything other than kidney transplants, thus, all of the marketing activities to these physicians was off-label and improper.

74. A bi-monthly business brief created by the Relators' direct manager, Wyeth Transplant Account Director ("TAD") Leslie Hatch for the Northeast Zone, dated February/March 2001, stated that one of her "Key Business Accomplishments" included notes that a physician at the University of Pittsburgh Hospital was using Rapamune in pancreas transplant patients. TAD Hatch also noted that Hahnemann Hospital had stopped using Rapamune due to four patients who developed lung disease, and noted "this adverse event needs to be put in perspective for these [ ] physicians."

75. In a similar bi-monthly report dated December/January 2001, TAD Hatch reported under "Key Business Accomplishments": 1) a Rapamune speaker would be featured at the National Pancreas Workshop, and noted that the University of Maryland had modified its protocol to include a Rapa/low dose FK combination; 2) at Newark's Beth Israel Hospital, the heart transplant program placed Rapamune on its *de novo* protocol; 3) Dr. Marcos at Strong Memorial was converting liver patients to Rapamune; and 4) Lahey Clinic, primarily a liver treatment and transplant center, had added Rapamune to their formulary.

76. In her business plan for 2000, TAD Hatch included market information for kidney, pancreas, liver and heart transplants. She recommended targeting the University of Pittsburgh account, commenting that it ranked number two in the United States in liver transplants.

77. TAD Scott Hughes presented a similar business analysis in 2001, detailing the numbers of heart, lung, liver, pancreas and kidney transplants in his region. Mr. Hughes supervised TAMs in the southern United States.

78. Also in 2001, TAD Ojar Mezulis presented a business analysis detailing the non-kidney transplant opportunities, including heart and liver transplants. Mr. Mezulis supervised TAMs on the west coast of the United States.

79. These internal business plans confirm that off-organ promotion and other off-label promotion for Rapamune was not limited to a certain geographic region – it was pervasive throughout the United States, and was a company-wide strategy.

80. TAMs were provided off-label studies, abstracts and lists of studies to use when marketing Rapamune for extra renal uses and other off-label uses. Neal Wasserman, a Wyeth Medical Science Liaison, provided Relator Sandler's Northeast sales region with a bibliography of studies to use for this purpose.

81. The FDA required a black box warning on the Rapamune label for liver transplants on January 23, 2003, and a black box warning for lung transplants on March 19, 2003. Wyeth reduced its off-label marketing for extra-renal uses by the end of 2002. Nevertheless and in spite of the FDA's black box warnings, Wyeth continued to work with physicians who used Rapamune off-label for other organs. Wyeth's prior off-label marketing efforts for extra-renal organs created a stream of revenue from which it (Pfizer) still profits

today. For example, after the black box warning was issued, Relator Sandler continued to work with the Director of the Liver Transplant Program at the University of Pennsylvania, Dr. Ari Shaked, who prescribed Rapamune for liver transplant patients.

82. The use of Rapamune for extra-renal transplants continued throughout the United States even after the black box warning was issued.

83. Before all American Transplant Congresses ("ATC") until 2006, Wyeth management painstakingly coordinated dinners for key physicians attending the conference and designed seating charts strategically to place kidney and extra-renal transplant physicians with positive experience using Rapamune next to transplant physicians with no experience using Rapamune so that Wyeth marketing and sales personnel could segue into off-label discussions of Rapamune and generate extra-renal and other off-label Rapamune sales. Wyeth Transplant Science Liaisons also attended these dinners for the purpose of influencing practitioners and generating increased use of Rapamune.

84. Up to about 2003, the Relators' supervisor, TAD Hatch, required TAMs in her district to attend ATC meetings for the purpose of taking notes on presentations and abstracts discussed by physicians in the meetings so that the information could be cataloged in a master spreadsheet for use by TAMs in marketing Rapamune to physicians for off-label uses, including extra-renal uses. Relator Sandler was told by TAD Hatch that the spreadsheet was provided to Gino Germano, Wyeth Excutive Vice President and General Manager and Jim Meyer, National Director of Rapamune Sales.

85. Wyeth also promoted off-label uses of Rapamune, including extra-renal uses, at ATC commercial booths. Relator Sandler recalls being told by Wyeth management to look closely at the name tags of individuals coming to the Wyeth booth or areas for medical

information on Rapamune so as not to discuss off-label uses with persons who could work for the FDA. Wyeth went so far as to identify cities in Maryland and other locations where FDA offices were located so that TAMs could examine the cities contained on conference name tags.

86. In addition, as detailed in Section C below, Wyeth also offered health care institutions and health care professionals kickbacks in the form of, but not limited to, donations, grants, and speaker fees to incentivize these health care professionals to prescribe Rapamune for off-label purposes.

2. Wyeth Marketed Rapamune For An Unapproved Dosing Regimen Which Wyeth Called "Conversion"

a. Rapamune Was Never Indicated For Conversion Use And In 2004 The FDA Required Wyeth To Place Warnings In Rapamune's Package Insert Pertaining To Side Effects Of Converting Patients On Other Immunosuppressant Regimens To Rapamune

87. Wyeth used and uses the term "conversion" to refer to off-label treatment regimens for transplant patients who did not receive Rapamune at the time of the transplant operation (which is known as *de novo* use), but who were subsequently placed on ("converted to") Rapamune months or years after the transplant operation. Wyeth refers to conversion protocols using terms such as "delayed start," "two-step," "Rapamune Maintenance Regimen" (also called "RMR") and "maintenance" protocols.

88. Since its approval in September of 1999, Rapamune has been indicated only for *de novo* use, which means that transplant patients begin to take Rapamune on a continuing basis as soon as possible following a kidney transplant procedure. Rapamune has never been approved for use as a substitute drug regimen by kidney transplant patients who are being successfully (or even unsuccessfully) maintained on other drug regimens. Rapamune also is not approved to be administered alone, as it is indicated only to be used as an "adjunctive" agent in

concert with other specific drugs within a certain treatment protocol. Rapamune's package insert states that it is "indicated for the prophylaxis of organ rejection in patients receiving renal transplants. It is recommended that Rapamune be used initially in a regimen with cyclosporine and corticosteroids."

89. The original indication for Rapamune required that the drug be used as soon as possible after transplant (*de novo* use) and in combination with corticosteroids and cyclosporine for the entire life of the patient. The use of Rapamune "as soon as possible after transplantation" is consistent with the studies that Wyeth provided to the FDA for approval of the drug. Indeed, an FDA Medical Officer's review pertaining to the New Drug Application ("NDA") for Rapamune noted that "all but 6 study participants started Rapamune 24-48 hours after transplant."

90. In 2003, Rapamune obtained an indication which allowed for the gradual reduction and eventual discontinuation of cyclosporine in low to moderate risk patients. After the indication changed in 2003 to allow for the withdrawal of cyclosporine from the treatment protocol, the "dosage and administration" portion of the package insert stated: "The initial dose of Rapamune should be administered as soon as possible after transplantation. For *de novo* transplant recipients, a loading dose of Rapamune of 3 times the maintenance dose should be given." The withdrawal regimen in Rapamune's package insert required the use of Rapamune, cyclosporine and steroids to be initiated after transplant. The package insert did not provide for conversion use of Rapamune in transplant patients.

91. In July 2004, Rapamune's package insert was changed, with FDA approval, to include a statement about "adverse reactions" associated with "conversion":

> The safety and efficacy of conversion from calcineurin inhibitors to sirolimus [Rapamune] in the maintenance renal transplant

> population has not been established. In an on-going study evaluating the safety and efficacy of conversion from calcineurin inhibitors to sirolimus in maintenance renal transplant patients ... [t]here was a higher rate of serious adverse events including pneumonia, acute rejection, graft loss and death . . .

See July 13, 2004 Rapamune Package Insert, Section 6.4. Indeed well before the 2004 Package Insert warning, Wyeth was aware of the negative side effects of Rapamune when used in conversion regimens. For example, a 2002 Business Plan for the Baystate Hospital indicated that a threat to sales was the fact that "[transplant] coordinators complain about adverse effects" and the action plan for that hospital stated "[f]requent calls to [transplant] coordinators … [needed to] stay on top of perceived adverse events." Even after Rapamune received FDA warnings in 2004, Wyeth continued to instruct its Rapamune sales force to market Rapamune for conversion.

92. Two years later, on November 13, 2006, Wyeth sales representatives and brand teams were warned in internal correspondence from Ryan Daufenbach, Rapamune Global Product Manager, that a new "precaution" had been issued regarding Rapamune:

> In a study evaluating conversion from calcineurin inhibitors to sirolimus [Rapamune] in maintenance renal transplant patients 6-120 months post-transplant, increased urinary protein excretion was commonly observed from 6 to 24 months after conversion to Rapamune. In general, those patients with the greatest amount of urinary protein excretion prior to sirolimus conversion were those whose protein excretion increased the most after conversion. New onset of nephritic proteinuria was also reported. Reduction in the degree of urinary protein excretion was observed following discontinuation of sirolimus. Periodic quantitative monitoring of urinary protein excretion is recommended. The safety and efficacy of conversion from calcineurin inhibitors of Rapamune in maintenance renal transplant population has not been established.

The above language became part of Rapamune's May 2, 2007 package insert. Proteinuria and nephric proteinuria are signs of serious kidney disease.

93. On October 17, 2007, an HHS letter to Wyeth added additional precautions about Rapamune "conversion," including "a 5-fold increase in the reports of tuberculosis."

94. On January 14, 2008, results from a clinical study of 830 patients who converted to Rapamune 6 months to 10 years after transplant were included in Rapamune's package insert. According to the package insert, the study demonstrated that there was "no benefit associated with conversion with regard to improvement in renal function and a greater incidence of proteinuria." In sum, conversion to Rapamune not only put kidney transplant patients at an increased risk of serious side effects, including serious kidney disease, but also demonstrated no benefits to patients in terms of improving the kidney's function.

b. Wyeth Conversion Studies Failed To Produce Results Which Justified Switching Kidney Transplant Patients Who Were Already Being Treated On Another Treatment Regimen To Rapamune

95. The "conversion" studies Wyeth hoped to complete to support conversion use for Rapamune were not even scheduled to begin until January 2000, approximately one and half years after Rapamune was approved. At the time the drug was approved, the FDA and Wyeth were aware that "conversion," among other uses, would be studied by Wyeth, in the future, as part of a "Phase IV Clinical Program." Phase IV included many different studies Wyeth hoped to commission in order to secure additional approved "indications" for Rapamune.

96. A Wyeth PowerPoint presentation, entitled "Phase IV Clinical Program" indicated that a North American sirolimus (Rapamune) "conversion" study was listed as a "study development" beginning in January 2000. According to an August 9, 1999 letter written by Wyeth's Senior Director of Global Medical Affairs, Dr. Gilles des Gachons, Wyeth "elected to delay the initiation of Phase IV clinical utility study," which included "conversion therapy in 'maintenance' patients" until Wyeth could engage the FDA in "discussions at an FDA Advisory Board Meeting." This letter was directed towards physicians whom Wyeth hoped would participate in these "conversion" studies, among other Phase IV studies.

97. A May 2005 Rapamune Diagnostic PowerPoint presentation, created by David Hartman from Wyeth's Global Market Reseach division, revealed that once the 316 "conversion" trial was underway, Wyeth expected their new indication for conversion by mid-2006. The report stated that this was an opportunity to "promote switching maintenance patients to Rapamune in a calcineurin inhibitor free regimen." According to the PowerPoint presentation, Rapamune already gained approximately 3,500 kidney transplant patients during 2004 with about a third of those gains generated through "switching" or conversion.

