UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

MEMORANDUM & ORDER
MOTION FOR CLASS CERTIFICATION

----------X

In re: ZYPREXA PRODUCTS LIABILITY LITIGATION

04-MD-1596

----------X

UFCW LOCAL 1776 AND PARTICIPATING EMPLOYERS HEALTH AND WELFARE FUND, ERIC TAYAG, and MID-WEST NATIONAL LIFE INSURANCE COMPANY OF TENNESSEE, on behalf of themselves and others similarly situated,

05-CV-4115
05-CV-2948

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

LOCAL 28 SHEET METAL WORKERS, on behalf of themselves and others similarly situated,

06-CV-0021

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

SERGEANTS BENEVOLENT ASSOCIATION HEALTH AND WELFARE FUND, on behalf of themselves and others similarly situated,

06-CV-6322

Plaintiffs,

vs.

ELI LILLY AND COMPANY,

Defendant.

----------X

APPEARANCES:

For the Plaintiffs: HAGENS BERMAN SOBOL SHAPIRO LLP
One Main Street, 4th Floor
Cambridge, MA 02142
BY: THOMAS M. SOBOL
DAVID S. NALVEN

LAUREN G. BARNES
KRISTEN A. JOHNSON

HAGENS BERMAN SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900
Seattle, WA 98101
BY: STEVE W. BERMAN
CHRISTOPHER O'HARA

MURRAY LAW FIRM
650 Poydras Street, Suite 2150
New Orleans, LA 70130
BY: JAMES R. DUGAN, II
DOUG PLYMALE, PH. D.

KENNEY, EGAN, MCCAFFERTY & YOUNG
3031C Walton Road, Suite 202
Plymouth Meeting, PA 19462
BY: BRIAN P. KENNEY
ERIC L. YOUNG

HANLY CONROY BIERSTEIN SHERIDAN
FISHER & HAYES LLP
112 Madison Avenue
New York, NY 10016
BY: JAYNE CONROY
PAUL J. HANLY, JR.
ANDREA BIERSTEIN

SIMMONS COOPER, LLC
707 Berkshire Blvd.
P.O. Box 521
East Alton, IL 62024
BY: TOR A. HOERMAN
GREG ERTHEAL

ZIMMERMAN REED PLLP
651 Nicollet Mall, Suite 501
Minneapolis, MN 55042
BY: RONALD S. GOLDSER
STACY K. HAUER
BRIAN C. GUDMUNDSON

IVEY & RAGSDALE
315 West 19th Street
Jasper, AL 35501-5323
BY: GARVE IVEY
BARRY RAGSDALE

CHARFOOS & CHRISTENSEN PC
5510 Woodward Avenue
Detroit, Michigan 48202

BY: ANN MANDT
DAVE PARKER

J. THOMPSON & ASSOCIATES LLC
26000 W. Twelve Mile Road
Southfield, MI 48034
BY: JASON J. THOMPSON

CHRISTOPHER A. NEAL & ASSOCIATES
300 Harwood
Bedford, TX 76021
BY: CHRISTOPHER A. NEAL

KAHN GAUTHIER LAW GROUP, L.L.C
650 Poydras Street, Suite 2150
New Orleans, LA 70130
BY: LEWIS KAHN
ERIC O'BELL

MURRAY LAW FIRM
909 Poydras Street, Suite 2550
New Orleans, LA 70112-4000
BY: STEPHEN B. MURRAY, SR.
STEPHEN MURRAY, JR.

SADIN LAW FIRM, P.C.
121 Magnolia, Suite 102
Friendswood, TX 77546
BY: ART SADIN

HARKE & CLASBY LLP
155 South Miami Avenue Suite 600
Miami, Florida 33130
BY: LANCE A. HARKE
HOWARD M. BUSHMAN

For the Defendant:

PEPPER HAMILTON, LLP
3000 Two Logan Square
Eighteenth & Arch Sts.
Philadelphia, Pennsylvania 19103
BY: NINA M. GUSSAK
THOMAS E. ZEMAITIS
ANTHONY VALE
ADAM B. MICHAELS
KENNETH J. GRUNFELD
PAUL V. AVELAR

PEPPER HAMILTON, LLP
620 Eighth Avenue
37th Floor
New York, NY 10018-1405
BY: SAMUEL J. ABATE, JR.

JACK B. WEINSTEIN, Senior United States District Judge:

Table of Contents

I. Introduction

A. Overview

Institutions and individuals sue on behalf of a class for overpayment on purchases of defendant Eli Lilly and Company's ("Lilly") antipsychotic prescription drug Zyprexa. Institutional plaintiffs are third-party payors ("TPPs") such as pension funds, labor unions, and insurance companies. They cover members' health benefits; they have paid for Zyprexa, as well as many other pharmaceuticals upon which people rely. Individual plaintiffs bought or paid a portion of the purchase price for Zyprexa for their own use.

Claimed is a substantive violation of the Racketeer Influenced and Corrupt Organizations Act ("RICO") through mail fraud, predicated on overpricing supported by excessive claims of

utility as well as disavowal of adverse secondary effects of the drug, primarily weight gain and diabetes. *See* 18 U.S.C. § 1964.

There is sufficient evidence of fraud under RICO to go to a jury. Proposed testimony of plaintiffs' experts would permit a jury to determine the excess price. Allocation of damages based on that excess, predicated on written receipts and other reliable information, is practicable. For the institutional plaintiffs' RICO claims, every element of Rule 23 of the Federal Rules of Civil Procedure has been satisfied. *See* Part XX, *infra*. Certification of these TPP claims is appropriate under federal substantive law.

Certification of individual payor claims is denied. It will be difficult to obtain the necessary reliable payment data in most cases. More important, the individual plaintiffs proposed as representatives cannot properly represent the proposed class of individual persons. They have a conflict of interest since they are suing Lilly for personal injury and could potentially sacrifice the proposed overpayment class for a better recovery in their related individual suits. Separate releases for the two claims do not overcome this conflict. *See* Aff. of Douglas R. Plymale 3, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 197; Parts II.A.2.a.iv, II.A.2.b.iv, XIX.B, *infra*. In any event, even if the individual plaintiffs were to be certified as a subclass, their separate counsel (needed to avoid ethical problems of conflicts) and different issues of proof would unduly complicate the trial. Were the case to be settled, the claims of individuals as well as of other possible plaintiffs, such as the United States and state attorneys general, could be folded into one class with subclasses. *See, e.g.*, Hr'g Tr., July 17, 2008.

State-based claims for a recovery are also made. No ruling on the certificability of those claims will be made at this time. Under the particular circumstances of this case, the state causes

of action would essentially be subsumed in the single federal RICO action. As certified for litigation purposes, state-based substantive claims are excluded. Were the case to be settled, inclusion as part of the settlement would be desirable to help bring the total litigation to closure and to avoid future claims. *See* Parts XIX.A.2, XIX.C, XXI.B, *infra*.

A single price was charged for uses of the drug approved by the United States Food and Drug Administration ("FDA") ("on-label") and those not so approved ("off-label"). Subclassing for these two categories of drug use is proposed, but is denied. There is evidence that off-label use of Zyprexa was excessive and may have been encouraged by Lilly. *See, e.g.*, Laurie Tarkan, *Doctors Say Medication* [*Including Zyprexa*] *Is Overused in Dementia,* N.Y. Times, June 24, 2008, at F1. A cause of action for Lilly's urging such off-label use may exist, but it is independent of the case as it is now being certified based solely on overcharging for use of Zyprexa in any form. Subclassing of on-label and off-label purchases can be reconsidered were there a total settlement. *See* Parts XIX.A.1.c-d, *infra*.

Damages sought are limited to four years before filing. No damages will be allowed beyond the initial complaint's filing date of June 20, 2005. By then all potential third-party payors and prescribers of Zyprexa should have been sufficiently aware of the alleged overpricing, especially considering the widespread publication that year of adverse clinical trial results. As a matter of substantive equity, no damages will be allowed before June 20, 2001, four years before the suit was commenced. Permitting recovery for overcharges before that date would be inappropriate since the specialists who are the third-party payors had a continuing duty to their clients to inquire and to be aware of the value of drugs for which they were paying. In these special circumstances, limits should be placed on losses attributable to plaintiffs' passivity.

This ruling will result in a maximum period of June 20, 2001 to June 20, 2005 for recoverable overcharges. A jury may reduce, or even eliminate, this window on finding that the third-party payors knew or should have known of Zyprexa's alleged overpricing before they commenced suit on June 20, 2005. This limitation on the recovery period by the court depends upon exercise of the court's discretion. *See* Part XX.B.4, *infra*.

The parties have proposed slightly different certification orders, including the definition of the class, and have agreed on the parameters of the plan of notice. *See* Pfs.' Proposed Order on Class Cert. attach. 1, Aug. 22, 2008, Docket Entry No. 227; Def.'s Proposed Order, Aug. 22, 2008, Docket Entry No.228 Ex. 1; *see* Part XXIV, *infra*. Defendant opposes any certification but has cooperated in providing appropriate forms of orders.

An interlocutory appeal is now certified on this court's order denying summary judgment. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007) (denying motion for summary judgment). Interlocutory appeal provisions of Rule 23(f) of the Federal Rules of Civil Procedure on certification of the class also apply. *See* Fed. R. Civ. P. 23(f). Further proceedings in this court are now stayed in the class action certified, *see* Part XXIII, *infra*; related Zyprexa actions not encompassed in this certified action may go forward. *See* Part I.C, *infra*. So, too, may the unsealing process. *See* Part II.C, *infra*.

Details on methods of administration of the litigation, beyond those outlined in this memorandum, appropriately await proceedings after a possible interlocutory decision by the Court of Appeals for the Second Circuit. No substantial difficulty in providing for the particulars of administrating this class action litigation is foreseen. Federal courts have handled class actions far more complex than this one with a relative ease of administration. *See* Part XXII,

infra. Despite its theoretical substantive and procedural simplicity, the case comes freighted with complex medical details, economic models, and important implications for our national health care system.

Allocation of scarce medical resources is reflected in large part by the cost of medications doctors prescribe. Drugs are primarily paid for by third-party payors rather than by the doctors who recommend them or the patients who use them. *See, e.g.*, Peter H. Schuck & Richard J. Zeckhouser, Targeting in Social Programs 56-57 (2006) ("[P]olicymakers and plan managers are relying on physicians to be vigilant stewards of scarce resources," even though they are often ineffective in controlling costs). TPPs include insurance funds and other health management organizations ("HMOs") such as the plaintiffs in the instant action. These screeners of drug use must have reasonably accurate and transparent sources of information if they are to make reasonable medical and economic choices. So too must doctors and their patients.

The FDA is expected to guard the quality of available information about the utility and risks of pharmaceuticals by regulating drug approvals and labeling requirements, monitoring adverse side effects, and requiring warnings and "Dear Doctor" letters. Non-governmental agencies, individual expert research, publications, meetings, and word-of-mouth supply an enormous amount of additional data on which doctors and other screeners of drug use rely. Tort law has an important function in guarding against the pollution of information the medical calling and patients receive, particularly since our federal agency, the FDA, is relatively impotent in protecting against misleading by drug manufacturers.

Sold under the brand name Zyprexa, olanzapine is one of a class of medications known as "atypical" or "second-generation" antipsychotics ("SGAs"). (This memorandum uses "Zyprexa"

and "olanzapine" interchangeably.) It is a prescription drug developed and manufactured by Lilly. The FDA first approved Zyprexa in 1996 for use in treating schizophrenia, a severe mental illness; Zyprexa was later approved for treating some types of bipolar disorders and other diseases. Olanzapine's main adverse side effects appear to be weight gain, diabetes, hyperglycemia, and other metabolic problems.

Zyprexa continues to be used by, and prescribed for, large numbers of people. There is a general consensus that it is useful for both FDA-approved indications and some off-label purposes. It has substantially increased the quality of life of some sufferers from severe mental problems. *See, e.g.*, Elyn R. Saks, The Center Cannot Hold: My Journey Through Madness 303 (2008) ("I began to take Zyprexa . . . . The change was fast and dramatic. . . . I felt alert and rested, energetic in a way I hadn't felt in a long time—so long, in fact, that I'd almost forgotten what those good feelings were like. . . . The clinical result was, not to overstate it, like daylight dawning after a long night—I could see the world in a way I'd never seen it before.").

Beneficial effects of Zyprexa are evidenced by the fact that the institutional plaintiffs continue to reimburse or pay for Zyprexa prescriptions for their members, with few or no restrictions on its use. Many treating physicians prescribe it for their patients, despite its now well-known metabolic side effects. Nevertheless, the utility of Zyprexa does not trump plaintiffs' legal claims for fraud and overpricing.

B. Plaintiffs' Claims

Plaintiffs claim overpayment through direct expenditures for Zyprexa. Individual patients buy Zyprexa for personal use pursuant to the prescriptions of their doctors, paying the full, or a portion of, market price according to particular insurance plans. Third-party payors pay the

remainder for their covered members, typically via pharmaceutical benefit managers ("PBMs"), which act as TPP agents in administering their prescription drug programs.

It is alleged that over the twelve-year period since Zyprexa's introduction in 1996 to today, Lilly has withheld information and disseminated misinformation about the safety and efficacy of Zyprexa and has promoted and marketed the drug for uses for which it was not indicated and for patients who would have been better served by less expensive medications. As a result, plaintiffs contend, Zyprexa commanded a higher price than it would have had the truth been known to those who prescribed, bought, or paid for the drug. The resulting alleged excess payments—estimated to range from $3.998 billion to $7.675 billion (per plaintiffs' expert Dr. Rosenthal) or to approximate $4.9 billion (per plaintiffs' expert Dr. Harris)—are claimed as damages. *See* Parts XVIII.A.2-3, *infra*. Having survived summary judgment, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, plaintiffs now seek certification of a class of third-party and individual payors.

Five causes of action are asserted: Counts I and II, violations of the Racketeer Influenced and Corrupt Organization Act ("RICO") under 18 U.S.C. §§ 1962(c) and 1962(d); Count III, violations of forty-five state consumer protection statutes; Count IV, common law fraud; and Count V, unjust enrichment. *See* First Am. Class Action Compl. (Redacted), Nov. 7, 2005, Docket No. 05-CV-4115, Docket Entry No. 14 ("Am. Compl").

Subject matter jurisdiction is based upon 28 U.S.C. § 1331 (action arising under the laws of the United States) and 18 U.S.C. §§ 1962 and 1964(c) (RICO). Plaintiffs also invoke jurisdiction pursuant to 28 U.S.C. § 1332(d)(2) ("Class Action Fairness Act"). Venue is placed in the Eastern District of New York pursuant to 28 U.S.C. § 1391(b) and (c) (requiring that a

substantial portion of the alleged improper conduct took place in the district where suit is commenced) and 18 U.S.C. § 1965 (RICO). As already noted, claims under Counts III, IV and V are not being certified.

C. Related Actions

Related Zyprexa actions provide the court and litigants with an extensive factual and evidentiary background. The present suit is part of a series of cases based on injuries allegedly resulting from Lilly's sale of Zyprexa. Thousands of mass tort product liability personal injury actions against Lilly on behalf of approximately 30,000 private litigants have been transferred to this court by the Judicial Panel on Multidistrict Litigation ("JPML") since April 2004; almost all of them have now settled. *See* JPML Order, *In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, Docket Entry No. 1 (E.D.N.Y.); 28 U.S.C. § 1407. The large number of related individual personal injury suits necessitated administration of the multidistrict litigation ("MDL") as a quasi-class action, with the use of matrices for settlement amounts, control over fees, cooperation with state courts and national settlements of liens. *See In re Zyprexa Prods. Liab. Litig.*, 451 F. Supp. 2d 458, 477 (E.D.N.Y. 2006) (recognizing the court's "obligation to exercise careful oversight of this national 'quasi-class action'") (citation omitted); *In re Zyprexa Prods. Liab. Litig.*, 433 F. Supp. 2d 268, 271 (E.D.N.Y. 2006) (finding that the case "may be characterized properly as a quasi-class action subject to the general equitable power of the court"); *In re Zyprexa Prods. Liab. Litig.*, 424 F. Supp. 2d 488, 491 (E.D.N.Y. 2006) (same); *In re Zyprexa Prods. Liab. Litig.*, 233 F.R.D. 122, 122 (E.D.N.Y. 2006) (same).

Various administrative measures were taken to control discovery and ensure appropriate representation for the personal injury plaintiffs. Two successive Plaintiffs' Steering Committees

("PSCs") were appointed. *See* Case Mgmt. Order No. 19, Aug. 16, 2006, Docket No. 04-MD-0159, Docket Entry No. 692; *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2004 WL 3520245 (E.D.N.Y. June 17, 2004) (outlining the PSC's responsibilities). Multiple special masters and a magistrate judge assisted.

Extensive and coordinated discovery led to creation of a national archive available to all parties. *See In re Zyprexa*, 424 F. Supp. 2d at 491 ("[A]ll litigants, whether in federal or any state court, have access to the materials obtained in pretrial discovery"). Those documents, including depositions, are available to the parties in the instant class action. The collection, maintained initially in a depository in Denver, Colorado, and currently in Mount Pleasant, South Carolina, has been available free of charge to the MDL and non-MDL plaintiffs in both state and federal courts who agree to adhere to the terms of the protective and related orders issued by this court. *See also* Case Mgmt. Order No. 20 at 1, Nov. 16, 2006, Docket No. 04-MD-1596, Docket Entry No. 928 (ordering special master's discovery and trial schedule for personal injury actions); *In re Zyprexa Prods. Liab. Litig.*, 375 F. Supp. 2d 190, 191 (E.D.N.Y. 2005); Case Mgmt. Order No. 15 at 5, May 15, 2006, Docket No. 04-MD-1596, Docket Entry No. 527 (directing MDL counsel to use best efforts to coordinate the scheduling of depositions with state court counsel, and providing for cross-noticing of depositions in federal and state court).

Because many of the personal injury suits were filed in state courts, coordination with state judges was desirable. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 898105, at *1 (E.D.N.Y. Apr. 16, 2006) ("Coordination and cooperation between state and federal courts has been encouraged."); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 197151 (E.D.N.Y. Jan. 30, 2006) (suggesting coordination and cooperation in a letter

to state judges with Zyprexa cases); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2004 WL 3520248, at *4 (E.D.N.Y. Aug. 18, 2004) (directing Lilly and the first PSC ("PSC I") to "confer regarding procedures for coordination of state court discovery with discovery in this MDL").

Over 8,000 personal injury claims, representing about 75% of the then-pending plaintiffs, were settled by Lilly in 2005 under the supervision of PSC I. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2005 WL 3117302 (E.D.N.Y. Nov. 22, 2005). A complex claims processing and payment procedure was established, administered via special settlement masters. *See In re Zyprexa Prods. Liab. Litig.*, 433 F. Supp. 2d 269 (E.D.N.Y. 2006); *see also In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443217 (E.D.N.Y. Aug. 24, 2006) (ordering payments to begin); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443249 (E.D.N.Y. Aug. 24, 2006) (establishing disbursement procedures). Another 18,000 such plaintiffs settled with Lilly in January 2007; settlement was largely administered by an appointed settlement administrator rather than the court. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, 2007 WL 37736 (E.D.N.Y. Jan. 5, 2007). Since then, many more plaintiffs have settled or agreed to settle. *See, e.g.*, *In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-1596, 2008 WL 1827486 (E.D.N.Y. Apr. 22, 2008) (ordering the administrative closure of over a thousand cases pending reinstatement should the contemplated settlements not be consummated).

Summary judgment motions in several individual plaintiffs' personal injury claims were addressed in June 2007. Analysis of the summary judgment motions required review of thousands of pages of material. *See* Appendices A-D of *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230 (E.D.N.Y. 2007) (including over 1500 pages of relevant depositions demonstrating

doctors' awareness of Zyprexa's association with patient weight gain). In one claim, defendant's motion was granted based on statute of limitations grounds. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230. Other personal injury lawsuits set for trial in this district in June 2008 were settled before summary judgment could be rendered. *See, e.g.*, *Godley v. Eli Lilly & Co.*, Docket No. 06-CV-04038 (E.D.N.Y.); *Smith v. Eli Lilly & Co.*, Docket No. 06-CV-04039 (E.D.N.Y.).

For the personal injury settlements, an attorneys' fees structure was ordered. *See In re Zyprexa Prods. Liab. Litig.*, 424 F. Supp. 2d 488 (capping fees at 20% of recovery for smaller, lump-sum claims, and at 35% for all other claims); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 2443248 (E.D.N.Y. Aug. 24, 2006) (limiting PSC costs charged to the individual settling plaintiffs); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 2458878 (E.D.N.Y. Aug. 22, 2006) (referring oversight of PSC I's fee claims to the magistrate judge).

Cases commenced in this district are being prepared for trial here in clusters of twelve. *See* Case Mgmt. Order Nos. 29, 30, Aug. 19, 2008, Docket No. 04-MD-1596, Docket Entry Nos. 1838, 1840. The expectation is that all will be tried, dismissed or settled by the spring of 2009. *See* Hr'g Tr., Aug. 11, 2008. Cases transferred from other districts will have general discovery completed at about the same time, when transfer will be suggested for the relatively few that have not been settled or dismissed. *See* Case Mgmt. Order No. 28, July 11, 2008, Docket No. 04-MD-1596, Docket Entry No. 1796.

Since many of the personal injury plaintiffs had coverage for health-related expenditures through state Medicaid and federal Medicare programs, a procedure for resolving outstanding government liens was executed. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006

WL 2385230 (E.D.N.Y. Aug. 15, 2006) (describing and approving Medicaid lien agreements between states and the PSC); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2385232 (E.D.N.Y. Aug. 16, 2006) (describing fee division issues); *In re Zyprexa Prods. Liab. Litig.*, 451 F. Supp. 2d 458 (creating a national mechanism to resolve outstanding Medicare and Medicaid liens on the recoveries of settling personal injury plaintiffs); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-01596, 2006 WL 3501263, at *1 (E.D.N.Y. Dec. 4, 2006) ("In compliance with this court's instructions . . . all fifty states as well as the federal government have resolved their Medicare and Medicaid liens" by agreeing to modify their lien demands to provide a national equitable system) (citation omitted); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2443217 (E.D.N.Y. Aug. 24, 2006) (describing and approving Medicare lien agreements between certain states, the federal government, and the PSC); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2385230 (E.D.N.Y. Aug. 15, 2006) (same); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 2095728 (E.D.N.Y. July 28, 2006) (ordering Lilly and the states to negotiate); *In re Zyprexa Prods. Liab. Litig.*, No. 04-MD-1596, 2006 WL 1662610 (E.D.N.Y. June 15, 2006) (setting initial conference regarding a possible holdback to satisfy government liens).

Non-governmental health insurance liens were dealt with on an individual basis. A private health insurance company sued the trustees of the first Zyprexa settlement fund for failure to resolve such liens; that matter has now been settled. *See Aetna, Inc. v. Seeger Weiss, LLP*, No. 07-CV-03559 (E.D.N.Y.).

In suits based on claims similar to those in the instant action, many state attorneys general have sued on behalf of their states' citizens claiming reimbursement for overpayments for

Zyprexa made with state and federal funds via state Medicaid programs. Currently pending in this court are actions on behalf of the citizens of Montana, Connecticut, New Mexico, Mississippi, West Virginia, and Louisiana. *See In re Zyprexa Prods. Liab. Litig.*, No. 07-CV-1933, 2008 WL 398378 (E.D.N.Y. Feb. 12, 2008) (Montana, denying remand); *Hood ex rel. Mississippi v. Eli Lilly & Co.*, No. 07-CV-645, 2007 WL 1601482 (E.D.N.Y. June 5, 2007) (Mississippi, denying remand); *In Zyprexa Prods. Liab. Litig.*, 375 F. Supp. 2d 170 (E.D.N.Y. 2005) (Louisiana, denying remand); *West Virginia v. Eli Lilly & Co.*, 476 F. Supp. 2d 230 (E.D.N.Y. 2007) (West Virginia, denying remand); *Connecticut v. Eli Lilly & Co.*, No. 08-CV-955 (E.D.N.Y.); *In re Zyprexa Prods. Liab. Litig.*, No. 07-CV-1749, 2008 WL 940102 (E.D.N.Y. Apr. 1, 2008) (New Mexico, scheduling discovery); *cf.* Alex Berenson, *Lilly Considers $1 Billion Fine to Settle Case*, N.Y. Times, Jan. 31, 2008 (federal and state negotiations with Lilly over a proposed fine). A putative qui tam action by a whistleblower representing California has been dismissed. Order, *California ex rel. Jaydeen Vincente v. Eli Lilly & Co.*, Apr. 23, 2008, Docket No. 08-CV-600, Docket Entry No. 84 (dismissing action). A number of state attorney general cases are pending in state courts. *See* Hr'g Tr., Aug. 11, 2008 (five cases). The one case originating in this district, that of Connecticut, will be tried on June 15, 2009 if it has not been settled or dismissed. *See* Order, Aug. 11, 2008, Docket No. 04-MD-1596, Docket Entry No. 1828. It is expected that by the summer of 2009, the five attorney general cases transferred to this court will have been settled, dismissed, or, with general discovery completed, transferred back to their originating jurisdictions. *Id.*

Some of Lilly's shareholders have filed suit because of the decline in share price. *See In re Eli Lilly & Co. Securities Litig.*, No. 07-CV-1310 (E.D.N.Y.). This litigation has been

dismissed on statute of limitations grounds. *See In re Zyprexa Prods. Liab. Litig.*, 549 F. Supp. 2d 496 (E.D.N.Y. 2008).

Current shareholders have sued in this court in the form of three separate shareholder derivative actions. *See Waldman v. Taurel*, No. 08-CV-560 (E.D.N.Y.); *City of Taylor Employees Retirement System v. Taurel*, No. 08-CV-1554 (E.D.N.Y.); *Robins v. Taurel*, No. 08-CV-1471 (E.D.N.Y.). Similar cases are pending in other courts. Settlement negotiations are ongoing. *See* Hr'g Tr., May 29, 2008.

The present suit must be considered in the context of the related Zyprexa actions. Materials previously submitted to the court in the MDL were, on consent of the parties, considered in deciding this class certification motion. *See* Transcript of Evidentiary Proceedings on Class Certification, March 28, 2008 through April 2, 2008 ("Tr."), at 5-6 (Mar. 28, 2008). Materials from the parties' previous summary judgment motions, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, are extensively cited.

In March 2008, Lilly settled with the state of Alaska for $15 million during trial in a related case. *See* Alex Berenson, *Lilly Settles Alaska Suit over Zyprexa*, N.Y. Times, Mar. 26, 2008 (reporting the settlement agreement reached after three weeks of trial before the case went to the jury). That state's lawsuit sought reimbursement for the medical costs of Alaska Medicaid patients who developed diabetes while taking Zyprexa; the state's claim to recover costs associated with Lilly's off-label promotion of Zyprexa was dismissed before trial. Alex Berenson, *Lilly E-Mail Discussed Off-Label Drug Use*, N.Y. Times, Mar. 14, 2008. Some of the materials introduced in that trial are available in this court.

D. Class Certification

Plaintiffs seek to consolidate many thousands of claims in the present class action on the ground that those who paid for Zyprexa were charged more than they would have been in the absence of Lilly's fraud. Claims include those of both patients and insurance companies. Various definitions of the putative class have been proposed. As outlined in plaintiffs' papers, the class may be generally defined as:

> All individuals and [non-governmental] entities in the United States and its territories who, for purposes other than resale, purchased, reimbursed, and/or paid for Zyprexa during the period from September 1996 through the present. For purposes of the Class definition, individuals and entities "purchased" Zyprexa if they paid for some or all of the purchase price.

Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert. 32, Apr. 21, 2008 (undocketed; filed under seal); *see* Red. Am. Compl.; Class Plaintiffs' Opening Brief on Class Certification ("Pfs.' Class Cert. Br."), Aug. 3, 2007, Docket No. 05-CV-4115, Docket Entry No. 131 (filed under seal).

Two subclasses are proposed: a Third-Party Payor Subclass and a Consumer or Direct-Payor Subclass. Further division into two groups, one for "on-label" (used for FDA-approved indications) purchases and the other for "off-label" (used for non FDA-approved indications) purchases has also been suggested by plaintiffs. Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert. 33; *see* Fed. R. Civ. P. 23(c)(5); Part XIX.A, *infra*.

The class will be certified on a more limited basis than that sought by plaintiffs. *See* Part XXI, *infra*. With adequate due process protections for both plaintiffs and defendant, restrictions on the litigation will permit the jury to determine, with sufficient precision, the monetary damages, if any, to institutions that allegedly overpaid for Zyprexa as a result of Lilly's fraud. The assistance of *Daubert*-cleared experts and a plan for efficiently managing the litigation as a

class action, as opposed to individual suits, provide substantial benefits to the community and the courts and litigants.

Certification will be granted to a class of third-party payors on the federal RICO claims only. *See also In re Zyprexa Prod. Liab. Litig.*, 493 F. Supp. 2d 571, 577, 579 ("Based on expert reports and available modes of economic analysis, a trier could determine that Zyprexa would have . . . been sold for a reasonably precise computable lesser amount than it was sold for were it not for Lilly's alleged fraud."). Plaintiffs' state claims will not be certified at this time by this court.

Establishment of class damages is practicable based upon the admissible opinions of plaintiffs' proffered experts. In these circumstances the Constitution requires a jury disposition. *See* U.S. Const. amend. VII. For purposes of the constitutional right to a civil jury, this is essentially a "suit at common law," even though plaintiffs rely on statutory substantive law and equitable class action practice. *See* Part XIX.D, *infra*.

Total denial of certification would constitute the death knell of the action. Almost all plaintiffs' claims would be too small to individually support this costly litigation. Under such circumstances, absent an unusual situation, the rule to be applied in deciding to deny certification is essentially that for summary judgment if all the elements of Rule 23 of the Federal Rules of Civil Procedure are satisfied—as they are here. *See* Fed. R. Civ. Proc. 23; Part XX, *infra*.

In arguing against class certification, defendant relies heavily on the Second Circuit Court of Appeals' reversal of *Schwab v. Philip Morris*, 449 F. Supp. 2d 992 (E.D.N.Y. 2006), in *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), *subsequently placed in doubt by Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008). Denial of some

aspects of defendant's motion for summary judgment was based in part on *Schwab*. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571. The instant action and that in *McLaughlin* superficially may appear alike: in both, consumers have sued for overpricing based on fraudulent health claims of the product—medication or cigarettes. *McLaughlin* is, as explained below, distinguishable from the present case. Assuming *McLaughlin* is still fully viable in view of the subsequent Supreme Court decision in *Phoenix Bond* expanding the reach of civil RICO actions, it is not an impediment to certification in the instant Zyprexa case. *See* Parts XX.B-D, *infra*.

E. Opportunity to Comment

Due to the enormous number of potential plaintiffs involved and the importance of the case, the court made a special effort to solicit and to incorporate in this memorandum and order the views of those who might be interested. To this end, the court issued a "Discussion Draft" of this class certification memorandum several months ago. *See In re Zyprexa Prods. Liab. Litig.*, No. 04-CV-4115, 2008 WL 2696916 (E.D.N.Y. June 2, 2008). Comments of interested persons or parties were solicited for a subsequent hearing on class certification:

> Because the class proposed to be certified in the draft opinion specifically excludes government and individual payors, the United States Attorney or other representative of the federal government, state Attorneys General or equivalent state officials, or any individual or representative of an interested group will be heard if so desired. Testimony at the previously held certification hearings related to government and individual payments, as well as to the activities of individual non-governmental organizations such as the American Diabetes Association and the National Alliance on Mental Illness.

In re Zyprexa Prods. Liab. Litig., No. 05-CV-4115, 2008 WL 2779068 (E.D.N.Y. July 14, 2008); Hr'g Tr., July 17, 2008; Oral Statement by the Court at Class Cert. Hr'g, July 17, 2008, Docket No. 05-CV-4115, Docket Entry No. 207; Order, July 17, 2008, Docket Entry No. 208.

Interested parties or persons were invited to participate in the court's September 4, 2008 hearing on the motions to unseal Lilly documents, until then confidential pursuant to a long-standing protective order. *See In re Zyprexa Prods. Liab. Litig.*, No. 05-CV-4115, 2008 WL 3245091 (E.D.N.Y. Aug. 6, 2008); Letter, Bloomberg L.P., Aug. 18, 2008, Docket No. 05-CV-1596, Docket Entry No. 1832; Mot. to Vacate CMO 3, Vera Sharav, Alliance for Human Research Protection & David Cohen, Docket No. 04-MD-1496, Docket Entry No. 1859; Letter, Kaiser Health Foundation Plan et al., Aug. 22, 2008, Docket No. 04-MD-1496, Docket Entry No. 1847. Although the court's efforts towards public participation may have somewhat delayed the proceedings, the opportunity to reflect and provide for public comment seems more important than speed in this instance. The court postponed issuance of this final order of certification in order to consider the public and private interests reflected in the comments and motions it has received.

F. Interlocutory Appeal

As suggested in the summary judgment opinion, *see In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d at 580-81, an interlocutory appeal from the order denying summary judgment should be, and is now, certified. *See* Part XXIII, *infra*. This will permit that issue to be considered along with any immediate appeal from the class certification order. 28 U.S.C. § 1292(b); Fed. R. Civ. Proc. 23(f).

II. Procedural History

A. Multiple Plaintiffs

1. Third-Party Payor Plaintiffs

On June 20, 2005, Mid-West National Life Insurance Company of Tennessee ("Mid-West") and Eric Tayag ("Tayag") filed a putative class action suit against defendant Eli Lilly and Company ("Lilly") regarding the alleged fraudulent over-promotion of olanzapine, sold under the brand name Zyprexa, and seeking economic damages. *See* Mid-West & Tayag Compl., June 20, 2005, Docket No. 05-CV-2948, Docket Entry No. 1. Similar suits were initiated by UFCW Local 1776 and Participating Employers Health and Welfare Fund ("UFCW"), *see* UFCW Compl., Aug. 25, 2005, Docket No. 05-CV-4115, Docket Entry No. 1, Local 28 Sheet Metal Workers ("Local 28"), *see* Local 28 Compl. (Redacted Version), Dec. 29, 2006, Docket No. 06-CV-21, Docket Entry No. 1, and Sergeants Benevolent Association Health and Welfare Fund ("SBA"), *see* SBA Compl., Nov. 21, 2006, Docket No. 06-CV-6322, Docket Entry No. 1. The United Federation of Teachers Welfare Fund ("Teachers") and ASFCME District Council 37 Health and Security Fund ("DC 37") later joined as additional class representatives. In the fall of 2006, Michael Pronto ("Pronto") and Michael Vannello ("Vannello") were added as co-lead individual plaintiffs and Tayag was dropped as a class representative.

In response to Lilly's September 29, 2005 motion for an order requiring the filing of a RICO case statement, Def.'s Mot. for Order Requiring Plaintiff to File RICO Case Statement, Sept. 29, 2005, Docket No. 05-CV-4115, Docket Entry No. 8, plaintiffs filed an amended complaint on November 7, 2005, alleging in great detail Lilly's misrepresentations and fraudulent over-promotion. First Am. Class Action Compl. & Demand for Jury Trial, Nov. 7, 2005, Docket Entry No. 14.

a. UFCW

The UFCW Fund is a Taft-Hartley trust fund created to provide cost effective, comprehensive medical and prescription drug benefits to the Local 1776 members of the United Food & Commercial Workers Union ("UFCW Local 1776"), whose employers are required to contribute financially pursuant to negotiated union contracts. *See generally* 29 U.S.C. §§ 141-197 *et seq*. (Taft-Hartley Act, i.e., enabling federal law pursuant to which the UFCW Fund was created). UFCW Local 1776 is a labor union based in Philadelphia, Pennsylvania, with over 20,000 active members, some of whom live in other states. Pfs.' Class Cert. Br. Typical of Taft-Hartley benefit trust funds, the UFCW Fund has no employees. Dep. Tr. of Regina Reardon on behalf of Plaintiff UFCW, Oct. 5, 2006, at 15 ("UFCW Dep."). Since 1996, the UFCW Fund has contracted with a third-party administrator that collects employer contributions, maintains records, pays claims, and conducts the day-to-day operations of the UFCW Fund. *Id.* at 16. It has overall annual expenditures of $70 million, an increase of almost fifty percent over the last five years. *Id.* at 172-73.

Like most other third-party payors, the UFCW Fund, with the assistance of its third-party administrator, contracts with a Pharmacy Benefit Manager ("PBM") to manage its pharmacy plan. *Id.* at 16. The UFCW Fund pays for eligible Zyprexa prescriptions directly through its PBM, currently National Medical Health Card ("NMHC"). *Id.* at 86, 39. To manage the UFCW Fund's pharmacy benefits, NMHC uses a formulary containing a list of preferred drugs. Many of the drugs on the preferred list are those for which the NMHC has rebate contracts with the manufacturers. *Id.* at 91. The UFCW Fund pays the cost, minus a co-pay, regardless of whether the drug is included in the formulary. *Id.* at 84. The co-pay is a percentage of the drug cost or a fixed amount per prescription paid by the actual user; it may vary depending on whether the

particular drug is on-formulary or off-formulary. *Id.* at 99. UFCW has no direct means of determining the indication for which a prescription is written and whether it is for an on-label or off-label purpose. On May 15, 2007, UFCW's PBM formally recommended that the fund impose a prior authorization requirement for all Zyprexa prescriptions to discourage potential off-label use of the drug.

UFCW alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's fraud, Opp'n to Eli Lilly & Co.'s Mot. to Compel Further Resps. by Pfs. to Interrogs. & Doc. Reqs. & to Compel Mid-West's Rule 30(B)(6) Witness to Answer Questions, Dec. 1, 2006 ("Opp'n to Mot. to Compel") at 7, and has produced such Zyprexa prescription information as cost, dose and date.

From January 1997 through January 2006, the UFCW Fund paid a total of $799,888.16 for Zyprexa. Between January 31, 1997 and April 10, 1997, it paid for 5,514 units; between June 9, 1999 and January 11, 2002, it paid for 3,226 units; between June 4, 2003 and June 16, 2003, it paid for 1,345 units; and between December 12, 2003 and January 5, 2006, it paid for 57,569 units. UFCW used various PBMs between 1996 and 2000; since not all of them maintained data on Zyprexa, there are some gaps in the records.

According to plaintiffs, Lilly sales representative call notes produced in discovery suggest that several physicians who prescribed Zyprexa to the UFCW Fund's insureds were deceived by Lilly before, or while, prescribing Zyprexa. Pfs.' Response to Def.'s Local R. 56.1 Statement of Undisputed Facts & Pfs.' Local R. 56.1 Statement of Disputed Facts, June 12, 2007, Docket No.

05-CV-4115, Docket Entry No. 113 ("Pfs.' SJ Fact Proffer"). These notes indicate that physicians who prescribed Zyprexa to UFCW Fund's insureds may have been falsely led into believing that Zyprexa was effective for a variety of problems for which it was not useful, including depression, mood disorders, anxiety, sleep problems, selective serotonin reuptake inhibitors ("SSRIs") failures, and dementia. *Id.*

b. Mid-West

Plaintiff Mid-West National Life Insurance Company of Tennessee ("Mid-West") is an insurance company based in North Richland Hills, Texas. Mid-West offers various insurance products, some of which include a prescription drug benefit. Dep. Tr. of Kip Howard on behalf of Plaintiff Mid-West at 100:8-20, Oct. 24, 2006 ("Mid-West Dep."). The numbers of persons covered by Mid-West for pharmacy benefits for the years 1999 through 2006 are as follows: 2,356 in 1999, 1,313 in 2000, 36,244 in 2001, 138,472 in 2002, 182,847 in 2003, 197,950 in 2004, 204,096 in 2005, and 223,069 in 2006. *See* Affidavit of Kip Howard at ¶ 3, Dec. 29, 2006 ("Mid-West Aff. 1"). No information is available on the number of persons covered for the years 1996, 1997, and 1998.