98. By August 2005, Wyeth's 316 "conversion" study did not produce the renal function benefit that Wyeth hoped and the Company again delayed filing for a new indication for Rapamune. Further, Wyeth faced problems with proteinuria in the patients it studied. Although Wyeth obtained a one year subanalysis of early vs. late conversion patients in terms of proteinuria outcomes, Wyeth never informed physicians that late conversions fared the worst. In short, there is no indication for the "conversion" of renal transplant patients from calcineurin-based regimens to Rapamune. Rapamune's current package insert and prescribing information contain the "adverse reactions" and "precautions" added to the label that relate to "conversion."

99. A Wyeth internal email made it clear that the Company was aware that marketing Rapamune for conversion, in unapproved combinations, and for extra-renal use was illegal. Specifically, on July 24, 2006, Bob Rapella, Wyeth Senior Vice President of Pharmaceutical Sales, wrote to Wyeth's Rapamune sales force:

> This message is going to all members of the Rapamune sales team. Recently the compliance office was contacted regarding possible off-label promotion of Rapamune. As a result, an investigation has been initiated to ensure a complete and factual understanding of the circumstances and any potential activity outside of policy 511 guidelines. If you are contacted regarding this matter, please cooperate openly and fully with the compliance officer per the Wyeth values. We recognize that transplantation is a complex

> clinical area, that treatment and patient management approaches can evolve quickly in an ongoing effort to improve clinical outcomes, and that your customers may expect you to engage in a dialogue related to the latest scientific or clinical developments. For example, physicians may be using Rapamune in heart, lung and liver transplants. Physicians may also use a different immunosuppressive agent at the time of transplantation (i.e. de novo) and then switch or convert the patient to Rapamune sometime later. This practice is sometimes referred to as conversion. However, because Rapamune has not been approved for these uses, they cannot be promoted by Wyeth and discussing these topics with your customers is inconsistent with Wyeth policy. Finally, it is important for you to understand that detailing Rapamune to healthcare professionals who do not treat kidney transplant patients is also inconsistent with Wyeth policy and you should not engage in these activities. If you have any questions about this direction, please contact me or a member of the compliance office.

c. Wyeth Misrepresented The Results Of The Rapamune Maintenance Regimen Study And Other Studies To Physicians In Order To Increase Off-Label Conversion Sales

100. Wyeth saw the stable transplant patient population as a fertile ground to increase Rapamune prescriptions. To that end, Wyeth created an off-label conversion marketing program around the Rapamune Maintenance Regimen ("RMR") Study 310, even though Study 310 did not support the use of Rapamune for conversion. Wyeth often used the term "RMR" or "RMR-like" to mean conversion even though it was a misnomer. Specifically, the RMR Study 310 formed the basis for Rapamune's dosing protocol that allowed the withdrawal of cyclosporine from the approved regimen of Rapamune, cyclosporine, and steroid for 2-4 months post-kidney transplant for moderate to low risk patients. Despite being used to justify the conversion of stable patients from one drug regimen to another, Study 310 did not address the conversion of kidney patients on other treatment regimens to Rapamune.

101. Wyeth management, and particularly National Director of Transplant Sales Joe McCafferty and Wyeth Area Account Directors, instructed Transplant Account Managers to tell

physicians that it was imperative to convert kidney transplant patients to Rapamune within the first year following a transplant in order to improve long-term patient and graft survival. Management instructed its sales force to make the argument that by eliminating any calcineurin inhibitors (like cyclosporine and Prograf) and adding Rapamune as the base immunosuppressive drug, patients would experience a decreased risk of dying from a cardiovascular event, while the chances of the long-term survival of their transplanted kidney grafts would significantly improve. This became a core marketing message continuing throughout Relators' tenure at Wyeth. Since 2003, Wyeth management instructed its sales force to use the following studies in support meritless conclusions as outlined below:

- Wyeth Study #310 demonstrated that withdrawing cyclosporine from a Rapamune-based regimen improves renal function and structure in low to moderate risk kidney transplant patients.
- A registry study by Dr. Meier-Kreische showed that improved renal function correlates to a decreased risk of dying from a cardiovascular event, and a retrospective analysis of registry data by Dr. Hariharan showed that improved renal function correlates to extended long-term survival of the transplanted kidney within the first year post-transplant.
- Therefore, even patients on stable, working treatment regimens should be converted to Rapamune because a Rapamune-based regimen improves renal structure and function and thereby decreases the risk of dying from a cardiovascular event and extends long-term survival of the transplanted kidney.

102. Wyeth's marketing claims were unsupported by the data cited to physicians, and Transplant Team management knew they were unsupported.

103. As stated above, Wyeth's Study 310 only compared treatment regimes using Rapamune in combination with steroids to those using Rapamune in combination with cyclosporine and steroids. Study 310 does not compare the efficacy or safety of converting patients on other immunosuppressive regimens to Rapamune or adding Rapamune to a patient's current treatment regimen. The study only shows that withdrawing cyclosporine from the

approved combination of Rapamune, cyclosporine, and a steroid combination two to four months post-transplant in low to moderate risk patients is less damaging than continuing to use cyclosporine with Rapamune and steroids.

104. The studies by Dr. Meier-Kreische and Dr. Hariharan upon which Wyeth management relied do not include Rapamune. The studies report, in general, that as kidney function improves post-transplant, the risk of death from a cardiovascular event decreases and the chances long term renal graft survival improve. These studies have nothing to do with conversion.

105. Joe McCafferty and Wyeth Area Account Directors instructed Wyeth's sales force to extrapolate from these studies a medical conclusion that is not supported by the data. At a June 2004 meeting with a transplant nephrologist at New York-Presbyterian Hospital, TAD Hatch advanced the conclusion that Rapamune conversion protocols would benefit the nephrologist's patients who were on other protocols. When the nephrologist requested data supporting TAD Hatch's assertion, neither she nor Wyeth's Global Medical Affairs department, which purportedly specializes in responding to physician's medical questions, was able to respond with any supporting data.

106. A 2005 PowerPoint entitled "Rapamune Diagnostic Report" by Wyeth's David Hartman, demonstrates that Wyeth encouraged marketing Rapamune for conversion using the RMR data. The PowerPoint stated, "RMR study allows current rep discussion of CNI sparing prior to the conversion indication." The 2005 PowerPoint also stated, "[t]he RMR study will lead into the renal conversion indication in 2006." However, it is clear that the RMR study had nothing to do with conversion. Moreover, Wyeth never received the "conversion" indication for Rapamune.

107. Wyeth's claims that kidney patients would experience improvement in renal function if converted to Rapamune were specifically disproven by Wyeth's own studies. Starting in 2008, Rapamune's Package Insert, at Section 14.4, included the following study results:

> Conversion from calcineurin inhibitors (CNI) to Rapamune was assessed in maintenance renal transplant patients 6 months to 10 years post-transplant (Study 5). This study was a randomized, multicenter, controlled trial conducted at 111 centers globally, including US and Europe, and was intended to show that renal function was improved by conversion from a CNI to Rapamune. Eight hundred thirty (830) patients were enrolled and stratified by baseline calculated glomerular filtration rate (GFR, 20-40 mL/min vs. greater than 40 mL/min). In this trial there was no benefit associated with conversion with regard to improvement in renal function and a greater risk of proteinuria in the Rapamune conversion arm. In addition, enrollment of patients with baseline calculated GFR less than 40mL/min was discontinued due to a higher risk of serious adverse events, including pneumonia, acute rejection, graft loss and death.

(Emphasis Added).

108. Despite a lack of scientific or medical support, Wyeth management directed sales representatives to push the RMR/conversion message aggressively. At a national POA sales meeting, TAM Mark Wasco was selected by Wyeth management to present his January 2004 marketing plan for Harrisburg Hospital, which included an action plan to seek conversion business through RMR.

109. At a national 2003 POA meeting, Relator Sandler and other TAMs were trained by Wyeth trainer, Tammy Lindsey, and Barb Arison to use specific "openers" to market RMR/conversion to transplant physicians. One such opener was: "Doctor, in the past you have been comfortable converting patients to Rapamune to get improved renal function. As it turns out the FDA agrees with you too. Here is a landmark study [Study #310] that shows you why."

110. Another marketing scheme related to the RMR/conversion scheme was the so-called "Two-step protocol." TAD Leslie Hatch and Wyeth sales manger, Carl Kincaid, told

Relator Sandler and TAMs in the Rapamune Northeast district to use a study by Dr. Nankivell, which did not study Rapamune, in order to market Rapamune for conversion. TAD Leslie Hatch told her team that RMR was a "two step proactive approach" in which a switch to Rapamune is planned from the very beginning, generally for stable patients. This marketing ploy has no basis in Rapamune's package insert, Study 310 or the study by Dr. Nankivell.

111. Transplant physician Dr. Nasser Youssef reported to Relator Sandler in mid-2004 that Wyeth needed to provide potential conversion patients with detailed educational materials outlining the benefits versus the increased risks of side effects associated with converting stable patients from currently efficacious treatment programs to Rapamune-based regimens. Dr. Youssef considered attempts to convert stable patients to Rapamune "an ethical dilemma" and insisted that patients be involved in treatment decisions when their current drug regimens were working for them. Ms. Sandler disclosed Dr. Youssef's concerns and his request to Wyeth's transplant team management in her sales reports, and communicated them again to Wyeth National Director of Transplant Sales Joe McCafferty by telephone. Wyeth took no action in response to her disclosure.

112. Relator Sandler opposed Wyeth's off-label marketing of Rapamune, but Wyeth persisted in its marketing efforts. In her notes dated September 2005, Relator Sandler noted that she felt she "crossed the ethics line" when she pushed RMR for stable maintenance patients, and had raised the issue with Wyeth management, specifically whether "GMA" knew about the sales and marketing push to switch stable maintenance patients using the RMR technique.

d. Wyeth Directed And Trained Its Sales Team To Off-Label Market Rapamune For Conversion Use From The Launch Of Rapamune Onwards

113. Before Rapamune's launch in September 1999, Wyeth believed the narrow *de novo* indication was one of several "threats" that Rapamune faced in the marketplace. In a

January 22, 1999 Marketing Plan ("Marketing Plan") issued nine months before the FDA approval of Rapamune, Wyeth stated that one of the weaknesses of Rapamune, compared to its competitors, is that "Rapamune will have a narrow indication at launch (renal indication only, *de novo* patients only)." The Marketing Plan also noted that "limited number of *de novo* patients available; market penetration will be slow." In the Marketing Plan, one of Wyeth's business objectives was to gain "Penetration of Maintenance Population – Because of the predominance of maintenance patients in the transplant market, this strategic imperative is critical to achieving our expected sales forecast." Wyeth estimated that there are "130,000 maintenance transplant patients in the U.S. requiring chronic immunosuppressive treatment." Wyeth anticipated that within 6 months, "sales [of Rapamune] are forecast at $12.9 million for 1999 and $34.4 million for 2000."

114. Rapamune's Marketing Plan targeted "maintenance patients." The Marketing Plan stated that one of Wyeth's "strategic imperatives" included the "business objective … "[f]or *maintenance* patients, achieve usage as a viable alternative to calcineurin inhibitors in 50 of the top 100 renal centers." (Emphasis in original).

115. Wyeth was methodical in its execution of the Marketing Plan. At the Rapamune Launch Conference in September 1999 ("Launch Conference"), one workshop was titled "Utilization and Management of Rapamune in the Maintenance Population 1 (Conversion, Rescue, Switch)." During sales training, sales teams were required to present off-label uses of Rapamune. National Director of Sales Jim Meyer assigned to Zone 1 TAMs the task of researching and presenting "Rapa[mune] use with FK [Prograf]" with emphasis on "[u]tilization and management of Rapa[mune] in the maintenance population . . . (to include maintenance switch and conversion)." Zone 3 was assigned to research and present steroid withdrawal

protocols. The September 1999 Launch Conference also included a marketing overview in which the primary message was that Rapamune was the "go-to" drug for the maintenance population. This conference was attended by the newly hired Rapamune TAMs, TADs, and upper level Wyeth managers and top executives including: Wyeth President and CEO Bernard Poussout, Wyeth Vice President of Sales Michael Marquard, Wyeth President of U.S. Pharmaceuticals Joe Mahady, Wyeth Senior Vice President Global Medical Affairs Dr. Joseph Carmado, Wyeth Executive Vice President and General Manager Gino Germano, Wyeth's National Director of Sales Jim Meyer, and Executive Director of Marketing of Rapamune Larry Bauer.