Mid-West's Plan A has a $50 deductible and a maximum annual coverage of $500. *Id.* Under Plan A, the insured receives a 25% discount on payments for brand-name drugs at the point of sale; the co-pay for generic drugs is a flat rate of $20 or $10 depending on how the prescription is filled. *Id.* Plan B has a deductible of $100 and a maximum annual coverage of $1000. Under Plan B, both generic and brand drugs are covered under a tiered flat co-pay of $15, $30, or $45, depending on whether the drug is generic, brand on-formulary, or brand off-formulary. *Id.*

Wholly owned by HealthMarkets, Inc. ("HealthMarkets"), Mid-West Aff. 1 at ¶ 2, Midwest has assets in excess of $25,000. Affidavit of Mid-West, Kip Howard, Jan. 5, 2007 ("Mid-West Aff. 2") at ¶ 2; Mid-West Dep. 13. From 1996 to present, either HealthMarkets or another company it wholly owns, MEGA Life and Health Insurance ("MEGA"), has contracted with a PBM to administer pharmacy benefits for Mid-West's insureds. Mid-West Aff. 1 at ¶ 2. Pharmacy benefits are administered by the PBM pursuant to contracts between HealthMarkets (or MEGA) and the PBM. *Id.*

The PBM that administered pharmacy benefits for Mid-West's insureds from 1996 through 1999 was Advanced Paradigm, Inc. (n/k/a Caremark, Rx, Inc.). Mid-West's Obj. & Answers to Lilly's First Set of Interrogs. ("Mid-West's Resps. to Interrogs., First Set") at No. 1. From 2000 through 2002, Mid-West's PBM was MedCo Health Solutions, Inc. *See id.* From 2003 through the present, Mid-West's PBM has been Caremark Rx, Inc. *See id.*

Mid-West always adopts the formulary of its PBMs; it does not create its own custom formulary. Mid-West Aff. 2 at ¶ 7. The formulary is set and controlled by its PBM. *Id.* Mid-West does cover non-formulary drugs, but its insureds pay a higher co-pay for them. *Id.* at ¶ 5. Zyprexa has always been on the formulary of Mid-West's PBM. *Id.* at ¶ 3.

Insureds of Mid-West with a prescription drug benefit are reimbursed, and have always been reimbursed, for eligible Zyprexa prescriptions. *Id.* at ¶ 4. Mid-West has never sought any utilization restrictions (including prior authorizations) for Zyprexa. *Id.* at ¶ 8. Since filing its complaint, it has not altered its practices or policies regarding its payment for Zyprexa. Mid-West Dep. 87-88; Mid-West's Resps. to Interrogs., First Set at No. 7. Mid-West pays a higher

price for Zyprexa now than when the Amended Complaint was filed; Zyprexa's market price has steadily increased at more than the cost-of-living.

Mid-West alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's alleged fraud. Opp'n to Mot. to Compel at 7. It has produced its prescription claim data in discovery, including information such as cost, dose, date, and identity of some prescribing physicians.

From January 2000 through April 2007, Mid-West paid for 1,617 Zyprexa prescriptions for 646 of its insureds. *See* Mid-West's Resps. to Interrogs., First Set, as supplemented. Mid-West does not possess claims data prior to January 2000. *Id.* Its documented payments for Zyprexa total $32,570. *See id.*

The plaintiff has communicated neither with its insureds nor their physicians about the safety or efficacy of Zyprexa. It has not shared the allegations of this lawsuit with them.

c. Local 28

Local 28, a New York Taft-Hartley health and welfare fund, provides a prescription drug benefit to active and retired member of the Local 28 Sheet Metal Workers Union. It provides coverage for members living in the five boroughs of New York City as well as in Nassau and Suffolk counties. Dep. of John McGrath on behalf of Plaintiff Local 28 at 13, Nov. 10, 2006 ("Local 28 Dep."). It has 2,800 working members, 400 apprentices, and 1,800 retirees, all of whom are eligible for health benefits for themselves and their families. *Id.* In total, Local 28's

Workers Fund provides benefits for approximately 10,000 people, *id.* at 43, 134, including eligible members in twenty-nine states. *Id.* at 13.

The pharmacy benefit plan for Local 28 is an "open plan;" payment is made for any drug as long as it is prescribed by a physician and is approved and non-experimental. *Id.* at 48-49. Since 2004, Local 28's formulary has been provided by its PBM, Specialized Pharmacy Solutions. The PBM has the exclusive authority to classify drugs in the formulary. *Id.* at 61-62. Local 28 pays any remaining balance for a prescription after a member provides the co-pay. *See also id.* at 84. It pays for Zyprexa and has not made any Zyprexa-specific changes to its policies. *Id.* at 33.

Alleged is that Local 28 has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. Am. Compl. at ¶¶ 472, 480, 535, 54, 546. It claims that every Zyprexa prescription for which it had paid was procured by Lilly's fraudulent conduct. Opp'n to Mot. to Compel 7. Local 28 has identified these prescriptions by producing claims data in discovery, including such information as cost, dose and date. Between 1998 and 2007, the Fund paid $198,906.73 for 848 Zyprexa prescriptions. Local 28 Dep. at Ex. 3.

Plaintiffs assert that certain call notes produced by Lilly indicates that Local 28's physicians were told that Zyprexa was effective for a variety of problems, including mood disorders, anxiety, sleep problems, SSRI failures and dementia; defendant disputes this interpretation. Lilly Physician Call Notes at ZY 1005511869, ZY 1005569827, ZY 1005599586.

d. SBA

The Sergeants Benevolent Association ("SBA") provides a prescription drug benefit, as well as other health benefits to sergeants in the New York City Police Department, retirees, and dependants. Dep. of Errol Ogman on behalf of Plaintiff SBA Health & Welfare Fund, Jan. 24, 2007 at 9:17-20 ("SBA Dep."). It provides pharmaceutical benefits for approximately 33,000 individuals. *Id.* at 9:17-20, 11:9-19, 145:10-15.

SBA pays for prescriptions, including those for Zyprexa, of covered members. *Id.* at 105:10-106:13. It has never used a formulary and does not distinguish between preferred and non-preferred drugs. *Id.* at 151-52. SBA has never imposed any restrictions (including prior authorizations, step therapy, or higher co-pays) for Zyprexa, *id.* at 150-51, 157, 159, although it has required prior authorization for other medications, including those used to treat schizophrenia. *Id.* at 212-14. SBA continues to pay for Zyprexa to this day. *Id.* at 36-37.

Third-party administrators handle SBA's routine benefit management. Until October 2003, SBA used General Prescription Program as its PBM. *Id.* at 162:24-163:10. In October 2003, SBA switched to a PBM named Caremark. *Id.*; SBA's Response to Interrogs. Caremark was the PBM for SBA from October 1, 2003 to July 31, 2005. SBA's Objs. & Answers to Lilly's First Set of Interrogatories, Jan. 17, 2007. In July 2005, SBA started a non-profit company called True Health Benefits to handle pharmacy benefit management. True Health Benefits then contracted with Innoviant Rx as a third-party administrator to handle the tasks of a normal pharmacy benefit manager. SBA Dep. at 50:8-20. SBA, acting through True Health Benefits, encourages participants to consider cost-effectiveness by requiring members to pay a percentage of the total drug cost rather than using a formulary. *Id.* at 147:6-148:4, 151:19-22.

SBA alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. *Id.* at 33, 36-37. It asserts that every Zyprexa prescription for which it has paid was procured by Lilly's alleged fraud. *Id.* at 35-36. (From July 2001 to June 2005, SBA did not pay for Zyprexa medications for non-Medicare members because of a special New York City program that covered psychotropics for those patients. *Id.* at 152-55.) During the class period, SBA spent $87,869 for Zyprexa; it has identified these prescriptions by producing claims data in discovery.

Lilly allegedly made misleading statements to Caremark, SBA's PBM from October 2003 to July 2005. In May 2002, for instance, Caremark was contacted by a Lilly representative with information on a recent study finding that most atypicals were "significantly associated with diabetes mellitus" and that Zyprexa's metabolic effects were not worse than other SGAs', which plaintiffs claim downplayed Zyprexa's link to diabetes. *See* Letter from Vicki Poole Hoffman, Associate Therapeutic Consultant, Lilly U.S.A., Medical Division, to Audrey Moyna, Caremark, May 8, 2002; Ex. C to Def.'s Mem. Relating to the Form of Order on Class Cert. 2, Aug. 22, 2008, Docket No. 05-CV-4115, Docket Entry No. 222. Lilly also used Caremark and other PBMs to communicate and market to physicians. *See* Email from Paula J. McCain, Eli Lilly & Co., to Joanne Delois Murphy et al., Sept. 11, 2003, at 4:52:38 p.m. In September 2003, Lilly utilized Caremark to mail out Zyprexa marketing material to physicians. *Id.*

In June 2007, SBA notified its members about the pending litigation and concerns about Zyprexa. *See* SBA's Supp. Response to Interrogs., June 1, 2007. SBA continues to communicate with its members through its delegates regarding this litigation and concerns about Zyprexa. SBA Dep. at 121:18-122:17.

e. Teachers

Based in New York, plaintiff United Federation of Teachers Welfare Fund ("Teachers") provides supplemental health benefits to covered members, teachers, paraprofessionals, and eligible dependents. Teachers' Objections and Resps. to Lilly' First Set of Interrogs. at No. 1 (Teachers' Resps. to Interrogs., First Set"); Dep. Tr. of Arthur B. Pepper on behalf of Plaintiff Teachers at 7, Jan. 15, 2008 ("Teachers Dep."). Teachers offers various health products to its participants, including a prescription drug benefit.

An annual $100,000 maximum on prescription drug benefits is imposed per family per calendar year. UFT Welfare Fund Health and Welfare Benefits for Employees and Their Families 2007 Edition, 35, 50-51. The UFT Fund generally does not pay for medications for eligible persons in rest homes, nursing homes, sanitaria, extended-care facilities, and like entities unless pre-authorization is applied for and granted. *Id.* at 50.

It is Teachers' policy not to pay for any medications prescribed for off-label uses. Teachers' Resps. to Interrogs., First Set at No. 27; Teachers Dep. 42. It is the responsibility of Teacher's PBM to ensure that only prescriptions for covered medications are paid for by the UFT Fund. The UFT Fund relies on its PBM for such enforcement and monitoring.

Teachers reimburses eligible Zyprexa prescriptions for its covered members. Teachers' Resps. to Interrogs., First Set at No. 7. The formulary used by its PBM actually places Zyprexa in a preferred status. Teachers Dep. 71; 2007 Express Scripts National Preferred Formulary for UFT Welfare Fund. Like SBA, Teachers did not pay for any Zyprexa prescriptions from July 2001 until June 2005 for non-Medicare members because of the New York City program covering psychotropics. Teachers Dep. 79. Teachers continues to pay for Zyprexa.

Teachers alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. It claims that every reimbursed Zyprexa prescription was procured by Lilly's fraudulent conduct and has identified these prescriptions by producing claims information about cost, dose, and date in discovery.

f. DC 37

Based in New York, plaintiff ASFCME District Council 37 Health and Security Fund ("DC 37") provides health benefits to member employees of the City of New York and their dependants. DC 37's Objections and Resps. to Lilly's First Set of Interrogs. at No. 1 ("DC 37's Resps. to Interrogs., First Set"); Dep. Tr. of Willie Chang on behalf of Plaintiff DC 37 at 24-25, Jan. 16 & Jan. 23, 2008 ("DC 37 Dep.").

DC 37 offers various health products to its participants, including a prescription drug benefit. Imposed is an annual $100,000 cap on prescription drug benefits. DC 37 Dep. 241. DC 37 does not pay for medicines administered to patients in rest homes, hospitals or other in-patient facilities. *Id.* at 242-43.

Adopting its PBM's recommendations, DC 37 does not independently seek to impose restrictions on particular drugs or classes of drugs. *Id.* at 158, 237. It has required prior authorization for other medications, including those used to treat schizophrenia, upon the advice of its PBM. *Id.* at 158-59, 235-37. It is DC 37's policy not to pay for any medications prescribed for off-label uses. DC 37's Resps. to Interrogs., First Set at No. 37; DC 27 Dep. 97, 147.

For covered participants, DC 37 reimburses eligible Zyprexa prescriptions. DC 37's Resps. to Interrogs., First Set at No. 1. From July 2001 until June 2005, DC 37 did not pay for psychotropics for its non-Medicare members because the City of New York program covered

those during that time, although it did cover Zyprexa prescriptions for Medicare-eligible retirees during that period. *Id.* DC 37 has not imposed or sought any restrictions (including prior authorizations, step therapy, or higher co-pays) or modifications to its formulary for Zyprexa. DC 37 Dep. 157-59, 237-38. It continues to pay for Zyprexa. *Id.* at 177.

DC 37 alleges that it has suffered economic harm as a result of Lilly's false and misleading statements about the safety and efficacy of Zyprexa. The Fund claims that every Zyprexa prescription for which it has reimbursed was procured by Lilly's alleged fraudulent conduct. It has identified these prescriptions by producing claims data in discovery, including information such as cost, dose and date.

2. Individual Plaintiffs

a. Michael Pronto

Plaintiff Michael Pronto, age 31, is a resident of Brentwood, New York. In April 2003, he became "sad and depressed" after a romantic setback. He sought counseling, and was referred to a nurse practitioner, Florence Wissert. Dep. Tr. of Florence Wissert at 27:3-9, Mar. 12, 2007 ("Wissert Dep.").

i. Use of Zyprexa

Pronto was first prescribed Zyprexa on April 28, 2003 through Nurse Wissert. *See* Pronto Dep. Ex. 4 at 5. He continued to receive prescriptions for Zyprexa from April 2003 through August 2003 and from April 2004 through the fall of 2006, at which time he stopped taking the medication. Dep. Tr. of Scott Sussman, N.P. at 79:24-80:15, April 23, 2007 ("Sussman Dep.").

Whether Pronto has bipolar disease is disputed. Nurse Wissert had no independent recollection of Pronto and her testimony was based solely on notes in his chart. Wissert Dep. 93:18-22. Medical records indicate that she used a screening tool, Lilly's one-page "Mood Disorder Questionnaire" ("MDQ"), to find that Pronto had bipolar disease, *id.* at 29:20-30:9, but the MDQ is not intended as a diagnostic tool. *See* Part XVIII.B.1.a, *infra*. Nurse Wissert also noted he had a history of alcohol abuse. Plaintiffs note that there is no evidence she performed a differential diagnosis, *see* Pronto Dep. Ex. 4 at 10, or used the criteria of the American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Washington DC, American Psychiatric Press Inc., 2000 ("DSM-IV-TR"). Neither did she utilize the Young Mania Rating Scale, which Lilly uses to evaluate patient improvement and efficacy of Zyprexa in treating Bipolar I., or the Axis V GAF. Sussman Dep. 79:24-80:15. *See generally* Pronto Dep. Ex. 4; Sussman Dep. Ex. 4.

Pronto was not treated by Nurse Wissert after August 8, 2003. Pronto Dep. Ex. 4 at 9. He did not receive medical care from anyone between that date and March 31, 2004, during which time it appears that he did not take Zyprexa. *Id.* Beginning March 31, 2004, Pronto was seen at the office of Dr. James Carlson. Sussman Dep. 38:11-21. Although Pronto received some care from Dr. Carlson, he was primarily seen by Scott Sussman ("Sussman"), a nurse practitioner. *Id.* From April 26, 2004 through October 23, 2006, Pronto was prescribed Zyprexa through Dr. Carlson's office. *Id.* at 50; Pronto Med. Rec. 6, 14-15.

When Nurse Sussman began treating Pronto on March 31, 2004, he prescribed Prozac for what he diagnosed as insomnia, depression, and anxiety. Pronto Dep. Ex. 5A at 1. At Pronto's next visit, on April 26, 2004, Sussman continued Prozac and added Ambien for insomnia.

Pronto Dep. Ex. 5 at 1. Nurse Sussman twice noted bipolar in Pronto's chart as a possible condition, but never attempted to determine whether Pronto actually had bipolar disorder. Sussman advised Pronto to see a psychiatrist, Sussman Dep. 52-53, 55, but he could not afford to do so. Dep. Tr. of Michael Pronto at 127:2-128:2, March 2-3, 2007 ("Pronto Dep.").

Pronto's diagnoses changed over the course of his treatment with Nurse Sussman and Dr. Carlson. Pronto Dep. Ex. 5 at 1. From December 17, 2004 onward, the focus of his treatment was a back and neck injury and its associated pain, Sussman Dep. 129:24-130:16, although Sussman noted Pronto's anxiety and panic disorder in his medical records that day. *See* Sussman Dep. Ex. 4.

In March 2006, Pronto advised Nurse Sussman that he had become aware of the Zyprexa litigation and wanted to have his blood sugar tested. Sussman Dep. 70-72. On September 25, 2006, he told a staff member in Dr. Carlson's office that he had been off Zyprexa for three months but wanted to resume treatment. *Id.* at 71-73, 146-47. On October 13, 2006, Pronto applied to Lilly's prescription drug program for free Zyprexa and received several months' supply. Pronto Dep. 149-52; Pronto Med. Rec. 12-13. It is unclear when Pronto actually last ingested Zyprexa.

ii. Payment for Zyprexa

During most of the relevant period, Pronto was insured through UFCW Local 1500, which provided a pharmacy benefit. The cost of his Zyprexa prescriptions was largely covered by insurance, except for a flat $25 co-payment per prescription. Pronto Dep. 49, 54. The total amount Pronto spent on Zyprexa is approximately $500.00. *Id.* at 19. When he lost his

insurance in June 2006, he was able to obtain Zyprexa free from his health care providers or directly from Lilly. *Id.* at 51-52, 56, 149-52; Pronto Med. Rec. 12-13.

iii. Effects of Zyprexa

Pronto claims he developed hypertension and high cholesterol and triglycerides as a result of Zyprexa. When he began the medication on April 28, 2003, Pronto weighed approximately 200 pounds. Wissert Dep. 33:22-34:7. In the first two or three months, he reportedly experienced a rapid weight gain of approximately forty to sixty pounds, Pronto Dep. 14:4-20, 62:6-63:1, complaining about it at his September 13, 2004 visit with Nurse Sussman. Sussman Dep. Ex. 4. After discontinuing Zyprexa in the fall of 2006, his weight dropped to 226 pounds by March 2, 2007. Pronto Dep. 14:19-20.

Pronto's baseline laboratory values were not recorded when he started taking Zyprexa. In April 2004, his blood pressure was moderately hypertensive. A month later, blood glucose levels, cholesterol, LDL, and triglycerides were all normal. In January 2005, Nurse Sussman diagnosed him as having hypertensive heart disease, unspecified. By April 2006, Pronto's glucose level was elevated and his triglyceride levels, LDL, and cholesterol were very high. *See* Pronto Med. Rec.

Lilly contends that the evidence shows that Zyprexa was effective for Pronto, highlighting his positive self-reporting noted in his medical charts. *See id.* at 1-3, 7, 8; Wissert Dep. at 51-52, 63; Sussman Dep. 65. Nurse Sussman continued to prescribe Zyprexa in April 2006 because "it was working for" Pronto. Sussman Dep. 76.

Plaintiffs allege, in contrast, that there is no evidence that Zyprexa was ever effective for Pronto. While Pronto did report he was "feeling better with his current medication," plaintiffs

note that such self-reporting is often unreliable; moreover, it is difficult to determine what medication he was on at the time of these comments and whether he was referring to his pain medication. *Id.* at 131:7-13.

While this individual's case is thin, there is enough to go to a jury. The claim of overpayment, based upon the evidence that the price charged was too high, could be accepted by a reasonable juror.

iv. Related Cases

To seek redress for his alleged physical injuries, Pronto has sued Lilly in a separate action. That case is in the process of settlement. *See Pronto v. Eli Lilly & Co.*, Docket No. 06-CV-6834 (E.D.N.Y.) (administratively closed, pending final consummation of settlement). The general releases being used in these personal injury cases prevent a case such as the instant one from being brought by this plaintiff.

In an affirmation filed on June 23, 2008, Pronto's counsel states that the plaintiff has not

> settled any of his claims against Lilly and [has not] executed any release whatsoever of any claims against Lilly. Moreover, as described below, during discovery, defendant Eli Lilly and Company ("Lilly") agreed to treat Mr. Vannello's claims for economic injury, based on his purchases of Zyprexa, separately from his claims for physical injury based on his ingestion of Zyprexa. Based on this separation of the two types of claims, it is my understanding that, even if Mr. [Pronto] were to settle his physical injury claims, he would not release, and would not be asked to release, his purchase claims.

Aff. of Douglas R. Plymale 3, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 197.

This portion of plaintiff's counsel's statement is contradicted by Lilly's response of June 23, 2008; Lilly indicates that Pronto is in the process of settling his case as part of a global settlement, with a "Master Settlement Agreement on behalf of . . . Zyprexa clients, including

plaintiffs" Michael Pronto and Michael Vannello. Def.'s Br., June 23, 2008, at 2 (filed under seal). Their cases were administratively closed by order of the court on March 18, 2008, with no objection or motion to set aside or modify the order. *Id.*

The release required by the Master Settlement Agreement covering the Pronto and Vannello claims is broad enough to cover overcharge claims for Zyprexa. It reads:

> Claimant KNOWINGLY AND VOLUNTARILY RELEASES, ACQUITS, AND FOREVER DISCHARGES Lilly from any and all claims and/or causes of action of whatever kind or character, which have accrued or may accrue, whether known or unknown, and includes, but is not limited to, those claims which Claimant ever had, or now has, or hereafter can, shall or may have in the future against Lilly arising out of, relating to, resulting from, or in any way connected with Zyprexa, including those claims and damages of which Claimant is not aware and/or that Claimant has not yet anticipated. Claimant expressly waives the provisions of any applicable law protecting against the release of unknown or unanticipated claims.

Id. at 3. It is probable that the settlement will ultimately be fully executed, making the release operative; it would likely result in dismissal of plaintiffs' individual economic claims based on the general exhaustive terms of the release.

If the tentative global agreement already reached falls through, there is a conflict of interest. Plaintiff may "sell out" the proposed economic class to achieve a higher award in his personal injury claim. He cannot represent a class or subclass seeking compensation for overpayment without appearing to violate fiduciary responsibilities to the class.

In any event, the individual plaintiffs who are settling, or have settled, their personal injury claims would have to be excluded from the class, as plaintiffs' counsel practically concedes:

> Because at least some plaintiffs who have settled personal injury claims may have released their over-payment claims, however, Plaintiffs provide an adjusted definition for the Consumer Class to reflect the exclusion from the class of individuals who

> have released their claims. Plaintiffs had previously acknowledged that such persons would be excluded from the class; the adjusted definition merely formalizes that position and incorporates it into the class definition for ease of application.

Pfs.'s Submission Regarding Consumer Class Members' Releases 2, June 23, 2008, Docket No. 05-CV-4115, Docket Entry No. 196. Such a possible large carve-out of some 30,000 plaintiffs would unduly complicate administration of the litigation.

It may be that some of the third-party payors in the class will seek reimbursement from their insureds based on the personal injury recoveries. This possibility is of such minor significance as to warrant its being ignored at this stage of the litigation.

b. Michael Vannello

Plaintiff Michael Vannello, aged 54, is a resident of Ridgewood, Queens, New York. In 1995, he developed panic attacks and fear associated with riding the subway in New York City. He left his longstanding messenger job at First Manhattan Company, Dep. Tr. of Michael Vannello at 36:6-23, 80:25-81:9, Mar. 1, 2007 ("Vannello Dep."), and applied for and was granted Social Security Disability Insurance. *See* Dep. Tr. of Ronald Vannello, April 30, 2007 ("Ron Vannello Dep.") at 23:23-24:5. His brother, Ronald Vannello, is his representative payee for his monthly disability payments. *Id.* at 8:23-9:9.

i. Use of Zyprexa

Vannello was treated with multiple medications during the 1990s, including antidepressants and anti-anxiety medication. He was initially prescribed Zyprexa by his treating psychiatrist in February 2000, and took Zyprexa almost continuously to October 2002. He did not take Zyprexa for schizophrenia or bipolar disorder.

In March 1995, Laszlo Papp, M.D., a psychiatrist and professor at Columbia University, diagnosed Vannello as having panic disorder and anxiety disorder. Dep. Tr. of Dr. Lazlo Papp, Apr. 24, 2007 ("Papp Dep.") at 11, 14, 16. Dr. Papp first prescribed Zyprexa on February 22, 2000 at a 5 mg level, after Vannello had complained that he was nervous and worried with mood swings and angry outbursts, and had trouble sleeping. *Id.* at 86; Select Medical Records of Michael Vannello 16-17 ("Vannello Med. Rec.").

In March 2000, Dr. Papp referred Vannello to an intensive outpatient treatment program at Zucker Hillside Hospital, where he continued to be prescribed Zyprexa. *Id.* at 22-30. All of Vannello's Zyprexa prescriptions were for off-label uses while he was being treated at Hillside. *See* Dep. Tr. of Dr. Michael Kahan at 146:18-147:20, Apr. 11, 2007 ("Kahan Dep."). On June 30, 2000, Dr. Michael Kahan, a psychiatrist and head of the hospital's outpatient anxiety disorder program, diagnosed Vannello with a panic disorder with agoraphobia and continued him on Zyprexa at 5 mg daily, along with Xanax 1 mg four times a day.

While at Hillside, Vannello attended group therapy, received individual counseling from a clinical social worker, and was prescribed medication. Kahan Dep. Ex. 2. He received a variety of medications in addition to Zyprexa. *Id.* Dr. Kahan discontinued Vannello's Zyprexa use for three months starting in January 2001, but in March he began it again at an increased dosage of 7.5 mg. On June 29, 2001, Dr. Kahan further increased the dosage to 10 mg, raising it to 15 mg on August 14, 2001. On September 19, 2001, Dr. Kahan again increased the dosage to 20 mg because Vannello's anxiety had been increasing. *Id.* at 41-42. Vannello took Zyprexa for general anxiety disorder and panic disorder with agoraphobia until September 27, 2002. Ron Vannello Dep. at 69; Vannello Med. Rec. 39-40, 53; Kahan Dep. 30-31, 44, 108.

ii. Payment for Zyprexa

Vannello paid approximately $5,932.00 in cash for his Zyprexa prescriptions. *See* Mem. Supp. of Pfs.' Mot. for Class Cert. 54; Michael Vannello Eckerd Drug Prescription Records. He also received free samples of Zyprexa from his doctors. Kahan Dep. 106; Vannello Dep. 55.

iii. Effects of Zyprexa

Before he began taking Zyprexa in 2000, Vannello had a history of obesity and diabetes. Since 1993, his doctors have recommended a weight reduction diet. Vannello Med. Rec. 5, 7-8. Vannello was first treated for hypertension in March 1991, *id.* at 1, for adult onset diabetes mellitus on March 21, 1995, Dep. Tr. of Dr. Lewis Bass, M.D., May 14, 2007 ("Bass Dep.") at 68-69, and for high cholesterol in November 1996. Vannello Med. Rec. at 19.

At the time of his initial diabetes diagnosis in 1995, Mr. Vannello weighed 293 pounds. *See* Kahan Dep. Ex. 10 at 57. He was able to control his weight and diabetes without medication, Bass Dep. 68:23-69:9, losing 90 pounds over the next two years. *See* Kahan Dep. Ex. 10 at 45. After Vannello's weight dropped, he had no symptoms of diabetes. *See id.* at 45.

When Vannello began to take Zyprexa in February 2000, he weighed 240 pounds, *see* Papp. Dep. Ex. 3 at 5, and he was not taking any diabetes medications. Bass Dep. 68:23-69:9. By March 21, 2000, Vannello had gained 16 pounds. *See* Papp. Dep. Ex. 3 at 6. Over the next two years while on Zyprexa, his weight increased dramatically, reaching 314 pounds by August 2002. *See* Kahan Dep. Ex. 10 at 36. Vannello's Zyprexa treatment was discontinued in October 2002, around the time he reached his peak weight. Bass Dep. Ex. 3.

Vannello was again diagnosed with diabetes mellitus in May 2003. Bass Dep. 54. His fasting blood glucose levels peaked at 388 mg/dl around this time. *See* Kahan Dep. Ex. 10 at 32.

Similarly, Vannello's triglycerides were measured at 404 in early 2004; he had no previous record of triglycerides or total cholesterol elevation prior to this time. It took almost three years to drop to his pre-Zyprexa weight of 242 pounds. *Id.* He currently takes Metformin to treat his diabetes. Vannello Dep. 10, 167.

Vannello underwent a number of echocardiograms before, during, and after his Zyprexa treatment. A pre-Zyprexa echocardiogram on November 9, 1999, showed evidence of left atrial dilation and left ventricular hypertrophy. *See* Bass Dep. Ex. 3. A post-Zyprexa echocardiogram on May 12, 2001 revealed a dilated left ventricle in addition to left atrial dilation and left ventricular hypertrophy. Bass Dep. Ex. 4. EKGs in December 3, 2002, *see* Bass Dep. 43, and 2006 suggested continuing ischemic heart disease. Bass Dep. Ex. 6. Vannello's obesity, combined with pre-existing hypertension, may have caused excess strain on the heart muscle, possibly resulting in permanent damage. Bass Dep. 100:23-102:3; Decl. of William Wirshing, M.D. 6-7, 16, 48-49, Jan. 31, 2007 ("Wirshing Decl."); Expert Witness Rep. & Decl. of David Allison, Ph.D. 10; 23-24, Feb. 12, 2007 ("Allison Rep.").

Lilly maintains that the evidence shows that Zyprexa was effective for Mr. Vannello, citing positive self-reports noted in his medical charts, such as feeling less irritable, under better control, less anxious, improved mood, and getting out more. Vannello Med. Rec. 17, 31-33, 37-38, 56; Vannello Dep. 99-100; Papp Dep. 47-48. Vannello's symptoms worsened when Dr. Kahan tried to take him off Zyprexa in January 2001, and he reported feeling better after restarting Zyprexa in March 2001. Kahan Dep. 31-32.

Plaintiffs note there is no objective medical evidence—as opposed to Vannello's own self-reports—to indicate that Zyprexa was efficacious in treating him. *See* Fed. R. Evid. 702.

During the course of his treatment at Hillside, his diagnoses remained consistent. *See* Kahan Dep. Ex. 2. At the time of Vannello's discharge in November 2002, his diagnoses were still panic disorder with agoraphobia and general anxiety disorder. *Id.* at 210-12. None of the treating doctors prescribing Zyprexa used the Young Mania Ratings Scale ("Y-MRS"). On Axis V of the DSM-IV-TR, another standard measure of mental/emotional function, Vannello showed no improvement; his Global Assessment of Functioning Scale ("GAF") was 50/60 when he was admitted on March 20, 2000 to Hillside Hospital. *Id.*

iv. Related Cases

Vannello has filed a separate personal injury action against Lilly claiming a diabetes injury as a result of Zyprexa ingestion. *See Vannello v. Eli Lilly & Co.*, Docket No. 06-CV-6839 (E.D.N.Y.) (administratively closed, pending final consummation of settlement). For the same reason as in Mr. Pronto's case, *see* Part II.A.2.a.iv, *supra*, Mr. Vannello cannot represent the proposed class or subclass.

B. Prior Submissions

Multiple prior submissions define the claims, evidence, and facts of the dispute. Except for the plaintiffs' original individual complaints, all submissions are docketed under Docket No. 05-CV-4115 (E.D.N.Y.). *See* First Am. Class Action Compl. & Demand for Jury Trial, Nov. 7, 2005, Docket Entry No. 14 (redacted); Def.'s Answer, Apr. 26, 2007, Docket Entry No. 107; Def.'s Mot. to Dismiss First Am. Compl., Jan. 12, 2006, Docket Entry No. 22; Pfs.' Mem. of Law in Opp. to Def.'s Mot. to Dismiss, Feb. 23, 2006, Docket Entry No. 27; Def.'s Reply Mem. of Law in Further Support of Mot. to Dismiss, Mar. 24, 2006, Docket Entry No. 31; Def.'s Mot. for Summary J., May 29, 2007, Docket Entry No. 109; Pfs.' Mem. of Law in Opp'n to Def.'s

Mot. for Summary J., June 12, 2007, Docket Entry No. 113; Def.'s Reply Mem. in Support of Def.'s Mot. for Summary J., June 18, 2007, Docket Entry No. 121; Def.'s Local R. 56.1 Statement of Undisputed Facts, May 29, 2007, Docket Entry No. 109; Pfs.' SJ Fact Proffer; Pfs.' Submission Regarding Consumer Class Members' Releases, June 23, 2008, Docket Entry No. 196; Def.'s Response Regarding Information on Settlement of Sub-Class Representatives' Claims, June 23, 2008, Docket Entry No. 198 (sealed); Pfs.' Reply Submission Regarding Consumer Class Members' Releases, June 25, 2008, Docket Entry No. 199; Def.'s Mem. Relating to the Form of an Order on Class Cert., Section 1292(b) Cert., Aug. 22, 2008, Docket Entry Nos. 228, 230.

C. Unsealing Motions

From its inception over four years ago, this litigation has been subject to a protective sealing order pursuant to Rule 26 of the Federal Rules of Civil Procedure, applying to the products of discovery and all derived documents. Case Mgmt. Order No. 3, Aug. 3, 2004, Docket No. 04-MD-1596, Docket Entry No. 61 (limited to cases alleging personal injury from ingestion of Zyprexa); *see* Fed. R. Civ. P. 26(c). An identical protective order specifically applicable to the third-party payors cases was issued on October 16, 2006, Case Mgmt. Order No. 3, Oct. 16, 2006, Docket No. 05-CV-4115, Docket Entry. No. 61, and a second one applicable to financial data a month later. Case Mgmt. Order No. 4, Nov. 17, 2006, Docket Entry. No. 72. Since the inception of the case, millions of documents produced by Lilly have been marked confidential.

Along with their first amended complaint, filed November 7, 2005, plaintiffs moved to declassify certain Lilly documents cited in the complaint. Notice of Pfs.' Action to Lift

Confidentiality Designations, Nov. 7, 2005, Docket Entry No. 15. Plaintiffs argued that Lilly's "documents cited in the First Amended Complaint do not 'contain trade secrets or other confidential research, development, or commercial information' or other material properly protected under Federal Rule of Civil Procedure 26(c)(7), and that the documents are improperly designated as 'confidential' under the protective order." *Id.* Both parties briefed the issue for decision by the special master supervising discovery. *See* Lilly Letter, Apr. 19, 2006, Docket Entry No. 37.

In January 2007, plaintiffs renewed their declassification motion, which had not yet been resolved. The motion was deferred, *see* Order, Feb. 7, 2007, Docket Entry No. 85, pending resolution of the injunction proceedings related to the *New York Times*' December 2006 publication of a series of articles revealing confidential information obtained illegally from the Zyprexa MDL. *See In re Zyprexa Injunction*, 474 F. Supp. 2d 385 (E.D.N.Y. 2007). Plaintiffs also challenged the confidentiality designations of all of defendant's documents cited in defendant's experts' reports, for the same reasons as in their previous motion. *See* Notice of Pfs.' Action to Lift Confidentiality Designations, Mar. 9, 2007, Docket Entry No. 91; *see* Pfs.' Letter, Mar. 23, 2007, Docket Entry No. 93 (requesting a hearing). The motion was referred to the special master to review the documents and determine which should be unsealed. Order, Mar. 30, 2007, Docket Entry No. 104.

On July 7, 2007, plaintiffs challenged the confidentiality designations of all the documents produced by defendant that were cited in plaintiffs' summary judgment and *Daubert* pleadings. Notice of Pfs.' Action to Lift Confidentiality Designations, July 7, 2007, Docket Entry No. 130. On April 2, 2008, plaintiffs wrote to the court requesting that the declassification

process by the special master be completed. As of that date, plaintiffs challenged the confidentiality of 351 documents produced by Lilly, as well as the marketing and sales data covered by Case Management Order No. 4. Pfs.' Letter, Apr. 2, 2008, Docket Entry No. 172.

Plaintiffs then moved under Rule 23(d) of the Federal Rules of Civil Procedure for an order permitting the publication of documents on the basis of which the parties made their dispositive motions, including class certification. *See* Pfs.' Notice of Mot. & Mem. in Support, Aug. 4, 2008, Docket No. 05-CV-4115, Docket Entry Nos. 215-16; Pfs.' Reply, Aug. 22, 2008, Docket Entry No. 225; Fed. R. Civ. P. 23(d)(1)(B)(iii) ("In conducting an action under this rule, the court may issue orders that: . . . require—to protect class members and fairly conduct the action—giving appropriate notice to some or all class members . . . (iii) the members' opportunity to signify whether they consider the representation fair and adequate, to intervene and present claims or defenses, or to otherwise come into the action."). Several non-parties also requested that the documents be unsealed. *See* Letter, Bloomberg L.P., Aug. 18, 2008, Docket No. 04-MD-1596, Docket Entry No. 1832; Mot. to Vacate CMO 3, Vera Sharav, Alliance for Human Research Protection & David Cohen, Docket No. 04-MD-1596, Docket Entry No. 1859; Letter, Kaiser Health Foundation Plan et al., Aug. 22, 2008, Docket No. 04-MD-1596, Docket Entry No. 1847. Defendant opposed, citing trade secrets and arguing the documents contain commercially valuable information. Def.'s Mot. in Opp'n, Aug. 18, 2008, Docket Entry No. 222. This motion was argued at a hearing on September 4, 2008.

Based on this country's long-standing tradition of open access to the courts and court records, the enormous number of people who have taken or will take Zyprexa, the involvement

of government regulatory bodies, absent class members' interest in the proceeding, and the age of the documents, the motions to unseal are granted. *See* Part XXIV, *infra*.

D. Dispositive Motions

1. Motion to Dismiss

On January 12, 2006, Lilly filed a Rule 12 motion to dismiss plaintiffs' Amended Complaint on the grounds that plaintiffs could not satisfy the causation element of their claims, that they lack standing, and that they suffered no direct injury. Def.'s Mot. to Dismiss First Am. Compl.; Def.'s Reply Mem. of Law in Further Support of Mot. to Dismiss. In response, plaintiffs assured the court that they would offer evidence that would demonstrate causation and reliance, Apr. 21, 2006 Hr'g Tr. on Def.'s Mot. to Dismiss 27, Docket Entry No. 36, and alleged as follows:

> [I]t will be proven as fact not presumption, that every influential sector of the mental health community was subjected to Defendant's misrepresentations and omissions, and that the broad-based fraudulent conduct had real-world, significant effect that was intended by the program.

Pfs.' Mem. of Law in Opp. to Def.'s Mot. to Dismiss 30.

Lilly's Motion to Dismiss was denied on April 21, 2006. *See* Minute Entry, Apr. 21, 2006, Docket Entry No. 36.

2. Summary Judgment

Instead of a motion to dismiss, the court preferred to rule on a summary judgment motion. It directed the parties to work with the Special Master to establish a limited discovery plan. Apr. 21, 2006 Hr'g Tr. 43-49; *see* Am. Case Mgmt. Order No. 1, June 19, 2006, Docket Entry No. 39. Discovery was confined to the grounds for summary judgment. *Id.* at 3-6; Apr. 21, 2006 Hr'g Tr.

43-49. The discovery undertaken by both parties is discussed at length in Lilly's May 29, 2007 Memorandum of Law in Support of its Motion for Summary Judgment. Plaintiffs were given access to all of the discovery taken in the personal injury litigation, which comprised over fifteen million pages of records and included the depositions of fifty-eight current and former Lilly employees.