116. At the Rapamune Launch Conference, Wyeth's instructions to TAMs to increase the market for the drug by marketing it off-label to physicians in order to get them to convert transplant patients who were currently on another immunosuppressant regimen had an immediate impact, as Wyeth personnel followed the instructions from the start. For example, in Wyeth TAM Bob Johnson's weekly summary from September 20, 1999, he wrote that at the University of Maryland Medical System, the transplant pharmacist Anne Wiland "has been quite active in encouraging attendings to convert to Rapamune." TAM Johnson also noted that Johns Hopkins University Medical Center was "poised to convert five patients from clinic right away."

117. In a weekly report dated September 24, 1999, Wyeth TAM Rick Reed noted that at three of his medical centers, Baystate Medical Center, Montefiore, and Westchester Medical Center, Rapamune would be used on rescue patients or patients who were MMF intolerant – in other words, the first use of Rapamune at those institutions would be in conversion protocols. Similarly, then-TAM Joseph McCafferty in his weekly summary submitted that same day noted that the University of Pittsburgh was using Rapamune in CellCept-intolerant patients (*i.e.*,

patients who were not successfully treated on CellCept, a competitor to Rapamune) and patients with creeping creatinines on tacrolimus.

118. TSL Lynn Fallon's contact report for September 1999 also details visits she made to physicians at the University of Maryland and Temple University. Fallon notes that she discussed patients' conversion with Dr. Anne Weiland of the University of Maryland, and that Dr. David Klasser, who mainly had kidney and pancreas transplant patients, "converted a patient when I was there." By December of 2000, then-TAM Joseph McCafferty noted that the University of Pittsburgh had switched to Rapamune for *de novo* use due to the University's prior experience with conversions to Rapamune for kidney and pancreas patients.

119. Wyeth also introduced one of its main illegal marketing schemes at the Rapamune Launch Conference, a program known as "Creatinine Creep" – the idea that Rapamune was appropriate in conversion use for patients whose levels of creatinine were unacceptably high. Wyeth believed that this concept would help its illegal marketing tactics and increase Rapamune's market share well beyond what it should have been, given its indication and physician prescribing patterns.

120. Early on, Wyeth's Marketing team began focusing on the ideas of "creatinine creep" and "preserving kidney health/preserving renal function" to market Rapamune off-label for "conversion." In September of 2000 in her Business Plan, TAD Hatch wrote that she needed "The Creep" program up and running as soon as possible. Wyeth developed the Creatinine Evaluation Education Program ("CREEP"), which "heightened awareness" that "calcineurin inhibitors" caused a slow gradual decline in renal function and Rapamune did not. TAMs were required to promote CREEP to transplant coordinators and nephrologists who were given a "call

for action" to perform "vigilant monitoring" of serum creatinine levels and "identify" patients at risk and "intervene" with Rapamune.

121. Wyeth considered "stable maintenance patients with creatinine creep" the "road to the holy grail." Relator Sandler's manager, TAD Hatch, recorded the phrase "holy grail" in this context in a memo outlining the topics of discussion presented at an April 5, 2000 POA meeting with Wyeth's National Director of Sales, Jim Meyer, and Wyeth's head of marketing, Larry Bauer. Relator was told that Gino Germano, Wyeth Executive Vice President and General Manager, coined the term "holy grail" as it related to securing Rapamune sales from stable maintenance patients with creatinine creep (or rising creatinine levels). In short, Wyeth hoped to convert patients on other regimens who were experiencing high creatinine levels to Rapamune.

122. In a memo from TAD Ojars Mezulis to his sales team ("Team T4000") on June 21, 2002, he notes that the Plan of Action "POA" meeting held from June 18 to 19, 2002 had been very successful and that as part of that meeting, he noted "The Creep Outreach tactics that Donna discussed should give you some additional ideas on how best to use this program. Certainly, the new slide kit regarding Creatinine Creep should be a useful tool to get this message out."

123. Wyeth used a variety of tactics to influence doctors to convert their patients to Rapamune, including grants, speaker honoraria, and using speakers vetted by Wyeth to spread false and misleading information about the efficacy of Rapamune conversion protocols for transplant patients. Wyeth referred to patients who were functioning without serious complications at the time their regimens were changed to include Rapamune as "stable maintenance" patients. Patients experiencing serious complications on other treatment regimens and then placed on Rapamune were referred to as "rescue" patients.

124. Wyeth was aware that a number of physicians resisted its efforts to switch their stable patients for fear of disrupting treatment regimens that were efficacious. To overcome this resistance, Wyeth used a variety of tactics, some bordering on coercion. Wyeth sales representatives were provided with drug combinations to use when discussing conversion of patients, either with MMF or without MMF. TAD Hatch, in a September 2000 Business Brief, describes how Rapamune use finally was expanding thanks to the conversion of maintenance patients to Rapamune at Yale University, the University of Pittsburgh, and other institutions. Indeed, getting Rapamune conversion use accepted at the higher-prestige transplant centers was part of Wyeth's scheme, described in the same Business Brief as a way to share "protocols from prestigious centers from around the country … to give slower adopters the confidence of 'how.'"

125. Wyeth used persuasion and lucrative speaking opportunities to change the prescribing habits of doctors who were originally hesitant to use Rapamune. In a memo dated April 15, 2000, Wyeth Sales Representative Kim Owen discussed her top account, Dr. Martin Zand of Strong Memorial Hospital in Rochester, New York. She noted that Dr. Zand was hesitant to try Rapamune and was "concerned with the lipid issue." Because Dr. Zand was scheduled to speak on the effect of immunosuppressants on lipids at an upcoming conference, Ms. Owen arranged meetings with him and Wyeth sales staff before the meeting "to address the lipid issue with Rapamune at length." The Wyeth representatives "coached him on this topic and prepared him to speak appropriately on Rapamune's effect on lipids." Wyeth encouraged its TAMs to "coach" physicians where necessary to increase Rapamune sales.

126. Sometimes, coaching was not enough. In a January 26, 2001 Business Brief, Relator Sandler described an interaction with transplant physician Dr. Youssef. Relator Sandler wanted Dr. Youssef to "meet my needs for 2001." To do this, she "aggressively leveraged a

large grant we gave him in December 2000." One of Relator Sandler's demands was that Dr. Youssef begin to "convert stable maintenance patients to Rapa/LDFK regimen." She noted that Dr. Youssef would "need to do some tenacious problem solving" to achieve this goal. In the same document, she describes challenging a doctor at the University of Pennsylvania, Dr. Brayman, to become a more proactive Rapamune advocate, asking him to "influence [Dr.] Bloom to expand [Rapamune] use in maintenance patients especially diabetics." However, Relator Sandler noted in the "Obstacles" portion of this report that Dr. Youssef had stopped converting stable patients to Rapamune because of a high incidence (20-25%) of side effects which were serious enough to discontinue use of Rapamune.

127. As stated, Wyeth's Brand Team and management directed and monitored TAMs' marketing efforts through the use of business plans, including standardized Territory Business Plans ("TBPs") developed by Wyeth. TAMs were told to keep their business plans updated at all times and available for Wyeth management, especially during management field visits (*i.e.*, managers accompanied TAMs to physician marketing calls to review and critique TAM performance).

128. The TBP used by TAMs to create their business plans is a uniform template, guiding the TAMs' marketing targets and efforts into a nationwide plan for Rapamune. Specifically, the TPB template stated, "The Territory Business Plan (TBP) organizes your activities in a local, focused way that's integrated with the national strategy for Rapamune. It ensures that all Sales and Marketing activity is conducted in a synergistic, functional way by giving TAMS and Management up-to-date information ..." Relator Sandler's TBP stated that "lack of conversion indication or data" is a sales problem. Because Wyeth management

reviewed these business plans to ensure a "national strategy for Rapamune" was implemented by the TAMs, it is clear Wyeth was aware of and encouraged off-label marketing.

129. As stated, TAMs were required to present their business plans at national and regional meetings. All national and regional meetings included sales, marketing, medical (such as MSLs and TSLs) and upper management. These business plans were used to train Wyeth sales representatives. Relator Sandler's 2005 Business Plan, which was directed by Wyeth and was presented to Joe McCafferty, Wyeth's National Director of Transplant Sales, and others at Wyeth, states that her 2004 "action plan" included a "focus on earlier conversions[,] increase awareness of Renal FC [function] as a predictor of long term graft survival." Another 2003 Business Plan called for her to target "delayed start," "early conversion" and "stable maintenance."

130. In a Business Brief for the Northeast Zone dated February – March 2001, TAD Hatch noted among her "key business accomplishments" that Dr. Nassar Youssef at Our Lady of Lourdes Medical Center reinitiated Rapamune as the standard of care for *de novo* and conversion patients as a result of Relator Sandler's influence. This was likely after she had succeeded in her "aggressive leveraging" of a prior grant to Dr. Youssef, as detailed above. In the same section, TAD Hatch notes that Westchester County Medical Center continued with Rapamune as the standard of care for conversions for patients with rising creatinines and other toxicities.

131. In a Business Brief dated December-January 2001, TAD Hatch noted among her "key business accomplishments" that at Massachusetts General Hospital, Dr. Hugh Auchincloss was converting diabetic patients to Rapamune. At Boston Children's Hospital, Dr. Harmon started a study to convert long-term patients to "Rapa/MMF no CI" (*i.e.*, Rapamune, Cellcept and no calcineurin inhibitor). However, TAD Hatch noted in the same business brief that among

the obstacles facing Rapamune was that "Youssef" (Dr. Nasser Youssef) stopped converting stable patients to Rapamune because of a high incidence (20-25%) of treatment emergent side effects that were serious enough to discontinue Rapamune.

132. A June 19, 2001 Business Brief noted that a University of Pennsylvania transplant physician, once a non-believer in Rapamune, had begun to convert his clinic patients after hearing Dr. MacDonald's presentation at the All City Kidney Transplant Conference. In the "Best Practice" section of the document, Relator Sandler described how she averted a problem at MCP Hahnemann Hospital located in Philadelphia, Pennsylvania regarding a physician concerns about Rapamune. Dr. Kumar's patients experienced serious side effects, including interstitial pneumonitis (serious lung disease) and death after being treated with Rapamune. After sending a team of four Wyeth personnel to meet with the physician, TAD Hatch reported that Dr. Kumar was comfortable using Rapamune again, and reinstated it for use in conversion of patients with rising creatinines and other toxicities.

133. Wyeth National Director of Transplant Sales, Joe McCafferty, requested 30, 60, and 90 day business plans in or about 2005. The 30-60-90 day business plans were directed at about 20 hospitals in which Wyeth believed it could increase sales of Rapamune quickly. TAMs were required to use every effort to gain more sales in these hospitals over a 90 day period. These plans contained strategies by TAMs to increase Rapamune off-label conversion sales. Mr. McCafferty was also aware that TAMs were using the TSLs to market "conversion/stable conversion." Mr. McCafferty, who worked at Wyeth's headquarters in Collegeville, Pennsylvania, tightly managed the marketing of Rapamune by Wyeth's Transplant Sales division. In addition to leading the sales efforts of the TAMs and TADs, Mr. McCafferty

attended meetings with physicians with TAMs, including Relator Sandler, for the purpose of marketing Rapamune for both on-label and off-label uses.