Lilly conducted Rule 30(b)(6) depositions of the four original named payor plaintiffs UFCW, Mid-West, Local 28, and SBA. Testimony was obtained from the four PBMs that provide pharmacy benefit advice to the named plaintiffs. Lilly also undertook discovery regarding the two individual plaintiffs, deposing them, their family members, and prescribers.

Both parties produced a number of expert witness reports and deposed the experts. Plaintiffs submitted expert reports by Meredith Rosenthal, Ph.D.; Jeffrey E. Harris, M.D., Ph.D.; John Abramson, M.D.; Steven G. Klotz, M.D.; Lon Schneider, M.D., and Robert Rosenheck, M.D. *See* Pfs.' Disclosure of Expert Testimony Pursuant to Fed. R. Civ. P. 26(a)(2), Feb. 27, 2007, Docket Entry No. 87 (designating plaintiffs' experts). Two plaintiffs' experts, Myron Winkelman, R.Ph., and Terry D. Leach, Pharm.D, proposed to testify about how PBMs function from economic and clinical perspectives. *Id.* Plaintiffs also relied on the following experts, previously disclosed in the personal injury litigation: David Goff, Jr., M.D.; David B. Allison, Ph.D.; Frederick Brancati, M.D., MHS; William Wirshing, M.D.; John L. Guerigian, M.D.; and Laura Plunkett, Ph.D., D.A.B.T. *Id.*; *see* Part XVIII, *infra*.

In support of its summary judgment motion, Lilly relied on five experts: Ernest R. Berndt, Ph.D.; Iain M. Cockburn, Ph.D.; David F. Feigal, Jr., M.D.; David Kahn, M.D.; and Jeffrey S. McCombs, Ph.D.

With a record developed by May of 2007, Lilly filed a motion for summary judgment on grounds similar to those in its motion to dismiss. Plaintiffs also filed a summary judgment motion. On June 28, 2007, the court denied both summary judgment motions and all of the various *Daubert* challenges to proposed expert testimony. *In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 579 (E.D.N.Y. 2007) ("While the case is close, plaintiffs have sufficiently demonstrated for purposes of this motion that genuine issues of material fact exist with respect to their RICO and state substantive law claims.").

Recognizing that the law underlying its decision was "in a state of flux and not free from doubt," the court declined to certify its summary judgment order for immediate interlocutory appeal pursuant to 28 U.S.C. § 1292(b), but noted that it would do so after deciding whether the case should proceed as a class action. *Id.* at 580-81.

E. Class Certification

On August 3, 2007, plaintiffs filed a motion for class certification. They proposed two subclasses: a nationwide third-party payor class of institutions that have paid for the cost of Zyprexa prescriptions, and a nationwide patient class of individuals who have paid out-of-pocket for some or all of the cost of Zyprexa prescriptions. Pfs.' Class Cert. Br. 58-59.

1. Briefing

Both parties filed extensive briefing. *See id.*; Class Plaintiffs' Proposed Trial and Apportionment Plan and Statement of State Law ("Pfs.' Trial Plan"), Dec. 4, 2007, Docket Entry No. 144; Defendant's Memorandum of Law in Opposition to Plaintiffs' Motion for Class Certification ("Def.'s Mem. of Law in Opp. to Class Cert."), Feb. 22, 2008, Docket Entry No. 150 (filed under seal); Defendant's Statement of Facts in Support of Defendant's Opposition to

Plaintiff's Motion for Class Certification ("Def.'s Fact Proffer"), Def.'s Local R. 56.1 Statement of Undisputed Facts, Feb. 22, 2008, Docket Entry No. 150; Plaintiffs' Reply Memorandum of Law in Further Support of Purchase Claim Plaintiffs' Motion for Class Certification (Pfs.' Reply Mem. of Law in Further Support of Purchase Claim Pfs.' Mot. for Class Cert.), Mar. 21, 2008; Plaintiffs' Response to Defendant's Local Rule 56.1 Statement of Undisputed Facts (Pfs.' Response to Def.'s Fact Proffer"), Mar. 21, 2008, Docket Entry No. 165; Plaintiffs' Post-Hearing Memorandum on Class Certification, ("Pfs.' Post-Hr'g Mem. on Class Cert."), Apr. 9, 2008, Docket Entry No. 176; Defendant's Post-Hearing Memorandum Opposing Class Certification, ("Def.'s Post-Hr'g Mem. Opp. Class Cert."), Apr. 9, 2008, Docket Entry No. 177.

2. Discovery

In filing their motion for class certification shortly after summary judgment was denied, plaintiffs indicated they did not believe additional discovery on class certification was necessary. *See* Pfs.' Class Cert. Br., Aug. 3, 2007. In response, Lilly moved for additional discovery on class certification. At a hearing on Lilly's motion on September 21, 2007, the court agreed that the record contained little evidence regarding differences in the ways that third-party payors in the putative class develop and maintain their formularies:

> What concerns me is the differences in the nature of these insurers and now how they went about doing their research, putting their formularies together, using experts, what their insurance plans called for in connection with reimbursement, whether they were reimbursing fully or whether there was also a requirement that the insured paid a portion.

Sept. 21, 2007 Hr'g Tr. 18-19. More information in these areas was necessary to determine whether the proposed class was sufficiently homogenous. *Id.* at 29.

On November 30, 2007, a conference was held to discuss the scope of additional class certification discovery, including the depositions of the named payors' insureds' prescribers. *See* Nov. 30, 2007 Hr'g Tr. While it was willing to permit the limited class certification discovery previously ordered by the special master to go forward as contemplated, *id.* at 35, the court also suggested that the information sought by the plaintiffs was not necessary for class certification. *Id.* at 23 ("I'm very skeptical about whether we need [additional call note and database production]"). Instead, the court recommended that the parties "just close [discovery] out at this stage and go forward with certification based on the enormous amount of papers and other material that we have in this case and in other cases." *Id.* at 35. The parties agreed; the only further discovery undertaken was Lilly's depositions of newly identified class representatives and one of UFCW's PBMs. *Id.* at 37-38. Depositions previously taken in this and other matters were to be used to present the class certification issue, although their admissibility could still be challenged at trial. *Id.* at 37. Case Management Order No. 9 reflected this agreement and was entered on December 21, 2007. *See* CMO 9, Nov. 21, 2007, Docket Entry No. 146.

3. Expert Reports

Preparing for an evidentiary hearing on class certification, both parties relied on the same experts presented to the court on the issue of summary judgment. *See* Part XVIII, *infra*. Defendants also presented a new expert, Dr. Eugene Kolassa. Additional expert reports were submitted on the issue of class certification.

All *Daubert* motions as to proposed expert witnesses, whether made as part of the class certification motion or in earlier proceedings, have been denied.

> Each of the challenged experts meets *Daubert* requirements. Each is a distinguished scientist whose expertise probably will be helpful in deciding relevant scientific and economic issues. Attacks on them . . . are primarily based on assessments of credibility best left for the trier. *In limine* motions respecting particular aspects of these and other experts' proposed testimony will be considered when it becomes clear what will be the detailed issues to be tried.

In re Zyprexa Prods. Liab. Litig., 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

Four days before the hearing, on March 24, 2008, Lilly filed a Motion to Strike as untimely and prejudicial the Supplemental Declaration of Robert Rosenheck, M.D., the Supplemental Declaration of William Wirshing, M.D. and the Second Supplemental Declaration of Meredith Rosenthal, Ph.D. *See* Def.'s Mot. to Strike, Mar. 24, 2008, Docket Entry Nos. 160, 161. At the March 29, 2008 hearing, defendant's motion was denied. *See* Transcript of Evidentiary Proceedings on Class Certification, March 28, 2008 through April 2, 2008 ("Tr."); *see also* Pfs.' Mot. to Strike Decl. of Alan G. White, Ph.D., June 12, 2007, Docket Entry Nos. 114, 115.

4. Evidentiary Hearing

On March 28-31 and April 1-2 of 2008 an extensive evidentiary hearing was conducted to comply with the certification standards set by the Court of Appeals for the Second Circuit. *See In re Initial Public Offering Securities Litigation* ("*In re IPO*"), 471 F.3d 24, 41 (2d Cir. 2006) (noting that even when there is overlap between a Rule 23 requirement and a merits issue, "the district judge must receive enough evidence, by affidavits, documents, or testimony, to be satisfied that each Rule 23 requirement has been met."). Extensive oral and written expert testimony was considered. More than 1,000 exhibits, the majority of which had been previously submitted, were admitted.

On April 2, 2008, the court granted leave to the parties to file post-hearing memoranda. *See* Pfs.' Post-Hr'g Mem. on Class Cert.; Def.'s Post-Hr'g Mem. Opp. Class Cert. Further argument was heard on April 10, 2008. Additional submissions were requested and received. *See* Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert.; Affirm. of Andrea Bierstein in Support of Purchase Claim Pfs.' Supp. Post-Hr'g Mem. on Class Cert (undocketed); Affirm. of Thomas Sobol in Connection with Damages Calculations, Apr. 24, 2008, Docket Entry No. 180; Def.'s Supp. Post-Hr'g Mem. of Law, Apr. 24, 2008, Docket Entry No. 181. Supplemental authority letters were submitted. *See* Letter from Lauren G. Barnes, May 20, 2008, Docket Entry No. 189 (noting *New England Carpenters Health Benefits Fund v. First Databank, Inc.*, 248 F.R.D. 363 (D. Mass 2008); Lilly Letter, May 22, 2008, Docket Entry No. 190 (same); Pfs.' Notice of Supp. Authority, June 9, 2008, Docket Entry No. 191 (noting *Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008)); Def.'s Mem. in Opp. to Notice of Supp. Authority, June 10, 2008, Docket Entry No. 192; Pfs.' Reply in Support of Notice of Supp. Authority, June 11, 2008, Docket Entry No. 193.

Further information about the status of the two individual plaintiffs' personal injury lawsuits against Lilly and their proposed settlement releases was requested. *See* Purchase Claim Pfs.' Submission Regarding Consumer Class Members' Releases, June 23, 2008, Docket Entry No. 196; Def.'s Response Regarding Information on Settlement of Sub-Class Representatives' Claims, June 23, 2008, Docket Entry No. 198 (sealed); Pfs.' Reply Submission Regarding Consumer Class Members' Releases, June 25, 2008, Docket Entry No. 199; Pfs.' Reply Affirmation of Kevin L. Oufnac, June 25, 2008, Docket Entry No. 200; Affirmation of Dr. Douglas R. Plymale, June 19, 2008, Docket Entry No. 197.

Additional briefing was requested on the combined impact of the Second Circuit Court of Appeals decision in *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), and the Supreme Court's opinion in *Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008), on the pending motion for class certification. *See* Order, June 16, 2008, Docket Entry No. 195.

After the court's discussion draft on certification was issued on July 2, 2008, the parties were given an opportunity to further brief and argue certification-related issues. *See* Hr'g Tr., July 17, 2008; Oral Statement by the Court at Class Cert. Hr'g, July 17, 2008, Docket No. 05-CV-4115, Docket Entry No. 207; Order, July 17, 2008, Docket Entry No. 208; Order on Potential Conflict of Interests, July 21, 2008, Docket Entry No. 210; Pfs.' Mem. in Response to the July 21, 2008 Order Regarding *Amchem* Issues, Aug. 4, 2008, Docket Entry No. 214; Def.'s Response to the July 21, 2008 Order Regarding Potential Conflicts of Interest, Aug. 4, 2008, Docket Entry No. 211; Purchase Claim Pfs.' Mem. Final Supp. Submission Regarding Class Cert. and Cert. Under 28 U.S.C. § 1292, Aug. 22, 2008, Docket Entry No. 226; Joint Notice Program, Aug. 22, 2008, Docket Entry No. 227; Def.'s Mem. Relating to the Form of an Order on Class Cert., Section 1292(b), Aug. 22, 2008, Docket Entry Nos. 228, 230. A full opportunity was given to the parties and interested members of the public to comment on this court's draft certification order of July 2, 2008. *See* Part I.E, *supra*.

Each side has submitted a proposed certification order fulfilling the requirements of Rule 23(c), consistent with, and incorporating, the analysis and findings in the prior tentative proposed draft of this memorandum and order. *See* Pfs.' Proposed Order on Class Cert. attach. 1, Aug. 22, 2008, Docket Entry No. 227; Def.'s Proposed Order, Aug. 22, 2008, Docket Entry No.228 Ex. 1; *see* Fed. R. Civ. P. 23(c). Defendant notes that submission of the order does not constitute

agreement with any portion of this memorandum. The order is incorporated in the conclusion. *See* Part XXIV, *infra*.

Both parties have, assuming *arguendo* that the present memorandum and order will be approved by the Court of Appeals for the Second Circuit, agreed upon the notification procedures to be used under Rule 23(c)(2), including opt-out provisions and the like. *See* Joint Notice Program, Aug. 22, 2008, Docket Entry No. 227 attach. 2. The Notice Plan is attached in Appendix A, *infra*.

The expert reports and testimony considered by the court and contested by the parties in the instant motion are individually discussed in Part XVIII, *infra*. The following Parts III-XVII present the background information necessary to understand the context of the motion for class certification.

III. Anti-Psychotic Medications

Lilly's prescription medicine Zyprexa, with a chemical name of olanzapine, is one of a class of medications known as "atypical" or "second-generation" antipsychotics ("SGAs") that treat schizophrenia and bipolar disease. Schizophrenia is a severe, debilitating mental illness that afflicts over one percent of the general population—2.5 million Americans—often beginning in late adolescence or early adulthood. *See* Robert Freedman, *Schizophrenia*, 349 (18) New Eng. J. Med. 1738, 1738 (2003); Gary D. Tollefson & Cindy C. Taylor, *Olanzapine: Preclinical and Clinical Profiles of a Novel Antipsychotic Agent*, 6 (4) CNS Drug Reviews 303, 304 (2000); U.S. Dep't of Health & Human Servs., Mental Health: A Report of the Surgeon General 273 (1999), http://www.mentalhealth.org/features/surgeongeneralreport/home.asp; DSM-IV-TR, *supra* at 308. One of the most complex and challenging of psychiatric disorders, schizophrenia is a

heterogeneous syndrome of disorganized and bizarre thoughts, delusions, hallucinations, inappropriate affect, and impaired psycho-social functioning. *See* DSM-IV-TR, *supra* at 298-302. The illness occurs when a patient suffers two or more of the following characteristic symptoms: (1) delusions, (2) hallucinations, (3) disorganized speech, (4) grossly disorganized or catatonic behavior, and (5) negative symptoms, *see id.*, or has bizarre delusions or hallucinations of voices commenting on the person's behavior or thoughts. Research has shown a variety of abnormalities in schizophrenic brain structure and function. Pharmacotherapy: A Pathophysiologic Approach (Joseph T. Dipiro et al., eds., 5th ed. 2002) (hereinafter "Pharmacotherapy") at 1219; *see* DSM-IV-TR, *supra* at 299. Causation is believed to be multi-factorial. Pharmacotherapy, *supra* at 121; *see* DSM-IV-TR, *supra* at 305-06, 309-11.

Bipolar disorder is a serious, lifelong mental illness marked by dramatic shifts in mood, from abnormally elevated, expansive, or irritable moods to states of extreme sadness and hopelessness, often with periods of normal mood in between. Nat'l Inst. of Mental Health, Bipolar Disorder, *available at* http://www.nimh.nih.gov/publicat/bipolar.cfm (last visited June 30, 2008); *see* Decl. of Steven Klotz, M.D. 2, Feb. 22, 2007, Docket Entry No. 99 ("Klotz Decl."). Bipolar I, characterized by the occurrence of one of more manic episodes or mixed episodes, often with major depressive episodes, and Bipolar II, characterized by one or more major depressive episodes accompanied by at least one hypomanic episode, are separate disease states. *See* DSM-IV-TR, *supra* at 382-92. Because of its complexity, bipolar disease can be difficult to diagnose; between seven and ten years of mis-diagnoses and incorrect treatment is typical for bipolar patients. Klotz Decl. 6. "[U]ntreated bipolar disorder can be disastrous; 10

percent of sufferers commit suicide." Mary Carmichael, *Welcome to Max's World*, Newsweek, May 26, 2008.

In the past five years there has been extensive research into diagnosing and recommending treatments for bipolar disorder, funded in part by pharmaceutical manufacturers. Klotz Decl. 3. There has been a corresponding growth of bipolar diagnoses—correct *and* incorrect—leading to an increase in patients and greater awareness of the disease; many patients labeled "bipolar" are mentally ill but, upon detailed psychiatric examination, not bipolar. *Id.* at 3-4. An estimated 5.7 million Americans are affected by the disorder.

Both schizophrenia and bipolar disorder, like many mental illnesses, display considerable biological and symptomatic differences. *See* Decl. of Richard G. Frank, Ph.D. at ¶ 7, Jan. 8, 2008, Docket Entry No. 148 ("Frank Decl."). Often, patients with these disorders have other psychiatric and physical problems. *Id.* Due to the illnesses' heterogeneity, different people respond differently to different psychotropic drugs. Which drug will work best for a new patient is often unknown until he or she tries it; thus clinical decision-making about psychotropic medications almost inevitably is based on "trial and error." *Id.* at 3-4 (citing H.A. Huskamp, *Managing Psychotropic Drug Costs: Will Formularies Work?*, Health Affairs 22(5):84-96 (2003)). As a result, third-party payors prefer not to place strong restrictions on the use of antipsychotic medications. *Id.* at 4.

While the two primary uses of second-generation antipsychotics remain the treatment of schizophrenia and bipolar disorder, antipsychotics are prescribed off-label, i.e., for non-FDA approved purposes, to treat symptoms related to agitation, anxiety, psychotic episodes, obsessive behavior, behaviors related to dementia, depression, obsessive compulsive disorder ("OCD"),

Post Traumatic Stress Disorder ("PTSD"), personality disorders, and Tourette's Syndrome. *See* Frank Decl. at 3 (citing Agency of Health Research and Quality, Off Label Use of Atypical Antipsychotic Drugs, *available at* http://effectivehealthcare.ahrq.gov/reports/topic.cfm?topic=8&sid=34&rType=10). "'Off-Label' prescriptions are a mainstay of the drug industry—an estimated 21% of drug use overall." Anna Wilde Mathews & Avery Johnson, *FDA to Propose Guidelines for 'Off-Label' Drug Use*, Wall St. J., Feb. 15, 2008; *see* Rosenthal Decl. 26 (noting that Zyprexa's "unapproved uses represent an average of 31% of Zyprexa mentions in the National Disease and Therapeutic Index (NDTI) database."). Examples of off-label use include using a drug to treat a condition for which it is not indicated, treating an indicated condition with different doses than those specified on the label, and prescribing a drug for a different patient population than that indicated (such as children, if it has only been approved to treat adults). Off-label uses of approved medications have not been subjected to the baseline FDA scrutiny required for on-label indications, and are thus considered riskier. *See id.* at 1021.

Two common off-label uses of SGAs are for dementia in the elderly and children with bipolar disorder. One in four nursing home residents take antipsychotic drugs, with sales in 2007 totaling over $13 billion. Kris Hundley, *Dementia Relief, with a Huge Side Effect: The Off-Label Use of Some Drugs Is Helping*, Tampa Bay Times, Nov. 18, 2007. "The use of antipsychotic drugs to tamp down the agitation, combative behavior and outbursts of dementia patients has soared, especially in the elderly." Tarkan, *supra* at F1. Use of the medications are particularly high in nursing homes. Sedatives and antipsychotics—despite their potentially severe side

effects, including increased risk of death—present a tempting option to overextended staff. *Id.* Of Zyprexa's $4.4 billion sales in 2006, 26.6% were to patients over 64. *Id.*

Off-label use of antipsychotics in children with bipolar disorder is a recent phenomenon. "Between 1994 and 2003, the number of children treated for bipolar disorder in the United States increased to more than 800,000 from 20,000." M. Alexander Otto, *Should Kids Get These Drugs? Plan Likely to Increase Scrutiny of Anti-Psychotics in Children*, News Tribune, May 12, 2008. At least some of those were diagnosed "no doubt . . . wrongly. The disease is hard to pin down." *See* Carmichael, *supra.* Just two SGAs have been approved for use by children, Risperdal and Abilify; Zyprexa is indicated for use by adults only.

A. First-Generation or "Typical" Anti-Psychotics ("FGAs")

Zyprexa is generally known as a "second-generation antipsychotic" or "SGA" to differentiate it from older, first-generation antipsychotics ("FGAs"), which were the standard drug therapy for schizophrenia until the 1990s. FGAs include chlorpromazine (Thorazine), fluphenzine (Proxilin), haloperidol (Haldol), molindone (Moban), thioridazine (Mellaril), loxapine (Loxitane), mesoridazine (Serentil), perphenazine (Trilafon), thiothixene (Navane), and trifluoperazine (Stelazine), some of which have been in use since the 1950s. Pharmacotherapy, *supra*, at 1224. FGAs are sometimes referred to as "typical" antipsychotics and SGAs as "atypical."

Although many different FGAs exist, they share similar levels of efficacy. They are, generally speaking, post-synaptic dopamine-receptor antagonists, i.e., they target dopamine receptors in the brain. *Id.* at 1220. A troubling side effect of typical antipsychotics is that the blockage of dopaminergic neurotransmission causes extrapyramidal syndromes ("EPS") such as

Parkinsonian effects or tremors. *Id.* at 1223. Tardive Dyskinesia ("TD"), a long-lasting movement disorder, frequently occurs with prolonged treatment. *Id.*

B. Second-Generation or "Atypical" Anti-Psychotics ("SGAs")

Because of FGAs' potential for severe side effects and their limited efficacy, many pharmaceutical companies searched for new drugs that would be more effective and cause less movement disorder. By the 1980s, clozapine, the first SGA, was being investigated on that hypothesis. Since it had an "atypical index" when measuring its effect on different parts of the brain, clozapine became known an "atypical" antipsychotic. 2007 Physicians Desk Reference at 2184-89. Clozapine has different effects than FGAs on areas of the brain that control movement; it was hoped that it would cause less movement disorder than other antipsychotics. *Id.* While clozapine turned out to be effective, its toxic side effects, including agranulocytosis (dramatic loss of white blood cells), limited its use to about ten percent of persons with schizophrenia. *Id.*; Decl. of Meredith Rosenthal at 6, Feb. 27, 2007, Docket Entry No. 101 ("Rosenthal Decl."). Although clozapine was the first atypical antipsychotic, it tends to stand on its own between FGAs and SGAs. Clozapine was approved by the FDA in September 1989 and was the only SGA available in the United States until 1993, although its potential toxicity assured only a small market share. *Id.* at Decl. 5. .

During the 1990s pharmaceutical companies, building on the "atypical" hypothesis, developed newer, second-generation antipsychotic drugs ("SGAs") attempting to capture the enhanced therapeutic effect of clozapine without its toxicity and or the side effects caused by traditional antipsychotics, such as EPS and TD. "The introduction of atypical antipsychotic medications was trumpeted by the manufacturers of these pharmaceutical agents as a major

advance in the treatment of schizophrenia with improved symptomatic control of the psychosis and a reduction in both tardive dyskinesia and extra pyramidal side effects." Wirshing Decl. 7.

In late 1993, risperidone became the first non-clozapine SGA to receive Food and Drug Administration ("FDA") approval. In early 1994, Janssen, a subsidiary of Johnson & Johnson, began marketing and selling risperidone under the brand name Risperdal. During the next two years, Janssen heavily marketed and promoted Risperdal for its approved indication, management of the manifestation of psychotic disorders, and, allegedly, for multiple non-approved uses, including attention deficit-hyperactivity disorder, bipolar disorder, and aggression associated with late-onset dementia. By late 1996, Janssen had a significant share of the United States antipsychotic drug market, and had demonstrated the sales potential of marketing SGAs for non-approved indications. When Zyprexa entered the market in 1996, Risperdal was seen as its primary competitor. *See* Strategy Integration Team, Eli Lilly & Co., Zyprexa in Serious Mental Illness (65 Plus Years)—A Strategy Review (undated).

The FDA first approved Zyprexa on September 30, 1996, for use in treating "the manifestations of psychotic disorders" seen in schizophrenia. Letter from Dr. Robert Temple, Director, Office of Drug Evaluation I, FDA, to Dr. Timothy R. Franson, Eli Lilly & Co., Sept. 30, 1996. Thereafter, the FDA approved Zyprexa for maintenance treatment of schizophrenia, FDA Nov. 9, 2000 Approval Letter; for the short-term treatment of acute manic episodes associated with bipolar I disorder as monotherapy, FDA March 17, 2000 Approval Letter; in combination with lithium or valproate, FDA July 10, 2003 Approval Letter; and for maintenance in the treatment of bipolar disorder. FDA Jan. 14, 2004 Approval Letter.

Multiple other second-generation antipsychotic drugs have been introduced since 1996. Atypical SGAs, in addition to clozapine (Clozaril), olanzapine (Zyprexa), and risperidone (Risperdal), now include quetiapine (Seroquel), aripiprazole (Abilify), and ziprasidone (Geodon). Pharmacotherapy, *supra* at 1224. Seroquel has been approved since 1997. Indicated for schizophrenia and acute manic or mixed episodes associated with bipolar disorder, Geodon entered the marketplace in March of 2001, and Abilify in November 2002. Abilify is also approved for treatment of depression. Transcript of Evidentiary Proceedings on Class Certification 827 ("Evid. Hr'g Tr."), March 28, 2008 through April 2, 2008.

C. Rapid Growth of Pharmaceuticals and SGAs

SGAs were and are marketed as providing more effective treatment with fewer side effects and better symptom reduction than the older—and far less expensive off-patent—FGAs. Expert Rep. of John Abramson, M.D., at 7, Feb. 28, 2007, Docket Entry No. 97 ("Abramson Rep."). Because of the severe and costly—in both human and economic terms—nature of the illnesses that SGAs treat, insurance companies, believing the newer drugs to be more effective, have been willing to spend billions of dollars on them, despite the fact that they can cost up to 100 times more than the older antipsychotic medications. *Id.* (noting that, for example, Zyprexa costs more than twenty times the cost of Haldol, an FGA).

In 1994, when Risperdal, the second SGA after clozapine, was introduced, only five percent of schizophrenic patients were being prescribed an SGA; national spending on antipsychotic medications was $1.4 billion. *Id.* Ten years later, about ninety percent of schizophrenic patients nationally were being treated with SGAs rather than FGAs, and $10

billion was spent annually on antipsychotic medications. *Id.*; *see* Frank Decl. 4 (noting that in 2003, IMS Health estimated United States antipsychotic drugs sales to total $8.1 billion).

The dramatic rise in the costs of prescription drugs over the past decade is in large part due to SGAs, which now make up a substantial proportion of increased national spending on medication. In 2004, for instance, prescription drug expenditures in the United States were estimated at $188.5 billion, nearly five times the $40.3 billion the nation spent fourteen years earlier. Prescription Drug Trends, Kaiser Family Foundation (June 2006). "Sales of newer antipsychotics like Risperdal, Seroquel and Zyprexa totaled $13.1 billion in 2007, up from $4 billion in 2000." Tarkan, *supra* at F1; *see* Alex Berenson, *Lilly Adds Strong Warning Label to Zyprexa, a Schizophrenia Drug*, N.Y. Times, Oct. 6, 2007.

SGAs now account for about ninety percent of all antipsychotics drugs prescribed for all psychiatric purposes, regardless of whether they were approved for those indications or not. *See* Jeffrey A. Lieberman, *Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia,* 353 N. Eng. J. of Medicine 1209, 1210 (2005). Off-label prescriptions make up a substantial proportion of overall SGA sales.

Because many patients treated with antipsychotics are severely disabled, Medicare and Medicaid, as public health insurers, are the largest buyers of the drugs. Between 1994 and 2003, total Medicaid spending on all prescription drugs increased by $25.9 billion, quadrupling from $8.4 billion to $34.3 billion; one-third of the increase, $8.5 billion, went towards increased expenditures on SGAs. Abramson Rep. 8. In 2003, three out of the top four drugs that Medicaid purchased were SGAs. *Id.* Zyprexa headed this list: Medicaid paid over $1.8 billion for olanzapine in each of 2003 and 2004, $500 million more than for any other single drug. *Id.*; *see*

CMS Medicaid Drug Utilization data, ranked by Drug, 2003-2006. In 2005, the most recent year for which data is available, Medicaid paid over $1.6 billion for Zyprexa.

D. Lilly, with Zyprexa, Has Been Successful

Zyprexa has been a phenomenal success for Eli Lilly. Approved in more than 80 countries, it has been prescribed to more than 23 million people since 1996. Lisa Demer, *State Claims Drug Maker Hid Data*, Anchorage Daily News, Mar. 6, 2008. Over 73 million Zyprexa and Zyprexa Zydis prescriptions had been written by the end of 2006. *See* Rosenthal Decl., Ex. E.1 (citing IMS Health TRx Data).

From its launch, Zyprexa rapidly cut into Risperdal and Clozaril's market shares, even while the overall market for atypical antipsychotics grew substantially. Rosenthal Decl. 6. For both FDA-approved and off-label indications, Zyprexa has the largest market share for SGAs in the United States, *see* Lieberman, *supra* at 1210, and in 2003, was the seventh best-selling drug in the country with sales of $3.3 billion. Rosenthal Decl. 6. Although 2005 sales dropped to $2.5 billion, *id.*, Zyprexa sales now total $4.2 billion annually. Abramson Rep. 8. During plaintiffs' proposed class period, Zyprexa sales exceeded $22 billion. *See* Pfs.' Mem. in Opp. to Def.'s Mot. for Summary J., June 12, 2007 (filed under seal). In the United States, government payments for Zyprexa totaled $1.5 million in 2007. Alex Berenson, *In Trial, Alaska Says Lilly Concealed Risks of Schizophrenia Drug*, N.Y. Times, Mar. 6, 2008.

Zyprexa now accounts for approximately 27 percent of Lilly's total revenues, down from a high of 33 percent in 2002, *Fitch Affirms Eli Lilly & Co.'s IDR at 'AA'*, Business Wire, Sept. 26, 2007, but constitutes nearly fifty percent of the company's profits. Pretax profits from Zyprexa total $2 billion annually. J.K. Wall, *$2 Billion Challenge: Lilly Under Gun to Replace*

Aging Blockbuster Zyprexa, Indianapolis Business J., Nov. 3, 2007. The average cost per prescription—roughly a month's supply—ranges from $250 to $350. *See* Summary J. Hr'g Tr. 74, June 22, 2007. At commonly prescribed doses, Zyprexa now costs about $8,000 per year. Berenson, *Lilly E-Mail, supra*. Its costs, along with Lilly's profits, is expected to sharply decrease when its patent expires in 2011.

IV. Pharmaceutical Industry

A. Pricing

Unlike those of the typical consumer good, sales of most branded pharmaceuticals are not sensitive to prices or price changes. Such an inelastic market behaves differently from the classic elastic market described by the sloping price and demand curves. Even when there is a wide variation in prices between competing pharmaceuticals, these price differences tend not to affect the unit sales of the products. Especially when a drug treats as serious a disease as a psychiatric disorder, the relative price of an agent has little, if any, affect on product use. Kolassa Decl. 10.

The pharmaceutical market's unique price stability results from the limited monopoly protection afforded by patents, and, where patents have expired, patients' reluctance to switch to generic drugs and physicians and third-party payors' hesitations about requiring such a switch:

> [O]nce launched, prices are unlikely to decline in the face of new warnings or other information because of the presence of brand loyalty. That is, once a drug has been on the market, there will be a segment of patients and physicians that believe that it works for them and will not switch even if significant risks are discovered . . . . When there are significant numbers of brand-loyal customers, a manufacturer in this situation may rationally maintain a high price and capture only the segment of the market that values the product most highly.

Rosenthal Decl. 38-39.

Even when negative information about a medication's safety or effectiveness is released, manufacturers are reluctant to reduce prices; such a move could "signal the market or the courts that the manufacturer accedes to the allegations that the drug is worth less than was initially promised." *Id.* The common result of negative information in sales of branded pharmaceuticals is a decline in quantity, not a decline in price. Quantity declines may thus reflect a reduction in the market's valuation of the drug.

Because of this price rigidity, pharmaceutical companies are able to independently fix and raise their prices routinely. Kolassa Decl 10. Lilly, like other firms, is free to set the price it chooses for its products. *Id.*; Harris Rep. ¶ 17. Competing medicines can somewhat limit a manufacturer's pricing freedom; Zyprexa's price growth, for example, has been consistent and generally paralleled that of most of the other SGAs. Kolassa Decl. 8; *see id.* at tbl. 1.

B. Marketing

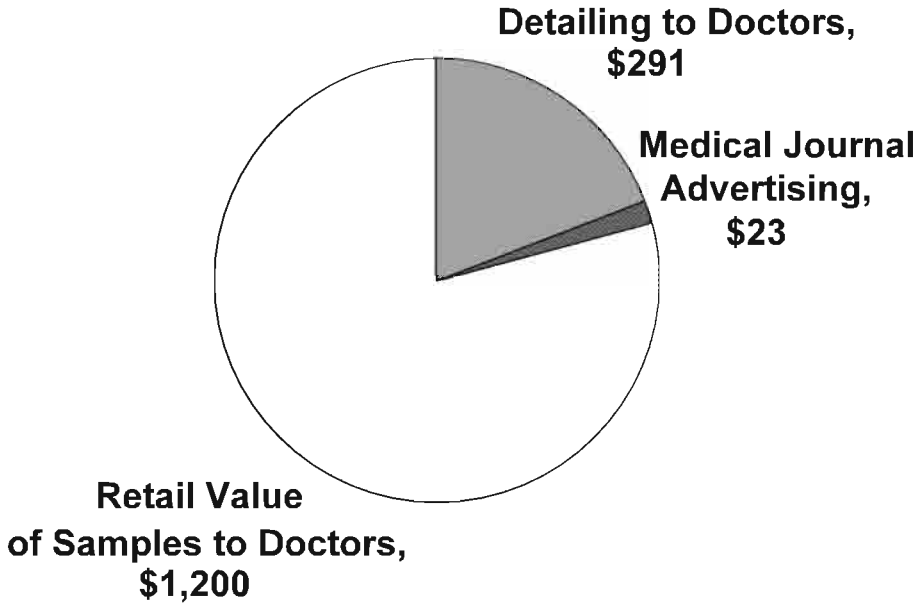
Marketing and advertising have been critical to the success of the pharmaceutical industry in the last two decades. Whether via increasingly common direct-to-consumer ("DTC") advertising or one-on-one physician detailing, drug companies spend billions on advertising. Gardiner Harris, *Group Urges Ban on Medical Giveaways*, N.Y. Times, Apr. 28, 2008; *see also* Rosenthal Decl. 15. In 2000, for example, total national prescription drug promotion expenditures totaled more than $15.7 billion. *See* Adriane Fugh-Berman & Shahram Ahari, *Following the Script: How Drug Reps Make Friends and Influence Doctors*, 4(4) PLoS Medicine 621, 621 (April 2007).

Drug detailing alone accounts for $4.8 billion. *Id.* "Detailing" is the one-on-one promotion of drugs to physicians by pharmaceutical sales representatives, usually through regular

office visits, free gifts, and friendly advice, when "drug reps go to doctors' offices to describe the benefits of a specific drug." Daniel Carlat, *Dr. Drug Rep.*, N.Y. Times. Mag., Nov. 25, 2007, at 67; *see also* Rosenthal Decl. 15. Drug companies hope that drug representatives will increase the sale of a particular drug by influencing physicians with "finely titrated doses of friendship." Fugh-Berman & Ahari, *supra.*

Like many other pharmaceutical campaigns, detailing—including free samples directly distributed to doctors—was the backbone of Lilly's marketing of Zyprexa. Over plaintiffs' putative suggested class period Lilly spent about $291 million on detailing (more than any other SGA) out of a total marketing budget of $1.5 billion, with an additional $1.2 billion going towards drug samples distributed primarily through detailers. *See* Rosenthal Decl. 25. Its Zyprexa sales representatives wrote over fourteen million call notes, each describing doctor interactions; Evid. Hr'g Tr. 744 (Abramson testimony); two thousand detailers were employed just for the primary care market alone. (Unlike many drug manufacturers, Lilly never condescended to advertising and marketing its drug directly to gullible lay consumers through maddeningly battological television and other media. *Id.* at 832-33 (Cockburn testimony).) The below chart and table illustrates Lilly's overall promotional spending on Zyprexa from 1996 through 2006.

Total Zyprexa Promotional Spending, 1996-2006 ($ millions)



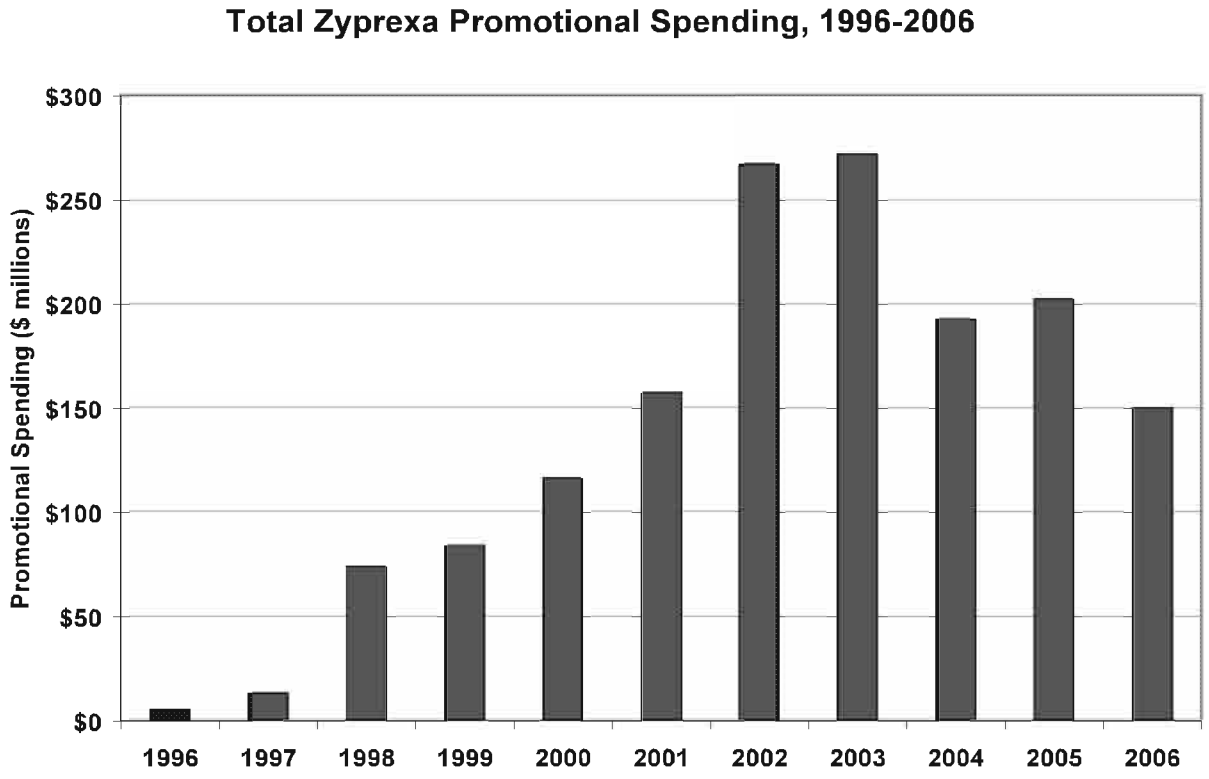
Pfs. Corr. Response 340.