134. In 2006, TAM Bill Bankert's Business Plan for Johns Hopkins in Maryland, included a "specific objective" to "have a conversion protocol for [sic] patients who are already on a CNI."

135. By the end of 2002, Wyeth collected detailed "center specific" data, which could track kidney patient counts, drug regimen combinations, and start times. This information was purchased by Wyeth from a third-party vendor. It was not provided to TAMs, but to Transplant Account Directors and other upper-level Wyeth executives and TAD Hatch, Relator Sandler's manager. When TAD Hatch accompanied TAMs in the field, she would share the data with TAMs on her computer screen, in order to help them target off-label sales. Relator Sandler understood that Wyeth did not want the actual report transmitted directly to TAMs, but ultimately Wyeth wanted her and other TAMs to use the information concerning each hospital's off-label use of Rapamune to increase sales.

136. Wyeth knew exactly which Rapamune regimens were being used by its targets, including those regimens that were not approved by the FDA. For example, according to slides from the U.S. Market Research Brand Team Meeting in December 2002, in the first quarter of 2000, 47% of Rapamune was used as directed with cyclosporine and steroids, but by the third quarter of 2002, only 17% of Rapamune was used as directed. The same document showed Wyeth's estimate that "14,500 patients are worth $9,135,000."

137. In September 2005, Wyeth management "upgraded" Salesworks, which was an electronic company system designed to record physician "calls" by TAMs. The "upgrade" was made so that TAMs could no longer place details about sales issues discussed with physicians in

the notes section. Relator Sandler believes that the change in the system stemmed from Wyeth's fear that the Company would be charged with off-label marketing several Wyeth drugs, including Rapamune. Wyeth management also advised TAMs not to use "alternative" methods like "handwritten notes or e-mail" to commemorate the selling interaction. Wyeth justified the change in Salesworks by stating, "[w]e believe that it is appropriate and will serve the Company's best interests in the future." Before Salesworks was updated, TAD Hatch told TAMs in her district not to use the "c-word," meaning TAMs should not discuss "conversion" marketing Rapamune when reporting on sales calls in Salesworks. In a May 22, 2002 email, Ms. Hatch also told her TAMs "[i]n the future, all weekly updates should be written in the 3rd person. IE. [sic.] that which the center or clinician is doing; not what you are doing." Relator Sandler understood this to mean that rather than writing that a physician had been convinced by the TAM to use Rapamune off-label, weekly updates should be written to make it appear that the physician had independently decided to use Rapamune for off-label purposes. By early 2005, Mr. McCafferty also told TAMs not to use the term "stable maintenance." Relator Sandler understood Mr. McCafferty's instructions to mean that TAMs should not report on their efforts to convert stable maintenance patients, not that they should suspend their efforts to market the drug in conversion protocol to physicians treating this group of patients.

138. At least through 2007, Wyeth actively marketed off-label conversion regimens throughout the country. In support of this strategy, Company sales records for Rapamune use in kidney transplant recipients, including the records on which Transplant Account Managers' bonuses are calculated, were divided into categories labeled *de novo*, "up to 7 months," and "after 7 months" conversion sales figures. Joe McCafferty noted in an email to the Rapamune sales force dated October 11, 2005 that the monthly metric report showing growth in the overall

kidney market share for Rapamune came in at "two distinct time points" – one, at *de novo* use, and the other at the two year or later time point. Similarly, an email dated May 15, 2005 from McCafferty attached several market reports, including TAM sales, compensation, and patient market repair forms, and informed them that several centers had reworked their drug protocols to incorporate delayed introduction of Rapamune.

139. In addition, as detailed in Section C *infra*, Wyeth also offered health care institutions and health care professionals kickbacks in the form of, but not limited to, donations, grants, and speaker fees to incentivize these health care professionals to prescribe Rapamune for off-label purposes.

3. Wyeth Marketed Rapamune In Combination With Other Drugs Not Encompassed By Rapamune's Package Insert

140. From the launch of Rapamune in 1999 until at least 2007, Wyeth encouraged its Rapamune sales force to engage in a number of marketing schemes that promoted Rapamune's use with drugs other than cyclosporine and steroids (*i.e.*, the only approved combination).

141. In general, FDA-approved immunosuppressant regimens for patients receiving transplants, such as kidney transplants, require the use of more than one drug in combination. This is because drugs used to suppress the immune system after a kidney transplant in order to keep the body from rejecting the new kidney are very strong and when used by themselves in high doses, cause very serious side effects including death. For that reason, most immunosuppressant regimens currently approved by the FDA require the use of multiple agents in lower doses in order to reduce the likelihood that patients will suffer serious side effects. As discussed above, Rapamune is only approved in combination with cyclosporine and steroids.

142. At the time of Rapamune's launch in 1999, Relator Sandler learned that a significant number of kidney transplant physicians had moved away from the use of cyclosporine

(an older generation immunosuppressant) to other newer immunosupressants, including but not limited to, tacrolimus (manufactured by Astellas under the trade name "Prograf" and also referred to as "FK") and mycophenolate mofetil (manufactured by Roche under the trade name "Cellcept" and also referred to as "MMF"). In order to combat the concomitant challenges of convincing kidney transplant physicians to use Rapamune, a new drug with an unproven track record, steroids, and cyclosporine (an older drug that was used less frequently), Wyeth trained and instructed its Rapamune sales force to market Rapamune in combination with any drug or combination of drugs that a physician could be convinced to prescribe. Specifically, Wyeth managers instructed the Rapamune sales force to market Rapamune as an "add on," meaning that the sales force should suggest to physicians that Rapamune could be used along with any other drugs, including Cellcept and Prograf, either *de novo* (*i.e.*, as soon as possible after transplant) or in other off-label "conversion" regimens. Wyeth mangers also encouraged TAMs to market Rapamune use for *de novo* patients without the use of cyclosporine or without the use of steroids.

143. The training of TAMs to market Rapamune in combination with drugs other than cyclosporine and steroids began before the launch of Rapamune. At the Prelaunch Meeting Agenda for the Northeast Transplant Team notes show that on September 8, 1999, Wyeth presented a session for TAM education called, "Launch Presentation Practice and Fine Tuning, Rapa with FK." In an email from TAD Hatch to Wyeth MSL Lynn Fallon a month before the "Prelaunch Meeting" (on August 10, 1999), Ms. Hatch explained the September 8, 1999 session pertaining to the use of Prograf and Rapamune further. Specifially, Ms. Hatch wrote to Ms. Fallon, "I have greatly appreciated your imput [sic] in helping plan Zone 1's [Northeast Transplant Team] Prelaunch/Launch Plan with respect to staff education, launch workshops, and acct bus [account business] planning … We've got 2 Hot!! Topics – Going for the Maintenance

Population and use with FK. Based on our plan, we should blow the doors off" (Emphasis in original).

144. TAMs followed through with Wyeth's instructions to off-label market Rapamune in combination with drugs other than cyclosporine, including Prograf. A 2001 business plan created by TAM Kim Owen stated that her 2001 "account goals and action steps" included a plan to encourage Strong Memorial Hospital to "start replacing MMF [Cellcept] with Rapamune on the *de novo* renal protocol and additional maintenance protocols. INSTEAD OF REPLACE [sic.] MMF LET SAY ESTABLISH [sic.] RAPA AS PRIMARY AGENT WITH LOW DOSE OF FK [Prograf] AND STERIODS." (Emphasis in original). Ms. Owen's business plan noted that Strong Memorial Hospital/University of Rochester, in Rochester, New York, was an "FK-based center," meaning that "FK is firmly entrenched in all protocols as primary immunosuppresssant- 'comfort zone.'" In short, TAM Owen encountered problems marketing Rapamune, in combination with cyclosporine and steroids, and thus formulated a plan – approved by her managers – to encourage physicians at Strong Memorial to use Rapamune in combination with FK (Prograf) in their protocols.

145. Another marketing slogan Wyeth encouraged TAMs to use in marketing Rapamune in unapproved combinations was "A CNI is a CNI," which meant that transplant physicians need not be limited to cyclosporine (a calcineurin inhibitor) but could use any calcineurin inhibitor in its place, such as Prograf. However, Rapamune has never been approved for use in combination with any CNI except for cyclosporine. This marketing ploy and slogan have no basis in Rapamune's FDA package insert.

146. Starting in about 2003, Wyeth managers also seized on Rapamune's new FDA-approved dosing regimen that allowed for withdrawal of cyclosporine after 2-4 months of

treatment for low-risk kidney transplant patients receiving Rapamune, cyclosporine and steroids *de novo* (or as soon as possible after kidney transplant) to encourage its TAMs to off-label market Rapamune for use with drugs other than cyclosporine and steroids. In this marketing scheme, Wyeth claimed that because the cyclosporine could be withdrawn in low to moderate kidney transplant patient after 2-4 months, Rapamune was therefore a "foundation drug," and as such could be used in combination with other drugs. The term "foundation drug" was not approved by the FDA and is not mentioned in Rapamune's package insert. The term was invented by Wyeth merely as a marketing ploy to increase sales of Rapamune in a competitive climate where physicians were hesitant to change their standard treatment regimens to include Rapamune.

147. Wyeth also paid physicians to speak about off-label combinations of Rapamune in order to convince other physicians to follow suit. TAMs were encouraged to develop potential speakers for national and local lectures on off-label uses, including unapproved combinations of Rapamune. TAD Hatch wrote in an email entitled "Weekly Update" to Joanne Crowley, on October 11, 2002, that in Maine, "Dr [sic.] Allan McDonald to speak on 12/16/02. Dr [sic.] Vella rethinking rapa/fk/pred [Rapamune, Prograf and prednisone] in a more favorable light. Dr. [sic.] MacDonald should help."

148. A speakers list also provided TAMs with a number of physicians who Wyeth engaged to speak on off-label combination uses to be used by TAMs in their marketing efforts. The speakers list includes approximately 18 physicians, including the following speakers and topics: (1) Dr. John Fung, a liver transplant physician at the University of Pittsburgh, who is listed with the terms "Rapa/FK" (*i.e.*, Rapamune and Prograf) (2) Dr. David Conti, Albany Medical Center, who is listed with the terms "[c]onversion experience w/ Rapa/MMF for

Chronic rejection;" (3) Dr. Rob Corry, a Pancreas transplant physician at the University of Pittsburgh, who is listed with the terms "Rapa/FK" (Rapamune and Prograf).

149. The speakers list also indicated that Dr. Stuart Flechner was available to speak on the use of Rapamune with Cellcept and IL2R ("an interleucken-2 receptor antagonist" or "IL-2 receptor" which is used also to prevent organ rejection) for "de novo protocol for low risk renal transplants" for an honorarium of $2000 or "prorated $15000."

150. With guidance from his manager, Relator Paris engaged Dr. Flechner to speak to kidney transplant physicians at Mt. Sinai Medical Center to discuss his protocol using Cellcept, IL-2 receptor antagonist and Rapamune. The physicians at Mt. Sinai had concerns that about using Rapamune with cyclosporine in any regimen because they believed that cyclosporine caused rejections. Wyeth paid Dr. Flechner to assist in the marketing of the unapproved combination of Cellcept, an IL-2 receptor antagonist and Rapamune in order to overcome these objections and secure Rapamune sales.

151. Wyeth marketed Rapamune in combinations not approved by the FDA, including the regimen proposed by Dr. Flechner, even though it did not have sufficient data to gain additional indications for the use of Rapamune with drugs other than cyclosporine and steroids. Wyeth's marketing efforts flatly disregarded the safety of renal transplant patients who were already placed at a significant disadvantage, in terms of overall health, caused by their transplants and the conditions that necessitated transplant. Specifically, by at least 2007, the "Warnings and Precautions" section of Rapamune's package insert was modified to warn against Rapamune's "*de novo* use without cyclosporine." Currently, Rapamune's package insert at section 5.12 states:

> The safety and efficacy of *de novo* use of Rapamune without cyclosporine is not established in renal transplant patients. In a

> multicenter clinical study, *de novo* renal transplant patients treated with Rapamune, myclophenolate mofetil (MMF), steroids and an IL-2 receptor antagonist had significantly higher acute rejection rates and numerically higher death rates compared to patients treated with cyclosporine, MMF, steroids, and IL-2 receptor antagonist. A benefit, in terms of better renal function, was not apparent in the treatment arm with *de novo* use of Rapamune without cyclosporine. These findings were also observed in a similar treatment group of another clinical trial.

152. This warning indicates that the Cellcept, Rapamune, IL-2 receptor antagonist and steroid protocol, similar to that advanced by Dr. Flechner in speeches paid for by Wyeth, actually caused significantly higher acute rejection and death.

153. A pharmaceutical company may provide speakers to educate and provide information to physicians on its products; however, when a pharmaceutical company directs, influences, and/or mandates the information or topics discussed by speakers at the educational program, an ostensibly "educational event" can be transformed into a vehicle for marketing. In these situations, the discussion of off-label uses of a drug by the speaker is considered "misbranding" the drug.

154. In addition, as detailed in Section C below, Wyeth also offered health care institutions and health care professionals kickbacks in the form of, but not limited to, donations, grants, and speaker fees to incentivize these health care professionals to prescribe Rapamune for off-label purposes.

4. Wyeth Targeted High-Risk African-American Patients For Off-Label Uses Despite Insufficient Data Concerning High-Risk Patients

155. Wyeth Transplant Team management was aware that there was limited data for Rapamune use in high-risk patients and/or African-American patients. African-American transplant recipients are considered high-risk because they exhibit more vigorous immune responses to transplants than other patient groups. Some physicians in Relator Paris' sales

district, were concerned that the combination of Rapamune, cyclosporine and steroids lacked efficacy in African American or high risk patient groups and believed that that if higher levels of the approved combinations were used, serious side effects would result.

156. Wyeth's 2002 Division Business Plan, "SWOT Analysis" ("Strengths, Weaknesses, Opportunities, and Threats"), lists as a Threat: "Limited data on use in high risk and special populations (African-American, Pediatric)." Another Threat listed is: "Limited data to support *de novo* dosing regimens -- FK, MMF, Induction agents."

157. Despite limited data on high-risk patients, Wyeth targeted transplant centers that catered primarily to African-American patients, typically in urban areas. In 2005, Wyeth's sales management (headed by National Director of Transplant Sales Joe McCafferty) selected Philadelphia's Einstein Medical Center as a center on which to focus a Wyeth marketing plan designed to rapidly increase or accelerate Rapamune sales in a 90 day period. Einstein's transplant patient population was approximately 75% African-American in 2005.

158. Wyeth management targeted SUNY Downstate Medical Center, whose patient population was in 2005 and still is predominantly African-American, for conversion protocols. Wyeth management arranged for Baltimore physician Dr. Walli to present to SUNY Downstate transplant staff his experiences in converting African-American patients to Rapamune, even though no approved data exists to show that conversion was safe or effective in high-risk patients. Dr. Walli reported some success with conversion in African-American patients. He also disclosed, when questioned, that he found an organ rejection rate of approximately 50% among the African-American patients he tried to convert to Rapamune. When questioned about the outcomes of those African-American patients who had experienced organ rejection, Dr. Walli had no data to support this conclusion. Several nephrologists at SUNY Downstate told Mr. Paris

that they were reluctant to convert African-American patients to Rapamune because no data existed to show that conversion to Rapamune was effective in high-risk patients.

159. Wyeth Managers also instructed TAMs to use journal articles, including one called "Outcomes of African American Kidney Transplant Recipients Treated With Sirolimus, Tacrilomus, and Corticosteroids," published in TRANSPLANTATION July 2002 by Dr. Donald Hricik *et al*., to off-label market Rapamune to African-Americans for combinations that were not approved by the FDA. The study describes the outcomes of 56 African-American transplant recipients treated with Rapamune, tacrolimus and steroids and compares this regimen to a group of 65 white patients treated with tacrolimus, mycophenolate mofetil (MMF) and steroids. The study results indicated that Rapamune used with lower doses of tacrolimus and steroids showed equivalent results compared to the Caucasian people studied with regard to acute rejection, graft survival, and patient survival. The combinations of Rapamune examined in this study are not approved in the Rapamune package insert.

160. Relator Paris was directed by Wyeth mangers to use Dr. Donald Hricik as a speaker to encourage transplant physicians to prescribe Rapamune in unapproved combinations for African-American patients.

161. Wyeth's business and marketing plans demonstrate that it continued to target transplant centers with significant African-American patient populations despite the dearth of data on this large patient pool.

162. In addition, as detailed in Section C *infra*, Wyeth also offered health care institutions and health care professionals kickbacks in the form of, but not limited to, donations, grants, and speaker fees to incentivize these health care professionals to prescribe Rapamune for off-label purposes.

5. In Using Transplant Science Liaisons To Further Rapamune Sales, Wyeth Management Disregarded Its Own Policies Proscribing Such Conduct In Its Pursuit Of Off-Label Revenue

163. Like other pharmaceutical companies, Wyeth employed a staff of medical professionals, called Transplant Science Liaisons or Medical Science Liaisons. The purported job function of TSLs was to provide specialized scientific and medial information (which could not be presented by Wyeth's sales force) about Rapamune to physicians seeking information about the drug. TSLs may present any data about Rapamune, including information on off-label uses, provided that the physician initiated the query unsolicited. Many physicians view TSLs as non-sales professionals that are a source of unbiased information. Instead of using its TSLs to meet the legitimate needs of physicians seeking important information about Rapamune, Wyeth used them to assist its sales team in marketing Rapamune for off-label uses. While it is permissible for TAMs to direct unsolicited off-label questions initiated by physicians to TSLs, Wyeth actively and openly encouraged TAMs to first discuss off-label uses of Rapamune to physicians and use Wyeth TSLs in further meetings with physicians to promote those uses.

164. Wyeth managers, including TAD Hatch, encouraged TAMs to use TSLs to assist in efforts to market Rapamune for off-label uses, including for off-label extra-renal use. In a weekly update to her manager dated March 24, 2002, Relator Sandler wrote:

> Alka [a Wyeth TSL] presented Rapa data to [the] heart transplant division at HUP and Temple with positive results – new Rapa Rx's from docs who previously had no interest in using our product.

165. In 1999, Lynn Fallon discussed meeting with various liver transplant surgeons in her field contact reports, stating that liver transplant surgeons were excited about using Rapamune for liver transplant patients. She further documented her discussions of various off-label drug combinations with these same surgeons. Although TSLs are prevented from engaging

in marketing activity, Fallon's report makes it appear that she is engaging inappropriate marketing activity.

166. TAM George Zorbas' business plan for St. Barnabas Hospital indicated how the TAM used TSL involvement to market Rapamune off-label for heart and lung transplant patients:

> Use of the TSL: Neal Wasserman and I have the best working relationship of any TAM and TSL. I use Neal's presence for affect or impact in certain situations where there may be a possibility to discuss a study opportunity for growth of the commercial business. When doing inservices to hear or lung transplant units, I have invited him for emphasis. He is a valued partner in my territory.

167. Unlike TAMS, who are sales representatives and therefore prohibited from discussing data regarding off-label uses of pharmaceuticals, Wyeth's TSLs – some of whom were pharmacists or nurses -- could legally disseminate and discuss data relating to off-label drug uses *if they receive an unsolicited request* from a physician or other health care professional. Wyeth written policy requires TAMs to forward all requests for such medical information to their TSLs, who in turn provide the requested information to the physician or health care professional. TSLs exist to answer medical questions that physicians may have about the drug; because of their access to and ability to discuss medical data relating to off-label uses of prescriptions drugs, TSLs are not part of the sales force and are not permitted to participate in sales and marketing efforts.

168. Wyeth's official policy forbade TAMs from soliciting off-label medical requests from physicians for the TSL's but Wyeth managers encouraged TAMs to proactively discuss off-label uses with physicians and then suggest that the physician request information from TSLs. In about 2006, TAMs' bonus criteria included compensation based in part on the number of medical requests they garnered from physicians.

169. Wyeth Managers directed TAMs to work closely with their TSLs to develop marketing strategies, gain Wyeth paid study placements at selected hospitals based on Wyeth's sales needs, select medical speakers, and accompany TSL meetings with transplant centers and hospitals in order to actively market Rapamune for on-label and off-label uses. TSLs also presented off-label lectures to physicians in conjunction with TAMs' marketing efforts. TSLs also helped coach physicians or created slide decks for physicians paid by Wyeth to speak on off-label uses of Rapamune. Wyeth mandated business plans approved by management and shared among TAMs to contain plans to "maximize" TSL involvement in sales efforts. TAD Hatch required TSLs Neal Wasserman and Alka Somani to provide activity reports to Hatch even though they were in the medical affairs division of Wyeth and she did not technically supervise their work.

170. In sum, Wyeth blended the marketing, sales and medical affairs divisions within the company to increase off-label sales of Rapamune.

171. There was significant conflict between the medical unit and the sales unit regarding the blatant off-label marketing activity. Some of the TSLs felt it was unethical to assist in Wyeth's illegal marketing efforts Wyeth directed them to engage in. As a result, some TSLs reported TAMS to upper level management for off-label marketing, documenting behavior such as the TAM having off-label discussions with physicians, then bringing the TSL in to handle ideas that were precipitated by the TAM, not the physician. In turn, TAMs complained that the Sales and Marketing group pushed them to focus on conversion, and a heavy portion of their compensation depended on off-label marketing.

172. Wyeth's improper use of medical reference representatives as sales tools caused false claims to be submitted to federal and state health care providers by promoting the off-label use of Rapamune.

6. Wyeth Trained Its Sales Force To Market Rapamune For Off-Label Uses

173. Wyeth trained all sales representatives to market Rapamune for both on-label and off-label uses through a course of home study; formalized training at Wyeth's headquarters in Collegeville, Pennsylvania; formalized training sessions at Rapamune annual and semi-annual national and district conferences; informal district meetings held by TADs throughout the year; and informal "Journal Club" meetings, often held weekly by TADs.

174. As stated, Wyeth's managers also used the business plans created by the TAMs and TADs and presented them at national and district meetings and informally throughout the year as training tools and examples of marketing techniques. The business plans, as detailed *supra*, often contained information regarding off-label marketing activities, including conversion, off-organ promotion, inappropriate marketing of unapproved drug combinations, and marketing for high-risk populations that were not covered under any approved Rapamune indication. Circulating these business plans also provided pressure on other sales representatives to replicate these tactics in their respective regions.

175. Wyeth provided off-label information to its Rapamaune sales force in the form of studies and other materials. While the training materials state they are unapproved for use with customers, Wyeth ensured that the sales force would have the necessary knowledge to address off-label questions in the field. There is no other reason for this type of training to be provided to sales representatives. For example, Wyeth created a detailed training module for the field representatives which discussed how Rapamune should be used in special patient subsets, such

as high-risk patients, pediatric patients, and rescue patients. Rapamune has never been approved for use in these patient populations, but the training slides instruct the field representatives on how to present the scenario, identify the problem or issue, explain how Rapamune fits the need, and how to anticipate the customer and competitive response.

176. Wyeth also used "Journal Clubs" to discuss medical journal articles that were not approved for detailing. Journal Club meetings were usually held by telephone conference call amongst TAMs in a single district with their TAD; often TSLs were present at the meetings. For Journal Club meetings, TAMs were assigned the task of reviewing a journal article, assessing its possible use in marketing Rapamune, and presenting their "conclusions" to the group. After the presentation, the group discussed the "conclusions" and TAMs were expected to use the information in marketing to transplant physicians. TAMs, TADs and other Rapamune sales personnel were not physicians and the "conclusions" they reached had no basis in Rapamune's package insert.