Lilly's expensive promotional effects were driven by a sense of urgency: with its patent for former bestseller Prozac running out, Zyprexa's success was crucial to Lilly's future. *See* Elizabeth Lopatto & Allan Dodds Frank, *Lechleiter, Replacing Taurel as Lilly Chief, Pushes Pipeline*, Bloomberg.com, Dec. 19, 2007, http://www.bloomberg.com/apps/news?pid=20601087&sid=aKo2Xxlu2bNg&refer=home ("Prozac generated $2.6 billion in annual sales before a U.S. appeals court stripped the drug of patent protection in 2001."). In 1995, Lilly valued the market for schizophrenia drugs at $1 billion, but believed it to have "the potential to be an estimated $3.5 billion market by 2000,"

possibly reaching $6 billion by 2006. Eli Lilly & Co., Zyprex [sic]—A Major Step Forward Toward a Health Care Solution for Psychosis, July 20, 1995, at 12.

Zyprexa's promotional expenditures began low, then rapidly increased until 2003, when they dropped almost as quickly. At the peak in 2003, Lilly spent approximately $275 million per year marketing Zyprexa, declining to $150 million by 2006. Spending on detailing peaked earlier, at $60 million in 2001, although its effects lasted for some time longer. (The "stock of detailing" can be thought of as slowly accumulating, and then depreciating, over time. Evid. Hr'g Tr. 889 (Cockburn testimony). Promotional effects are long-lived; once physicians and or patients are motivated to try a drug, they tend to stay with it. Rosenthal Decl. 20-21.)

The table and graph below, based on IMS Health data, show Lilly's total promotional spending as well as its combined expenditures on Zyprexa detailing and sampling alone, broken down by year.



Year	Combined Nominal Expenditures on Detailing and Sampling of Zyprexa ($millions)
1998	71.5
1999	82.2
2000	114.1
2001	151.6
2002	262.4
2003	256.2
2004	177.5
2005	194.1
2006*	170.2

Harris Rebuttal 11 tbl. 1.

*Projected to full year, based on first 10 months.

Lilly's advertising and detailing budget was not unusual. Other companies spent similar amounts promoting their SGAs. Detailing expenditures for Abilify, for example, have risen to at least $40 million, Evid. Hr'g Tr. 831 (Cockburn testimony); its DTC advertising budget in 2001 totaled about $40 million per quarter. *Id.* at 832-33.

C. Wholesale Influence of Drug Marketing

It is undisputable that expenditures for drug marketing increase sales. The billions spent by the pharmaceutical industry attests to that. Physicians, despite what most claim, *are* influenced both consciously and unconsciously by commercial promotional messages. Scientific knowledge and judgment are not impervious shields against fraudulent product claims. Rosenthal Decl. 18; *see id.* at 16 (noting recent studies demonstrating that "despite their extensive training, physicians are influenced by marketing messages even when they are flawed or contradicted by scientific evidence."). One study, for instance, showed that the majority of doctors held beliefs about two classes of drugs that were consistent with the detailing message

but at odds with the scientific evidence, even though the same physicians reported that commercial sources of information had little influence on their prescribing. *Id.* at 17 (also noting that doctors deny that gifts and payments have any effect on their own prescribing behavior).

The medical community appears to be only beginning to grasp the extent and influence of pharmaceutical companies over the medical system and prescribing decisions. According to the American Medical Student Association, most medical schools do not adequately restrict the money, gifts, and free drug samples that drug companies routinely provide doctors and trainees. Gardiner Harris, *Survey of Medical Schools Is Critical of Perks*, N.Y. Times, June 3, 2008, at A20. A new model policy by the Association of American Medical College governing interactions between medical schools and the drug industry "recommend[s] that gifts of free food and gifts to students and teachers be banned and that schools discourage faculty involvement in industry-sponsored speakers' bureaus." Harris, *Group Urges Ban, supra.* Even Congress has taken notice: a proposed bill, the Physician Payments Sunshine Act would require the pharmaceutical industry to report gifts, payments, travel reimbursements and donations over $500 to the medical field—but exempts product samples, training and educational opportunities; the bill has been endorsed by Lilly. Daniel Barlow, *State: U.S. Bill Would Undermine* [*Vermont*] *Drug Maker Gift Rules*, Rutland Herald, May 27, 2008.

Intense pharmaceutical marketing saturates the industry and appears in many forms—some of which could be characterized as disguised. Lilly's marketing efforts are central to plaintiffs' allegations. To support their claims that as soon as Zyprexa launched, Lilly began a pattern of misleading the public and the healthcare community, minimizing the known side effects of the drug and overstating its efficacy as well as fraudulently and illegally promoting it

for off-label use, plaintiffs point to evidence that Lilly utilized all the various channels of information through which pharmaceutical companies can market their products to propel Zyprexa's brand message. *See* Part XVIII.A.6, *infra* (testimony of plaintiffs' expert Dr. Abramson); *see, e.g.*, Lisa Demer, *Defense Opens in Zyprexa Trial*, Anchorage Daily News, Mar. 22, 2008 (reporting that David Kahn, a professor of psychiatry at Columbia University Medical Center and a defense witness for Lilly in the Alaska trial, confirmed during his testimony that there is no source of information in which Lilly is not involved); Sheri Qualters, *Drug Makers Look at New Ethics Code*, Nat'l L.J., Aug. 4, 2008 (reporting the Pharmaceutical Research and Manufacturers of America's ("PhRMA") massive overhaul of its ethics code governing interactions with health care professionals to restrict marketing by limiting free meals and banning certain gifts, institute strict protocols for speaking and consulting arrangements, and train sales representatives on laws, regulations, and industry codes; emphatically endorsed by the U.S. Department of Health and Human Services, it will probably be implemented by Lilly starting next year). Those channels—today highly susceptible to industry influence—are described below.

1. Drug Labels

The most obvious source of information about a medication is its own prescription label. Abramson Rep. 9. "[L]abels are the primary means of providing prescribing physicians and their patients with important information on a drug's risks and benefits." Karen Baswell, Note, *Time for a Change: Why the FDA Should Require Greater Disclosure of Differences of Opinion on the Safety and Efficacy of Approved Drugs*, 35 Hofstra L. Rev. 1799, 1803 (2007). Approved indications and respective dosage information appear on the label. 21 U.S.C. §§ 352, 355(d).

Although a pharmaceutical company must obtain the FDA's approval for its drug's label, the label is the property of the manufacturer, not the FDA. *Id.* Initially drafted by the manufacturer, labels are then subject to negotiations between the federal agency and the manufacturer. *Id.* Because the FDA depends solely on drug safety and efficacy information provided by pharmaceutical companies, it cannot effectively object to a label's shortcomings if it never received the data from the manufacturer showing the drug's drawbacks. *See* Part V, *infra.*

2. Clinical Trials

Clinical trials provide the empirical data upon which the FDA determines a drug's safety and efficacy and doctors make professional judgments about the relative risks and benefits of a drug—and whether it is appropriate to prescribe it for their patients. The pervasive commercial bias found in today's research laboratories means studies are often lacking in essential objectivity, with the potential for misinformation, skewed results, or cover-ups. One of the plaintiffs' experts described how he saw this situation:

> [C]orporate influence now permeates every aspect of this process, from the design of clinical studies (including the population included in the trial, the choice of drugs, doses, and duration of the trial, and the outcome and safety measures to be tracked), to control of the data, data analysis, the writing of manuscripts for articles, and publication decisions.

Abramson Rep. 14.

Such bias is a recent phenomenon. Before 1980, the National Institute of Health ("NIH") funded most clinical trials. During the 1980s, its budget was slashed; in response, drug industry funding went up six-fold from 1977 to 1990. *Id.*; Evid. Hr'g Tr. 722. By 1991, drug companies funded 70% of all clinical trials, though 80% of commercially funded trials were still performed at universities. Abramson Rep. 14; Evid. Hr'g Tr. 723. By 2004, only 26% of commercially

funded trials took place at universities. Abramson Rep. 15. Today 80% to 90% of all trials are commercially funded, *id.*; between 66% and 75% of the clinical studies published in the most prestigious medical journals are commercially funded. *Id.* at 16. Study design and control are increasingly in the hands of drug companies. Evid. Hr'g Tr. 727. Published studies often do not reflect their commercial ties or authorship; they may be "ghostwritten" by company employees, use proprietary data not accessible to the scientific community, or simply fail to acknowledge their authors' financial ties to drugmakers. *See e.g.*, Rob Waters, *Harvard Doctors Failed to Disclose Fees, Senate Says*, Bloomberg.com, June 9, 2008 (reporting that Harvard Medical School doctors who helped pioneer the use of psychiatric drugs in children violated federal and school rules by failing to disclose at lease $3.2 million from drug makers, including Lilly); Editorial, *Hidden Drug Payments at Harvard*, N.Y. Times, June 10, 2008, at A22.

Sponsorship is not insignificant. *Cf. Exxon Shipping Co. v. Baker*, 128 S. Ct. 2605, 2626 n.17 (2008) ("Because this research [supporting defendant Exxon's position] was funded in part by Exxon, we decline to rely on it."). Even those trials performed at academic institutions are often partly to almost wholly controlled by the sponsor. *See* Abramson Rep. at 15. Sponsorship significantly increases the chance of positive results; the odds are 5.3 times greater that commercially funded studies will conclude that the sponsor's drug is the treatment of choice compared to non-commercially funded studies of exactly the same drug. Evid. Hr'g Tr. 724; Abramson Rep. 16. Odds of a trial favoring a drug also greatly increase if the trial's researchers had a financial conflict of interest with a manufacturer. Abramson Rep. 18. "For those studies that had both industry sponsorship and at least one author with a conflict of interest the odds were 8.4 times higher that the study would favor the sponsor's drug." *Id.*

Not only does commercial bias affect the probable outcome of a study, it also often controls whether and when a study is published. Because drug manufacturers often delay or suppress negative results from clinical trials they or their affiliated research institutions conduct, "doctors, formulary committees, and policy makers [may base] their decisions on an unrepresentative fraction of the available scientific evidence." *Id.* at 19 (giving the example that when such authorities opined on the safety of antidepressants for children, only six out of a total of fifteen completed studies had been published); *see* Benedict Carey, *Researchers Find Bias in Drug Trial Reporting*, N.Y. Times, Jan. 17, 2008, at A20 ("The makers of antidepressants like Prozac and Paxil never published the results of about a third of the drug trials that they conducted to win government approval, misleading doctors and consumers about the drugs' true effectiveness, a new analysis has shown."); Alex Berenson, *Accusations of Delays in Releasing Drug Results*, N.Y. Times, Apr. 1, 2008, at C7 (reporting a lead investigator's allegations that his study's commercial sponsor deliberately delayed for two years the release of his trial results, which reflected negatively on the sponsor's drug, "to hide something."); *cf.* Alan Finder, *At One University, Tobacco Money Is Not Taboo*, N.Y. Times, May 22, 2008, at A29 (reporting that the Virginia Commonwealth University's formerly secret 2006 contract with Philip Morris for tobacco research gives the company the sole power to decide whether to publish by defining all university-created material as its proprietary information).

3. Journal Articles

Clinical trials are made public via research and review articles in medical journals. Doctors value keeping up-to-date with medical literature, and journal articles are their primary source of best practices and current developments. Evid. Hr'g Tr. 721, 718. Research articles

describe individual primary clinical trials; review articles summarize results from multiple trials on the same subject. *Id.* at 721. Both are subject to systemic industry bias. Abramson Rep. 20. Because of the increase in commercially-funded trials, the number of commercially funded journal publications has likewise dramatically increased. Today, two-thirds to three-quarters of trials published in the four most respected medical journals are commercially funded. *Id.* at 725; Abramson Rep. 16. Several editors of preeminent medical journals have gone so far as to say that their publications "have devolved into information-laundering operations for the pharmaceutical industry." *Id.* at 728; Abramson Rep. 20. For example, by April 16, 2002, the Zyprexa product team had published 125 full manuscripts and submitted an additional 100 for publication. Evid. Hr'g Tr. 731.

4. Drug Detailing

As discussed above in Part IV.B, medical detailing is a large field, employing over 90,000 sales representatives, or one detailer for every 4.5 doctors. Abramson Rep. 10. The vast majority of doctors—eighty-five to ninety percent—speak with drug detailers, and most consider them and the information they provide helpful and accurate. Evid. Hr'g Tr. 743; Abramson Rep. 10. Drug representatives ostensibly provide useful information for physicians since they address "difficult problems in treating patients." Jonna Perala et al., *Lifetime Prevalence of Psychotic and Bipolar I Disorders in a General Population,* 64 Archives of Gen. Psychiatry 19, 1892 (2007).

But company-controlled and produced information has great potential to mislead: one Journal of General Internal Medicine article "shows that nearly half (forty-two percent) of the material given to doctors by drug reps made claims in violations of FDA regulations. And only thirty-nine percent of the material provided by drug reps provided scientific evidence to back up

claims." Abramson Rep. 25. Pharmaceutical sales representatives are prohibited from promoting off-label uses; they may legally only provide information about off-label uses if a physician specifically requests the information. *See* Part V.C, *infra*. In the present case, plaintiffs make extensive allegations of Lilly's misleading and extensive off-label detailing. *See, e.g.*, Part IX.A, *infra*.

5. CME Course and "Thought Leaders"

Another key source of drug information for doctors is continuing medical education ("CME") courses, usually medical lectures held locally featuring prominent "thought leaders" as speakers. *See id.* at Rep. 21-22; Schneider Rep. 12. Required to maintain medical licenses and to stay current with new developments to give patients the best medical care, many CME courses provide expert syntheses of clinical trial information. Evid. Hr'g Tr. 735-36.

Like clinical trials themselves, the percentage of CMEs that are commercially funded has increased sharply, from 48% in 1998 to 58% in 2002. Abramson Rep. 22; *see* Evid. Hr'g Tr. 736. Sixty percent of CMEs have direct commercial sponsorship; indirect sponsorship (e.g., via non-profits funded by company money) accounts for a large portion of the remainder. Total industry contributions towards continuing medical education is estimated to be 70% or higher and in the hundreds of millions of dollars. Abramson Rep. 22 (noting that commercial sponsorship grew from $400 million in 1998 to $700 million in 2002).

Lecture fees are used to recruit recognized clinical experts, well-known and respected in their field and referred to as "thought leaders" or "key opinion leaders," to join company "speakers bureaus" and conduct CMEs. *Id.* at 21. "[O]ne recent study indicates that at least 25 percent of all doctors in the United States [approximately 200,000 physicians] receive drug

money for lecturing to physicians or for helping to market the drugs in other ways." Carlat, *supra,* at 67; *see also* Gina Kolata, *Citing Ethics, Some Doctors Are Rejecting Industry Pay*, N.Y. Times, Apr. 15, 2008 (reporting that a small number of prominent academic scientists have decided to stop accepting payments from food, drug and medical device companies in response to accusations of ethical conflicts inherent in these arrangements). In many of these presentations, the slides used have been "created by drug makers, not the speakers. That's like ghost-talking." Harris, *Group Urges Ban, supra*; *see id.* ("Speakers' bureaus and drug samples are pillars of the industry's marketing operations").

Studies have shown that commercial sponsorship does result in biased CMEs. Evid. Hr'g Tr. 737; *see* Abramson Rep. 10. "Drug company-sponsored lectures are two-and-a-half to three times more likely to mention the sponsor's drug in a positive light and the competitors' drugs in a neutral or negative light than are non-commercially sponsored lectures." *Id.* at 22-23. Increased formulary requests, the prescribing of new brand-name drugs instead of older generic products, and the prescribing of the specific product promoted have all been demonstrated to increase after exposure to pharmaceutical promotion and company-sponsored CMEs. *See id.* at 26 (effect of drug detailing).

6. Clinical Practice Guidelines and Nonprofit Organizations

Clinical Practice Guidelines ("CPGs") are an important source of drug information for physicians. Evid. Hr'g Tr. 765-66. Summarizing expert opinions and often used to identify the standard of care, CPGs are closely followed by prescribers, who prefer not to depart from the identified standards to avoid charges of medical malpractice. Abramson Rep. 25-26. Guidelines are typically formulated by panels of experts under the auspices of quasi-governmental

organizations, medical professional societies, or non-profit organizations like the National Alliance of the Mentally Ill ("NAMI"), the American Psychiatric Association ("APA"), and the Texas Medication Algorithm Project ("TMAP"). Abramson Rep. 68 ("Guidelines and algorithms advanced by these organizations have a significant effect on the standard of care and the prescribing decisions of doctors.").

Such entities "have been particularly active in promoting treatment of the mentally ill with atypical antipsychotics." *Id.*

> A host of practice guidelines and algorithms drafted before the publishing of many of the recent, independent studies on atypical antipsychotics advanced the idea that SGAs should be used as first line treatment for schizophrenia and bipolar disorder. For example, the Expert Consensus Guideline Series, Treatment of Schizophrenia 1999 recommended SGAs for first line treatment, acute exacerbation, failure of FGA at low doses, and failure of another SGA. The American Psychiatric Association instituted the second edition of its Practice Guideline for the Treatment of Patients with Schizophrenia in 2004 and recommended SGAs as first line treatment for patients in the acute phase of schizophrenia. The Texas Medication Algorithm Project ("TMAP") recommend[ed] SGAs rather than FGAs for Stage 1 and 2 of antipsychotic treatment.

Id. at 68 (footnotes omitted). (In November 2007, TMAP reversed its earlier position on the basis of recently published studies and issued a revised consensus judgment by leading experts suggesting that there is no advantage for chronic schizophrenics of SGAs over FGAs. *See* Rosenheck Supp. Decl. 7.)

Many organizations are partially or fully financially supported by pharmaceutical manufacturers. *Id.* at 26. NAMI, for instance, received $544,500 from Lilly in the first quarter of 2007. Avery Johnson, *Under Criticism, Drug Maker Lilly Discloses Funding*, Wall St. J. Online, May 1, 2007, http://online.wsj.com/article/SB117798677706987755.html. And panel experts often have economic ties to the industry via research grants or speaker fees. Every single

expert, for example, who worked on the sections devoted to severe mental illness, including schizophrenia, in the 1994 edition of the DSM-IV, the APA's most important diagnostic handbook, had financial links to drug makers; more than half the task force members who will oversee the next edition have such connections. Tara Parker-Pope, *Psychiatry Handbook Linked to Drug Industry*, N.Y. Times Blog, May 6, 2008, http://well.blogs.nytimes.com/2008/05/06/psychiatry-handbook-linked-to-drug-industry/.

V. Role of the Food and Drug Administration

A. Approval Process

Under the Food, Drug, and Cosmetics Act ("FDCA"), new pharmaceutical drugs cannot be marketed in the United States unless the sponsor of the drug demonstrates to the satisfaction of the FDA that the drug is safe and effective for each of its intended uses. 21 U.S.C. §§ 355(a), (d). A drug receives FDA approval only for treatment of specified conditions, referred to as "indications." 21 U.S.C. §§ 352, 355(d). For each indication sought a manufacturer must provide condition-specific safety and efficacy information. *Id.* The FDA also determines the particular dosage (or range of dosages) considered safe and effective for each indication.

To determine whether a drug is "safe and effective," the FDA relies on information provided by a drug's manufacturer; it does not conduct any substantial analysis or studies itself. Applications for FDA approval (known as New Drug Applications or "NDAs") must include "full reports of investigations which have been made to show whether or not such drug is safe for use and whether or not such drug is effective in use." 21 U.S.C. § 355 (b)(1)(A). FDA approval of prescription drugs is wholly dependent upon the accuracy of information provided by drug manufacturers. *See* Abramson Rep. 11. *See generally* Wayne A. Ray & Michael Stein, *Reform*

of Drug Regulation—Beyond an Independent Drug-Safety Board, 354(2) New Eng. J. Med. 194 (Jan. 12, 2006).

Not only does the FDA depend upon industry-supplied data, but it also relies on direct financial support from the industry. "By law, makers of brand-name drugs pay application fees to the F.D.A. in exchange for the agency's commitment to act within 180 days." Bloomberg News, *F.D.A. Revises Its Letter for Nonapproval of Drugs*, N.Y. Times, July 10, 2008. "[S]ince the enactment of the Prescription Drug User Fee Act of 1992 . . . the pharmaceutical industry provides between twenty to fifty percent of the funding for the FDA's activities. The regulating agency is therefore dependent on those it is supposed to be regulating." Baswell, *supra* at 1828.

As a result, some have alleged that the FDA and the pharmaceutical industry have many close ties:

> [F]ederal drug policy seems to currently favor the commercial pharmaceutical industry. Differences of opinion regarding drug safety and efficacy in a new drug application seem to be decided in favor of the manufacturer (at least initially). After approval, challenges to a drug's safety or to the adequateness of the drug's label regarding risks are seemingly set aside until the effects of the risks become so egregious that the manufacturer or the FDA is forced to address them. This set-aside period allows the manufacturer to maximize profits before removing either an indication for a drug or the drug itself.

Id. at 1829; *see also* Gardiner Harris, *Potentially Incompatible Goals at F.D.A.: Critics Say a Push to Approve Drugs Is Compromising Safety*, N.Y. Times, June 11, 2007, at A14 (reporting that "several F.D.A. safety reviewers in recent years have been punished or discouraged after uncovering . . . drug dangers").

FDA approval does not require that a new drug be more effective or safer than other drugs approved to treat the same condition. Neither does it require that the drug be cost-

effective. *See* Robert Rosenheck, *The Growth of Psychopharmacology in the 1990s: Evidence-Based Practice of Irrational Exuberance*, 28 Int'l J. Law & Psychiatry 467 (2005). A drug must only be shown to be more effective than a placebo in treating a particular condition and be without any statistically significant adverse safety findings. *See* Abramson Rep. 11-13; Ray & Stein, *supra*, at 194. Comparative data showing performance as against that of existing drugs is not required; the FDA has no basis for determining that one drug is better than another drug. *See* Ray & Stein, *supra*, at 194.

Because short-term studies are accepted, drug applications often do not contain long-term data on the safety or efficiency of the drug. Abramson Rep. 11. Approval of a new drug generally contains a requirement that the manufacturer pursue further long-term studies, but two-thirds of the promised studies never materialize and the FDA lacks any enforcement authority. *Id.* at 12-13. Many of the effects of newly approved drugs could not possibly be known at the time of FDA approval, particularly the long-term effects of taking a medication, given the short length of, and relatively few participants in, the clinical trials conducted for approval. *See AP Analysis: How a Drug's Risks Emerge*, N.Y. Times, May 23, 2007. There is no systematic provision requiring drug companies to conduct—or provide results from—post-marketing studies. *Id.*

A manufacturer wishing to market an approved drug for indications other than those already approved must resubmit the drug for a series of clinical trials similar to those required for the initial FDA approval. *See* Food and Drug Administration Modernization Act of 1997 ("FDMA"), 21 U.S.C. §§ 360aaa(b), (c); *see also* 21 C.F.R. § 314.54 (outlining the administrative procedure for filing an application for a new indication); 21 U.S.C. §§ 301 *et seq.*

A supplemental NDA must be filed. Unless and until an additional indication is approved by the FDA, the unapproved use is considered to be "off-label."

As the primary gatekeeper of drugs with potentially life-saving or life-changing effects, the FDA often finds itself between a rock and a hard place: "Safety and speed are the yin and yang of drug regulation. Patients want immediate access to breakthrough medicines but also want to believe the drugs are safe. These goals can be incompatible." Harris, *Potentially Incompatible Goals*, *supra* at A14.

B. Drug Labeling

Critical for conveying a drug's approved uses and known warnings to prescribers, a drug's labeling must also be approved by the FDA as part of the original application. "Labels" include all marketing and promotional materials relating to the drug as well as the printed insert included in its packaging. They may not describe intended uses for the drug that have not been approved by the FDA. 21 U.S.C. §§ 331, 352.

Manufacturers and the FDA typically negotiate over the wording and content of the label, especially in regards to adverse information about the drug. The FDA aims to strike a balance between too-strong warnings, which may scare away patients who would substantially benefit from the drug, and inadequate warnings, which can lead patients incurring injurious side effects. *See, e.g.*, Benedict Carey, *Caution, Not Panic, Seen After Drug Warnings*, N.Y. Times, Jan. 8, 2008, at F6 (reporting that a new study has found that recent suicide warnings on anti-depressants have "seemed to prompt caution rather than panic.").

After a drug is approved, the FDA continues to exercise control over the product's labeling. To protect patients from safety concerns, the FDA may require a label change to reflect

the increased risk of various side effects or interactions, restrict a drug's indications, or, in extreme cases, force a withdrawal from the market. *See* 21 C.F.R. § 201.57(3); Abramson Rep. 13. Negotiation over proposed modifications is common, *see* 21 U.S.C. § 355(d); Ray & Stein, *supra*, at 194-95, and compromise often results. *See* Raymond L. Woosley, *Drug Labeling Revisions—Guaranteed to Fail?*, 284(23) JAMA 3047 (Dec. 20, 2000); *see, e.g.*, Part XI, *infra*. A manufacturer may independently change its product label upon learning new safety information.

C. Drug Marketing, On and Off-Label

FDA regulations restrict how drug companies may market and promote approved drugs. *See* 21 U.S.C. §§ 331, 352; 21 C.F.R. § 314.81. The FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC") is charged with overseeing the marketing and promotion of FDA-approved drugs to ensure that advertisements are not false or misleading, provide a fair balance between the benefits and risks of the drug, and do not promote "off-label" uses. *See* Statement by Janet Woodcock, M.D. (Director, Center for Drug Evaluation and Research ("CDER"), FDA) Before the Senate Special Committee on Aging.

Promotional materials, both professional- and consumer-oriented, must be consistent with the FDA-approved product labeling. Rosenthal Decl. 15. Only claims that are supported by scientific evidence (according to strict scientific procedures) and which are not false or misleading may be asserted by drug companies. *Id.* FDA oversight is supposed to ensure a "fair balance" in all marketing claims and materials, *id.*; its regulations require that the risks as well as the benefits must be clearly identified and given appropriate prominence. *Id.* at 14-15; *see, e.g.*, Part VI.D, *infra*. This restriction pertains to the clinical indications for which the drug has been

approved as well as the dosing regimen that is supported by the clinical trials that were undertaken to establish safety and efficacy. Rosenthal Decl. 14-15. Illegal "misbranding" or encouragement of off-label use can result in criminal penalties. *See* 21 C.F.R. § 333. The Justice Department has reached a number of legal settlements, for example, with drug companies accused of such illegal marketing. Mathews & Johnson, *supra*.

In general the FDA's effectiveness in regulating drug promotion is limited. In 2003, DDMAC's entire staff consisted of forty members, with twenty-five reviewers responsible for reviewing all pharmaceutical advertisements and promotional materials. *Id.*; Abramson Rep. 12. Moreover, such materials do not have to be pre-approved; FDA review of promotional materials occurs, if it does at all, after the materials have already appeared in public. Woodcock Statement, *supra*. Upon finding a violation, DDMAC generally requests, but does not require, the company to stop using the promotional materials. *Id.*; Andrew Eder, *AstraZeneca Defends Drug's Soaring Sales*, Delaware Online, Aug. 3, 2008 (reporting that "a recent report by the Government Accountability Office found that when FDA finds a drug company promoting an off-label use, it takes the agency an average of seven months to issue a warning, followed by four more months for the company to fix the problem"); *see, e.g.*, Part VI.D, *infra*. *But cf* "There's Danger Here, Cherie!" Richard C. Ausness, *Liability for the Promotion and Marketing of Drugs and Medical Devices for Off-Label Uses*, 73 Brook. L. Rev. 1253 (2008) (arguing that more off-label use should be recognized by governmental agencies). Sponsors occasionally are required to publicly correct product misimpressions created by false, misleading, or unbalanced materials. Woodcock Statement, *supra*.

Any use of an approved drug for a purpose other than those indicated in the labeling, whether for a different population, medical condition, or dosage, is considered to be "off-label." *Buckman Co. v. Plaintiff's Legal Committee*, 531 U.S. 341, 350 (2001); *see* David C. Radley, *Off-Label Prescribing Among Office-Based Physicians*, 166 Archives of Internal Medicine 1021 (May 8, 2006). Physicians may prescribe drugs for off-label uses at their discretion. *See* 21 U.S.C. § 396; *Sita v. Danek Medical Inc.*, 43 F. Supp. 2d 245, 263 (E.D.N.Y. 1999) ("[D]octors commonly exercise professional medical judgment and prescribe drugs for uses not within the indications articulated by the FDA."); Gregory J. Radomisli, *Liability for Off-Label Use*, N.Y.L.J., June 20, 2008, at 4 (discussing doctors' freedom to prescribe off-label and quoting *Buckman* and *Sita*). It is generally agreed that "off-label prescribing can benefit both individual patients and patient populations as clinical experience leads to the formation of hypotheses to be tested in structured clinical trials." Rosenthal Decl. at 11. As one of plaintiffs' experts testified,

> The lack of an indication in the label should not be an issue, however, in the concerned physician's managing of patients and prescribing a medication "off-label." Physicians and the community recognize that many drugs effective for a condition may not be labeled for that condition and may not have a strong body of evidence for or against their use. When considering off-label prescribing, physicians depend on the patient-specific evidence they have available to them. This includes the particular patient, the severity of his problems, the successfulness of prior treatment, and the risks of not treating.

Schneider Decl. 11-12.

There are loopholes to prohibitions against off-label promotion. Off-label information may be distributed by sales representatives if requested by a health care provider. 21 U.S.C. §§ 360aaa-366. "[D]octors may freely discuss off-label uses with other doctors at continuing medical education events, which are often sponsored by drug makers." Eder, *supra.* In a move

welcomed by the drug industry, the FDA is now developing guidelines on how drug and medical-device manufacturers can provide doctors with reprints of medical journal articles that deal with uses of drugs and devices that have not won FDA approval. Mathews & Johnson, *supra*.

D. Monitoring of Adverse Side Effects

Once a drug has been approved, the FDA's statutory authority is limited to requesting label changes, negotiating restrictions on distribution with the manufacturer, and petitioning for the withdrawal of the drug from the marketplace. Ray & Stein, *supra*, at 195. Title 21 of the Code of Federal Regulations requires that "as soon as there is reasonable evidence of a serious hazard with a drug," the "Warnings" section of the label should be revised accordingly. "Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box," 21 C.F.R. § 201.57 (e), commonly known as a "black box" warning.

The FDA's Office of Surveillance and Epidemiology ("OSE") is responsible for overseeing the safety of approved drugs. Abramson Rep. 12. Like DDMAC, OSE is underfunded and understaffed. *Id.* For example, "[t]he F.D.A. has 200 inspectors, some of whom audit clinical trials part time, to police an estimated 35,000 testing sites." Gardiner Harris, *Report Assails F.D.A. Oversight of Clinical Trials*, N.Y. Times, Sept. 28, 2007, at A1; *see* Gardiner Harris, *Advisers Say F.D.A.'s Flaws Put Lives at Risk*, N.Y. Times, Dec. 11, 2007, at A12 (reporting on an FDA Advisory Board's conclusion that the "FDA is falling further and farther behind in carrying out its responsibilities and understanding the science it needs to do its many jobs."); Gardiner Harris, *Report Assails F.D.A. Oversight of Clinical Trials*, N.Y. Times, Sept. 28, 2007, at A1 (noting another government report's conclusion that "the agency's

oversight of clinical trials is disorganized and underfinanced . . . . [F]ederal health officials did not know how many clinical trials were being conducted, audited fewer than 1 percent of all testing sites and, on the rare occasions when inspectors did appear, generally showed up long after the tests had been completed."); *cf.* Marcia Coyle, *FDA-Regulated Officials Face Tougher Penalties*, Nat'l L.J., May 12, 2008, at 7 ("Underfunded, undermanned and under criticism for its enforcement effort in recent years, the agency has sought a broad range of [sentencing] guideline changes which, if approved, would have stiffened sentences dramatically . . . . 12 years ago, the FDA sought wholesale revisions to the guideline covering nonfraud violations of the FD&CA, but the [sentencing] commission withdrew the proposals after negative industry reaction."); Gardiner Harris, *Tainted Drugs Put Focus on the F.D.A.*, N.Y. Times, Mar. 17, 2008, at A13 (discussing recent deaths from tainted heparin produced in China and the FDA's inability to conduct inspections of foreign manufacturing plants); Barry Meier, *Calling for a Warning System on Artificial Joints*, N.Y. Times, July 29, 2008, at A1 (FDA's ability to monitor medical devices overwhelmed). *See also* Gardiner Harris, *More Money for Food Safety Is Sought: After Outbreak of Salmonella, Department Asks for $275 Million*, N.Y. Times, June 10, 2008, at A17.

Although drug companies are under a continuing obligation to report serious adverse events, with required safety reports to be filed every three months during the first few years of marketing of a drug, the FDA's adverse event reporting system is largely voluntary. *See* Phil B. Fontanarosa et al., *Postmarketing Surveillance—Lack of Vigilance, Lack of Trust*, 292 JAMA 2647, 2647 (2004). There was some evidence presented at the evidentiary hearing that a major problem with this country's system of ensuring postmarketing drug safety is that it is "the drug

makers themselves who are largely responsible for collecting, evaluating and reporting data from postmarketing studies of their own products." Abramson Rep. 13 (quoting Fontanarosa, *supra*). Drug companies have an incentive to minimize reporting.

Through the FDA's Safety Information and Adverse Event Reporting Program ("MedWatch"), consumers and healthcare professionals may voluntarily report "serious problems that they suspect are associated with drugs." What is MedWatch?, FDA MedWatch Homepage, http://www.fda.gov/medwatch/What.htm (last visited July 12, 2008); *see* Gardiner Harris, *F.D.A. to Expand Scrutiny of Risks from Drugs After They're Approved for Sale*, N.Y. Times, May 23, 2008, at A17 ("The agency now relies on an unsystematic system in which doctors, patients, and manufacturers report problems with drugs and medical devices when they deem them important. . . . The agency estimates that it receives reports for only a fraction of actual drug effects"). *But see id.* (reporting on the FDA's announcement of a new "Sentinel Initiative" system to allow officials to monitor drug safety using Medicare claims data).

Health care professionals are not required to report serious adverse events suspected to be caused by medications, and are not even encouraged to report adverse events other than those classified as "serious." *See* Timothy Brewer, *Postmarketing Surveillance and Adverse Drug Reactions*, 281(9) JAMA 824 (Mar. 3, 1999). Doctors may not easily or immediately recognize a causal connection between a new drug and a deleterious side effect. Adverse events are thus significantly underreported; reported events are thought to represent only 1% to 10% of total complications. *See* A. S. Rogers et al., *Physician Knowledge, Attitudes, and Behavior Related to Reporting Adverse Drug Events*, 148(7) JAMA (July 1, 1988); Lots La Grenade et al., *Underreporting of Hemorrhagic Stroke Associated with Phenylpropanolamine*, 286 (24) JAMA

3081, 84-86 (Dec. 26, 2001); *see also* Making Health Care Safer: A Critical Analysis of Patient Safety Practices. Rockville, MD: Agency for Healthcare Research and Quality (K.G. Shojania et al., eds., 2001), at chap 4: Evidence Report/Technology Assessment No. 43, AHRQ publication 01-E058 (finding that only 1.5% of all adverse events result in an incident report, and only 6% of adverse drug events are identified properly).

In recent years, multiple drugs have been pulled off the market after new evidence of their lack of efficacy or increased safety concerns is revealed. *See, e.g.*, Alex Berenson, *Panel Doubts Two Drugs Used to Fight Cholesterol*, N.Y. Times, Mar. 31, 2008, at C1 (noting a two-year clinical trial of two widely prescribed cholesterol drugs showed the drugs did not slow arterial plaque growth; the drugs' initial FDA approval was based on short-term limited studies and not outcome trials). As one commentator noted,

> Perhaps the most terrifying aspect of the aforementioned "bad drug" cases [referring to Avandia, Vioxx, Fen-phen, Parlodel, DES, Ortho Evra, and Paxil] is not that negative or harmful side effects were ultimately linked to the drugs, but the amount of time the drugs remained on the market *without adequate warning to the consumers*, after the manufacturers knew (or had reason to know) of either the dangerous risks or the general ineffectiveness of the drugs.

Baswell, *supra,* at 1803 (original emphasis) (arguing that the FDA should require drug companies to provide all scientifically supported interpretations to doctors and consumers so that consumers may make a truly educated choice); *see, e.g.*, Gardiner Harris, *Heart Surgery Drug Pulled from Market: Bayer, Under Pressure, Acts After New Signs of a Fatality Risk*, N.Y. Times, Nov. 6, 2007, at A35 (reporting on Bayer's withdrawal of its drug Trasylol after a study suggested it increased death rates); Gardiner Harris & Alex Berenson, *Drug Companies Near an Old Goal* N.Y. Times, Apr. 6, 2008 (reporting on the Ortho Evra birth control patch lawsuit

against Johnson & Johnson based on allegations the company concealed research showing safety dangers for six years, delaying the eventual imposition of an FDA label change).

In part, delays in drug withdrawals are built into our pharmaceutical industry as it is currently structured and regulated.

> [O]nce a drug is approved, halting its sales is extremely difficult. Experts on [FDA] advisory panels are often loath to take widely used medicines out of doctors' hands, even when their safety is uncertain. This history also shows how vulnerable the F.D.A.'s drug approval system can be to unwelcome surprises.

Harris, *Heart Surgery Drug*, *supra*.

VI. FDA Approval and Regulation of Zyprexa

Plaintiffs' claims for overpricing span a period of twelve years, from Zyprexa's approval in 1996 to the present. The summary below of Zyprexa-related events that occurred during that time is by no means a complete account of what actually happened or what is reflected in the millions of documents produced by Lilly during discovery. Some of the information has already been discussed in this court's prior Zyprexa opinions.

A. Pre-Approval Studies

In the early 1990s, Lilly began seeking FDA approval of olanzapine for use in treatment of psychotic disorders. Before applying for FDA approval of Zyprexa for treatment of schizophrenia in 1996, Lilly performed a variety of studies to test the drug's safety and efficacy. Early studies revealed Zyprexa was associated with weight gain. Lilly's 1993 HGAV study reported that "weight gain was evident and uniform in all subjects, with an average gain of nearly 9 pounds." Jason A. Plassard, & Brian D. Beato, Olanzapine in Human Plasma, Final Report, Lilly Study FID-LC-HGAV (Nov. 1993), at 48. Statistical analysis of HGAV data performed in

April 1995 noted that "weight gain was evident and uniform in all subjects, with an average gain of nearly 9 pounds over the study duration," or approximately one and a half pounds per week. *Id.* at 47.

In August 1995, in the "Olanzapine Integrated Summary of Safety" report prepared for submission to the FDA, which included data from 3139 patients involved in approximately fifty worldwide olanzapine studies, Lilly noted that nearly 30% of patients on olanzapine in those trials reported incidences of weight gain. Olanzapine Integrated Summary of Safety: Psychosis, Lilly Research Laboratories, Aug. 31, 1995, at 111; *see* Wirshing Decl. 36. Compared with Haldol, an FGA, weight gain occurred more frequently in patients treated with Zyprexa. Olanzapine Integrated Summary of Safety at 166 ("A potentially clinically significant weight gain (≥7% from baseline) was experienced by 20.3% of olanzapine-treated patients compared with 5.0% of haloperidol patients.").

B. Initial Approval for Schizophrenia

Lilly was not required to, and did not, show that Zyprexa was better than, or even as good as, existing antipsychotics, or that it was safer or had fewer side effects than drugs already available to treat psychotic disorders. In seeking FDA approval, Lilly relied on two controlled studies showing Zyprexa to be superior to a placebo in the management of the symptoms of psychotic disorders in patients with schizophrenia during short-term, six-week-long studies. News Release, Lilly's Zyprexa (olanzapine) Cleared for Marketing for Treatment of Psychotic Disorders, Eli Lilly & Co., Oct. 1, 1996, at 2 [hereinafter Lilly News Release, Oct. 1, 1996]. "[F]or a drug anticipated to be used for lifetime treatment of an incurable disease, only 301 patients received at least 1 year of treatment while only 876 received at least 6 months of

treatment." Wirshing Decl. 36 (citing C.M. Beasley et al., *Efficacy of Olanzapine: An Overview of Pivotal Clinical Trials*, 58 J. Clin. Psychiatry 7-12 (1997)).

Before approving Zyprexa, the FDA expressed some concerns about both the long-term effectiveness and Lilly's claims of the comparative efficacy of Zyprexa. While Dr. Paul Leber, M.D., Director of the FDA's Division of Neuropharmacological Drug Products, had no reservations about the FDA review team's unanimous recommendation to approve Zyprexa, he "d[id] have a number of observations about olanzapine and the sponsor's development program that are of potential importance in regard to the kind of promotional claims that it may or may not be appropriate to allow Lilly to advance for Zyprexa." Leber Memo 2, Zyprexa NDA File, Aug. 18, 1996. With respect to long-term effectiveness, Dr. Leber noted that:

> The evidence adduced in the sponsor's short term (nominally 6 week long) studies, although it unquestionably provides compelling proof *in principle* of olanzapine's acute antipsychotic action, does not, because of 1) the highly selected nature of the patients admitted to study, 2) the high incidence of censored observations in the controlled trials, and 3) the indirect means used to assess the product's antipsychotic effects, provide a useful quantitative estimate of how effective (even in the short run) olanzapine actually will be in the population for whom it is likely to be prescribed upon marketing.
>
> The relatively short duration of the controlled clinical trials the sponsor relies upon, as might be anticipated, leaves us largely uninformed both about how effective a "maintenance" treatment olanzapine will be in extended use, and how best to administer it (i.e., dose and regimen) for that use.

Id. at 2-3 (emphasis in original) (footnote omitted).

As to comparative efficacy claims, Dr. Leber believed "the data adduced in the Zyprexa NDA is . . . insufficient to permit the sponsor to make claims asserting the product's superiority to haloperidol [Haldol, an FGA]." *Id.* at 5. While offering criticisms of some of the studies offered in support of the assertion, Dr. Leber specifically noted:

> The problem in schizophrenia outcome assessment is that some of the so-called "negative" signs and symptoms of that illness are indistinguishable from the pseudoparkinsonian signs and symptoms that are known side effects of antipsychotic drugs like haloperidol. It would be reckless, therefore, to assume that a drug-haloperidol difference detected on an instrument that registers negative symptoms is actually measuring a difference in antipsychotic effectiveness.

Leber Mem., Aug. 30, 1996, at 3; *see also* Leber Mem., Aug. 18, 1996, at 5-7.

C. Initial Label

Before approving Zyprexa for use in treatment of the manifestations of psychotic disorders, primarily those associated with schizophrenia in September 1996, *see* FDA Approval Letter (Sept. 30, 1996), the FDA made several recommendations regarding the placement and prominence of warnings about weight gain in the planned labeling for Zyprexa.

Detailed regulations cover the type of information required in a drug label and how that information is presented. *See* 21 C.F.R. § 201.57. Different subsections within the label indicate the various dangers associated with the drug; in 1996, the negative side effects with the greatest incidence were listed in the "Warnings" subsection, those with lesser risk under "Precautions," and finally those of little risk fell below the "Adverse Reactions" headings. *See id.* (1996).

The Warnings section was required to "describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 C.F.R. § 201.57(e) (1996). Dr. Wirshing, one of the plaintiffs' experts, described the significance of the Warnings section: "[It] is a much more focused section [than the other

subsections] that says: 'This is the type of problem we believe to be associated with the drug. Pay attention. Heads up, doc. This can happen.'" Evid. Hr'g Tr. 383.

For Zyprexa's initial label, the FDA proposed placing weight gain in the "Precautions" section rather than as a Warning or Adverse Reaction. Pfs.' Fact Proffer ¶ 378; *see* 21 C.F.R. § 201.57(f) (1996) (mandating the precautions subsection to "contain information regarding any special care to be exercised by the practitioner for safe and effective use of the drug").

Lilly suggested an alternate placement, arguing that weight gain belonged instead in the "Adverse Reactions" section, further down the label: "In light of the additional supporting data . . . that demonstrates that a significant portion of patients who experienced a weight increase on olanzapine started out with a low body mass index at baseline, we feel weight gain is improperly placed as a precaution." Pfs.' Fact Proffer ¶ 378. "Adverse Reactions" were defined as "an undesirable effect, reasonably associated with the use of the drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence." 21 C.F.R. § 201.57(g) (1996). As plaintiffs' expert Dr. Wirshing explained in non-legalese, the adverse experience section is a "compedium of human maladies that occurred during the controlled clinical trials. . . . Everything that happens to a person during [the length of the clinical trial] is supposed to get into the adverse experiences, every cold, every broken bone, every arrest . . ." Evid. Hr'g Tr. 383. Listing weight gain under this subsection rather than Precautions de-emphasized Zyprexa's demonstrated association with this side effect.

Lilly's argument was persuasive. At launch, weight gain was listed as an adverse event. Its frequency and magnitude was described as follows:

> In placebo-controlled, 6-week studies, weight gain was reported in 5.6% of [Zyprexa] patients compared to 0.8% of placebo patients. [Zyprexa] patients gained an average of 2.8 kg, compared to an average 0.4 kg weight loss in placebo patients: 29% of olanzapine patients gained greater than 7% of their baseline weight, compared to 3% of placebo patients. . . . During long-term continuation therapy (238 median days of exposure), 56% of olanzapine patients . . . gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 5.4 kg.

Zyprexa Package Insert, Oct. 2, 1006. Also listed under "Other Adverse Events Observed During the Premarketing Evaluation of Olanzapine," diabetes mellitus, hyperglycemia, ketosis and diabetic acidosis were indicated as infrequent (i.e., 1/100-1/1000 patients) or rare (i.e., fewer than 1/1000 patients) side effects observed in patients during clinical trials. *Id.*; *see* 21 C.F.R. § 201.57(g)(2) (1996).

Plaintiffs argue that this labeling was misleading at best and an outright fraud at worst. *See* Part XVIII.A.4.b, *infra* (testimony of Dr. Wirshing). As of the latest October 2007 label change, weight gain, hyperglycemia, and hyperlipidemia are listed under the Warnings heading. *See* Def.'s Letter, Oct. 8, 2007, Docket No. 04-MD-1596, Docket Entry No. 1424; Part XV.C, *infra*.

D. Warning Letter

On October 1, 1996, one day after the FDA's approval of Zyprexa, Lilly Research Laboratories Vice President Dr. Gary Tollefson led an interactive teleconference. Plaintiffs allege that Lilly's strategy of false promotion and misrepresentation began here: Dr. Tollefson implied Zyprexa was superior in efficacy and lack of side effects to the other antipsychotics, a message that the FDA found to be "false and misleading, and in violation of the [Federal Food, Drug, and Cosmetic] Act." Letter from Kenneth R. Feather, Senior Advisor, DDMAC, to Charles R. Perry, Jr., Director, Pharmaceutical Communications and Compliance, Eli Lilly &

Co., Nov. 14, 1996, at 1 [hereinafter FDA Warning Letter]. It subsequently issued Lilly a warning; this was the only warning from the FDA Lilly ever received about Zyprexa. *Id.* The company's whole promotional campaign, the FDA concluded, seemed to be "lacking in appropriate balance, thereby creating a misleading message about Zyprexa." *Id.*

In particular, the FDA highlighted Dr. Tollefson's response to a question about weight gain, along with certain other statements and promotional and labeling materials made or used during the teleconference:

> When asked a question about weight gain, Dr. Tollefson's response turned an adverse event into a therapeutic benefit. He states, "So we went back and analyzed our data and saw that the vast majority of weight gain reported initially as an adverse event, in fact, was weight gain occurring in patients who had baseline before starting treatment, had been below their ideal body weight. **So we really look at this, with the majority of patients, as being a therapeutic recovery rather than an adverse event. And that data, I think is fairly compelling, because it was included in our labeling.** (Emphasis added)."
>
> The information on weight gain was indeed included in the approved labeling, but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading.

Id. at 5 (emphasis in original). The agency also warned that,

> The promotional materials emphasize efficacy data but do not provide sufficient balance relating to adverse events and cautionary information. Further, they do not adequately or prominently discuss several important adverse events specifically selected for emphasis in the approved labeling. These events include orthostatic hypotension, seizures, transaminase elevations, weight gain, dizziness, and akathisia.

Id. at 1.

Other promotional materials were considered to also include "implications of superiority over other antipsychotic products that are unsubstantiated" and "present a misleading impression

of Zyprexa as a superior, highly effective, virtually free of side effects, easy to use product . . . . contrary to the approved labeling." *Id.* at 2-3. Further, the FDA noted, "[t]he entire thrust of [Lilly's promotional] campaign is to point out that Zyprexa is different and safer than older antipsychotic drugs. Therefore, it is necessary to properly emphasize those adverse events that do occur, that require caution when using Zyprexa." *Id.* at 2.

For example, Lilly publicized the fact that Zyprexa did not require blood monitoring. Dr. Tollefson explained this supposed benefit at the launch teleconference:

> With some of the other agents, such as Clozapine or clozaril that you may be familiar with, of course there are prerequisites for blood monitoring on a weekly basis because of some of the safety concerns with those drugs. Of course this is very troublesome to patients and very costly. We're very pleased that we have no requirements for any type of blood monitoring with Zyprexa.

Tr. of Zyprexa FDA Approval Conference Call, Eli Lilly & Co., Oct. 1, 1996 at 4. The assertion was reemphasized in a press release on the FDA's approval of Zyprexa offered the same day. Lilly News Release 2, Oct. 1, 1996.

Although it was not included in the FDA's warning letter, plaintiffs allege that this instance embodies Lilly's misleading marketing: from pre-approval clinical trials, the company already knew of the drug's metabolic weight-gain effects—and thus presumably the need for regular blood glucose testing. *See id.* at 4 ("[T]he most frequently observed treatment-emergent events associated with olanzapine at an incidence statistically greater than placebo [included] weight gain."). In response, Lilly notes that its statement that "Zyprexa patients would not have to submit to weekly blood monitoring tests" was related to the fact that unlike clozapine, Zyprexa was not associated with agranulocytosis. *See* Lilly News Release 3-4, Oct. 1, 1996.

The FDA warning letter specifically forbid Lilly from making four claims about Zyprexa: 1) that Zyprexa caused fewer EPS side effects; 2) that Zyprexa was superior for schizophrenia; 3) that Zyprexa did not cause TD; and 4) that Zyprexa did not lead to Parkinson's disease. FDA Warning Letter; Evid. Hr'g Tr. 745 (Abramson). Plaintiffs allege that Zyprexa continued to make all of these claims, in addition to promoting the drug for unapproved off-label uses. *See* Parts XVIII.A.4-6, *infra*.

VII. Events from 1996 to 2000

Zyprexa sales grew substantially from 1996 to 2000, despite the facts that at launch it cost approximately twice as much as Risperdal, the only other SGA on the market at the time, and that a third SGA, Seroquel, was introduced in 1997. Evid. Hr'g Tr. 381 (Wirshing). While Lilly's marketing efforts were highly successful, the numbers of adverse event reports ("AERs") submitted to the FDA and made available to Lilly through the MedWatch database also steadily increased. For example, in one Periodic Adverse Drug Event Report, Lilly reported five instances of diabetic acidosis and two instances of diabetic coma between September 30 and December 30, 1997. Most Serious Adverse Events by Body System/IND Safety Reports, Olanzapine Annual Report, Eli Lilly & Co. (Oct. 1, 1997 to Sept. 30, 1998). Another report listed three incidents of ketoacidosis from April 1 to June 30, 1998. Line Listing of Non-Alert Reports: Quarterly Review Period Ending June 30, 1998, Eli Lilly & Co. By the end of 1998, after two years on the market, the diabetes-related AERs for Zyprexa totaled nearly 200. By the end of 2000, that number was approximately 600.

Given that the number of reported events typically reflects 1% to 10% of the total estimated population of all complications, *see* Part V.D, *supra*, the diabetes-related AERs for

Zyprexa were much higher. Yet Zyprexa's label from October 1996 to April 12, 2000 only mentioned diabetes-related conditions in its Adverse Events section, which also included such conditions as "chills and fever" and "heart arrest," and listed the known pre-launch incidence of diabetes, hyperglycemia adverse events, or diabetic ketoacidosis as "infrequent" or "rare."

VIII. Events in 2000

A. FDA Approval for Manic or Mixed Bipolar

In 2000, Lilly sought to increase sales of Zyprexa by obtaining FDA approval to treat additional indications, including bipolar mania, maintenance of treatment response in schizophrenia, psychotic disorders, and use for adolescents. *See* NDA 20-592; Letter from Russell Katz to Gregory Brophy (Oct. 12, 2000). Early that year, the FDA approved the use of Zyprexa in the treatment of manic or mixed episodes of bipolar disorder.

B. European Investigation

By 2000, European officials were expressing concern about the risks and side effects of Zyprexa. On February 21, 2000, the European Agency for the Evaluation of Medicinal Products ("EAEMP") contacted Eli Lilly Ltd. UK and ordered the company to expedite its review of risk factors and provide the information quickly. Telefax Message from Dr. Juhana Idänpään-Heikkilä, Scientific Administrator, European Agency for the Evaluation of Medicinal Products, to Mr. J. C. Saunders, Eli Lilly Ltd UK (Feb. 21, 2000), at 1 ("Reports of myocarditis, cardiac failure, cardiomyopathy and eosinophilia should be reviewed cumulatively for the next PSUR [Periodic Safety Update Report] and the increase in triglyceride levels and reports of hyperlipidemia are potential signals which should be reviewed thoroughly for the next PSUR,

including possible risk factors such as diabetes and weight gain."). The EAEMP also requested full review of all known cases of diabetic ketoacidosis:

> We would like to inform you that CPMP [the European Union's Committee for Proprietary Medicinal Products] . . . concluded that there have been several reports of diabetic ketoacidosis, some with fatal outcome and a cumulative review should be provided of all known or suspected cases as soon as possible.

Id.

C. FDA Requests Information on Hyperglycemia and Diabetes

On May 1, 2000, the FDA requested more information from Lilly on Zyprexa's relationship to hyperglycemia and diabetes. *See* Note to Reviewer 1, Eli Lilly & Co., July 31, 2000 (responding to the FDA's request that Lilly "investigate the possibility of collaborating with organizations having large pools of patients treated with atypical antipsychotics to examine the evidence of hyperglycemia or new-onset diabetes mellitus temporally associated with olanzapine."). Specifically, the FDA asked for:

> A thorough assessment of all Phase 1, 2, and 3 studies in the olanzapine NDA and any subsequent supplements for evidence of new-onset diabetes mellitus, hyperosmolar coma, diabetic ketoacidosis, weight gain, and hyperglycemia. This should include the frequency of deaths, serious adverse events, total adverse events, and dropouts due to events related to abnormalities of glucose metabolism listed above, data regarding mean changes from baseline in plasma glucose level, and the percentage of patients meeting criteria for a markedly abnormal plasma glucose concentration from an appropriate pool of placebo-controlled Phase 2/3 studies. Any deaths, dropouts, or serious adverse events should have an accompanying detailed narrative summary.

Letter from Gregory T. Brophy, Director, Lilly Research Lab., to FDA at 2 (July 31, 2000) (quoting FDA Letter, May 1, 2000) [hereinafter Brophy Letter]. In addition, the FDA required a "review of spontaneous postmarketing reports for new-onset diabetes mellitus, hyperosmolar coma, diabetic ketoacidosis, weight gain, and hyperglycemia" as well as "a comprehensive

review of all preclinical data pertaining to hyperglycemia." *Id.* (quoting FDA Letter, May 1, 2000).

Lilly's partial response on July 31, 2000, included an analysis of seventy-eight controlled trials as well as "a review of published literature, a historical review of preclinical data and previously submitted Phase I, II and III studies, and analysis of current, complete clinical trial database, a review of spontaneous postmarketing reports with an estimate of patient exposure, and copies of correspondence with foreign regulatory agencies." Eli Lilly and Co., Hyperglycemia, Weight Gain, and Olanzapine 17 (2000).

Plaintiffs suggest that most of the submitted information was misleading, especially as it pertained to full disclosure of the risks of prolactin, weight gain, and hyperglycemia. For example, Lilly suggested that Zyprexa did not elevate prolactin levels. *See id.* at 21 ("[M]ost atypical antipsychotics, in contrast to typical antipsychotics, have not been associated with significant hyperprolactinemia. Risperidone is the one atypical antipsychotic associated with sustained prolactin elevations above the upper limit of normal"). Yet Lilly's own proposed label of October 2000 admitted the risk of heightened prolactin: "As with other drugs that antagonize dopamine D2 receptors, olanzapine elevates prolactin levels, and a modest elevation persists during chronic administration." Pfs.' Fact Proffer ¶ 622.

With regards to olanzapine's metabolic effects, Lilly dispersed blame for weight gain among antipsychotics generally, stating that "[w]eight gain has been reported during treatment with nearly every antipsychotic drug on the market . . . . Weight gain occurs during treatment no matter what the patient's age, sex, or race and is seen with both oral and depot drug formulations." *Id.* Although Lilly noted that "the average weight gain observed in the clinical

pharmacology studies was 8.9 +- 7.1 pounds (mean +- standard deviation)," it downplayed the results, suggesting that all patients enrolled in studies gain weight and thus weight gain could not be attributed to olanzapine:

> The clinical meaning of the weight gain is difficult to assess, since in the experience of the investigator over 20 years, patients generally tend to gain weight while enrolled in studies at the Lilly Clinic. The reasons for weight gain may be attributed to lack of exercise and liberal access to high fat meals.

Id. at 47. Plaintiffs note that Lilly did not mention that its own 1993 study had shown "uniform" and consistent weight gain among olanzapine patients. Plassard & Beato, *supra* at 48.

Similarly, Lilly tried to obfuscate the incidence of hyperglycemia, citing pre-disposed factors among schizophrenic patients. Its response to the FDA stated that,

> On the basis of [] case studies it appears as though patients that may develop hyperglycemia in temporal association with olanzapine are patients that are typically at risk for DM-II based on race, obesity, or family history. It is unclear at this point whether or not the number of cases of olanzapine in temporal association with DM-II exceeds the expected incidence for the development of DM-II in patients with schizophrenia.

Eli Lilly and Co., Hyperglycemia, Weight Gain, and Olanzapine (2000). Plaintiffs point out that Lilly's explanation overlooks the fact that an increased incidence of diabetes in Zyprexa users appears in studies in which all subjects are diagnosed schizophrenics.

D. Lilly Debates Label Change

Beginning in February 2000, Lilly officials internally debated whether—but ultimately chose not—to change Zyprexa's labeling and acknowledge the risk of hyperglycemia. While perhaps somewhat puzzled by the mechanism by which Zyprexa was causing hyperglycemia, Lilly did understand the drug's link to weight gain.

> It is not immediate [sic] apparent, based on the known pharmacology of olanzapine why it would cause hyperglycemia. The blockade of serotonin receptors by olanzapine along with its antihistaminic activity can explain associated weight gain . . . . Glucose levels greater than 600 mg/dL was reported in half of the spontaneous reports of hyperglycemia.

Olanzapine Labeling Change on Hyperglycemia for 02/22/2000 GPLC e-Meeting, Global Operations Labeling Department, Eli Lilly & Co., at 3.

In a confidential internal document, Lilly observed that patients taking Zyprexa were three and a half times as likely to develop high blood sugar as those who took nothing: "[r]ecent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment-emergent hyperglycemia in the olanzapine group (3.6 %) was higher than that in the placebo group (1.05%)." *Id.* at 1. The company was also aware that hyperglycemia has been reported uniformly since the introduction of Zyprexa: "The first report of hyperglycemia associated with olanzapine was received in October of 1996 and the last report was received in September of 1999. The reporting frequency of hyperglycemia has not changed over the 36 months of marketing (September 1996 through 1999) olanzapine." *Id.* at 2. While Lilly publicly asserted that Zyprexa only poses a risk for patients with pre-existing risk factors, the documents acknowledge that "[t]he spontaneous safety database also has a number of hyperglycemia cases in which the patient has no history or known risk factors for diabetes." *Id.*

Lilly did not provide this information to the FDA. In documents later submitted to the regulatory agency, Lilly narrowed the gap between the tested populations, stating that 3.1% of Zyprexa patients developed high blood sugar while 2.5% of patients taking a placebo developed the same. Pfs.' Fact Proffer 175 n.978.

In October 2000, following a meeting with members of one of Lilly's academic advisory boards, Lilly executives discussed the reactions of the board endocrinologists to the company's data on Zyprexa and weight gain, hyperglycemia, and diabetes. Email from Robert W. Baker, Eli Lilly & Co., to Charles M. Beasley et al., Eli Lilly & Co., Oct. 9, 2000, at 2:31 p.m.; Email from Robert W. Baker to Charles M. Beasley et al., Oct. 10, 2000, at 9:00 a.m. Dr. Robert Baker, then Lilly's Medical Advisor and Senior Clinical Research Physician, expressed some concern:

> Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic. . . .
> They were however concerned by our spontaneous AE reports, and quite impressed by the magnitude of weight gain on olanzapine and implications for glucose. . . . Disconcertingly, one member compared our approach to Warner-Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class.

Oct. 9, 2000 Baker Email. In response, Dr. Thomas Brodie reiterated that "clearly, this group of Endocrinologists . . . are very concerned with the approach Lilly is taking towards the issue that Zyprexia [sic] leads to diabetes." Email from Thomas M. Brodie, Eli Lilly & Co., to Robert W. Baker & Eugene R. Thiem, Eli Lilly & Co., Oct. 9, 2000, at 3:10 p.m. Continuing, he added "I do believe they made a very strong point that unless we come clean on this, it could get much more serious than we might anticipate." *Id.*

Dr. Charles Beasley, a former Senior Research Physician and Lilly Advisor on the olanzapine team, responded at length, acknowledging the side effects and concerns about how to deal with them.

> There is the marketing approach and then the scientific analyses approach. There are 2 issues—weight gain and hyperglycemia.
> These guys were really concerned about the weight gain, not only because of a diabetes risk but all the other potential health risks . . . . When they understood .

> . . that olanzapine is the worst offender, other than clozapine, they advocated a different marketing strategy than we are taking. They believe we should "aggressively face the issue" and work with physicians to address methods of reducing weight gain . . . There does not seem much to say about scientific analyses of weight gain, we know it's a weighty problem. When you translate 1-2% gain of 40+ kilos into the absolute number based on 5 million patients, the number is 50,000 to 100,000. 100,000 people putting on 90 pounds of weight is a lot. . . .
> . . .
> With regard to the marketing side of this issue of impaired glucose tolerance [sic] / diabetes, the message was clear. Don't get too aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents until we are sure of the facts and sure that we can convince regulators and academicians. W-L [Warner-Lambert] with Resulin [sic] was the example.

Email from Charles M. Beasley, Jr., to Alan Breier, Oct. 10, 2000, at 8:33 a.m.

E. FDA Approval for Schizophrenia Maintenance

On October 12, 2000, the FDA approved the use of Zyprexa for the maintenance of treatment response in schizophrenia. Letter from Russell Katz to Gregory Brophy (Oct. 12, 2000). The FDA only agreed to approve this new indication on the condition that Lilly adopt the FDA's proposed labeling revisions. *Id.* One of these revisions included greater emphasis on the narrow indication for which Zyprexa was approved, using the phrases "treatment of schizophrenia" and "in schizophrenia" and eliminating any reference to the broader category of psychosis or psychotic disorders.

Another of these revisions concerned the communication of information about Zyprexa's effect on plasma glucose levels and the risk of diabetic coma. On May 9, 2000, Lilly proposed making a change to the Zyprexa label to include data from the olanzapine clinical trial database that would list effects on random plasma glucose levels as an adverse reaction in the Laboratory Changes section and diabetic coma as an adverse reaction in the Postintroduction Reports section. Brophy Letter; Michele Sharp, Eli Lilly & Co., Draft Chronology of FDA Interactions

Re: Glucose, Triglycerides and Pancreatitis (Apr. 24, 2003). Lilly claimed that this label change was based on "[t]he results from the analysis of our clinical trial safety database . . . and review of our spontaneous case reports," and not in response to the May 1, 2000 letter the company had received from the FDA requesting information on "hyperglycemia or new-onset diabetes mellitus temporally associated with olanzapine." Brophy Letter at 1; Eli Lilly and Co., Hyperglycemia, Weight Gain, and Olanzapine 17 (2000).

F. "Diabetic Coma" Added to Label

The FDA approved the addition of the phrase "diabetic coma" to the label via a letter to Lilly dated October 11, 2000. The FDA, however, rejected Lilly's proposed "inclusion of data from the olanzapine clinical trial database with respect to random plasma glucose levels." Pfs.' Fact Proffer ¶ 617. The FDA based its rejection on the grounds that Lilly's proposed revision was misleading. Lilly's proposed text stated:

> In the olanzapine clinical trial database, as of September 30, 1999, 4577 olanzapine-treated patients (representing approximately 2255 patient-years of exposure) and 445 placebo-treated patients who had no history of diabetes mellitus and whose baseline random plasma glucose levels were 140 mg/dL or lower were identified. Persistent random glucose levels >= 200 mg/dL (suggestive of possible diabetes) were observed in 0.8% of olanzapine-treated patients (placebo 0.7%). Transient (i.e., resolved while the patients remained on treatment) random glucose levels >= 200 mg/dL were found in 0.3% of olanzapine-treated patients (placebo 0.2%). Persistent random glucose levels >= 160 mg/dL but <200 mg/dL (possibly hyperglycemia, not necessarily diabetes) were observed in 1.0% of olanzapine-treated patients (placebo 1.1%). Transient random glucose levels >= 160 mg/dL but <200 mg/dL were found in 1.0% of olanzapine-treated patients (placebo 0.4%).

Id. This language suggests that random glucose levels were the same for patients taking olanzapine and patients taking a placebo. On October 11, 2000, Dr. Russell Katz of the FDA

wrote to Gregory T. Brophy of Eli Lilly expressing his opinion that the proposed label change was misleading:

> The descriptive data that is provided expresses a certain level of implied safety with respect to treatment emergent hyperglycemia. This reassuring language is not appropriate for submission under 21 CFR 314.70(c) as a 'Special Supplement – Changes Being Effected' (CBE). A more complete submission of glucose data, and additional discussion of pooling and analysis of this data is necessary before an appropriate review of treatment emergent hyperglycemia and diabetes can take place.

Letter from Dr. Russell Katz, FDA, to Gregory T. Brophy, Eli Lilly & Co. (Oct. 11, 2000). To Dr. Katz and the FDA, olanzapine was not as safe as Lilly made it out to be. Because there was not enough data to support Lilly's proposed revision to the label, the FDA would not permit Lilly to use the label as a marketing device to infer "a certain level of implied safety" that was not proven to exist.

G. Malaysian "Dear Doctor" Letter

During this same time period, other countries requested or required Lilly to make changes to the Zyprexa label. In November 2000, at the request of the Malaysian Regulatory Authority, Lilly sent a "Dear Doctor" letter to Malaysian physicians advising them of a change in Zyprexa's package insert and an increased risk of hyperglycemia and/or diabetes as it relates to Zyprexa use. The "Dear Doctor" letter also advised Malaysian physicians to monitor patients with risk factors for the development of diabetes. Letter from John See, Regulatory and Scientific Affairs Manager, Eli Lilly & Co., to Doctor, Malaysian Regulatory Authority (Nov. 2000).

IX. Events of 2001

A. Off-Label Marketing Campaign to Primary Care Doctors

As an antipsychotic drug, Zyprexa has been and is most commonly prescribed by psychiatrists and other mental health specialists who treat patients with relatively rare schizophrenia and bipolar disorders, diseases traditionally beyond the ken of the average family doctor. Primary care physicians ("PCPs"), in contrast, do treat patients diagnosed with anxiety, depression, irritability, dementia, and Alzheimer's disease—all off-label uses vis a vis Zyprexa.

In order to expand the potential number of Zyprexa prescribers and patients and thus increase sales, Lilly began directing its marketing efforts towards PCPs in late 2000. Plaintiffs allege that the campaign was intended to, and did, largely (and illegally) promote off-label use by PCPs.

As recounted in one of this court's previous Zyprexa opinions, this strategy was outlined by the company as follows:

> Following several months of study by the LillyUSA Zyprexa Brand Team, the affiliate approved the recommendation that Lilly actively promote Zyprexa to selected current primary care prescriber targets . . . . We believe there to be significant unmet medical need among office-based primary care physicians . . . . Zyprexa's profile is ideal for primary care (safe, simple, well-tolerated, effective, versatile). Zyprexa would enjoy first mover advantage in this segment . . . .
> . . .
> Challenges: Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers. Many PCPs will refer patients in need to psychotropic treatment to a specialist rather than treat the patient. Key barriers to uptake include PCP's lack of training in this category, limited time with patients, and an aversion to perceived risk. Zyprexa's primary indications—schizophrenia and bipolar—are not viewed as PCP-treated conditions, so there's not a specific indication for Lilly reps to promote in the PCP segment
> . . .
> Position: Zyprexa: The safe, proven solution in mood, thought, and behavioral disorders. We will emphasize safety to address barriers to adoption . . . . The word 'solution' speaks to unmet medical need, and enables the PCP to take control of clinical situations that previously had led to referrals and/or poor outcomes. 'Mental disorders' is intentionally broad and vague, providing latitude to frame the discussion

around symptoms and behaviors rather than specific indications.

In re Zyprexa Prods. Liab. Litig., 489 F. Supp. 2d 230, 251 (E.D.N.Y. 2007).

The resulting PCP-directed marketing campaign, titled "Viva Zyprexa," was announced at a national sales meeting in March 2001. Evid. Hr'g Tr. 754 (Abramson). Prior to this time, Zyprexa had been prescribed almost exclusively by psychiatrists. An essential part of Lilly's marketing plan was encouraging PCPs to think differently about both their patients and Zyprexa. Rather than advertising its use for specific disorders, Lilly marketed Zyprexa for symptoms commonly encountered by PCPs, encouraging doctors to treat patients without making a diagnosis at all:

> One-third of all patients, all psychiatric patients, do not fit into a DSM category. They have ooms, they just don't neatly fit into a category. But yet you got to treat anxiety, agitation, depression where it exists.

Pfs.' Fact Proffer at II.C.2.c. (While the symptoms of dementia and depression overlap to some extent with those of schizophrenia and bipolar mania, these are different and distinguishable diagnoses.)

Although the FDA had never approved Zyprexa as a "solution [for] mood, thought and behavioral disorders," it was Lilly's plan to do just that—to "redefine" the way PCPs treated those diseases. Marketing Zyprexa as a "mood stabilizer," Lilly asserted that "Zyprexa safely stabilizes behavioral symptoms." The company told its sales force:

> The [primary care] doctor is thinking that he does not see schizophrenic or bipolar patients, but he probably does see patients with symptoms of behavior, mood or thought disturbances. Need to focus on symptoms and patient types . . . Even if the doctor does not have diagnosis, he should treat anyway."

Pfs.' Fact Proffer ¶ 607.

Based on the market research it had commissioned and the greater incidence of the disease, Lilly viewed bipolar disorder as a more important market segment than schizophrenia. By marketing to symptoms, Lilly believed it could essentially "create" a "bipolar market." Lilly's "Mood Disorder Questionnaire" ("MDQ") handout, distributed to primary care physicians, contained a series of questions Lilly sales representatives indicated were to help "diagnose" the patient. Formally a "self-administered screening tool," the MDQ instructed physicians they "have a positive screen [for patients who would benefit from use of Zyprexa] if the patient answers . . . 'Yes' to seven or more of the 13 items in question 1 AND . . . 'Yes' to question 2." Yet the MDQ was not designed to function as a diagnostic tool.

To better focus its marketing towards symptoms rather than diseases, Lilly also created hypothetical patient profiles, with names and symptoms, and used them as examples of patients that PCPs might treat with Zyprexa. *See, e.g.*, Zyprexa Primary Care Sales Force Resource Guide, Eli Lilly & Co., June 2002. These included "Martha," "Donna," "Mark" and "Christine." *See* Zyprexa Patient Profiles, Pfs. Ex. 480. "Donna," for example, was described as "a single mom in her mid-30s appearing in your office in drab clothing and seeming somewhat ill at ease. Her chief complaint is that she feels anxious and irritable." Creative Street, Inc., Zyprexa Primary Care 2002 Q-2 Updates, Draft 7 Script - 02/15/02 at 6. Sales representatives were trained to "demonstrate how Zyprexa can and does provide dependable control that you [the doctor] and your patients can rely on for relief" for this type of patient, and to tell doctors:

> Now when we look at efficacy in a patient like Donna, Zyprexa has been shown to improve mood, anxiety levels, and disrupted sleep patterns. In fact, when looking at depressive symptoms that are present in bipolar patients, Zyprexa has shown significant improvement in these symptoms. So what Zyprexa will mean to a patient

> like Donna is that she will have less anxiety, less irritability and be able to sleep better.

Id. at 7.

But, as plaintiffs note, "Donna" is not described as having bipolar disorder and having been so diagnosed; moreover, Zyprexa has not been shown to improve mood, anxiety levels, or disrupted sleep patterns in patients with Donna's symptoms who do not have bipolar I disorder. When Lilly told doctors that Zyprexa had been shown to help patients "like Donna," plaintiffs allege that the statement was false and misleading: no data had ever shown any benefit associated with the use of Zyprexa in a patient with Donna's symptoms.

In addition to touting the symptomatic relief provided by Zyprexa regardless of diagnosis, Lilly also, plaintiffs assert, actively promoted off-label sales of Zyprexa for dementia and depression. *See* Part XVIII.A.5, *infra* (testimony of Dr. Schneider). The company created a separate 280-person "long-term care" sales force to "drive the nursing home business." Zyprexa Primary Care Presentation 14, Mike Bandick, Zyprexa Brand Manager, Eli Lilly National Sales Meeting, March 13, 2001. At least some Lilly officials referred to nursing homes and assisted living facilities as an "opportunistic" market. Email from Denice Torres, Eli Lilly & Co., to Peter D. Feldman, Eli Lilly & Co., July 15, 2002, at 5:53 p.m.

Lilly's "Strategy #1" was to "establish Zyprexa as a first line choice in the treatment of the elderly patient who are [sic] experiencing behavior or cognitive symptoms." Zyprexa PCP Opportunity 3, Eli Lilly & Co. (undated). Certain marketing materials for dementia patients, plaintiffs point out, state that Zyprexa provided "[s]afety in agitation associated with dementia in a clinical trial" and that it was the "[f]irst and only psychotropic indicated for the treatment of

agitation associated with dementia." Zyprexa has never been approved for the treatment of dementia. Another Lilly brochure from 1999, entitled "Programs Emphasizing Zyprexa's Efficacy for Depressive Symptoms," stated that Zyprexa "improves depressive symptoms."

Representatives of Lilly were also instructed to inform doctors that Zyprexa may help patients with "symptoms of social withdrawal, apathy and flat affect." Training materials directed the sales force to tell doctors that "[p]sychiatrists refer to these as 'negative symptoms,'" but a "patient's family may say it more simply: 'She's not herself anymore.'"

Compared to the hypothetical patient profile "Donna," the elderly patient "Martha" was designed to "reinforce Zyprexa as a nursing home drug." Zyprexa Primary Care Presentation 14; *see* Part XVIII.A.5.b.ii, *infra*. Like Donna, Martha had no diagnosis, but only symptoms of agitation, restlessness, and paranoia. Yet according to plaintiffs, not only was there a lack of evidence that Zyprexa was beneficial for patients like "Martha" with dementia, Lilly actually had evidence to the contrary: the company's study results had shown "that olanzapine actually statistically significantly worsened cognitive function in patients with Alzheimer's disease compared to placebo patients." Schneider Decl. 17 (citing the 1999-2001 HGIC trial).

Lilly's marketing efforts succeeded in greatly increasing the number of off-label sales of the drug; without off-label marketing, Zyprexa—originally approved for the treatment of conditions affecting less than one percent of the population—could not have become the seventh best-selling drug in the world. In 2003, Zyprexa sales by diagnosis broke down into nursing home 9%, schizophrenia 26%, bipolar 28% and other 40%. Brand Council III at 16, Eli Lilly & Co. Within the bipolar segment, Lilly differentiated between bipolar mania, depression and maintenance. In 2002, Lilly sales figures for bipolar mania totaled $200 million, for bipolar

depression $136 million, and for bipolar maintenance, $225 million. Yet use of Zyprexa for bipolar depression alone has never been approved; bipolar maintenance became an approved indication only in 2004. Thus, in 2002, almost two-thirds of Lilly's revenue in the bipolar market came from off-label use. Lilly estimated its revenues from the same segments for 2003 and 2004, and the percentages held constant. Pfs.' Fact Proffer ¶ 720.

B. Japan Launch

In preparation for Zyprexa's launch in Japan in or about June 2001, Lilly attempted to persuade Japan's Ministry of Health and Welfare ("MHW") that the Zyprexa package insert did not need to include a requirement that blood glucose monitoring be conducted in certain patients due to the reports of diabetes and hyperglycemia. Email from Masashi Takahashi, Lilly Representative to Japan, Eli Lilly & Co., to Charles M. Beasley, Oct. 5, 2000, at 4:36 a.m. Lilly's concern was that such a disclosure would drive down demand for the drug. MHW wanted to "to rank weight gain (and hyperglycemia) issues higher in the safety section of the package insert," because, as the Lilly Japan Representative himself noted, the Ministry "recognizes that olanzapine causes weight gain more than other [antipsychotics] and weight gain is a widely accepted risk factor for diabetes." *Id.* In order to "avoid a request from MHW of forced blood glucose monitoring at launch," Lilly Japan thought "it would be clever to make a deal with MHW by ranking weight gain (and hyperglycemia) at higher places so as to look similar to SPC [Summary of Product Characteristic] description . . . ." *Id.*

X. Events of 2002

A. Japanese Label Change

In March 2002, in response to a request from the MHW for an "analysis of Eli Lilly global trial data on weight gain and hyperglycemia associated with the use of olanzapine," Lilly prepared a report. Eli Lilly & Co., Review of Glycemic Related Studies (2002). In the "Conclusions" section of the review, the company stated

> An increased risk of developing diabetes compared to a general reference population was observed in the AdvancePCS prescription database cohorts during treatment with either conventional or atypical antipsychotics. Though the risk of developing diabetes was significantly greater for patients in the Risperidone [Risperdal] cohort than in the Haloperidol cohort, this analysis did not demonstrate a generally elevated risk between the atypical and conventional antipsychotic cohorts. It remains unclear whether the observed increases are related to factors intrinsic or extrinsic to those psychotic conditions commonly treated with antipsychotic drugs.

Id. at 6.

Lilly's attempts to convince the MHW of the safety of atypical antipsychotics did not fully succeed. In April of 2002, after reports of nine serious cases of hyperglycemia and diabetic ketoacidosis among Zyprexa users in Japan, the MHW required Lilly to issue an "Emergency Safety Information" letter to physicians about Zyprexa's risks. The Japanese agency further required that Zyprexa's warning be adjusted to include a contraindication against use of Zyprexa by diabetics and instructions to monitor patients' blood glucose with an initial fasting blood glucose test, and periodic tests, thereafter while they were using Zyprexa.

Lilly found " '[t]he impact of the label change in Japan . . . very profound,' two senior executives commented in a July 1, 2002 memo. 'There has been a 75% drop in new patients being put on the drug.' " Alex Berenson, *One Drug, Two Faces*, N.Y. Times, Mar. 26, 2008.