177. TAMs also used Wyeth approved studies to market Rapamune to physicians for both on-label and off-label uses. Even when Wyeth presented articles that were approved for sales use, representatives were taught to "cherry pick" information, painting a false picture of Rapamune's efficacy and safety.

178. TAMs also used Wyeth-approved slide decks, ostensibly designed for physicians to use when presenting lectures on Rapamune, to detail physicians on off-label uses. In many cases, TAMs were encouraged to mix information contained in slides from various approved slide decks to create off-label slide presentations to be used in marketing Rapamune to transplant physicians. The "homemade" slide decks were presented and practiced in role plays at national

and district meetings as teaching tools for TAMs. Relator Sandler was asked by Wyeth management to present a "homemade" slide deck at a national POA meeting in 2005.

7. Wyeth Urged And Encouraged Representatives To Attend Hospital Rounds And Engage In Patient Care Conferences With Hospital Personnel

179. Wyeth's managers, including National Director of Transplant Sales, Jim Meyer and his successor Joe McCafferty, strongly urged and encouraged attendance by TAMs on hospital rounds. From 1999 through at least 2003, Wyeth TAMs routinely accompanied transplant physicians on hospital rounds, sometimes wearing white lab coats. Some physicians introduced the TAMs to patients as pharmaceutical sales representatives, but others said nothing about them to their patients. Occasionally, TAMs even attended transplant surgeries. After rounds, TAMs frequently attended physicians' meetings during which the physicians would discuss patients' treatment regimens. During these meetings, TAMs often suggested that specific patients might benefit from Rapamune as part of their treatment regimens.

180. As part of Mr. Paris's sales training in 2002, Wyeth arranged for him to accompany doctors on hospital rounds and encouraged him to gain access to clinical discussions with transplant physicians. Relators also attended transplant surgeries. Not until sometime in 2003 did Wyeth management instruct TAMs to cease attending rounds at transplant centers.

C. KICKBACKS: WYETH PAID PHYSICIANS AND MANIPULATED RESEARCH GRANTS AND CONTINUING MEDICAL EDUCATION SPEAKER PROGRAMS TO ILLEGALLY INCREASE RAPAMUNE PRESCRIPTIONS

181. Wyeth offered hospitals, transplant centers, and individual physicians kickbacks in the form of donations, funding research "grants-in-aid" (single-center clinical trials) and speaker fees in exchange for increased prescriptions of Rapamune for both on-label and off-label uses.

1. Wyeth Paid Kickbacks To Physicians Through Speaker Programs And Continuing Medical Education Events

182. Pharmaceutical companies are allowed to engage speakers to educate and provide information about their products to physicians. Physicians or hospitals may also request an unrestricted educational grant from a pharmaceutical company, including funds to pay for Continuing Medical Educational programs ("CME") or other educational programs. However, payments to physicians or hospitals for the purpose of unlawfully influencing prescription sales are deemed kickbacks and are unlawful.

183. Wyeth improperly used CMEs and other speaker's events to reward physicians for prescribing Rapamune. Prior to 2003, Wyeth operated two speaker programs: (1) Wyeth's Visiting Speakers Bureau or "VSB" and (2) a CME speakers program. Wyeth paid speakers honoraria, travel, hotel, and meal expenses, to lecture physicians and Wyeth personnel. While speakers typically received $1,500 to $2000 per lecture, some speakers were paid up to $10,000 per lecture. Dr. Barry Kahan, a kidney transplant surgeon from Houston, Texas, received $6,000 per lecture.

184. Wyeth targeted physicians who helped market Rapamune for both on-label and off-label uses. In a 2002 Business Plan written by Rich Reed, for the New Haven area, one page was devoted to "2002 Targeted Clinician Development," "2002 Targeted Clinician Penetration Goals" and "2002 Targeted Transplant Centers." The tables contained data on the prescribing habits of certain physicians, whether these physicians were "advocates" or "partners" for Rapamune, what percentage of their prescriptions were for Rapamune, goals that were set for 2002 based on 2001 prescribing data, and the overall goals for certain targeted transplant centers in the New Haven area.

185. An April 15, 2000 memo by TAM Kim Owen demonstrated Wyeth's strategic thinking in selecting physicians to partner with in the Company's scheme to market Rapamune for off-label use. For example, Dr. Conti of Albany Medical Center, Albany, New York, was reluctant to use Rapamune in any setting other than a single-center study. TAM Owen justified giving Dr. Conti the study as "a wise business decision" because, among other things, Dr. Conti was considered an "influential opinion leader," a physician able to persuade others to write prescriptions for the drug, which the memo explained was worth $200,000 per year in sales.

186. Wyeth selected physicians who would speak favorably about the drug's potential off-label uses. TAD Hatch described a dispute with a coworker on May 30, 2001, in which her choice of physician speaker Marc Lorber, then of Yale University, was dismissed because he was seen as "too neutral." Instead, Dr. Francesca Egidi was selected as a speaker "because of her experience with conversion."

187. Through aggressive marketing, Wyeth persisted in its effort to change physicians' views. Dr. Marc Lorber of Yale, for example, was dismissed as "too neutral" in 2001, but in 2000, TAD Hatch noted that Dr. Lorber had been "developed" by sales representative Rick Reed from a resistant physician into one of Wyeth's most effective [cyclosporine] using advocates."

188. Wyeth rewarded physicians who said "the right things" as Rapamune advocates and speakers. Relator Sandler stated in a September 20, 2002 weekly update that she was targeting Dr. Simon Goral as a speaker because she "has an excellent grasp of the data and is targeting patients for Rapa conversion." Joe McCafferty circulated an e-mail in September, 2000 stating, "The Rapamune speakers list is attached . . . the list will grow as more clinicians gain experience with Rapamune. The list is divided into two sheets at this point – kidney and liver speakers."

189. Prior to 2003, National Director of Transplant Sales Jim Meyer and the TADs developed preferred speaker lists that included heart, liver, and lung transplant specialists as well as nephrologists and kidney transplant specialists. A University of Pittsburgh pediatric liver surgeon, Dr. Rakesh Sindhi, participated so frequently in Wyeth's speakers program, promoting Rapamune's off-label uses in liver and pediatric transplant patients as well as kidney conversion protocols, that his hospital placed a limit on the honoraria he could receive from Wyeth.

190. Wyeth managers developed a speakers list that highlighted each speaker's preferred use of Rapamune to treat kidney transplant patients, including but not limited to, Rapamune's use (1) in unapproved combinations (*i.e.*, other than Rapamune with cyclosporine and steroids); (2) in various stages post-transplant such as *de novo*, "delayed start" or maintenance/conversion protocols; and (3) in various populations, such as "high risk" patients including African-Americans.

191. Wyeth managers, including Joseph McCafferty, informed TAMs and TADs when speakers from the "VSB" were scheduled to "tour" their geographical sales regions to perform lectures. Wyeth managers encouraged TAMs to book these touring speakers for as many engagements as possible. Relator Sandler and other TAMs routinely booked these speakers for four lectures over a two day period. In 2005, Joe McCafferty sent an email to TAMs and TADs encouraging them to use a particular physician who had complained to Wyeth management that Company TAMs failed to engage him frequently enough for paid lectures.

192. Wyeth's CME speaker program was designed to provide presentations to hospitals requesting information on specific topics. Wyeth managers encouraged TAMs to approach physicians and suggest programs and speakers who might be of interest to their transplant operations, for both on-label and off-label uses of Rapamune.

193. Up until about 2003, Wyeth paid CME and VSB speakers directly. Thereafter Wyeth began funneling payments for lectures through an intermediary called Institute for Continuing Healthcare Education (the "ICHE") and other third party vendors. Wyeth's change in policy regarding the mechanism for paying speakers was part and parcel of a larger written policy, which purported to sever the promotional arms of the Company from the scientific arms of the Company by, among other things, prohibiting the Rapamune sales force from selecting speakers and molding the "message." Wyeth's speaker's policy, however, was nothing more than window dressing designed to conceal the Company's efforts to unlawfully reward physicians for prescribing Rapamune. In reality, Wyeth orchestrated a scheme to determine which physicians would speak at ICHE events. Wyeth management was able to exclude speakers who did not promote Rapamune, and reward those who did so with repeated speaking engagements and resulting honoraria.

194. Wyeth's Transplant Team management required TAMs to attach to every suggestion or request for a speaker a hand-written Return-on-Investment or "ROI" analysis that predicted the immediate or long-term potential increase in Rapamune market share or account development that could be achieved as a result of each presentation. Management explicitly required the Return-on-Investment analyses to be hand-written and not part of the speaker request itself.

195. After each speaker's presentation, Wyeth Transplant Team management required the TAM responsible for requesting the speaker to write a review of the presentation, including the speaker's attitudes and views about Rapamune. If the speaker's presentation included remarks that were unfavorable or even unenthusiastic toward Rapamune, Wyeth managers

required TAMs to contact the speaker to question the speaker about his remarks and to suggest ways in which the speaker might treat Rapamune more favorably.

196. According to a Wyeth internal document, "Visiting Speakers Bureau: General Guidelines for Promotional Programs": "[A]ny speaker we support is subject to the same regulations that prohibit our sales force from promoting Wyeth products for unapproved uses or in any way that is false and misleading. Only the approved indications for our products may be discussed during the lectures and presentations involving products and must be within approved labeling." In reality, Wyeth speakers rarely restricted their talks to approved slide decks and usually discussed and promoted Rapamune's off-label uses. Management attended these presentations and never complained of the off-label presentations, nor did managers do anything to restrict off-label discussions.

197. As an example of Wyeth's control over paid speakers, National Director of Transplant Sales, Jim Meyer, instructed his Area Account Directors in a December 12, 2002 e-mail: "Please see attached. His talk confirms what Joe and I saw in Philly. Do not use D.K." The attachment states: "He views Rapamune and Cellcept [an alternative treatment regimen to Rapamune] as equivalent in performance in solitary kidney transplantation. Clearly, he does not view Sirolimus as base therapy referring to high AR rates [acute rejection rates] with Alan Kirk and Stuart Knectle CI sparing studies." Wyeth personnel were thereafter instructed not to use this speaker, demonstrating one method by which Wyeth marketing managers hand-picked speakers and rejected others based on their willingness to promote Rapamune off-label.

198. Moreover, Relator and other TAMs were encouraged to hold "Rapamune Day," where key heart, liver and kidney transplant specialists at a specific transplant center were invited by Wyeth to meet managers and executives from Wyeth's research and development,

medical affairs department, sales, and marketing departments. TAMs and TADs also attended. The purpose of Rapamune Day was to discuss funding for the transplant center, study needs, patient management issues, and sales issues with physicians. In other words, Wyeth and the transplant center would find way to meet each other's needs.

199. Wyeth also sponsored "All City" Transplant Programs in which key transplant physicians from an entire metropolitan area were invited to attend a CME dinner and roundtable, ostensibly sponsored by third parties such as a Transplant Center or hospital, but paid for and primarily developed by Wyeth. For example, Relator Sandler conducted annual All City Transplant Programs in the greater Philadelphia area, often "sponsored" by Jefferson Hospital, which were really paid for and orchestrated almost entirely by Wyeth. Jefferson Hospital had some input in the event, but left most of the important decisions about the program to the discretion of Relator Sandler who handpicked the speakers, selected the topics to be discussed, and devised the list of key physicians invited to attend. The speakers' topics often included off-label uses of Rapamune, including but not limited to extra-renal uses. Wyeth provided Jefferson Hospital with the funds to pay honoraria to the speakers. All City meetings were attended by senior Wyeth sales and marketing managers for the purpose of using the All City event as a vehicle to market Rapamune. In this way, Wyeth used Jefferson Hospital as a conduit to conduct illegal CME speaker programs designed to market Rapamune for both on-label and off-label uses.