Lilly immediately set about reconciling the Japanese label change with its sales pitch that Zyprexa does not cause diabetes. In response, two Lilly officials authored an internal

memorandum regarding how to "proactively" discuss with "formulary decision makers" Japan's decision to force a Zyprexa label change. Pfs. Fact Proffer ¶ 713. Lilly's message was that it "strongly disagreed" with the conclusion drawn by the Japanese regulators, notwithstanding reports of several deaths in connection with Zyprexa use and severe hyperglycemia. *Id.* at ¶ 714. Further, the memorandum emphasized that "we expect this outcome in Japan will not affect the Zyprexa label in the United States. It is important to keep in perspective the benefits of Zyprexa to patients with schizophrenia and bipolar mania." *Id.* The Lilly memorandum also highlighted six "points to note" while emphasizing the safety and cost effectiveness of Zyprexa and that the label change in Japan "does not affect the value of Zyprexa." *Id.* (emphasis added). Finally, the Lilly memorandum affirmed that "Lilly stands by its science, and is exploring several options to correct this regulatory injustice." *Id.* (emphasis added).

B. Mexican and Australian Label Changes

In July 2002, the Mexican government requested that Eli Lilly revise its package insert regarding hyperglycemia for Zyprexa. Email from Elizabeth Brunner, Eli Lilly & Co., to Patrizia Cavazzoni, Eli Lilly & Co., July 8, 2002, at 2:52 p.m. Shortly thereafter, Lilly completed negotiations with the Australian Regulatory Board about a required label change noting the increased prevalence of diabetes in patients with schizophrenia. *See* Email from Anthony M. Fiola to Lilly PMs, August 28, 2002, at 15:43.

C. Lilly's Response to Foreign Label Changes

The foreign label changes, in particular that of Japan, were serious challenges to Zyprexa's future. Following the announcement of that label change, at the request of the FDA, Lilly performed an "Analysis of Japanese Data on Hyperglycemic and Diabetic Spontaneous

Serious Adverse Events Associated with Use of Zyprexa." The analysis was based upon thirteen serious adverse event reports of hyperglycemia, including two deaths from diabetic coma, in patients taking Zyprexa in Japan. In response, Lilly claimed that the Japanese cases were anecdotal; the Japanese patients were injured due to other pre-existing risk factors; the events in Japan were due to unspecified confounding causation factors; and that because the Japanese Zyprexa package insert had a stronger warning regarding diabetes than in the United States, Japanese physicians were, therefore, more likely to blame glucose-related adverse events on Zyprexa than American doctors. Pfs.' Fact Proffer ¶ 716.

On October 15, 2002, Dr. Russell Katz and Steve Hardeman of the FDA took part in a conference call with Lilly representatives Alan Breier (Vice President and Zyprexa Team Leader), Gregory Brophy (Director, US Regulatory Affairs), Melanie Bruno (Senior Regulatory Research Scientist), and Patrizia Cavazzoni (Medical Director). Telephone Communication: FDA Meeting and Briefing Document, Oct. 15, 2002. The purpose of the conference call was to discuss the FDA's concerns about glucose "dysregulation" connected with Zyprexa use. *Id.* Dr. Katz noted that the FDA had concerns about Lilly's use of data and methodologies with regard to reports of treatment emergent diabetes and informed Lilly that the FDA was awaiting the results of a VA study in its efforts to determine its position with regard to glucose dysregulation and Zyprexa. *Id.*

Handwritten notes on a document prepared for the meeting note that "John Buse has seen around 20 cases DKA that just appeared w/o patient having been identified as diabetic I or II type. Concerned about good drug/bad drug perception by prescribers and patients if drugs are labeled individually and differently." *See* Eli Lilly & Co., October 17, 2002 Glucose

Dysregulation FDA Meeting Preparation Document 7. The document coached Lilly officials on how to respond to FDA inquiries about label changes in other countries. Lilly officials were told that the FDA might ask, "[a]re you going to change your label in the US since the labeling has been changed in Japan, Australia, New Zealand and potentially Canada and there is already more information in the EU label than the US label?" *Id.* at 3. As detailed in the Preparation Document, Lilly officials were supposed to tell the FDA that "labeling changes in Japan and other countries has not been based [sic] full consideration of the available data, but rather forced upon Zyprexa." *Id.*

XI. Events of 2003

A. Pancreatitis Added to Label

Early in 2003, the FDA agreed that Lilly should include pancreatitis as an adverse event in the Postintroduction Reports section of the Zyprexa label. Pfs.' Fact Proffer ¶ 721.

B. Canadian Approval

On March 17, 2003, Canadian regulators approved olanzapine for the treatment of bipolar mania. In the "Precautions" section of the product monograph, however, the Canadian regulatory agency forced Lilly to add language warning of the risks of the drug in worsening pre-existing diabetes or other metabolic concerns:

> As with some other antipsychotics, exacerbation of pre-existing diabetes, hyperglycemia, diabetic ketoacidosis, and diabetic coma including some fatal cases have been reported very rarely during the use of ZYPREXA, sometimes in patients with no reported history of hyperglycemia . . . In some cases, a prior increase in body weight has been reported which may be a pre-disposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus.

Pfs.' Fact Proffer ¶ 741.

Lilly was also required to include the following language about the incidence of weight gain among patients taking Zyprexa, acknowledging here that nearly ten times as many patients on Zyprexa, as opposed to a placebo, gained clinically significant amounts of weight (more than seven percent of baseline body weight) in six weeks:

> During acute therapy (up to 6 weeks) in controlled clinical trials comparing ZYPREXA with placebo in the treatment of schizophrenia, the percentages of patients with weight gain >= 7% of baseline body weight at any time were 29% for ZYPREXA and 3% for placebo, which was a statistically significant difference. The average weight gain during acute therapy in patients treated with ZYPREXA was 2.8 kg.

Id. at ¶ 742.

C. European Label Change

European regulators, in a May 26, 2003 Assessment Report, highlighted a number of problems they had with Lilly's analysis of and explanation for various side effects of Zyprexa. They further required the addition of several warnings to the product information. First, regulators informed Lilly that it would need to change its label to reflect the risk of tardive dyskinesia. Markku Toivonen & Eric Abadie, Rapporteur's and Co-rapporteur's Joint Response Assessment Report 45 (May 26, 2003). In response to Lilly's claim that tardive dyskinesia tremors were not the fault of Zyprexa but were instead "confounded by recent antipsychotic use or pre-existing EPS, were mild, or were transient," the regulators observed that whether "events were mild and transient is not a reason to conclude that these events were not clinically significant enough to be mentioned . . . ." *Id.*

Regarding weight gain, the European regulators concluded that Zyprexa's product labeling "must be revised to highlight the high percentage of patients experiencing clinically

significant weight gain during olanzapine treatment." *Id.* at 48. After a back and forth on treatment-emergent diabetes and possible explanations for the occurrence of such in nine patients lacking risk factors for the disease, the regulators chided Lilly for an inappropriate analysis and refused to accept the company's rationale for the problems:

> The further analysis of the 9 patients in the schizophrenia database who appeared to lack risk factors for diabetes and who experienced treatment-emergent diabetes is not reassuring. It is not considered appropriate to label a patient as having hypertension based on isolated hypertensive blood pressure and, therefore, having a risk factor for diabetes. Similarly, the approach taken to consider isolated total cholesterol values as risk factors for diabetes is not considered appropriate. These new analyses do not change the conclusion that treatment-emergent diabetes has been observed in cases with no definite risk factors.

Id. at 50.

Consequently, European regulators required the following modifications of the European label:

> Hyperglycemia and/or development or exacerbation of ~~preexisting~~ diabetes occasionally associated with ketoacidosis or coma, has been reported very rarely, including some fatal cases. In some cases, a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable particularly in diabetic patients and in patients with risk factors for the development of diabetes mellitus (see also section 4.8 Undesirable effects).

Id. at 53 (strikeouts to be eliminated, underlined to be added).

The regulators dropped the first several words of this warning, which had been proposed by Lilly: "As with some other antipsychotics . . . ." *Id.* at 54. Lilly had been able to keep this class-wide language in its FDA-approved labels, but the European regulators rejected it, insisting on their cleaner version. *Id.* In fact, the regulators directly pointed out a link between weight gain and diabetes that Lilly had been loathe to admit:

> The Rapporteurs strongly disagree with the wording proposed by the MAH to be included in SmPC section 4.4. In fact, olanzapine treatment-induced weight gain is a risk factor for the development of diabetes! It is important to emphasize the development of diabetes in the wording. Otherwise the message is diluted. What the MAH is now proposing is a step backwards. Furthermore, it does not add any relevant information to draw the attention to other neuroleptics in the beginning of the sentence, it merely shifts the focus from the important message.

Id.

D. FDA Class-Wide Diabetes Label Change

In September 2003, the FDA required Lilly and all other SGA manufacturers to add a warning about treatment-emergent diabetes and hyperglycemia to the labels for those drugs. After "an extensive review of data available for patients treated with atypical antipsychotics over a number of years," Olanzapine—Screening and Monitoring for Metabolic Adverse Events 2 (2003), the FDA had concluded that "epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with atypical antipsychotics." *Id.* (quoting Communication to Eli Lilly & Co. from the FDA, Sept. 2003). As a result, the FDA requested "class-labeling for all atypical antipsychotics to include a warning about hyperglycemia-related adverse events." *Id.*

On September 15, 2003, the FDA advised Lilly and the other SGA manufacturers that they would be required to change their labeling to include warnings about diabetes and hyperglycemia. Letter from Robin Pitts Wojcieszek, Senior Regulatory Research Scientist, Eli Lilly & Col., to Russell Katz, Division Director, FDA (Dec. 17, 2003) (responding to FDA). The FDA "requested" that Lilly "add a WARNING with regard to Hyperglycemia and Diabetes Mellitus" as a "labeling revision." *Id.* The FDA did not require Lilly to make an Zyprexa-specific change as regards to diabetes or hyperglycemia; the agency had determined that there

was not enough evidence to conclude that there was a difference in rates of diabetes or hyperglycemia among the various atypical antipsychotics, and indicated that comparisons between drugs as to weight gain were inappropriate. Evid. Hr'g Tr. 393 (Wirshing). *But see id.* (testifying that he was "aghast" at the FDA's opinion there was insufficient evidence to rank the drugs at that time).

The FDA included certain "recommendations" of language to be included in the revised labels but negotiated with Lilly about the actual language to be used. FDA, Olanzapine—Screening and Monitoring for Metabolic Adverse Events 2-3 (2003). Lilly hoped to include a sentence stating that the FDA had not ranked the comparative risk of the atypical antipsychotics in this regard: "The available data are insufficient to provide reliable estimates of differences in hyperglycemia related adverse event risk among the marketed atypical antipsychotics." Letter from Dr. Russell Katz, Division Director, FDA, to Michele Sharp, Eli Lilly & Co. (Dec. 16, 2003), at 1.

The FDA required Lilly to omit that sentence from its warning and avoid an implication that all atypical antipsychotic medications carried an equal risk of treatment-emergent diabetes and hyperglycemia. *Id.* Similarly, the FDA required Lilly to include language in the new warning about the necessity of conducting blood glucose testing "at the beginning of treatment" for "[p]atients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics." *Id.*

After all the revisions were taken into account, the FDA required Lilly to adopt the following "WARNING" about hyperglycemia and diabetes mellitus in its label:

Hyperglycemia and Diabetes Mellitus

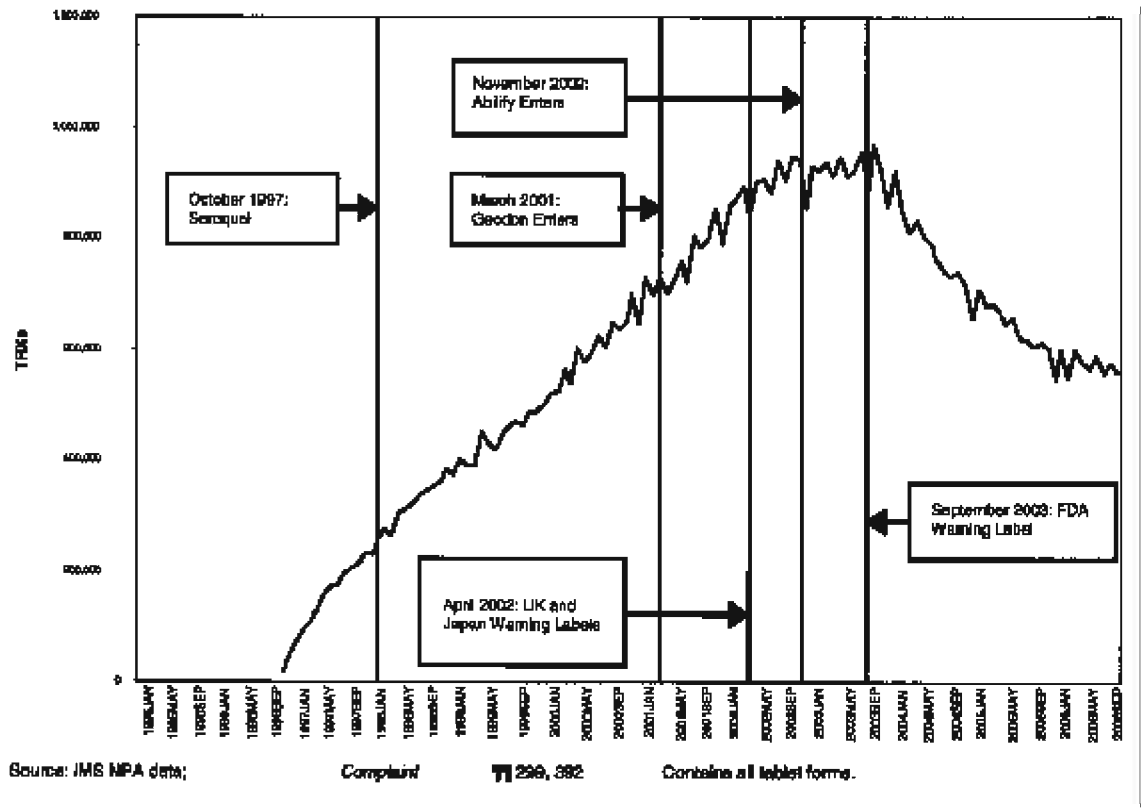
> Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including Zyprexa. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.
>
> Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Id. Apparently, weight gain was not listed under the "warnings to patients" section. The revised warning was added to the Zyprexa label on September 16, 2003 and a press release issued the following day.

E. Effect of Label Change on Zyprexa Sales

The September 2003 label change required by the FDA apparently had a profound influence on forcing down sales of Zyprexa compared to those of other antipsychotics. *See also* analyses of Dr. Harris' reports, Part XVIII.A.3, *infra*.

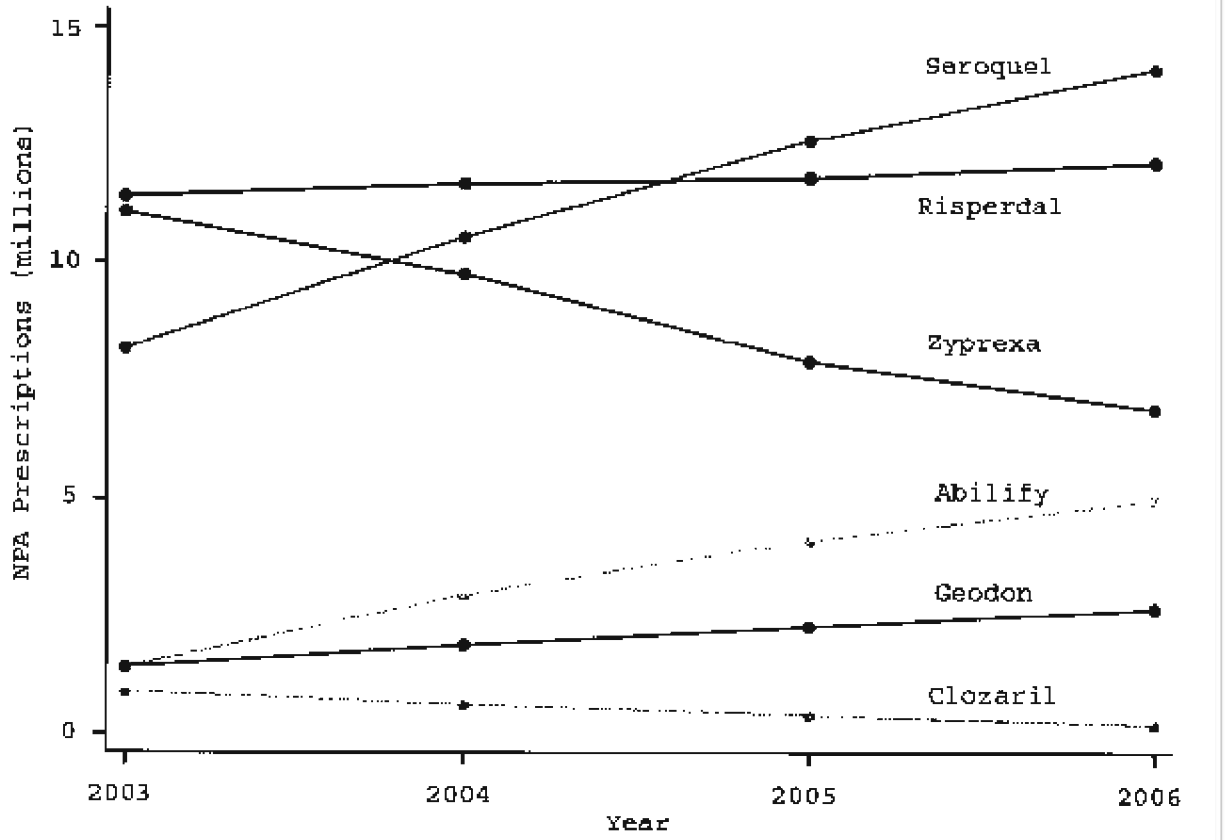
Zyprexa Prescriptions and Market Events



Zyprexa TRXs [Prescriptions] and Market Events, Rosenthal Rep. at Ex. 8, attch. C.1.b

"The only other brand-name atypical antipsychotic to decline after 2003 was Clozaril, approved by the FDA in September 1989, which was also identified by clinicians as more prone to induce weight gain and increase diabetes risk, and which had been available as a generic clozapine since December 1997." Harris Rep. Ex. 2. Since 2003, prescriptions of Zyprexa have decreased fifty percent. Alex Berenson, *One Drug, Two Faces*, N.Y. Times, Mar. 26, 2008.

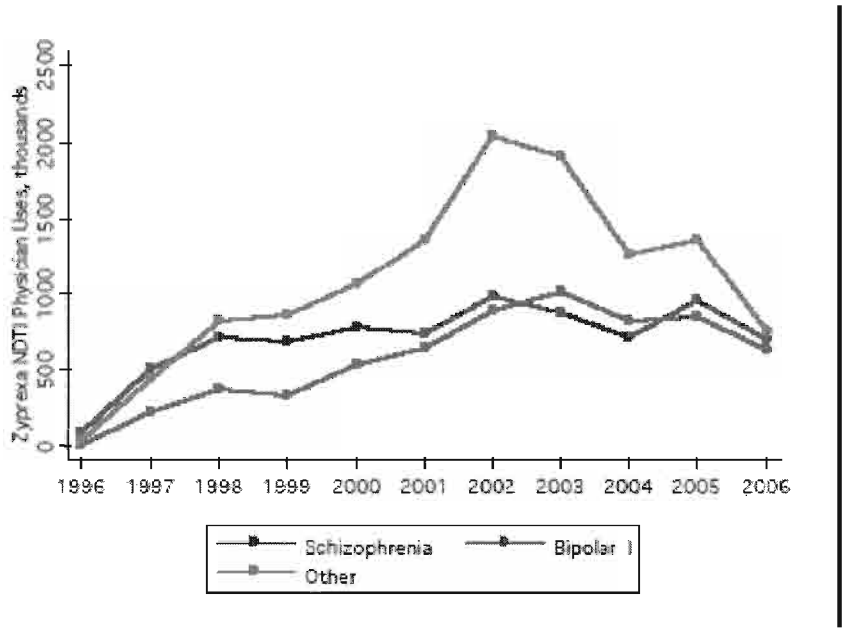
SGAs Sales



Harris Rep. Ex. 2.

"[T]he overall decline in Zyprexa use since the peak of 2002-2003 corresponded almost entirely to a decrease in prescriptions written for diagnoses other than Schizophrenia and Bipolar I disorder." *Id.* at ¶ 24.

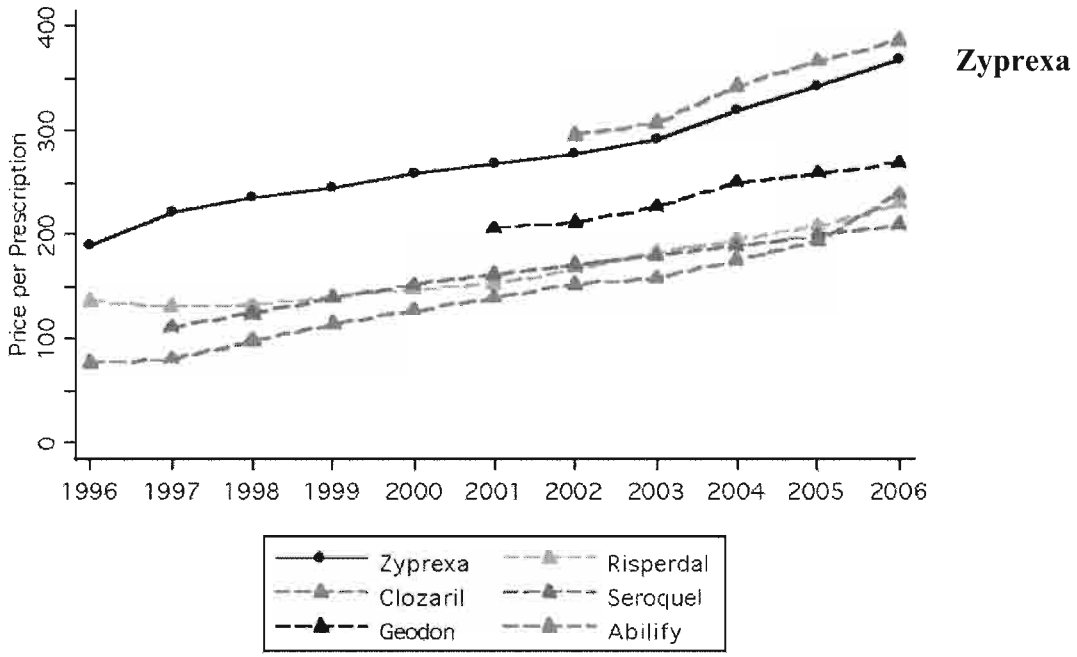
Reasons for Prescriptions



Because of Lilly's monopoly control over the price of its patented drug, decreased demand after 2003 did not lead to a price reduction relative to other atypical antipsychotics.

"Lilly maintained the price differential between Zyprexa and the three comparison drugs Seroquel, Risperdal and Clozaril even after the introduction of Geodon and Abilify. Even after the FDA-mandated change in warning label in 2003 and the consensus report of the American Diabetes Association in 2004, there was little change in the relative prices of the six branded atypical antipsychotics." Harris Rep. ¶ 32, Ex. 3.

Price Per Prescription



Zyprexa

F. VA Cooperative Study 451

The Department of Veterans Affairs Cooperative Study Group on the Cost-Effectiveness of Olanzapine ("VA Cooperative Study 451") was a large multi-site trial evaluating the cost-effectiveness of Zyprexa as compared to Haldol. *See* Rosenheck et. al., *Effectiveness and Cost of Olanzapine and Haloperidol in the Treatment of Schizophrenia*, 290 J.A.M.A. 2693 (2003); Rosenheck Decl. 6; Abramson Rep. 33-33. Although the study was funded with $5 million from Lilly, Dr. Rosenheck deems the study independent. *See* Evid. Hr'g Tr. 11.

Initiated in 1997 and published in November 2003, the results showed no advantage for Zyprexa over Haldol on any measure of symptoms, social functioning, or quality of life, no superiority on measures of tardive dyskinesia or higher abstract cognitive functions, but a small benefit for Zyprexa on measures of akithesia, fine motor movement, and memory. The study also showed that Zyprexa was associated with a significantly higher risk of weight gain and a greater annual cost of between $3,000-4,000 and $9,000-$10,000, due to the greater price of the medication. Rosenheck Decl. 6; *see* Abramson Rep. 33. Unlike the ICT study, however, the VA study found "no statistically or clinically significant advantages of olanzapine for schizophrenia on measures of compliance, symptoms or overall quality of life, nor did it find evidence of reduced inpatient use or total cost.'' *Id.* Further, the study noted, "[p]erhaps the most unexpected difference was the lack of any significant advantage for olanzapine on measures of retention, termination due to adverse effects, or EPS other than akathisia." *Id.*

XII. Events of 2004

A. American Diabetes Association Consensus Statement

In February 2004, the American Diabetes Association ("ADA"), the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity collectively issued a Consensus Development Statement on the interplay between antipsychotic medications, obesity, and diabetes, which was published in the ADA's official journal, Diabetes Care. *Diabetes Consensus Statement*, 27(2) Diabetes Care 596 (February 2004). The Statement was the result of a consensus development conference convened in November 2003, where an eight-member panel reviewed most of the relevant peer-reviewed English language scientific articles and heard presentations from fourteen experts drawn from the fields of psychiatry, obesity, and diabetes, as well as FDA representatives and drug manufacturers. *See In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 249 (E.D.N.Y. 2007).

The Consensus Statement concluded that Zyprexa and Clozaril posed an increased risk of diabetes as compared to other atypical antipsychotic drugs, and that these relative risks "should . . . influence drug choice." In part the report concluded:

> There is **considerable evidence**, particularly in patients with schizophrenia, that **treatment with [atypical antipsychotics] can cause a rapid increase in body weight in the first few months of therapy that may not reach a plateau even after 1 year of treatment.** There is, however, considerable variability in weight gain among the various [atypical antipsychotics] . . . . Clozapine [Clozaril] and **olanzapine [Zyprexa] . . . produce the greatest weight gain**.
>
> . . .
>
> Despite limitations in study design, the data consistently show an **increased risk for diabetes in patients treated with** clozapine or **olanzapine** compared with patients not receiving treatment with [first-generation antipsychotics] or with other [atypical antipsychotics]. The risk in patients taking risperidone and quetiapine is less clear; some studies show an increased risk for diabetes, while others do not. The two most recently approved [atypical antipsychotics], aripiprazole and ziprasidone, have relatively limited epidemiological data, but available clinical trial experience with these drugs has not shown an increased risk for diabetes.

. . .

> **[T]he risks of obesity, diabetes, and dyslipidemia have considerable clinical implications in this patient population and should . . . influence drug choice.** Even for those medications associated with an increased risk of metabolic side effects, the benefit to specific patients could outweigh the potential risks. For example, clozapine has unique benefits for treatment-refractory patients and those at significant risk for suicidal behavior. Since treatment response in many psychiatric conditions is heterogeneous and unpredictable, physicians and patients can benefit from the availability of a broad array of different therapeutic agents.
>
> . . .
>
> These three adverse conditions [obesity, diabetes, and dyslipidemia] are closely linked, and their prevalence appears to differ depending on the [atypical antipsychotic] used. Clozapine and **olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia**. Risperidone and quetiapine appear to have intermediate effects. Aripiprazole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as other agents. **The choice of [atypical antipsychotic] for a specific patient depends on many factors. The likelihood of developing severe metabolic disease should also be an important consideration.**

See In re Zyprexa Prods. Liab. Litig., 489 F. Supp. 2d 230, 249-50 (E.D.N.Y. 2007) (quoting *Diabetes Consensus Statement*, *supra*) (emphases added).

The Statement suggested that "both hunger and satiety may be altered in people taking olanzapine and clozapine because of their known affinities to serotonin, norepinephrine, dopamine, and particularly histamine-H1 receptors, all of which have been implicated in the control of body weight." Wirshing Decl. 14 (citing Eder at 598). Patients treated with olanzapine and clozapine have higher fasting and post-prandial insulin levels than patients treated with FGAs, even after adjusting for body weight.

Figure R4, below, reproduces a table from the Consensus Statement comparing the metabolic effects of SGAs.

SGAs' Metabolic Abnormalities

Drug	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/−	−	−
Ziprasidone*	+/−	−	−

+ = increase effect; − = no effect; D = discrepant results. *Newer drugs with limited long-term data.

[Zyprexa]

Figure R4.
Source: American Diabetes Association & American Psychiatric Association [38].
Clozapine = Clozaril; Olanzapine = Zyprexa; Risperidone = Risperdal; Quetiapine = Seroquel; Aripiprazole = Abilify; Ziprasidone = Geodon

Harris Rebuttal Rep. 19.

In response to the Consensus Statement, Lilly issued a press release entitled "Lilly Expresses Concern with Opinion of ADA Panel On Antipsychotic Drug and Obesity and Diabetes: Company Reaffirms 2004 Earnings Guidance." The release stated that "Eli Lilly and Company does not agree with a controversial conclusion of an opinion paper issued by an American Diabetes Association-sponsored panel, which states that second generation antipsychotics (SGAs) differ in their diabetes risk profiles." The Statement's "controversial" findings were, in Lilly's opinion, "not supported by the total body of evidence available on the subject."

B. "Dear Doctor" Letter

When the FDA mandated the classwide label change in September 2003, Lilly immediately changed the label, issued press releases, and sent out letters to physicians. Its formal "Dear Doctor Letter" warning physicians of the new warnings for diabetes and hyperglycemia did not, however, go out until March 1, 2004. *See* Letter from Dr. Russell Katz, Director, FDA Division of Neuropharmacological Drug Products, to Dr. Michele Sharp, Eli Lilly & Co., Dec. 23, 2000; Letter from Paul Eisenberg, Vice President, Eli Lilly & Co., to Doctor (Mar. 1, 2004) ("Eli Lilly and Company would like to inform you of important labeling changes regarding Zyprexa (olanzapine). The Food and Drug Administration (FDA) has asked all manufacturers of atypical antipsychotic medications, including Lilly to add a Warning statement describing the increased risk of hyperglycemia and diabetes in patients taking these medications, including Zyprexa.").

After the FDA notified Lilly that it sought "updated product labeling for all atypical antipsychotics to include a warning about additional information on hyperglycemia and diabetes," Lilly tried to downplay the seriousness of the new warnings, responding that "[t]he requested labeling echoes what Lilly has said for several years: that there is an increased risk of diabetes mellitus in patients with schizophrenia, along with an ever-increasing incidence of diabetes in the general population." U.S. Sales Organization Backgrounder and Verbatim: FDA Notification of Class Labeling for Atypical Antipsychotics Regarding Hyperglycemia and Diabetes 1, Eli Lilly & Co. (undated). Yet, Lilly had worked for years to prevent such warnings from being added to the Zyprexa label.

Various exchanges with the FDA led up to this critical label change. On February 24, 2003, Steven Hardeman of the FDA sent an email to John Roth of Lilly requesting further

information about the risks that olanzapine posed for treatment-emergent diabetes. Email from Steven Hardeman, Senior Regulatory Project Manager, FDA, to John Roth, Eli Lilly & Co., Feb. 24, 2005, at 9:58 a.m. Mr. Hardeman noted that the FDA "has been reviewing the analysis of treatment emergent diabetes (TED) with olanzapine (submitted 10/2/02)." *Id.* The FDA figured out the misleading manner in which Lilly had been comparing itself to clozapine instead of simply describing the effects of olanzapine. The FDA asked them to stop:

> Your proportional hazards analysis relied on comparison of risk with olanzapine to the pooled risk with other antipsychotics. Table 3.5 (p.31) suggests that clozapine may be different, that is, it appears to have a higher risk for glucose elevations, when compared to the rest of the non-olanzapine antipsychotics. We are interested in viewing the results of an analysis that compares olanzapine to non-olanzapine antipsychotics excluding the clozapine data.

Id. This was not the first time the FDA had asked for data excluding clozapine. As Lilly's Dr. Patrizia Cavazzonia noted, "This is the same question [FDA official] Russell Katz asked during our [telephone conference] in October, and I had clarified it for him verbally." *Id.*; Ex. C to Def.'s Mem. Relating to the Form of Class Cert. Order 10, Aug. 22, 2008, Docket No. 05-CV-4115, Docket Entry No. 230.

On June 20, 2003, in a document titled "Update to Olanzapine and Glucose Homeostasis (Prepared for FDA)" and submitted to the FDA, Lilly noted that since the FDA's 2002 letter of inquiry, Lilly's "researchers and clinicians have been focusing increased attention on the topic of serious mental illness and diabetes." Eli Lilly & Co., Update to Olanzapine and Glucose Homeostatis 3 (June 20, 2003). Lilly reviewed some recent studies, including one with "1362 patients not known to be diabetic," and found that 1.63% of the olanzapine patients developed

treatment-emergent diabetes as opposed to .59% of the haloperidol patients and .95% of the divalproex patients. *Id.* at 49 tbl. 2.1.

Despite the increased percentage of treatment emergent diabetes associated with olanzapine, Lilly discouraged the FDA from singling out Zyprexa, stating that "[d]ifferential labeling would ultimately not be in the best interest of patients and caregivers," using the following rationale:

> It is the opinion of Eli Lilly and Company that the cumulative data currently available, representing multiple lines of evidence, do not demonstrate clinically relevant or consistent differences in the risk for diabetes, or in changes in markers of glucose regulation, in patients treated with olanzapine compared with other atypical antipsychotics.

Id. at 59.

Even at this late stage in 2003, Lilly continued to try to convince prescribers that Zyprexa's adverse effects were no different from those in the class of atypical antipsychotics at large. It also continued to deny any link to diabetes whatsoever: "At the same time, the cumulative data do not currently allow us to establish whether treatment with antipsychotic mediation contributes to the increased risk of diabetes observed in the seriously mentally ill." *Id.*

Prior to the September 2003/March 2004 label change, Zyprexa's label did not warn of diabetes or hyperglycemia. Despite having the ethical obligation to make label changes as more data emerged regarding side effects and adverse events, this change was only made after the FDA required Lilly to include in the Zyprexa label a warning about the risk of developing diabetes and hyperglycemia and the need for baseline screening and glucose monitoring. *See* 21 C.F.R. § 201.57.

Despite Lilly's adamant denial of any link between diabetes and olanzapine, data suggests that these warnings were appropriate. The American label change in September 2003/March 2004—though far overdue—was still not adequate to warn of the significant and potentially catastrophic risks and was made far too late to affect ingrained physician prescribing habits. This is specifically supported by 21 C.F.R. § 201.57(e)'s requirement that "[t]he labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with the drug; a causal relationship need not have been proved." This shift in tone coincided with the FDA's decision to require all atypical antipsychotic medications to carry a warning about the risk of treatment-emergent diabetes and hyperglycemia they carried.

The injectable form of Zyprexa (Intramuscular) was approved in March 2004 for the treatment of agitation associated with schizophrenia and bipolar I mania. Harris Rep. 10. Since then, the FDA has approved no additional indications for the drug beyond patients with schizophrenia and bipolar I disorder. *Id.*

C. FDA Responds to Consensus Statement

In response to the ADA's Consensus Statement, representatives of the FDA's Division of Neuropharmacological Drug Products ("DNDP") wrote a letter to *Diabetes Care*, disagreeing with the Statement's ranking of diabetes risks among the atypical antipsychotics. Gerard Boehm, et al., *Response to Consensus Statement*, 27 Diabetes Care 2088 (2004). As the letter explained:

> Although the ADA ranked the diabetes risk for second-generation antipsychotics (SGAs), the . . . [DNDP] does not believe that the evidence currently available allows such a ranking . . . .
>
> [W]e must point out that the clinical trial data have not provided strong evidence of a diabetes risk for any of the SGAs. It is not clear whether this is due to the timing of glucose measurements (random in most cases), the low absolute frequency for

> diabetes events, the short duration of many of the trials, or other factors. Therefore, the DNDP does not consider the absence of a signal in clinical trial data to rule out the risk of diabetes with SGAs.
>
> Based on a review of epidemiological studies, the ADA concluded that there is an increased risk of diabetes with olanzapine and clozapine and discrepant results with quetiapine and risperidone. The ADA correctly identifies many of the limitations of these epidemiological studies, including "their retrospective nature, heterogeneity of methodology, selection or ascertainment bias, and absence of appropriate or well-characterized control subjects, . . . relatively short periods of study, failure to control for a possible treatment sequence bias in 'switchover' studies, and . . . not always using clinically equivalent dosages of the medications." The DNDP believes that although these studies support an increased risk of treatment-emergent hyperglycemia or diabetes, compared with patients treated with older antipsychotic drugs, the limitations of these studies preclude firm conclusions about the relative risk for diabetes among the studied SGAs.
>
> The ADA asserts that "weight gain and changes in body composition may account for many of the purported metabolic complications associated with SGA therapy, e.g. diabetes . . . ." The ADA correctly points out that SGAs have different weight gain liabilities. Although weight gain may be a factor in explaining the increased diabetes risk for these drugs is wholly or in part due to treatment-emergent weight gain. Although weight gain is widely recognized as a risk factor for diabetes in the general population, the clinical trial and epidemiological evidence has not shown a direct link between these treatment-emergent side effects. A substantial proportion (-25%) of adverse event reports submitted to the U.S. Food and Drug Administration do not mention weight gain as part of the presentation of SGA-associated hyperglycemia or diabetes.

Id. at 2088-89.

The DNDP explained that, while it agreed with the ADA's recommendation "to monitor patients treated with SGAs for evidence of diabetes," it did not believe "that the available evidence allows the ranking of diabetes risk for these drugs at this time." *Id.* at 2089. The DNDP explained that it "agree[d] with the ADA that additional studies are needed to clarify many of the issues surrounding the diabetes-SGA risk relationship," and recommended in the

meantime that "clinicians remain vigilant in monitoring all patients treated with SGAs to assure their safe use." *Id.*

XIII. Events of 2005

A. Class-Wide Black Box Dementia Warning

In May of 2005, the FDA required the manufacturers of Zyprexa, Risperdal, Seroquel, and Abilify to add a black box warning to the labels advising of the increased risk of death when using these drugs in treating the elderly for dementia. *See* Lindsey Tanner, *Dementia Drugs Can Increase Death Risks in Elderly Dementia Patients*, ABC News (2005).

Lilly had initially hoped that Zyprexa would be approved to treat dementia in the elderly. Between 1996 and 2000, Lilly engaged in and submitted to the FDA the results of at least two additional studies designed to support approval of an indication for treatment of dementia in the elderly. *See* Eli Lilly & Co., Note to Reviewers: Meeting Report (undated) (reflecting submissions of the results of the HGEU and HGGV to the FDA in 1998 and 1999). But, by 2003, Lilly admitted to the FDA that Zyprexa had no proven efficacy in treating psychosis associated with dementia. *Id.* at 2.

In December of that year, Lilly requested a meeting with the FDA's Center for Drug Evaluation and Research and provided information on seven clinical studies of Zyprexa it had conducted in elderly patients with dementia. The point of the request was not to focus on Zyprexa's efficacy or lack thereof for dementia. (Most of the studies "were designed and conducted to support a clinical development plan for the treatment of psychosis associated with dementia", but Lilly acknowledge that the "efficacy results from these studies were not sufficient to support the intended new indication." *Id.* at 1-2.)

Rather, Lilly wished to discuss a label change addressing the finding that in its clinical trials, elderly patients taking Zyprexa for treatment of dementia faced a much higher risk of death than those taking a placebo, stating, "[i]n placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs. 1.5%, respectively)." *Id.* at 2. Afraid that a Zyprexa-specific "label change regarding mortality in elderly based on dementia studies . . . [would] likely be disadvantageous to our positioning vs. the competition," *see* Oct. 2003 "Zyprexa Business Summary," Lilly encouraged the FDA to instead consider a class-wide warning for all atypical antipsychotics, rather than simply a warning on Zyprexa:

> Based on the safety comparisons of olanzapine [Zyprexa] with risperidone [Risperdal] and conventional antipsychotics in our integrated safety database, along with our understanding of the aripiprazole [Abilify] safety data, an increased risk of mortality in patients with dementia-related psychosis strongly suggests a class effect.
>
> Does the Division believe that this safety result may represent a class effect and should lead to updated antipsychotic labeling across the class?

Note to Reviews: Meeting Request 5. Lilly suggested that the following proposed language to be inserted in the WARNINGS section of the label:

> Safety Experience in Elderly Patients with Dementia-Related Psychosis—In elderly patients with dementia-related psychosis, the efficacy of olanzapine has not been established. In placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs. 1.5%, respectively). After adjusting for differences in duration of treatment, the exposure-adjusted mortality rate in olanzapine-treated patients was not significantly different from placebo-treated patients . . . .

Id. at 2. The FDA agreed, requiring a class-wide warning in 2005, allowing Lilly to avoid increased competition in the elderly market.

Since the class action certification hearing, the FDA has imposed a new requirement for a black box warning for all antipsychotics—FGAs as well as SGAs—warning of the increased risk of death associated with prescribing antipsychotics to older people with dementia. *See Antipsychotics and the Elderly*, N.Y. Times, June 17, 2008.

B. Publication of Clinical Studies Disputing Zyprexa's Safety and Efficacy

Since 2005, the results of several influential studies challenging Zyprexa's safety and efficacy have been published. Among the most significant are *Clinical Antipsychotic Trials of Intervention Effectiveness Study* ("CATIE"); J.P. McEvoy et. al. *Effectiveness of Clozapine vs Olanzapine, Quetiapine, and Risperidone in Patients with Chronic Schizophrenia Who Did Not Respond to Prior Atypical Antipsychotic Treatment*, 163 Am. J. Psychiatry 600 (2006) ("CATIE II-McEvoy"); T. Scott Stroup, *Effectiveness of Olanzapine, Quetiapine, and Risperidone in Patients With Chronic Schizophrenia After Discontinuing Perphenazine*, 164 Am. J. Psychiatry 415 (2007) ("CATIE-II Stroup"); Robert A. Rosenheck, et al., *Cost-Effectiveness of Second-Generation Antipsychotics and Perphenazine in a Randomized Trial of Treatment for Chronic Schizophrenia*, 163 Am. J. Psychiatry 2080 (2006) ("CATIE-III"); Lon Schneider et al., *Effectiveness of Atypical Antipsychotic Drugs in Patients with Alzheimer's Disease*, 355(15) New Eng. J. Med. 1525 (Oct. 12, 2006) ("CATIE-AD"); and P.B. Jones et. al, *Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study*, 63 Arch. Gen. Psychiatry 1079 (2006) ("CUtLASS").

1. CATIE

CATIE was sponsored and funded by the National Institutes of Mental Health ("NIMH") and remains the single largest government funded clinical study to date, costing $40 to $60

million. Evid. Hr'g Tr. 60; *see* Rosenthal Decl. 10; Rosenheck Supp. Decl. 2-7; Abramson Rep. 34-35. NIMH initiated the study to test the relative effectiveness, side effects, and costs of atypical second-generation antipsychotic drugs ("SGAs") in treating schizophrenia and Alzheimer's disease by providing study subjects with either a first-generation antipsychotic ("FGA")—perphenazine—or one of four SGAs: quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon), and olanzapine (Zyprexa). Jeffrey A. Lieberman, *Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia*, 353 N. Eng. J. of Medicine 1209, 1209 (2005); Rosenheck Decl. at 11; Pfs.' Slides: Hr'g on Pfs.' Mot. for Class Cert.: Robert Rosenheck, M.D. ("Rosenheck Slides"), at 13. Of the five comparators, the first four are all SGAs and currently under patent; only perphenazine, a FGA drug, is available in generic form (and thus costs the least). Rosenheck Decl. 9. Perphenazine was chosen as the representative FGA because it "falls in the midrange of antipsychotic drug potency—lower than the high potency drugs like [Haldol], but higher than more sedating drugs like [Thorazine]." Rosenheck Decl. 11.

Conducted between January 2001 and December 2004 at fifty-seven U.S. clinical sites across twenty-three states, patients were initially randomized to receive flexible-dose treatment double-blind conditions. Rosenheck Slides at 14. The study involved 1,493 patients who had been diagnosed with schizophrenia for the last ten to fifteen years and lasted eighteen months. Lieberman, *supra*. A clinical team with doctors from the University of North Carolina, Yale University, Duke University, and Columbia University oversaw the study and published the results in the September 22, 2005 issue of the New England Journal of Medicine. *See id.*

CATIE's results were published in several phases. Released in 2005, Phase I results concluded that on CATIE's primary outcome—time-to-all-cause discontinuation—Zyprexa performed better than Seroquel and Risperdal, but had no statistically significant difference compared with perphenazine or Geodon. Evid. Hr'g Tr. 19; Rosenheck Decl. 12; *see also* Lieberman, *supra*, at 1209-23. (Time-to-all-cause discontinuation is, in other words, the amount of time a patient stays on a drug before stopping or switching to something else, and is considered a surrogate measure for effectiveness.)

Established by CATIE was that increases in weight were substantially greater with Zyprexa than the other medications; the greatest increases in levels of glucose and lipid metabolism were also found in patients given Zyprexa. Rosenheck Decl. 12. CATIE reaffirmed that Zyprexa was associated with greater weight gain and increased measures of glucose and lipid metabolism (all features of metabolic syndrome) than all the other drugs. *Id.* at 1218. The study indicated that schizophrenia patients showed similar rates of extrapyramidal symptoms ("EPS") regardless of whether they took perphenazine or any of the four SGAs. This result surprised the researchers to a certain degree, given that the decreased frequency of EPS has been heralded as a significant advantage of SGAs over FGAs. CATIE further confirmed that the few limited measures in which Zyprexa scored higher than perphenazine were "moderate," and that Zyprexa's greater weight gain and increase in glycosylated hemoglobin, cholesterol, and triglycerides may have serious implications with respect to medical comorbidity, e.g., the development of the metabolic syndrome. *Id.* at 1218.

2. CATIE-II: McEvoy and Stroup

CATIE II compared clozapine, the first of the SGAs, to other SGAs. McEvoy, *supra*, at 600; Stroup, *supra*, at 415. The second phase of CATIE involved 543 patients who wanted to switch from perphenazine or their initial SGA because they were dissatisfied with the results; they were then randomized to a different SGA or clozapine. *Id.* Results from CATIE II were published as two separate articles in the American Journal of Psychiatry, one regarding the efficacy pathway and the other reporting the results of the intolerability pathway. *Id.*

Clozapine performed the best in CATIE II. *See* McEvoy, *supra*, at 608. The researchers described clozapine as being remarkably effective and substantially better then all the other SGAs, including Zyprexa. *Id.* Forty-four percent of patients who received clozapine were able to stay on the drug for the remainder of the study, whereas only eighteen percent who received another SGA were able to stay on that drug to complete the study. *Id.* at 607-08. Participants taking clozapine remained on it for an average of ten months, compared to an average of three months for those taking any of the other three SGAs. Those taking clozapine had the greatest symptom reduction rate of any of the medications. *Id.* at 608.

In an editorial in the American Journal of Psychiatry and subsequently in her deposition, Lilly's own expert, Carol A. Tamminga, M.D., agreed that clozapine was the superior medication "by far." Indeed, as Dr. Tamminga put it, CATIE "strongly confirms what we have seen before, that clozapine is our most effective drug for schizophrenic psychosis." Carol Tamminga, *Practical Treatment Information for Schizophrenia*, 163(4) Am. J. Psychiatry 563 (April 2006).

XIV. Events of 2006

A. Additional Critical Studies

1. CATIE-III

At the conclusion of the CATIE trials, Dr. Robert A. Rosenheck led a team that analyzed the results for cost effectiveness. *See* Rosenheck, *Cost-Effectiveness, supra.* His cost-effectiveness analysis of CATIE was published in 2006. Rosenheck Decl. 12; *see* Robert A. Rosenheck, et al., *Cost-Effectiveness of Second-Generation Antipsychotics and Perphenazine in a Randomized Trial of Treatment for Chronic Schizophrenia*, 163 Am. J. Psychiatry 2080 (2006) ("Rosenheck, *Cost-Effectiveness*"). The results "showed that Zyprexa had no significant advantage over perphenazine on symptoms, but was superior to" Risperdal and Seroquel. Rosenheck Decl. 13; *see* Rosenheck Slides 19; Evid. Hr'g Tr. 55-56. Since none of the drugs demonstrated any savings on inpatient, outpatient, or residential care, the cost-effectiveness of each treatment was primarily driven by the price of the drug; perphenazine costs $300 less per month than Zyprexa. (The overall medical costs associated with Zyprexa use were less, however, than the costs associated with Seroquel and Risperdal. Rosenheck, *Cost-Effectiveness, supra* at 2083, tbl. 2 (2006); *see* Evid. Hr'g Tr. 565-66.)

The study found that during the eighteen months of the CATIE trial, initial assignment to perphenazine, the FGA, was less costly but not less effective than assignment to each of four SGAs. *Id.* at 2085-86. The cost of treatment during the initial treatment periods, including the costs of the drugs, was $1,404.00 per month for Zyprexa versus $960.00 per month for perphenazine, a 46% increase in costs per month for Zyprexa. *Id.* at 2086.

The researchers found no statistically significant difference in overall effectiveness between perphenazine and the SGAs, with regard to symptom relief and side effect burden. *Id.* at 2087. (Notably, the CATIE study was not long enough to detect differences in time-dependent longer-term side effects such as diabetes and cardiovascular disease. *Id.* at 2087.) The study

thus cast doubt on the notion that SGAs are more effective than the FGAs; instead, the data suggest that perphenazine and other FGAs may be just as beneficial for some patients. *Id.* Rosenheck and the CATIE II authors concluded "[t]hese results should encourage consideration of older intermediate potency drugs like Perphenazine when a medication change is indicated." *Id.* at 2087.

2. CATIE-AD

The CATIE-AD study was also funded by the NIMH and sought to assess the effectiveness of SGAs in outpatients with Alzheimer's disease. *See* Part XVIII.A.5, *infra*; Schneider, *supra*; Abramson Rep. 35-36. More than 400 outpatients with Alzheimer's disease and psychosis, aggression, or agitation were randomly assigned to receive Zyprexa, Seroquel, Risperdal, or a placebo for up to thirty-six weeks. Schneider, *supra* at 1526. No significant differences among treatments with regard to the time to discontinuation of treatment were found. CATIE-AD concluded that adverse effects offset advantages in the efficacy of SGAs for the treatment of psychosis, aggression, or agitation in patients with Alzheimer's disease. *Id.* at 1537.

3. CUtLASS

The Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study ("CUtLASS 1") was funded by the British National Health Service. It was designed to test the hypothesis that schizophrenic patients requiring a change in medication who were randomly assigned to take an SGA (of their doctor's choosing) would experience an improved quality of life compared to those assigned to take an FGA (of their doctor's choosing). Abramson Rep. 33.

It involved 277 people diagnosed with schizophrenia and related disorders in fourteen community psychiatric services in the United Kingdom. Jones, *supra*. Subjects were

randomized between either FGAs or SGAs (other than clozapine) and measured on quality of life scores, symptoms, adverse effects, participant satisfaction, and cost of care. Abramson Rep. 33.

Participants reported no clear preference for either drug group, and costs were similar. The clinicians concluded that "the results of this pragmatic randomized trial refute the hypothesis that the use of SGAs is superior to the use of FGAs in terms of quality of life at one year," and specifically stated, "[w]e emphasize that we do not present a null result; the hypotheses that SGAs are superior was clearly rejected." Jones, *supra* at 1083, 1085; Abramson Rep. 33 ("In people with schizophrenia whose medication is changed for clinical reasons, there is no disadvantage across 1 year in terms of quality of life, symptoms, or associated costs of care in using FGAs rather than non-clozapine SGAS."). Further, the researchers stressed that "a range of adverse effects of FGAs and SGAs is emerging. Serious weight gain, diabetes mellitus, and hyperlipidemia may all adversely affect quality of life." Jones, *supra* at 1086.

B. *New York Times* Articles

In December 2006, the *New York Times* published a series of articles revealing confidential information obtained illegally from the Zyprexa MDL. *See In re Zyprexa Injunction*, 474 F. Supp. 2d 385 (E.D.N.Y. 2007). The articles raised questions about Lilly's misleading the medical profession about the efficacy and safety of Zyprexa. *See* Alex Berenson, *Eli Lilly Said to Play Down Risk of Top Pill*, N.Y. Times, Dec. 17, 2006; Alex Berenson, *Drug Files Show Maker Promoted Unapproved Use*, N.Y. Times, Dec. 18, 2006; Alex Berenson, *Disparity Emerges in Lilly Data on Schizophrenia Drug*, N.Y. Times, Dec. 21, 2006.

XV. Events of 2007

A. FDA Requests Additional Information in Response to *NYT* Articles

A few weeks later on January 12, 2007, the FDA contacted Lilly to request additional safety information regarding Zyprexa not previously disclosed to the agency:

> Recent articles in the New York Times reported on clinical trial data from 70 clinical trials on Zyprexa that showed patients taking Zyprexa experienced high blood sugar levels and weight gain that may have differed from information Eli Lilly revealed publicly and to the FDA.
>
> . . .
>
> [W]e further request that you submit to the agency all data and information . . . that bear on the safety of Zyprexa. In particular, we are interested in receiving data and analyses bearing on these concerns about weight gain and hyperglycemia that have not already been submitted to the agency. Additionally, if you are in possession of other information not specifically required to be submitted by statute or regulation, but that would nevertheless be useful to FDA in evaluating the safety of Zyprexa regarding these concerns of weight gain and hyperglycemia, we request that you please submit this information to us as well.

Letter: Dr. Thomas Laughren, Director, Division of Psychiatry Products, Office of Drug Evaluation I, Center for Drug Evaluation and Research, to Dr. Gregory T. Brophy, Eli Lilly & Co., Director, US Regulatory Affairs, Jan. 12, 2007. Lilly responded to the FDA's query in four parts between February 2007 and February 2008.

B. FDA Requests More Information for Lilly's Symbyax Supplemental NDA

In March 2007, the FDA raised additional questions about weight gain and hyperglycemia and suggested that Lilly has not been forthcoming with additional data. Lilly had submitted to the FDA in September 2006 a supplemental New Drug Application ("NDA") for approval to market Symbyax— a combination of Zyprexa (olanzapine) and Prozac (fluoxetine)—for Treatment Resistant Depression. *See* 2006 Physicians Desk Reference 1820. Responding to this application, the FDA stated:

> A primary concern with this application and the primary basis for our not taking a final action is our view that we lack important safety information needed to adequately update the labeling with all relevant risk information. In particular, we

> are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine. You must fully address these concerns before we will be able to take a final action on this application.
>
> Our overall goal is to improve labeling with regard to these findings so that clinicians will be better informed on what the risks are for their patients. They cannot make reasonable treatment decisions until they have such information. We do not feel that current labeling for either Symbyax or Zyprexa, provides sufficient information on these risks, and we fully intend to insure that these labels are enhanced with the best available information to characterize these risks.

Letter: Thomas Laughren, FDA to Robin Pitts Wojcieszek, Eli Lilly & Co., Mar. 27, 2007. Laughren also noted that Lilly's "recent February 20, 2007 response to our January 12, 2007 letter regarding the New York Times story has not been particularly helpful in addressing these concerns."

C. FDA Directs Zyprexa-Specific Label Change

On August 28, 2007, the FDA directed Lilly to "make the labeling changes [delineated in the letter] pertaining to the effect of olanzapine and Symbyax on body weight, lipids, and glucose." The changes would affect labels for both Zyprexa and Symbyax. Continuing, the agency indicated that these would likely not be the last changes mandated:

> We anticipate that additional labeling changes will be necessary when we have reviewed the results of the additional analyses that we have requested. Given that your [sic] completing these analyses and our review of them will take some time, we believe that it is in the best interest of the public health to make interim labeling changes now based on the data that we already have available.

Letter: FDA to Robin Wojcieszek, Eli Lilly & Company, Aug. 28, 2007, labeled "ZYAK-AG20030164" and submitted in *State of Alaska v. Eli Lilly & Co.*, 3AN-06-06530, in March 2008; *see* Margaret Cronin Fisk & Elizabeth Lopatto, *Lilly May Need Stronger U.S. Warning on Zyprexa Label (Update3)*, Bloomberg.com, July 30, 2008.

The specified changes included adding information about hyperglycemia, weight gain, and hyperlipidemia to the WARNINGS section of the Zyprexa label. The FDA's proposed language regarding hyperglycemia focused on the risks to patients taking olanzapine:

> Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine . . . . Olanzapine (and clozapine) treatments have been associated with a greater potential to induce hyperglycemia than other atypical antipsychotics.

Id.

In response, Lilly proposed language that eliminated any reference to a causal relationship between olanzapine and hyperglycemia. The current Zyprexa label contains no reference to such a causal relationship:

> Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including Zyprexa.
> While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Letter from Eli Lilly, Oct. 8, 2007, *In re Zyprexa Prod. Liab. Litig.*, Docket No. 04-MD-1596, Docket Entry No. 1424. Zyprexa's label does now, for the first time, acknowledge that the drug is associated with high blood sugar *more than* other SGAs, but it does not make clear that the drug is associated with diabetes more than other SGAs. *See* Alex Berenson, *Lilly Adds Strong Warning Label to Zyprexa, a Schizophrenia Drug*, N.Y. Times, Oct. 6, 2007.

Lilly continues to deny a causal relationship exists between Zyprexa and high blood sugar or Zyprexa and diabetes. As the company's Director of United States Regulatory Affairs testified in March 2008,

Q: But you took about—you took out any reference to language that indicates a causal relationship?
A: We—we did not include that in our proposal.
Q: Okay. And, in fact, to this day, Lilly denies that olanzapine can induce or cause hyperglycemia, correct?
A: We don't feel that the—that we have data to support that particular statement FDA included.

Testimony of Robin Wojcieszek, R.Ph., Assoc. Director of U.S. Regulatory Affairs for Lilly, entered into evidence on March 11, 2008 in *State of Alaska v. Eli Lilly & Co.*, 3AN-06-06530; *see* Lisa Demer, *Defense Opens in Zyprexa Trial*, Anchorage Daily News, Mar. 22, 2008 (quoting Lilly's medical expert as testifying that "Zyprexa does not cause diabetes" or affect insulin resistance or production). *See generally* Douglas L. Weed, *Truth, Epidemiology, and General Causation*, 73 Brooklyn L. Rev. 943, 954-955 (2008) (noting that epidemiologist experts' obligation to testify to "nothing but the truth" regarding disease causation is a high standard).

The new label also indicates that patients taking Zyprexa may continue to gain weight for as long as two years after starting therapy; one in six patients who take Zyprexa will gain more than 33 pounds after two years of use. *See* Alex Berenson, *Lilly Adds Strong Warning Label to Zyprexa, a Schizophrenia Drug*, N.Y. Times, Oct. 6, 2007

D. Change in TMAP Formulary

In November 2007, the Texas Medication Algorithm Project ("TMAP") issued a revised consensus judgment by leading experts suggesting that there is no advantage to using SGAs rather than FGAs for chronic schizophrenics—reversing its earlier judgment on the basis of CATIE and other studies. *See* Part IV.C.6, *supra*; Rosenheck Supp. Decl. 7.

XVI. Events of 2008: Classwide Warning for SGAs for Dementia

Since the class action certification hearing, the FDA has warned about the dangers of prescribing antipsychotic drugs to older people with dementia, that could increase the risk of death. The drugs include Zyprexa and Risperdal. Over the last decade, they have been widely used in nursing homes:

> The use of antipsychotic drugs to tamp down the agitation, combative behavior and outbursts of dementia patients has soared, especially in the elderly. Sales of newer antipsychotics like Risperdal, Seroquel and Zyprexa totaled $13.1 billion in 2007, up from $4 billion in 2000, according to IMS Health, a health care information company. Part of this increase can be traced to prescriptions in nursing homes. Researchers estimate that about a third of all nursing home patients have been given antipsychotic drugs.

Laurie Tarkan, *Doctors Say Medication* [*Including Zyprexa*] *Is Overused in Dementia,* N.Y. Times, June 24, 2008, at F1. Now the labels of all antipsychotics, both SGAs and FGAs, will contain a "'black box' label warning of an increased risk of death:

> Last week, the FDA required a similar warning on the labels of older antipsychotics. The agency has not approved marketing of these drugs for older people with dementia, but they are commonly prescribed to these patients 'off label.' Several states are suing the top sellers of antipsychotics on charges of false and misleading marketing. . . . Nursing homes are short staffed, and insurers do not generally pay for the attentive medical care and hands-on psychosocial therapy that advocates recommend. It is much easier to use sedatives and antipsychotics, despite their side effects.

Id. at F2; *see Antipsychotics and the Elderly*, N.Y. Times, June 17, 2008.

XVII. Pharmaceutical Distribution

Pharmaceutical companies often employ private manufacturers to produce medicine; collectively they provide 64% of all pharmaceuticals directly to wholesalers for distribution. Cong. Budget Office, 110th Cong., Prescription Drug Pricing in the Private Sector, 5 fig. 2 (Jan. 2007) ("CBO Paper"); Kolassa Decl. 2. Wholesalers and pharmaceutical manufacturers send

drugs to retail and nonretail providers, who then supply them to consumers. CBO Paper 1. (Examples of non-retail providers include hospitals, health maintenance organizations (HMOs), clinics, etc.) "Consumers obtain about three-quarters of their prescription drugs from retail pharmacies and the remainder from nonretail providers." *Id.*

In order for this system to operate, three separate sets of price negotiations must take place: (1) retail pharmacies and nonretail providers negotiate with pharmaceutical manufacturers and wholesalers, (2) payors (often through PBMs) negotiate with pharmaceutical manufacturers and wholesalers, and (3) payors negotiate with retail pharmacies and nonretail providers. *See id.* at 2. PBMs pass through or share the rebate negotiated with the manufacturers with their clients, in accordance to the terms of their contracts. Decl. of Edward Adamcik ("Admacik Decl.") ¶ 18; Decl. of Myron D. Winkelman, R.Ph. ¶ 38, Feb. 7, 2007, Docket Entry No. 90 ("Winkelman Decl."). Manufacturers pay rebates based on the volume of the medications reimbursed. Adamcik Decl. ¶¶ 11-12; CBO Paper 7.

For Zyprexa the matter was simpler, since there were relatively few rebates available. Records will permit computation of which "overcharges" found by the jury involved those standard rebates.

A. Pharmacy Benefit Managers ("PBMs")

Plaintiffs tendered two expert witnesses concerning PBMs, Terry D. Leach and Myron D. Winkelman. Decl. of Terry D. Leach, Pharm.D., Jan. 11, 2007, Docket Entry No. 89 ("Leach Decl."); Dep. of Terry Leach, Apr. 4, 2007 ("Leach Dep."); Winkelman Decl. ¶ 8; Dep. Tr. of Myron D. Winkelman, R.Ph., Apr. 12, 2007 ("Winkelman Dep."). Additionally, Plaintiffs' expert Richard G. Frank described how PBMs fit into the overall scheme of institutions that

influence the prescribing of anti-psychotic medications. *See* Decl. of Richard G. Frank, Ph.D., Jan. 8, 2008, Docket Entry No. 148 ("Frank Decl.").

1. Expert Witnesses

a. Myron Winkelman, R.Ph.

Plaintiffs' expert Mr. Winkelman is a registered pharmacist with over eighteen years of service as a Senior Pharmacy Executive for a large retail drug store chain, eight years of MIS experience with retail pharmacies and experience working directly as a Senior Manager with a large PBM. *See* Winkelman Decl.

Mr. Winkelman opined that: (i) PBMs do not influence physicians to prescribe any particular drug for a specific condition; (ii) PBM formularies generally include atypical antipsychotic drugs such as Zyprexa because PBM Pharmacy & Therapeutics ("P&T") Committees are loath to interfere with the plan of care for plan recipients with severe, persistent mental illness; (iii) Pharmaceutical and Therapeutics Committees of PBMs do not place drugs on their formularies for therapeutic uses that are not approved by the FDA; and (iv) P&T Committees are reactive and not proactive in their deliberations—they perform no independent clinical or laboratory work, and base their deliberations on the product information provided by drug manufacturers. *See id.*

Lilly did not file a *Daubert* motion with respect to Mr. Winkelman. In any event, he met *Daubert* standards. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

b. Terry D. Leach, Pharm.D.

Plaintiffs' expert Dr. Terry D. Leach, Pharm.D, has had key roles throughout his career in formulary management and on the P&T Committees of PBMs. He has held senior management positions in managed care pharmacies at firms such as Horizon BlueCross and BlueShield of New Jersey and Mid Atlantic Medical Services and as a consultant. He has served as a P&T vice chairman, developed and presented drug monographs to P&T Committees, created formulary kits and dossiers, and attended major PBM P&T meetings. *See* Leach Decl. 2-3.

Dr. Leach declared that third-party payors who offer prescription drug benefits rely upon their contracted pharmacy benefit manager to develop and maintain a sound prescription drug benefit. In turn, PBMs maintain the formulary management system based upon publicly available clinical information, which itself is largely derived from the drug manufacturers. As a result, in situations where relevant and accurate clinical data has not been released by drug companies, P&T committees' formulary decisions recommending coverage of medication may not be in the best interests of the TPP or the beneficiaries. *See id.*

Lilly did not file a *Daubert* motion with respect to Dr. Leach. He met *Daubert* standards. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

c. Richard G. Frank, Ph.D.

Plaintiff's expert Dr. Richard Frank is the Margaret T. Morris Professor of Health Economics at Harvard University Medical School. *See* Frank Decl. He provided an overview of the institutions that influence the prescribing of anti-psychotic medications, focusing on how institutions such as PBMs and public and private health insurance institutions affect the prescribing of antipsychotic agents. Included in his expert opinion was a discussion of the role of formularies and physician prescribing practices. *See id.* at 2.

People with major mental disorders such as schizophrenia and bipolar disorder are often disabled from work. Many are eligible for public health insurance. *Id.* at 4. As a result, a large percentage—70% to 80%—of sales of antipsychotic drugs in the United States are to Medicaid and Medicare. *Id.* at 4 (citing R.G. Frank, R.M. Conti & H.H. Goldman, *Mental Health Policy and Psychotropic Drugs*, Milbank Quarterly 83(2):271-298 (2005)). Thus, most patients prescribed antipsychotic medications pay little or no out-of-pocket costs; drug choice is driven by physician advice based on information that flows to doctors rather than patients. *Id.* at 5.

The ultimate consumer's role in mental health care is especially weak, either through inability to participate in decision-making or influence or coercion by others. *Id.* at 5 (citing Institute of Medicine, Improving the Quality of Health Care for Mental and Substance-Use Conditions (2006)). Moreover, little information about comparative effectiveness is readily available in a user-friendly form. *Id.* (citing S.J. Tannenbaum, *Evidence-Based Practice as Mental Health Policy: Three Controversies and a Caveat*, Health Affairs 24(1): 163-73 (2005)).

The terms of drug coverage as defined by health insurance plans and utilization controls potentially affect most consumer choices of antipsychotic drugs—to the extent that patients really choose. *Id.* at 6. As noted earlier, most public and private health insurance plans are reluctant to place effective restrictions on the ability of physicians to prescribe particular antipsychotic medications. As a result, third-party payors, including Medicare and Medicaid, do not place strong restrictions on the use of antipsychotic medications. *Id.* at 4. State Medicaid plans, for example, frequently exempt antipsychotic drugs from preferred drug lists and prior authorization provisions. *Id.* at 7 (citing C. Koyanagi, S. Forquer, & E. Alfano, *Medicaid Policies to Contain Psychiatric Drug Costs*, Health Affairs 24(2):536-44 (2005)). While most

physicians—especially those providing Medicaid and Medicare services—may more or less freely choose among SGAs, this unfettered discretion, when combined with the prescribers' difficulty in obtaining reliable information about new drugs, has led to overprescribing, particularly among such patient populations as the children and elderly. *Id.* at 8-9.

Dr. Frank summarized the effect of the lack of candid information to the prescriber, who can be influenced by inappropriate and incomplete anecdotal information:

> Because schizophrenia and bipolar disorders are severe illnesses and create much disability, large portions of the people that suffer from these illnesses are supported by public programs (SSI/DI). This means that antipsychotic medications are overwhelmingly purchased by public health insurance programs. The vulnerability of people with severe mental illnesses has led policy makers to exercise great caution in the application of utilization and cost controls to the treatments for schizophrenia and bipolar disorders. The result is that formulary designs and utilization controls under the Medicare and Medicaid programs allow for a great deal more flexibility in clinical decision making than occurs for many other illnesses. The implication of this flexibility is that physicians treating severe mental disorders have relatively wide discretion in making treatment recommendations.
>
> Obtaining information on the range of new treatments has long been a difficult task for most physicians. The physician's practice environment has only become more complex over time. Psychiatrists, it appears, rely little on decision supports such as guidelines and electronic prescribing to aid them in making therapeutic choices. Thus, it appears that they rely on less systematic influences in making choices. This may result in raising the importance of casual recommendations from colleagues, past experiences with drugs, promotional information from companies and their own trial and error. Thus, in the area of antipsychotic medications, there is a wide set of influences that may drive treatment choices and these extend beyond institutions that can apply evidence based principles to the management of care.

Id. at 9-10 (internal citation omitted).

2. Generally

Plaintiffs' experts offered only general, and not case-specific, testimony about the PBM industry and how PBMs operate. Leach Dep. 27, 202-06, 224-25, 236-41, 264-67; Winkelman

Dep. 17-19, 24. Both agreed that the descriptions of PBM operations presented in the affidavits and deposition from the PBMs for the payors in this case are consistent with their understanding of how PBMs operate. Winkelman Dep. 23; Leach Dep. 170-71.

Many health insurance plans contract with companies known as Pharmacy Benefit Managers ("PBMs"). Winkelman Decl. ¶ 8. "PBMs manage pharmacy benefits on behalf of their clients, which include health plans, HMOs, and self-insured employer-based plans." CBO Paper 10. PBMs handle such tasks as collecting funds from health plans and using those funds to pay network pharmacies, process claims, answer questions as to coverage parameters, and negotiate with drug companies. Winkelman Decl. ¶ 9; *see also* Leach Dep. at 32-34. PBM services include the management of formularies and rebates.

PBMs administer drug plans for more than 210 million Americans. Br. for Pharm. Care Mgmt. Ass'n as Amicus Curiae Opposing Proposed Settlement 5, *New England Carpenters Health Benefits Fund v. First Databank, Inc.*, No. 05-CV-11148 (D. Mass. Dec. 20, 2007). They exert a major influence on the economics of the pharmaceutical industry. Winkelman Dep. 80-85. "PBMs are the 800-pound gorillas of pharmaceutical reimbursement." *In re Pharm. Indus. Average Wholesale Price Litig.*, 230 F.R.D. 61, 71 (D. Mass. 2005).

Offered by PBMs are expertise in the management of pharmacy benefits, providing services such as formulary development, negotiations with pharmaceutical companies, rebate management, and claims processing. Winkelman Decl. ¶¶ 9, 11-12. They are essentially administrators of prescription drug benefits. Through their contracts with companies and funds offering healthcare plans, they cover millions of patient "lives" and manage about seventy-five percent of all outpatient drug claims. *Id.* at ¶¶ 9, 11. They create and maintain a preferred drug

list known as a formulary. A formulary is a list of drugs that are covered under the prescription drug benefits provided by a health plan. *Id.* at ¶ 13; *see also* Dep. of Raulo Frear (on behalf of PBM Express Scripts), Nov. 18, 2006 ("Express Scripts Dep.") 36:23 - 37:13; *see also* Leach Decl. 1-2.

The process for selecting drugs for placement on a formulary begins with a PBM's P&T Committee. Winkelman Decl. ¶ 14. P&T Committee members include physicians and clinical pharmacists. *Id.* The P&T Committee makes recommendations concerning which drugs should be included or excluded from the PBM's formulary. *Id.* PBM P&T Committees do not place drugs on their formularies for therapeutic uses that are not approved by the FDA. *See id.* at ¶ 3.

Theoretically, the P&T Committee acts to ensure the drug's safety and efficacy; their primary focus, however, remains on rebates and economic efficiency. *See* Winkelman Dep. 71-72. The health plan sponsors, or TPPs, that contract with the PBMs for prescription benefit management generally have little expertise in this complex area and tend to rely fully on the PBM and its formulary decisions. *See* Winkelman Decl., ¶ 20; *see also* Local 28 Dep. 61:17-62:4; UFCW Dep. 90:24-91:19; *see also* Leach Dep. 33:19-34:24. They tend to adopt without question or change the formulary recommendations provided to them by their PBM and indeed did so in this case. *See* Winkelman Decl., ¶ 20; *see also* Local 28 Dep. 61:17-62:4; UFCW Dep. 90:24-91:19. While TPPs do have the authority to decide which drugs they will cover and to reject the suggestions of their PBM, this power is almost never exercised, given that TPPs rely upon their PBMs for guidance. *See* Decl. of Keith Bradbury (on behalf of PBM Medco) ("Medco Decl.") ¶¶ 8-10; *see also* Decl. of Marsha Moore (on behalf of PBM Caremark) ("Caremark Decl.") ¶¶ 7-8; Leach Dep. 33:19-34:24.

Even where a TPP chooses to customize its formulary, it typically does so in consultation with the PBM's P&T Committee, *see* Medco Decl. at ¶ 9; *see also* Caremark Decl. ¶ 8, and relies for rebates on the PBM's relationships with drug manufacturers. *See* Winkelman Decl. ¶ 20. The agreements between PBMs and their client TPPs often prevent the client TPP from negotiating on its own with drug manufacturers. *See id.* When developing a drug formulary, P&T Committees do not conduct clinical research, review, or laboratory analysis on drugs. *See* Leach Decl. 2; *see also* Winkelman Decl. ¶ 32.

In short, although PBMs administer prescription drug benefits, including processing prescriptions, they act as middlemen in the prescription drug benefit process, *see* Winkelman Dep. 122:25-123:3, and do not influence the prescribing of particular drugs to particular patients. *See* Winkelman Decl. ¶ 1.

As a result of this passivity, doctors can prescribe whatever medication they think desirable for a condition, with no input from the PBM. *See id.* at ¶ 43. Once a drug is on the formulary, the PBM exerts no control over whether a particular drug is used for any particular condition. *See id.* PBMs have insufficient control to limit the use of a particular medication to FDA-approved uses. *See* Winkelman Dep. 15:1-12. When considering formulary placement of a particular prescription drug, P&T Committees generally limit their discussions to the approved uses of a drug. *See* Medco Decl. ¶¶ 18, 37, 48; *see also* Caremark Decl. ¶¶ 37, 38, 40, 47; Winkelman Dep. 103:14-23. Moreover, once a drug is on the formulary, a PBM will take no position on whether one drug is better than another. *See* Express Scripts Dep. 46:18-22. Although PBM P&T Committees do not place drugs on their formularies for non-FDA-approved

therapeutic uses, once a drug is on the list, they do not monitor off-label drug use. *See* Winkelman Decl. ¶ 32; Leach Decl. 2.

PBM P&T Committees rely on the clinical pharmacy departments of PBMs to present the most up-to-date information available to the public regarding the drug. *See id.* This publicly available clinical information is derived from the drug manufacturers, who are generally the only members of the industry, other than the FDA, that have all such data. *See id.* As with all product launches, there little information about the drug available in the public domain beyond what the company chooses to share. *See id.* This clinical information, primarily provided by the drug manufacturers, sets the foundation for formulary development and management. *See id.*; *see also* Winkelman Decl. ¶¶ 30-32.

PBM formularies generally include atypical antipsychotic drugs such as Zyprexa because PBM P&T Committees are unwilling to interfere with the plan of care for individuals with severe, persistent mental illness. *See* Winkelman Decl. ¶ 19. PBMs generally believe that all atypicals should be available for patients for whom this class of drugs may be prescribed. *See* Medco Decl. ¶ 49; *see also* Caremark Decl. ¶ 48; Express Scripts Dep. 74:10-12.

Other rationales for providing access to all available drugs in a class is that the diseases they treat are serious and most prescribing for these drugs is done by highly trained and board-certified specialists. In addition, results are highly variable, and even small deviations in drug therapy can be either harmful or helpful to patients. Winkelman Decl. ¶ 19. The nature of atypical antipsychotic medicine and the diseases for which they are prescribed have led to an industry-wide consensus that formularies should include all such drugs with no hindrances (such

as prior approval or step therapy), leaving doctors with the widest discretion to prescribe the drug they deem most appropriate. *See* Winkelman Dep. 82.

There are limited occasions where PBM P&T Committees approve a therapeutic interchange program for a particular pharmaceutical. A therapeutic interchange program prefers one drug over others in a class. *See* Winkelman Decl. ¶ 24. A PBM may suggest an alternative pharmaceutical to a physician who prescribes a prescription drug that is the subject of a therapeutic interchange program. *See* Medco Decl. ¶ 14; Caremark Decl. ¶ 14.

"Step therapy" is another possible limitation that a PBM may rarely place upon a prescription. Rules are established by the PBM that mandate the sequence in which patients must try drugs. *See* Winkelman Decl. ¶ 28. If the clinical results are not satisfactory with the first drug, the patient is then allowed access to another. *See id.* Step therapy programs are not, however, used for atypicals. *See* Express Scripts Dep. 104:25-105:3; *see also* Winkelman Dep. 111:7-112:10. Express Scripts never required step therapy for any atypical antipsychotic. Express Scripts Dep. 104: 20-24. Mr. Winkelman that testified he has never seen a client implement a prior authorization or step therapy program for an atypical. *See* Winkelman Dep. 116-19:-117:3.

Neither the P&T Committee nor the PBM tracks "off-label" use of a drug or has the ability to do so. *See* Medco Decl. ¶ 19; *see also* Caremark Decl. ¶¶ 17, 19; Winkelman Dep. 103:9-13. When a prescription is supplied to a retail pharmacist or a PBM mail-order facility, the information provided is limited and generally includes only the drug, dose, and other basic facts about the prescription. *See* Medco Decl. ¶ 19; *see also* Caremark Decl. ¶¶ 17, 19. It does not contain a diagnostic code. *See* Express Scripts Dep. 86:18-87:18, 90-17:22. Because there is

no diagnosis provided with the prescription information, PBMs are unable to record the indication for which a drug is prescribed. *See id.* The individual physician who prescribed the drug alone knows why the particular drug was prescribed. *See* Medco Decl. ¶ 20; *see also* Caremark Decl. ¶ 18; Winkelman Dep. 103:24-104:2.

A PBM can track off-label use of a drug only when it is prescribed pursuant to a prior authorization program. *See* Winkelman Dep. 15:11-17. A prior authorization program requires approval of a prescription by the PBM before a prescription is filled. *See* Express Scripts Dep. 99:9-19; *see also* Winkelman Decl. ¶ 24. Prior authorization programs have little overall impact on the number of additional off-label prescriptions written for Zyprexa because they are limited to less than two percent of prescriptions. *See* Winkelman Dep. 106:25-107:8. A prior authorization process is quite burdensome so it is utilized judiciously. Winkelman Decl. ¶ 25. In the real world, the process is impractical. *See* Winkelman Dep. 107:21-108:5. All major PBMs agree that prior authorization programs for atypicals are not appropriate. Medco Decl. ¶¶ 44, 49-50; *see also* Caremark Decl. ¶ 48; Express Scripts Dep. 101: 12-20.