2. Wyeth's Payment For Grants And Placement Of Paid Studies Were Designed To Improperly Influence Physician Prescribing Of Rapamune

200. Wyeth targeted transplant centers as well as physicians. In a March 11, 2001 memo, Jim Meyer wrote to TADs asking them to identify accounts (transplant centers) that they wanted targeted for future Phase IV activity, in the form of trials for either *de novo* or conversion

protocols. Mr. Meyer asked the TADs to rank their accounts in order of importance to their zone, both from a commercial and from an influential perspective. Wyeth kept charts of Rapamune's status at various centers, including the rank of the center in terms of number of transplants conducted, how many patients were on Rapamune, and whether the center followed a maintenance protocol in addition to a *de novo* protocol.

201. Wyeth provided inappropriate funding to hospitals and physicians in exchange for increased market share of Rapamune. For example, in an effort to increase Rapamune's market share in liver transplant departments, Wyeth donated at least $4,000.00 per year in the years 2001, 2002, and 2003 to Dr. Emry, the Director of pediatric liver transplants at Mt. Sinai and Mt. Sinai's liver transplantation program in New York. In 2004, Wyeth also agreed to sponsor a pediatric liver conference at the request of Dr. Emry. Wyeth's efforts to improperly influence the prescribing habits of Dr. Emry and other physicians at Mt. Sinai also put patients at increased risk of serious injury and death. Wyeth had never established the efficacy and safety of Rapamune's use as a immunosuppressive therapy for liver transplant patients and, at the very least, knew by January 2003 that the side effects were so serious for liver transplant patients that a "black box" warning was required. Specifically, the FDA's warning states the use of Rapamune for use in liver transplant patients "is not recommended." *See* Wyeth Package Insert at 5.2. The "Warnings and Precautions" section of Rapamune's package insert also describes the statistically significant incidences of excess deaths, Hepatic Artery Thrombosis ("HAT"), and graft loss occurring in three studies. These studies included regimens where Rapamune was used (1) *de novo* with cyclosporine (similar to its approved use for kidney transplant patients); (2) *de novo* with tacrolimus (another calcineurin inhibitor like cyclosporine); and (3) in a "conversion"

protocol where stable liver transplant patients who were previously on a calcineurin based regimen were switched to Rapamune 6-144 months after transplant.

202. An internal Wyeth spreadsheet from about 2002 called "Grants In Aid" indicates that approximately 35 separate Rapamune trials were approved for physicians among Wyeth's four Rapamune sales districts. While Wyeth only provided free drugs for some of the studies, the majority were paid studies, in which some of the physicians and/or hospitals conducting these studies received as much as $300,000 to $400,000. The Grants In Aid document indicates that approximately $7 million was being spent at this time for these studies collectively. The 2002 spreadsheet also tracks the number of prescriptions that were being written at the centers in which Wyeth had paid Grants in Aid.

203. In studies where Rapamune was not provided free of charge from Wyeth, the Company also stood to profit from prescription sales. For example, a February 11, 2000 memo from Wyeth TSL Neal Wasserman to Wyeth Senior Director of Global Strategy for Rapamune, Robin Gasoli, noted in a request for funding for Albany Medical Center that "[t]he business potential for the product with this study is also significant. Assuming an average dose per patient of 2.5mg/day … we can anticipate annual sales of $378,000 year one, and $366,950 year two."

204. Other forms of compensation, such as gifts, were also used to induce physicians to prescribe Rapamune. A 1999 letter from Dr. Brayman, of the University of Pennsylvania, to Wyeth's Larry Bauer thanked Mr. Bauer for Cuban cigars. Mr. Bauer's written notes on the letter (which were forwarded in hard copy to Gino Germano, and copied to Jim Myer (Wyeth National Director of Transplant Sales), TAD Hatch, and Relator Sandler) stated, "The skids are greased!!" Mr. Bauer's handwritten notes also indicated that the value of the cigars was

$350.00. Mr. Bauer wrote, "I can't expense them since they are from my personal collection. You [TAD Hatch] and Marlene will just have to make him 'work it off.'"

205. Wyeth also purchased an IMX Platform Assay machine that cost at least $150,000.00 for the University Pennsylvania, where Wyeth wanted to form an allegiance with a prestigious transplant center.

206. Wyeth's conduct regarding CME presentations and grants also violated the Stark Law. 42 U.S.C. § 1395nn(a)(1), (h)(6). Stark prohibits payment of Medicaid claims for prescriptions rendered in violation of its provisions. 42 U.S.C.§ 1395nn(a)(1), (g)(1). The honoraria, donations, and grants described above created non-exempt financial relationships between Wyeth on one hand and hospitals and physicians on the other, and therefore violated the Stark Law.

D. SIGNIFICANT PATIENT HARM HAS RESULTED FROM WYETH'S AGGRESSIVE OFF-LABEL MARKETING OF RAPAMUNE

207. Off-label use of Rapamune has resulted in documented harm to patients.

208. Rapamune exacerbates three serious and possibly life-threatening side effects of transplant surgery: proteinuria, which always reflects kidney damage; liver failure; and delayed wound healing, which increases risks of infection (especially dangerous because immunosuppression therapy is designed to compromise the patient's ability to fight infection). Rapamune also exacerbates anemia, which occurs dramatically more frequently in patients taking Rapamune than in those on other treatment regimens. Other documented side effects of Rapamune are thrombocytopenia, bone-bone arthralgia, edema, leukopenia, mouth ulcers, and hyperlipidemia.

209. Management directed TAMs to minimize Rapamune's role in documented increased cases of proteinuria and anemia. TAD Hatch repeatedly told Wyeth TAMs that if

doctors really wanted to use Rapamune, they would "work through the side effects" and "push on through to the other side" for the patient's benefit. However, there is no evidence that continuing to use Rapamune despite the side effects benefits patients in any way. Nevertheless, Wyeth urged its sales force to market Rapamune for off-label uses despite life-threatening side effects caused and exacerbated by the drug.

210. In conversion protocols, patients may also suffer harm by being unnecessarily removed from treatment regimens that are already working or showing promise of working after their transplants. Often, when the patient is converted to Rapamune, there are side effects, including one or more of the those mentioned above, that were not suffered as part of the original treatment regimen.

211. Kidney transplant recipients receiving treatment regimens marketed by Wyeth have died. A nephrologist at Columbia University Hospital has stopped converting kidney transplant recipients to Rapamune-based treatment regimens because of adverse events and patient deaths associated with Rapamune.

212. Dr. David Alexrod from Mary Hitchcock Hospital also reported that some of his patients converted to Rapamune and Cellcept developed infections very quickly, some of which were life threatening.

213. Wyeth Transplant Team management's response to reports of side effects has been to blame the surgeons and post-operative care-givers for these problems. Throughout 2003 and 2004, for example, Mr. McCafferty and Area Account Directors repeatedly instructed Transplant Account Managers to insist to physicians that surgical techniques played a greater role in wound-healing complications than did Rapamune. Neal Wasserman, a Wyeth Transplant Science Liaison, represented to Robin Boardman, a pharmacist at Mt. Sinai Hospital, that hepatic

artery thrombosis ("HAT") occurred in liver transplant patients primarily because of the surgical procedure itself and not because of the use of Rapamune after the surgery. Mr. Wasserman's representations directly contradict the FDA's Black Box warning, which states that "sirolimus in combination with cyclosporine or tacrolimus was associated with an increase in HAT."

214. At a Rapamune National POA meeting in about 2006, TAM Anne O'Keefe revealed in open sessions at the meeting that the Mayo Clinic was experiencing very serious side effects from using Rapamune and that these concerns had been raised with Wyeth Global Medical Affairs in 2005, but nothing was done. She expressed that Mayo Clinic was frustrated with Wyeth for failing to address critical patient safety issues.

215. Relator Sandler also understood that Dr. Barry Kahan raised issues with proteinuria with Wyeth in 2004, but was ignored.

216. Wyeth's off-label marketing efforts also harmed patients financially. Rapamune protocols cost as much as $20,000.00 annually, significantly more than alternative treatment programs. Even when patients have insurance, they more quickly exhaust their annual or lifetime benefits under the Rapamune regimen than they do under less expensive and effective protocols. The additional costs of treating the exacerbated side effects further injures patients financially. For example, at least one physician, Dr. Pascuale from Buffalo General Hospital, indicated that the cost of anemia caused by immosuppressants, such as Rapamune, may cost patients as much as $20,000 a year to address. Dr. Pascuale indicated that anemia was the "hidden cost" of Rapamune.

217. The Federal and State Governments are harmed when Medicaid and Medicare patients incur increased costs associated with treating these serious side effects.

COUNT ONE
Federal False Claims Act, 31 U.S.C. § 3729(a)(1)(A)[6]
(Against Both Defendants)

218. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

220. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented false or fraudulent claims for the improper payment or approval of prescriptions of Rapamune.

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

222. 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)[7]
(Against Both Defendants)

223. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

[6] To the extent wrongdoing occurred prior to May 20, 2009, this Amended Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3730 (a)(1).

[7] To the extent wrongdoing occurred prior to May 20, 2009, this Amended Complaint should be deemed to include violations of the Federal False Claims Act prior to its recent amendments, *e.g.*, 31 U.S.C. § 3730 (a)(2).

225. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly made, used, or caused to be made or used false records or statements material to a false or fraudulent claim.

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

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

COUNT THREE
Arkansas Medicaid Fraud False Claims Act, Ark. Code Ann. § 20-77-901
(Against Both Defendants)

228. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

229. This is a claim for treble damages and civil penalties under the Arkansas Medicaid Fraud False Claims Act, Ark. Code Ann. § 20-77-901.

230. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Arkansas Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT FOUR
California False Claims Act, Cal. Gov't Code § 12651 et seq.
(Against Both Defendants)

233. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

235. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the California Medicaid Program (*i.e.*, Medi-Cal) false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT FIVE
Delaware False Claims Act, Del. Code Ann. tit. 6, § 1201 et seq.
(Against Both Defendants)

238. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

240. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Delaware Medicaid Program false or fraudulent claims for payment or approval and/or

knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT SIX
Florida False Claims Act, Fla. Stat. Ann. § 68.081 et seq.
(Against Both Defendants)

243. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

245. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Florida Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT SEVEN
Hawaii False Claims Act, Haw. Rev. Stat. § 661-22 et seq.
(Against Both Defendants)

248. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

250. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Hawaii Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT EIGHT
Illinois Whistleblower Reward and Protection Act, 740 Ill. Comp. Stat. 175/1 et seq.
(Against Both Defendants)

253. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

255. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Illinois Medicaid Program false or fraudulent claims for payment or approval and/or

knowingly accomplished these unlawful acts by making, or causing to be made or used a false record or statement.

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

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

COUNT NINE
Indiana False Claims and Whistleblower Protection Act, Indiana Code § 5-11-5.5
(Against Both Defendants)

258. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

259. 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.

260. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Indiana Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT TEN
Louisiana Medical Assistance Programs Integrity Law,
La. Rev. Stat. Ann. § 46:439.1 et seq.
(Against Both Defendants)

263. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

264. 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*.

265. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Louisiana Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT ELEVEN
Massachusetts False Claims Act, Mass. Ann. Laws ch. 12, § 5(A)-(O)
(Against Both Defendants)

268. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

270. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented

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

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

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

COUNT TWELVE
Nevada False Claims Act, Nev. Rev. Stat. §357.010 et seq.
(Against Both Defendants)

273. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

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

275. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Nevada Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT THIRTEEN
New Hampshire Medicaid Fraud and False Claims, N.H. Rev. Stat. Ann. § 167:61-b, et seq.
(Against Both Defendants)

278. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

279. 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-b, *et seq*.

280. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the New Hampshire Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT FOURTEEN
New Mexico Medicaid False Claims Act, N.M. Stat. Ann. 1978, § 27-14-1 et seq.
(Against Both Defendants)

283. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

284. This is a claim for treble damages and civil penalties under the New Mexico Medicaid False Claims Act, N.M. Stat. Ann. 1978 § 27-14-1 *et seq*.

285. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented

to the New Mexico Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used a false record or statement.

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

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

COUNT FIFTEEN
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.
(Against Both Defendants)

288. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

289. 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*.

290. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Tennessee Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT SIXTEEN
Texas Medicaid Fraud Prevention Act, Tex. Hum. Res. Code Ann. § 36.001 et seq.
(Against Both Defendants)

293. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

294. 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*.

295. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Texas Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT SEVENTEEN
Utah False Claims Act, Utah Code Ann. § 26-20-1, et seq.
(Against Both Defendants)

298. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

299. This is a claim for treble damages and civil penalties under the Utah False Claims Act, Utah Code Ann. § 26-20-1, *et seq.*

300. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Utah Medicaid Program false or fraudulent claims for payment or approval and/or

knowingly accomplished these unlawful acts by making, or causing to be made or used a false record or statement.

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

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

COUNT EIGHTEEN
Virginia Fraud Against Taxpayers Act, Va. Code Ann. § 8.01-216.1 et seq.
(Against Both Defendants)

303. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

304. This is a claim for treble damages and civil penalties under the Virginia Fraud Against Taxpayers Act, Va. Code Ann. §8.01-216.1 *et seq*.

305. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Virginia Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT NINETEEN
New York False Claims Act, N.Y. State Fin. Law § 187 et seq.
(Against Both Defendants)

308. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

309. This is a claim for treble damages and civil penalties under the New York False Claims Act, N.Y. State Fin. Law § 187 *et seq.*

310. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the New York Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT TWENTY
Georgia False Medicaid Claims Act; GA. Code Ann. § 49-4-168 et seq.
(Against Both Defendants)

313. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint.

314. This is a claim for treble damages and civil penalties under the Georgia False Medicaid Claims Act, GA. Code Ann. § 49-4-168 *et seq.*

315. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Georgia Medicaid Program false or fraudulent claims for payment or approval and/or

knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT TWENTY-ONE
Michigan Medicaid False Claim Act, MCLA § 400.601 et seq.
(Against Both Defendants)

318. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Second Amended Complaint

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

320. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the Michigan Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

COUNT TWENTY-TWO
District of Columbia False Claims Act, D.C. Code § 2-308.14 et seq.
(Against Both Defendants)

323. Relators re-allege and incorporate by reference the allegations contained in the preceding paragraphs of this Complaint.

324. This is a claim for treble damages and civil penalties under the District of Columbia False Claims Act, D.C. Code § 2-308.14 *et seq*.

325. By virtue of the kickbacks, misrepresentations and submissions of non-reimbursable claims described above, Defendants knowingly presented or caused to be presented to the District of Columbia Medicaid Program false or fraudulent claims for payment or approval and/or knowingly accomplished these unlawful acts by making, or causing to be made or used, a false record or statement.

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

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

WHEREFORE, Relators request that judgment be entered against Defendants, ordering that:

(i) Defendants cease and desist from violating the False Claims Act, 31 U.S.C. § 3729, *et seq*., and the State False Claims Acts;

(ii) Defendants pay 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 Defendants' actions, plus the appropriate amount to the States under similar provisions of the State False Claims Acts;

(iii) Relators 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;

(iv) Relators 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;

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

(vi) Defendants disgorge all sums by which they have been enriched unjustly by their wrongful conduct; and

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

REQUEST FOR TRIAL BY JURY

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

DATED: May 24, 2010

Respectfully submitted,

BY: /s/ *John C. Kairis*

John C. Kairis*
Traci L. Goins (PA Bar No. 210218)
Alessandra C. Phillips (PA Bar No. 209937)
Grant & Eisenhofer P.A.
1201 N. Market Street
Wilmington, DE 19801
Telephone: (302) 622-7000
Facsimile: (302) 622-7100
jkairis@gelaw.com
tgoins@gelaw.com
aphillips@gelaw.com

Jay W. Eisenhofer (PA Bar No. 46584)
Francis P. Karam (PA Bar No. 77910)
Grant & Eisenhofer, P.A.
485 Lexington Avenue, 29th Floor
New York, NY 10017
Tel: 646-722-8500
Fax: 646-722-8501
jeisenhofer@gelaw.com
fkaram@gelaw.com

Reuben A. Guttman (PA Bar No. 61206)
Traci Buschner*
Grant & Eisenhofer P.A.
1920 L Street, NW, Ste. 400
Washington, DC 20036
Telephone: (202) 783-6091
Facsimile: (202) 350-5908
rguttman@gelaw.com
tbuschner@gelaw.com

Attorneys for Relators

***** Admitted *Pro Hac Vice*

Christine Humphrey
C. Humphrey & Associates, P.A.
801 Brickell Avenue, Suite 900
Miami, FL 33131
Telephone: (305) 755-7444
Facsimile: (305) 675-0621

CERTIFICATE OF SERVICE

I hereby certify that a copy of the Relators' Second Amended Complaint was filed with the Court by hand delivery and will be delivered via first class mail to the following persons this 24th day of May, 2010, as set forth below:

s/ *John C. Kairis*
John C. Kairis

VIA First Class Mail:

Christine Humphrey, Esquire
Fuerst Humphrey Ittleman
1001 Brickell Bay Drive, Suite 2002
Miami, FL 33131
Phone: 786 245-0439
Fax: 305-371-8989

Attorney General Edmund G. Brown, Jr.
California Attorney General
Justice Department
1300 I Street
Sacramento, CA 95814
Phone: (916) 322-3360
Fax: (916) 323-5341

Attorney General Joseph R. Biden, III
Delaware Attorney General's Office
Carvel State Office Building
820 N. French Street
Wilmington, DE 19801
Phone: (302) 577-8512
Fax: (302) 577-2496

Alex Sink
Chief Financial Officer
Florida Department of Financial Services
Division of Legal Services
c/o Pete Dunbar
200 East Gaines Street
Tallahassee, FL 32399-0333

Victoria Kizito
Assistant Attorney General
Office of the Georgia Attorney General
State Health Care Fraud Control Unit
Building 1, Suite 200
2100 East Exchange Place
Tucker, GA 30084

The Honorable Lisa Madigan
Attorney General of Illinois
Office of the Attorney General
Attn: Phillip Robertson,
Special Litigation
100 W. Randolph Street, 11th Floor
Chicago, IL 60601

Attorney General Andrew Cuomo
c/o John Miller
Special Assistant Attorney General
Office of the Attorney General
Medicaid Fraud Control Unit
The Capitol
Albany, NY 12224-0341

Attorney General Greg Abbott
Office of the Attorney General
300 W. 15th Street
Austin, TX 78701
Phone: (512) 463-2100
Fax: (512) 475-2994

Kathleen F. Warner
Asst. Attorney General
Civil Medicaid Fraud Division
P.O. Box 12548
Austin, TX 78711-2548
Phone: (512) 936-1449

The Honorable Mark Shurtleff
Attorney General of Utah
Office of the Attorney General
Utah State Capitol Complex
East Office Bldg, Suite 320
P.O. Box 142320
Salt Lake City, UT 84114-2320

Adelina O. Berumen
Deputy Attorney General
1455 Frazee Road, Suite 300
San Diego, CA 92108
Phone: 619-688-6043
Fax: 619-688-4200

The Honorable Greg Zoeller
Attorney General of Indiana
Office of the Attorney General
Indiana Government Center South
302 W. Washington St.
Indianapolis, IN 46204

Attorney General Martha Coakley
Office of the Attorney General
McCormack Building
One Ashburton Place
Boston, MA 02108-1698
Phone: 617-727-2200

Attorney General Mike Cox
c/o Mark Matus
Assistant Attorney General
Healthcare Fraud Division
2860 Eyde Parkway
East Lansing, MI 48823

Attorney General Michael A. Delaney
Attorney General of New Hampshire
33 Capitol Street
Concord, NH 03301
Phone: (603) 271-3658
Fax: (603) 271-2110

Attorney General Catherine Cortez Masto
Nevada Department of Justice
100 North Carson Street
Carson City, NV 89701
Phone: (775) 684-1100
Fax: (775) 684-1108

Randall M. Fox
Special Assistant Attorney General
Office of the New York Attorney General
Medicaid Fraud Control Unit
120 Broadway
New York, New York 10271

James G. Sheehan
New York State
Medicaid Inspector General
Riverview Center – 4th Floor
150 Broadway
Albany, NY 12204

Attorney General Kenneth T. Cuccinelli, Jr.
Office of the Attorney General
900 East Main Street, 6th Floor
Richmond, VA 23219
Phone: 804-786-2071
Fax: 804-786-1991

Ms. Erica Bailey
Assistant Attorney General
900 East Main Street, 6th Floor
Richmond, VA 23219
Phone: (804) 786-2452
Fax: (804) 786-0807

Brian McCabe, Esquire
Commercial Litigation Branch
Civil Division – Fraud Section
Patrick Henry Building, Room 9915
601 D Street, N.W.
Washington, D.C. 20002
Phone: 202-616-4875

The Honorable Dustin McDaniel
Attorney General of Arkansas
Office of the Attorney General
Attn: Judy Kaye Mason, Director
Medicaid Fraud Control Unit
200 Cartlett-Prien Tower
323 Center Street, Suite 200
Little Rock, AR 72201-2610

Jeffrey S. Cahill, Director
Medicaid Fraud Control Unit
Office of the Attorney General
33 Capitol Street
Concord, NH 03301
Phone: 603-271-1246
Fax: 603-271-2110

L. Timothy Terry, Director
Medicaid Fraud Control Unit
Office of the Attorney General
198 North Carson Street
Carson City, NV 89701-4717
Phone: 775-684-1185
Fax: 775-684-1192

Lara Silva
Assistant Attorney General
Antitrust and Civil
Medicaid Fraud Division
Capitol Station
P.O.Box 12548
Austin, TX 78711-2548
Phone: (512) 936-1302

Peter Nickles
Attorney General
for the District of Columbia
Attention: Stephane Latour, Chief
Civil Enforcement Section
Public Advocacy Division
Office of the Attorney General
441 Fourth Street, Suite 650 North
Washington, DC 20001

Attorney General Bill McCollum
PL-01 The Capitol
Tallahassee, FL 32399-1050
Phone: (850) 414-3600
Fax: (487) 487-9475

The Honorable Mark J. Bennett
Attorney General of Hawaii
Department of the Attorney General
425 Queen Street
Honolulu, HI 96813

The Honorable James Caldwell
Attorney General of Louisiana
P.O. Box 94005
1885 N Third Street, 6th Floor
Baton Rouge, LA 70802

Elizabeth Valentine
Assistant Attorney General
Healthcare Fraud Division
2860 Eyde Parkway
East Lansing, Michigan 48823

Attorney General Robert E. Cooper, Jr.
Office of the Attorney General
500 Charlotte Avenue
Nashville, TN 37243
Phone: 615-741-5860

Attorney General Thurbert Baker
Georgia Attorney General's Office
40 Capitol Square, SW
Atlanta, GA 30334

Dave Thomas
Inspector General of Indiana
150 West Market Street, Room 414
Indianapolis, IN 46204

Attorney General Gary King
Office of the Attorney General
P.O. Drawer 1508
Santa Fe, NM 87504-1508

Virginia Gibson, Esquire
Michael Blume, Esquire
Assistant U.S. Attorney
United States Attorney's Office
Eastern District of Pennsylvania
615 Chestnut Street, Suite 1250
Philadelphia, PA 19106-4476
Telephone: (215) 861-8355
Fax: (215) 861-8349