At the end of the day, it is the manufacturer who decides what their drug is going to be sold for. *See* Winkelman Dep. 118:22-24. The relationship between the plaintiffs' TPPs and PBMs is that of a service contract: the TPPs remain responsible for prescriptions costs and the well-being of their members, but completely rely on the expertise of the PBMs to create their formularies and operate the P&T committees. *See* Winkelman Decl. ¶ 20; *see also* Local 28 Dep. 59:10-24; UFCW Dep. 84:12-85: 3; Midwest Dep. 111:7-14.

3. Plaintiffs' PBMs

During the relevant time period, each of the named payor plaintiffs engaged PBMs to administer the prescription drug benefit they provide to their insureds. *See, e.g.*, Mid-West's Resps. to Interrogs., First Set at No. 1; UFCW's Resps. to Interrogs., First Set at No. 1; Local 28's Resps. to Interrogs., First Set at No. 1; SBA's Resps. to Interrogs., First Set at No. 1. These PBMs include Caremark, Inc. ("Caremark"), used by Mid-West and SBA; Express Scripts, Inc. ("Express Scripts"), used by UFCW; and Medco Health Solutions, Inc. ("Medco"), used by Mid-West. Mid-West's Resps. to Interrogs., First Set at No. 1; UFCW's Resps. to Interrogs., First Set at No. 1; Local 28's Resps. to Interrogas., First Set at No. 1. These three PBMs dominate the industry and manage over half of all retail prescriptions. Winkelman Decl. ¶ 11.

In the course of the instant litigation, both parties conducted discovery of these three PBMs. Each PBM produced documents related to Zyprexa. Caremark provided an affidavit (Caremark Decl.), Express Scripts provided deposition testimony and an affidavit, (Express Scripts Dep., Affidavit of Rodney Gerald Wilson ("Wilson Aff.")), and Medco provided two affidavits (Adamcik Decl., Medco Decl.). Lilly also conducted two depositions of National Medical Healthcard Systems, Inc., which provides PBM services to UFCW.

Caremark, Express Scripts and Medco each reviewed Zyprexa soon after its entry onto the market and each placed it on their respective formularies. Medco Decl. ¶ 41; Caremark Decl. ¶ 41; Express Scripts Dep. 40-41. Zyprexa was subject to later review by each PBM. Medco Decl. ¶¶ 43-44; Caremark Decl. ¶¶ 42, 49; Express Scripts Dep. 133-35. Each PBM considered and was aware of the side effect profiles of Zyprexa and the other atypical antipsychotics well before the September 2003 label change. Medco Decl. ¶¶ 43-44; Caremark Decl. ¶¶ 42, 49;

Express Scripts Dep. 133-35. In fact, Caremark sent communications to physicians addressing topics related to the side effects of atypical antipsychotics. Caremark Decl. ¶ 49.

In addition to removing a medicine from the formulary, a P&T Committee may remove it from "preferred" status, impose prior authorization, or initiate step therapy. Leach Dep. 148-50; Winkelman Dep. 73-74. For example, Express Scripts addressed safety concerns with Geodon by determining that it was not required to be listed on the formulary. Express Scripts Dep. 22, 46.

Zyprexa was on all the major PBM standard formularies. *See* Medco Decl. ¶ 41; *see also* Caremark Decl. ¶¶ 41, 44; Express Scripts Dep. 41:6-18; Rosenthal Decl. 13. Because Zyprexa is an atypical antipsychotic, most P&T Committees added the medication to their PBM's drug formularies, with or without restrictions, based solely upon the drug's classification and the information provided by Lilly. *See* Leach Decl. 7. Dr. Frear of Express Scripts testified that, to his knowledge, all his clients had Zyprexa on their formularies. Express Scripts Dep. 42:23-43:3, 60:9-14.

None of the nation's largest PBMs has a therapeutic interchange program for Zyprexa. *See* Medco Decl. ¶ 49; *see also* Caremark Decl. ¶ 48; Express Scripts Dep. 74:10-12. The P&T Committee never considered a therapeutic interchange program for Zyprexa. *See* Medco Decl. ¶ 49; *see also* Caremark Decl. ¶ 48; Express Scripts Dep. 74:10-12. Dr. Frear testified that he did not recall any conversations among the clinical group about off-label uses of atypical drugs. *See* Express Scripts Dep. 132:23-133:1. None had a prior authorization program for Zyprexa. Medco Decl. ¶¶ 44, 49-50; *see also* Caremark Decl. ¶ 48; Express Scripts Dep. 101: 12-20.

None considered a prior authorization program for any atypical or Zyprexa at the request of any client. Express Scripts Dep. 100: 4-11.

Despite having several options to respond to safety concerns related to a medication, only one of the PBMs—Express Scripts, on behalf of plaintiff UFCW—has relatively recently taken action regarding Zyprexa. Express Scripts now requires prior authorization for UCFW members, instituted at UFCW's request.

B. Health Insurance

The prescription pharmaceutical market is unique because of the widespread presence of insurance coverage. In 1996, 77% of non-elderly Americans had drug coverage, and in 2001, 64% of Medicare recipients had prescription drug coverage through either a commercial or public insurance plan (e.g., Medicaid). In 1996, nearly 70% of all prescription drug spending was paid for by insurance. Rosenthal Decl. 12.

The relatively small share of prescription drug spending that is paid for out-of-pocket by consumers reflects the prevalence of fixed dollar copayments as the most common form of cost sharing. Because copayments only represent a small share of the full retail price of a drug, patients and their physicians are relatively insensitive to the prices of prescription drug therapies. See chart below summarizing doctors' attitudes; Rosenthal Decl. 12. *But see* Gina Kolata, *Co-Payments Go Way Up for Drugs with High Prices: Insurers Shift Burden: Fees for Costliest Class of Medications Soar Tenfold or More*, N.Y. Times, Apr. 19, 2008, at A1 (reporting that health insurance companies are rapidly adopting a new pricing system for very expensive drugs, ceasing copayment options and requiring patients to pay a percentage of the cost).

Third-party payors who cover most spending for drugs, including the majority of Zyprexa costs, usually exert only indirect control over therapeutic choice. They are under pressure from patient groups and doctors to offer generous coverage for drugs that treat serious conditions such as schizophrenia and bipolar disorder. In light of their concerns that restrictions on access to medication may cause overall increases in medical spending, TPPs are very hesitant to impose any limitations on antipsychotics or similar medications.

Potential for formularies to combat or challenge the impact of high prices on spending is extremely limited. While patients may cut back on medications, switch to generics, and use mail order service in the face of higher and tiered copayments, prescription drug spending and costs are relatively inelastic. Pricing for drugs like Zyprexa is unresponsive to cost-sharing or market pressure from TPPs or their agents. Rosenthal Decl. 13.

While some controls have been imposed by TPP health insurers, they have had little effect on doctors' prescription of antipsychotics. Restrictions are minimal and generally do not encourage doctors to use one drug rather than another.

Tier Status of Selected Antipsychotics

	Zyprexa	Abilify	Geodon	Seroquel	Risperdal	Invega
Plan	Tier - Restrictions	Tier - Restrictions	Tier - Restrictions	Tier - Restrictions	Tier -Restrictions	Tier - Restrictions
Aetna	2nd tier - QL	3rd tier - QL	3rd tier - QL	2nd tier - QL	3rd tier - QL	3rd tier - QL / ST
Aetna: Medicare Part D	2nd tier	3rd tier - QL / ST	3rd tier - QL / ST	2nd tier - QL	2nd tier - QL	3rd tier - QL / ST*
CIGNA	2nd tier	3rd tier	3rd tier	2nd tier	2nd tier	3rd tier
Harvard Pilgrim	2nd tier	2nd tier	2nd tier	2nd tier	2nd tier	3rd tier
Humana	2nd tier / DL	2nd tier / DL	2nd tier / DL	2nd tier / DL	2nd tier / DL	2nd tier / DL
Humana: Medicare Part D	2nd tier / QL	2nd tier / QL	2nd tier / QL	2nd tier / QL	2nd tier / QL	2nd tier / QL*

KEY:

DL - Dispensing Limit (There is a limit on coverage based on the length of time or amount that can be dispensed for this medication to ensure the appropriate dose and usage based on the FDA label recommendations.)
QD - Quantity Duration
QL - Quantity Limits
ST - Step Therapy

C. Doctors

The prescription pharmaceutical market is unique because the consumers of the product—patients—are not free to choose the medicines they take. Prescription drugs, unlike typical commodities, can only be purchased under a physician's oversight. Thus, physicians act as a trusted intermediary—a learned gatekeeper—in prescription drug (and all health care) decision making. While patient preferences play a role in the choice of therapy, physicians have enormous influence over health care decisions, particularly for serious medical conditions. Professional

norms require physicians to use their clinical skills, knowledge, and experience to make therapeutic choices that are in the best interest of their patients. Rosenthal Decl. 11.

While the pharmaceutical companies, PBMs and third-party payors play an integral role in the delivery of prescription medicine, doctors make the final decision: whether a particular patient should be treated with a particular medicine.

Physicians obtain and review clinical information about prescription medicine from a variety of different sources, including medical literature, medical school, continuing medical education, professional meetings, guidelines, algorithms, the FDA, exchanges between colleagues, their own experience using the medication, and factors specific to their individual patients, as well as pharmaceutical marketing from manufactures and competitors. Kahn Report 5; Wirshing Dep. 160-65; Schneider Dep. 188-90, 194-99; Klotz Dep. 197-99. In practice, they face numerous constraints, including limited time and cognitive ability to digest the enormous flow of information about available treatments. Physicians are often not aware of the latest scientific evidence on appropriate regimes. They rely heavily on commercial sources of information, such as pharmaceutical company promotional materials. Rosenthal Decl. 11.

Doctors typically choose treatments based on what works best for each individual patient, not on the relative costs of the medications. Kahn Report 8; Schneider Dep. 190-94; Harris Dep. 93-95; Rosenthal Dep. 93. The price of a medicine plays little role in the prescription decision. Kolassa Decl. 9. Physicians are generally unaware of the price of the products they prescribe. *Id.* at 10 (citing various research studies).

They may prescribe any medication they deem appropriate. *See* Food & Drug Admin., *Use of Approved Drugs for Unlabeled Indications*, 12 FDA Drug Bulletin 4, 5 (1982);

Washington Legal Found., 202 F.3d at 333 (D.C. Cir. 2000); Expert Rep. of John Abramson ¶ 65, M.D., Feb. 28, 2007, Docket Entry No. 97 ("Abramson Rep."). Off-label prescribing is an important function of a physician. It can benefit both individual patients and patient populations; off-label clinical experience may lead to the formation of hypotheses to be tested in structured clinical trials. There is justified concern over the extent of off-label prescribing and the potential for waste or even patient harm that may result when drugs are prescribed for uses with little or no scientific support. Rosenthal Decl. 11. FDA regulations attempt to protect off-label prescribing from commercial influences because of the potential conflict between what is best for the patient and what is best for the pharmaceutical manufacturer. *Id*; *see* Part V.C, *supra.*

As Dr. Harris testified regarding this phenomenon of persistence, physicians are reluctant to change a patient's medication in light of safety concerns if the medication appears to be helping the patient:

> [T]he clinical community doesn't immediately adopt or discontinue—a recommendation or immediately discontinue a drug, although these consensus or blue ribbon reports can sometimes have a great impact. And one of the reasons is a well-known phenomenon which is basically called persistence. There are patients and doctors who believe that a drug is working and they stay with the drug. There are some doctors who may have heard about the report, but they are busy and maybe they read an article, maybe a colleague has mentioned it to it. But the idea of instantaneously changing clinical practice does occur in some cases, but in many cases it's gradual as the information continues to diffuse.

Evid. Hr'g Tr. 250 (Harris).

Analysis of Zyprexa Prescriber Depositions							
Type of Doctor	**Total Number of Doctors in Sample**	**"I weigh the risks and benefits of drugs when making prescription decisions"**	**"I rely on multiple sources of information about drugs when making prescription decisions."**	**"I am visited by Zyprexa sales representatives**	**"My decisions to prescribe is not impacted by price."**		**"My decision to prescribe is not impacted by PBMs, formularies, and/or health plans."**
					Yes	**No**	
Psychiatrist	46	45	45	42	42	4	46
Primary Care	15	13	11	13	15	0	15
Nurse Practitioner	1	1	1	1	1	0	1
Other (Physician's Assistant, Psychopharmacologist)	2	2	2	2	2	0	1
Family Practitioner	4	2	2	2	4	0	4
TOTAL	68	63	61	60	64	4	68

Analysis of Sales Representative Depositions								
Type of Sales Rep	**Total Number of Sales Reps in Sample**	**Promoted Zyprexa as a Mood Stabilizer**	**Told doctors the risks of diabetes/weight gain are the same for all atypicals**	**Told prescribers Zyprexa treats symptoms of anxiety, agitation, and/or irritability**	**Used patient profiles, including Donna, Marty, Melvin**	**Used the MDQ, help to rule out bipolar first (ROBF)**	**Told prescribers about Lilly weight loss tools, such as "Solutions for Wellness"**	**Only gave prescribers information that came directly from Lilly**
Primary Care & Pediatrician	5	1	3	2	5	5	4	4
Psychiatrists	11	9	9	6	7	0	9	11
TOTAL	16	10	12	8	12	5	13	15

Analysis of Prescriber-Specific Zyprexa Call Notes							
Type of Prescriber	**Total Number of Prescribers in Sample**	**Lilly Promoted Zyprexa as a Mood Stabilizer**	**Lilly said the risks of diabetes/weight gain are the same for all atypicals**	**Told prescribers Zyprexa treats symptoms of anxiety, agitation, and/or irritability**	**Used patient profiles, including Donna, Marty, Melvin**	**Used the MDQ of DIGFAST, encouraged me to rule out bipolar first (ROBF)**	**Lilly Told prescribers about Lilly weight loss tools, such as "Solutions for Wellness"**
Primary Care & Pediatrician	7	7	0	5	7	7	1
Psychiatrists	30	26	19	14	19	4	23
TOTAL	37	33	19	19	26	11	24

D. Patients

In the psychiatric community it is axiomatic that "different people respond differently to different psychotropic drugs." Frank Decl. ¶ 7; Kahn Report 8; Harris Dep. 66, 79-80. This variation in reactions is particularly important with respect to patients suffering from schizophrenia and bipolar disorder, where psychiatrists often employ "trial and error" to determine the best medication for the patient. Frank Decl. ¶¶ 7, 18. For some patients, Zyprexa is the most effective medication. Kahn Report 8; Wirshing Dep. 156-58, 160-62; *see, e.g.*, Elyn R. Saks, The Center Cannot Hold: My Journey Through Madness 303 (2008).

XVIII. Evidentiary Hearing Expert Testimony

A. Plaintiffs' Witnesses at Hearing

Plaintiffs proffered six witnesses at the evidentiary hearing on the certification issue: (1) Dr. Robert Rosenheck, *In re Zyprexa Prods. Liab. Litig.* Transcript of Evidentiary Proceedings on Class Certification ("Evid. Hr'g Tr."), March 28, 2008 through April 2, 2008 at 7-80; (2) Dr. Meredith Rosenthal, Evid. Hr'g Tr. 82-191 (Mar. 28, 2008); (3) Dr. Jeffrey Harris, *id.* at 204-343 (Mar. 29, 2008); (4) Dr. William Wirshing, *id.* at 349-463 (Mar. 31, 2008); (5) Dr. Lon S. Schneider, *id.* at 464-549 (Mar. 31, 2008); and (6) Dr. John Abramson, *id.* at 708-806 (Apr. 1, 2008). All met *Daubert* and Federal Rule of Evidence 702 standards: "(1) the[ir] testimony is based upon sufficient facts or data, (2) the[ir] testimony is a product of reliable principles and methods, and (3) [they] ha[ve] applied the principles and methods reliably to the facts of the case." Fed. R. Evid. 702; *see Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993); *see also In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007) (denying summary judgment); *In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007) (at Part IV, outlining criteria for meeting *Daubert* requirements).

1. Robert Rosenheck, M.D.

Dr. Rosenheck is a Professor of Psychiatry, Epidemiology and Public Health at Yale University School of Medicine and the Yale Child's Study Center. Decl. of Robert Rosenheck, M.D., at 2, Jan. 9, 2007, Docket Entry No. 87 Ex. 5 ("Rosenheck Decl."). For twenty years, he has been the Director of the Department of Veterans Affairs ("VA") Northeast Program Evaluation Center ("NEPEC"), a national arm of the VA Central Office in Washington. *Id.* at 3. In that capacity, he is responsible for monitoring and evaluating mental health initiatives in the United States Veterans Health Administration, which provides mental health services to 900,000 veterans annually. *Id.*

Board-certified in psychiatry, Dr. Rosenheck has devoted himself full-time since 1988 to mental health services research focusing "on the evaluation of treatments used in 'real world' clinical settings and their implications on policy." *Id.* He has authored or coauthored over 400 articles, *id.*, and published the results from three major studies of the cost-effectiveness of antipsychotic medications, including the VA Cooperative Study 451 and CATIE, which he conducted and oversaw as lead investigator. *Id.* at 5.

At the evidentiary hearing, Dr. Rosenheck testified substantially as set forth in his three previous declarations. Evid. Hr'g Tr. 8 ff. (Mar. 28, 2008); *see* Rosenheck Decl.; Rebuttal Decl. of Robert Rosenheck, M.D., Apr. 5, 2007, Docket Entry No. 164 attmt. B ("Rosenheck Rebuttal"); Supp. Decl. of Robert Rosenheck, M.D., Mar. 17, 2008, Docket Entry No. 161 Ex. B (Rosenheck Supp. Decl."). Lilly did not file a *Daubert* motion with respect to Dr. Rosenheck.

To a reasonable degree of medical and scientific certainty, it is Dr. Rosenheck's view that: (i) the current state of research shows little independent evidence of superiority of Zyprexa as compared to other first-generation antipsychotics ("FGAs") or second-generation antipsychotics ("SGAs") in the treatment of schizophrenia, Rosenheck Decl. 2 (ii) manufacturer-sponsored trials

that attempt to show superiority of Zyprexa are methodologically biased, *id.*; and (iii) there is no credible evidence that Zyprexa is more cost-effective in the treatment of schizophrenia than any other antipsychotic medication and some evidence that it is less cost-effective than some earlier drugs. *See id.*; *see also* Rosenheck Rebuttal. While earlier randomized trials suggested that Zyprexa was superior to FGAs and had fewer effects, more recent studies, including his own VA Cooperative Study 451 and CATIE, have found no advantages for Zyprexa on symptom measures or quality of life, minimal advantages on neurological side effects, and greater risk of obesity and metabolic disorder. *Id.* at 5; *see* Evid. Hr'g Tr. 24, 38 (Rosenheck); Troy Moore et al., *The Texas Medication Algorithm Project Antipsychotic Algorithm for Schizophrenia: 2006 Update Journal of Clinical Psychiatry*, J. Clin. Psychiatry 1751-1762 (November 2007) (noting that the Texas Medication Algorithm Project ("TMAP"), for example, stated in November 2007 that for chronic schizophrenics, there is no reason to prefer SGAs to FGAs). These recent studies have also demonstrated that higher Zyprexa drug costs result in greater annual total health costs by $2,400 to $6,000 per patient, in part because of the emerging "consensus . . . that olanzapine causes weight gain and probably diabetes." Rosenheck Decl. 5.

a. Independent Study Results Found No Advantage for Zyprexa

Dr. Rosenheck testified at length about the results of the VA Cooperative Study 451 and the CATIE cost-effectiveness study that he oversaw. Both found no advantages for Zyprexa. Evid. Hr'g Tr. 11, 16 ff; *see* Parts XI.E, "VA Cooperative Study 451," "CATIE," *supra* at XIII.B – XIV.A. The VA study compared Zyprexa with Haldol, an older FGA, and showed "no advantage for olanzapine over haloperidol on any measure of symptoms, social functioning, or quality of life; no superiority on pseudoparkinsonian symptoms; and no advantage on measures of tardive dyskinesia . . . ." While a small benefit for Zyprexa was found "on measures of akithesia,

fine motor movement, and memory[, t]he study also showed olanzapine to be associated with significantly greater risk of weight gain, and $4,000-$10,000 greater annual costs." Rosenheck Decl. 6. The CATIE cost-effectiveness study found that "1) olanzapine showed no significant advantage over perphenazine [a low-cost generic FGA] on symptoms as measure by the most widely used measure of schizophrenia symptoms (the PANSS total score), but was superior to [Risperdal] and [Seroquel]; and 2) olanzapine had no significant advantage on total days of hospitalization or any of four measures of quality of life." *Id.* at 13. He emphasized that "[a]ll publications completed thus far [have] found no statistically significant advantage for [Zyprexa] over perphenazine on any outcome." *Id.* at 12; Evid. Hr'g Tr. 34, 10 ("[T]he research of the last five years, which has been large independent studies, suggests that there is no net clinical benefit" of Zyprexa as compared to perphenazine). Dr. Rosenheck now believes that Zyprexa should be the last option for schizophrenic patients because of its metabolic risks; Risperdal would be the first-line treatment. *See* Evid. Hr'g Tr. Ex. 742.

At the time of their publication, the results of both the VA Cooperative Study 451 and the CATIE trial were surprising. They conflicted with the outcome of other earlier studies, most of which were designed and authored by Lilly employees, concluding that Zyprexa was superior to conventional antipsychotics. Rosenthal Decl. 6-9; *see* Evid. Hr'g Tr. 13 (discussing the 1997 Lilly-sponsored International Collaborative Trial ("ICT") study showing improvement over Haldol); *see also id.* at 10, 19, 34, 40, and 42. Dr. Rosenheck opines that these Lilly studies and reviews were biased.

b. Deficiencies of Lilly-Sponsored Trials

The unanticipated results obtained in the VA study arose from the study's use—as would be typical in clinical practice—of prophylactic anticholinergic medication to counter Haldol's side

effects *before* they occurred. Rosenheck Decl. 7. In the VA study, Zyprexa performed the same, but Haldol performed much better than in Lilly-sponsored studies administered without prophylactics. *Id.* at 7, 8 (noting that his 2005 summary of research literature revealed that the vast majority of favorable studies of atypical antipsychotics, including Zyprexa, used Haldol without prophylactics); Evid. Hr'g Tr. 13; *see also id.* at 10, 19, 34, 40, and 42; Rosenheck Decl. 8-9 (describing ICT study analysis and results). "[T]he vast majority of favorable studies of atypical antipsychotics, including olanzapine, used haloperidol *without* preventative side effect medicines." Rosenheck Decl. 8.

Lilly's International Collaborative Trial ("ICT"), the source of data for numerous publications by Lilly employees, suffered from significant flaws: it did not use preventative side effect medication, ceased data collection early, and depended upon possibly biased analytic and statistical methods. *Id.* In reviewing the ICT, the Director of the Division of Neuropharmacological Drug Products of the FDA concluded that ". . . the data adduced in the Zyprexa NDA [New Drug Application] is . . . insufficient to permit the sponsor to make claims asserting the product's superiority to haloperidol." *Id.* at 9. A subsequent memo by the same person said:

> The problem in schizophrenia outcome assessment is that some of the so-called "negative" signs and symptoms of that illness are indistinguishable from the pseudoparkinsonian signs and symptoms that are known side effects of antipsychotic drugs like haloperidol. It would be reckless, therefore, to assume that a drug-haloperidol difference detected on an instrument that registers negative symptoms is actually measuring a difference in antipsychotic effectiveness.

Id. at 10. But two Lilly publications subsequently asserted Zyprexa's superiority over Haldol. *Id.*

Dr. Rosenheck's rebuttal and supplemental reports respond to Dr. Kahn's, Dr. McCombs', and Dr. Kolassa's criticisms of CATIE. The jury can resolve the scientific issues between the parties with the assistance of good advocacy.

2. Meredith Rosenthal, Ph.D.

Dr. Rosenthal, an Associate Professor of Health Economics and Policy at the Harvard School of Public Health, has researched and written extensively about the impact of pharmaceutical marketing and promotion on pharmaceutical sales and the economics of the health care industry. *See* Decl. of Meredith Rosenthal at 3-4, Feb. 27, 2007, Docket Entry No. 101 ("Rosenthal Decl."). She is also an Academic Affiliate of Greylock McKinnon Associates, a consulting and litigation support firm. *Id.* at 3. Her reports described the extensive body of health care economics that she has studied, and, in particular, how pharmaceutical marketing increases drug sales and how its impact can be measured and quantified over time.

Dr. Rosenthal worked independently of Dr. Harris. *See id.* At the evidentiary hearing, Dr. Rosenthal testified substantially as set forth in her previous reports. *See* Rosenthal Decl. 11; Rebuttal Decl. of Meredith Rosenthal, Apr. 5, 2007 ("Rosenthal Rebuttal"); Supp. Decl. of Meredith Rosenthal in Support of Plaintiffs' Motion for Class Certification, Jan. 8, 2008, Docket Entry No. 147 ("Rosenthal Supp. Decl."); Second Supp. Rep. of Meredith Rosenthal, Mar. 20, 2008, Docket Entry No. 161 Ex. D ("Rosenthal Supp. Rep."); Dep. of Meredith Rosenthal, Apr. 12, 2007 ("Rosenthal Dep."); Second Supp. Dep. of Meredith Rosenthal, Mar. 21, 2008 ("Rosenthal Second Supp. Dep."). Lilly's *Daubert* motion with respect to Dr. Rosenthal was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

As requested by plaintiffs' counsel, Dr. Rosenthal undertook to: (1) examine whether economic theory and evidence suggest that Lilly's allegedly unlawful Zyprexa sales, marketing, and promotional practices resulted in a common economic impact on the putative class; (2) quantify damages to the class based on a "loss-of-value" theory, i.e., as the difference in economic value that class members were allegedly led to believe they would obtain from Zyprexa and the

actual economic value of the drug in light of limitations known to Lilly; (3) estimate the number of units sold of Zyprexa that resulted from Lilly's alleged promotion of Zyprexa for off-label uses and apply the "loss-of-value" approach to estimated damages associated with these units; and (4) quantify the amount by which Lilly incrementally profited from the allegedly unlawful practices. Rosenthal Decl. 1.

Dr. Rosenthal concluded that if the alleged unlawful conduct regarding Lilly's marketing and lack of disclosure of complete information about product risks and efficacy of Zyprexa were true, it resulted in economic harm to the putative class. *Id.* at 2. Her conclusion was based on two key ideas supported by standard economic theory, empirical studies and academic literature: (1) promotion positively affects sales, *see id.* at 16-18; and (2) prices of prescription drugs are influenced by product characteristics, including the perceived value of the drug relative to alternative therapies. *Id.* at 2, 28-30.

After finding that it was feasible to perform an economic analysis to quantify the effect of the alleged wrongful conduct using a class-wide "loss-of-value" approach, Dr. Rosenthal did just that, identifying and quantifying a significant amount of damages. Her work suggests that the lower- and upper-bound estimates for nominal "loss-of-value" for the putative class period proposed by plaintiffs of ten years—September 1, 1996 to December 31, 2006—are $4.0 billion and $7.7 billion, respectively. *Id.* at 2; *see* Part XVIII.A.2.c, Table, "Summary of 'Loss-of-Value' Damages" and Table, "Dr. Rosenthal's "Yardstick" Model Damage Estimate, *infra*. Since this period is greater than will be allowed by the court—four years—*see* Parts I, *supra*, and XIX.B.4, *infra*, considerably less damages might be proven by her approach.

a. Damage Model Assumptions

To determine these figures, Dr. Rosenthal assumed that the following allegations were true:

a) From the time of launch, Lilly obscured and downplayed serious side effects associated with Zyprexa. In particular, Lilly failed to adequately test Zyprexa despite knowing of a well-established effect for increasing the risk of hypoglycemia and diabetes. In the limited testing conducted by Lilly, it failed to inform the medical community that Zyprexa was especially insidious with respect to these side effects. Zyprexa's original label, and all label changes until 2004, did not adequately warn of these adverse effects.

(b) Most seriously, until required to do so by the FDA in September 2003, Lilly failed to adequately warn the public, including Class members and their physicians, about the increased risk of diabetes and hyperglycemia and of the related need to provide baseline diabetes screening and ongoing glucose monitoring for patients treated with Zyprexa.

(c) Lilly's strategy to maximize the market potential of Zyprexa relied on targeted research and marketing efforts that would establish the drug as a relatively safe and effective alternative that could be used to treat not only approved indications but also "mood and thought disorder" symptoms of other mental health and neurological problems for which the drug had not been approved (nor in many cases studied).

(d) Beginning in 1996, Lilly's marketing and promotional campaign, planned and executed by its own staff and a wide range of collaborating organizations and consultants: "(i) falsely and deceptively oversold the efficacy of Zyprexa as compared to other antipsychotics, (ii) failed to adequately warn of, and affirmatively mislead [sic] the medical community regarding the severe side effects of Zyprexa such as weight gain, hyperglycemia, diabetes and cardiovascular effects, and (iii) unlawfully promoted Zyprexa for usage in populations for which it had not received FDA approval and for which the efficacy and side effects had not been established through adequate clinical evidence."

(e) The specific tactics Lilly used in its campaign to promote Zyprexa included supporting the production of articles favorable to Zyprexa, disseminating biased information through continuing medical education programs, and paying physician thought leaders to represent Zyprexa favorably to their colleagues. In addition, given the central role Medicaid financing plays in the reimbursement of antipsychotics, Lilly manipulated and paid state agencies to promote the use of Zyprexa in the Medicaid population.

(f) Lilly's efforts to misrepresent the safety and efficacy of Zyprexa thus were delivered not only through traditional pharmaceutical promotional strategies

such as detailing and sampling, but also through channels that have the appearance of independence and legitimacy, including scientific journals, continuing medical education programs, and state agencies. All of these efforts reinforced Lilly's strategy of positioning Zyprexa to appear higher-value to physicians, patients, and payers than Lilly knew the drug to be.

(g) In addition to overstating Zyprexa's value for approved indications, Lilly sought to expand Zyprexa's use in patients with symptoms and conditions that were completely unrelated to schizophrenia (and, later, to bipolar mania, for which Zyprexa was approved). For many of these off-label indications, Lilly's efforts involved promoting Zyprexa to primary care physicians, who are generally less familiar with antipsychotic medications.

(h) Lilly "sought to position Zyprexa as a 'foundational mood stabilizer' by focusing on 'behavior treatment' and 'reducing symptoms associated with mood, thought, and behavioral disturbances.'" Sales of Zyprexa associated with treatment of depression, for which it has never been approved, are estimated to have reached nearly $3 billion from 1999 to 2005. In addition, Lilly promoted the utilization of Zyprexa in the elderly for symptoms of dementia, a use for which a black box warning was ultimately added to Zyprexa's label due to an increased mortality risk. Finally, Lilly promoted the use of Zyprexa in children for a wide range of indications including Tourettes Syndrome, poor impulse control, bipolar disorder and stuttering.

(i) In summary, Lilly failed to adequately warn about Zyprexa's known association with diabetes and diabetes-related injuries and of the need to provide baseline screening and monitoring to prevent such complications from occurring, while overselling the comparative effectiveness of the drug. Moreover, Lilly undertook promotion and sales of Zyprexa for unapproved uses, many of which were unsupported by clinical evidence.

Rosenthal Decl. 7-9 (footnotes omitted). A jury could find these assumptions, findings and calculations and those of the other plaintiffs' experts accurate.

Assuming these allegations will be proven, Dr. Rosenthal found the economic effect on the putative class was the following:

a) the economic value of Zyprexa to the class is less than that conveyed by Lilly's sales, marketing and promotional efforts; that is, there is a difference between the economic welfare of the class in reality compared with the perception Lilly allegedly created; and
b) the prices and quantities of Zyprexa sold during the class period were higher than they would be absent the allegedly unlawful practices.

Id. at 10.

b. Lilly's Unlawful Marketing Increased Sales: The "Quantity Effect"

The impact of promotion on pharmaceutical sales is well-documented. *Id.* at 20; Evid. Hr'g Tr. 95-96, 134; *see* Part IV.B, *supra*. Dr. Rosenthal found that the data showed a clear relationship between Lilly's promotional spending and the number of Zyprexa prescriptions. Off-label promotion patterns are associated with off-label use. By demonstrating on an aggregate basis that supposed off-label promotional activities resulted in more off-label prescriptions of Zyprexa than would otherwise been the case, she found that a substantial share of Zyprexa prescriptions were for unapproved indications. *Id.* at 27.

Using data on Lilly's promotional expenditures described in Lilly's own strategic marketing documents, as well as the prices and promotional spending of the other SGAs (not including clozapine) based on IMS data, she undertook an econometric analysis to determine the ratio of total promotion expenditures to total sales. To quantify the impact of Lilly's off-label marketing on sales, she applied that ratio to a set of expenditures that she identified as "off-label." *See id.* at 20-28.

Because she only had access to marketing data from 2002 and 2003, Dr. Rosenthal computed both a lower and an upper bound of damages, depending on how far the 2002-03 data is extrapolated. *Id.* at 35. She first identified the percentage of Lilly's 2002 and 2003 salesforce spending, 13.7%, which was targeted towards the long-term and pediatric care markets; she used these as her primary measures of the challenged off-label promotions. *Id.* at 34.

To arrive at the lower bound, she assumed that plaintiffs would be able to prove their allegations *only* with regard to pediatric and long-term care indications—not other off-label uses, like primary care—and that Lilly's off-label promotion occurred *only* during 2002 and 2003. She

estimated fraud-free spending by subtracting the 13.7% of salesforce spending associated with those two off-label markets. *Id.* at 36.

To estimate the upper bound of damages, Dr. Rosenthal assumed that essentially *all* salesforce efforts to target all long-term care doctors and primary care physicians—a far greater number than just pediatric and long-term care doctors—would be proven to be illegal. She also assumed that Lilly's promotional spending in 2002 and 2003 could be applied to the entire putative class period, from 1996 to 2006. Rosenthal Decl. 36. According to this model, Lilly's fraud-free promotional spending was its actual promotional spending, less the average share, 50.3%, of salesforce spending identified as targeting primary and long-term care physicians, applied throughout the class period. *Id.*

Relying on economic analysis, she estimated that approximately every $200 spent promoting Zyprexa resulted in one decision to prescribe. Evid. Hr'g Tr. 134; Rosenthal Decl. 26. The $200 ratio could then be applied to derive the number of "extra" off-label prescriptions caused by Lilly's alleged illegal promotional activities. For each "extra" prescription derived using this methodology, Dr. Rosenthal assigned it *zero* value based on her understanding that "the evidence suggests that [Zyprexa had] no effectiveness for off-label uses." Evid. Hr'g Tr. 187. The entire price of the prescription then constituted the measure of damages for each "extra" off-label prescription. *Id.* at 186-88. All these figures and computations and the assumptions on which they are based could be accepted by the jury in whole or in part.

Lilly offers substantial criticism of Dr. Rosenthal's model. Her key assumptions, they note, are debatable: (1) that actual expenditures matched the budgeted marketing expenditures shown on Lilly documents produced in discovery; (2) that all expenditures for marketing to long-term care facilities and primary care practitioners were for the promotion of off-label use of

Zyprexa; and (3) that (for the higher bound) the same long-term and primary care marketing expenditures in 2002 and 2003 occurred every year of the class period. (Plaintiffs themselves allege that marketing to primary care practitioners did not begin in earnest until September 2000. Am. Compl. at ¶ 155). By assuming that the *entire* prescription price is the measure of damages for each "extra" off-label prescription, Dr. Rosenthal ignored the possibilities that even if a prescription was induced by off-label promotion, (a) the medication may have conferred a benefit or value on the patient; (b) the use of Zyprexa may have reduced other costs incurred by the payor, such as hospital costs; and (c) had that prescription not been written, the physician would likely have written a prescription for another medication, possibly even more expensive. The jury can accept much of this criticism as valid while giving substantial weight to her analyses and damage estimates.

c. "Loss of Value" Pricing Theory

Dr. Rosenthal also provided an opinion on the value of Zyprexa and attempted to quantify the monetary difference between what was represented and paid for and what the class received. *See* Rosenthal Decl. 28 ff. She began with the basic premise of health economics that people are willing to pay higher prices for high-quality health care than for lower-quality health care. *Id.* She notes that Dr. Kolassa, one of Lilly's own experts, describes pharmaceutical pricing just that way:

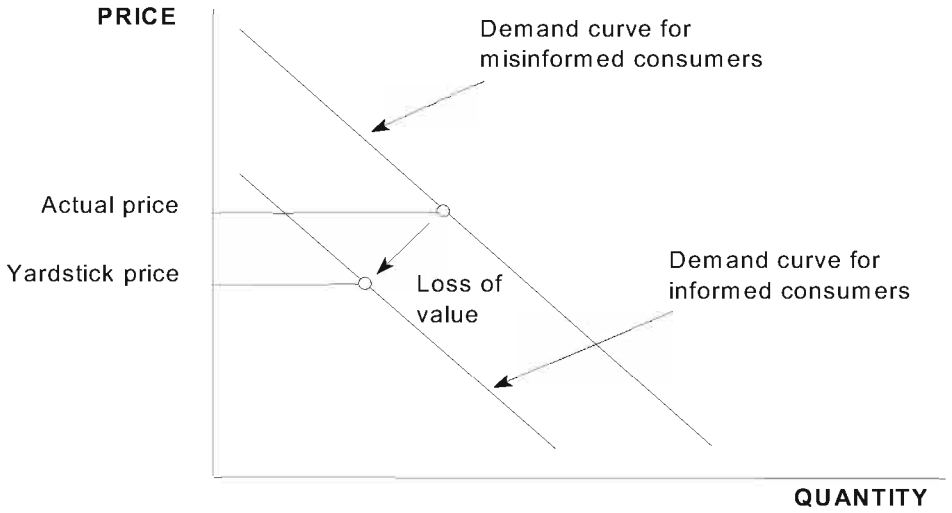
> "The primary principle that should guide every pricing decision is that the price should reflect the value of the product to the customer."
> "When a product delivers better outcomes, it deserves to be priced at a premium relative to competitors. Should the outcomes not differ from competitive products, a parity price is in order. Worse relative outcomes should be reflected by a price that is lower than prevailing levels."

Id. (quoting E.M. Kolassa, *Pharmaceutical Pricing Principles*, *in* Pharmaceutical Marketing: Principles, Environment, and Practice (M.C. Smith & E.M. Kolassa, et al., eds. 2002) at 189,

212). Although the pharmaceutical market is unique in many ways, *see* Part IV.A, *supra*, "this basic premise has been shown to hold true in pharmaceutical pricing as well." Rosenthal Decl. 28.

Her "loss of value" methodology attempts to demonstrate that the expected value of Zyprexa to patients was inflated by Lilly's allegedly fraudulent behavior. (A "loss of value" damage model is different from a "but-for" calculation of the effect of Lilly's alleged fraud on Zyprexa's prices. Evid. Hr'g Tr. 162.) The following chart demonstrates the relationship between loss of value and misinformation:

Demand Curve Change From Lilly Unlawful Conduct



Pfs.' Reply Mem. 53.

To determine estimated damages, Dr. Rosenthal employed standard "yardstick" techniques used by healthcare economists. She selected two of Zyprexa's comparators, Seroquel, a branded SGA launched in 1997, and perphenazine, a generic FGA, as yardsticks against which she measured Zyprexa's value. They were chosen after she considered, and rejected as less valid, other possible sources of willingness-to-pay estimates. According to the QALY scores from the CATIE cost-effectiveness study comparing the value of second-generation atypical antipsychotics and the first-generation typical antipsychotic perphenazine, *see* Part XIV.A.1, *supra*, the two medications are of "equal economic value" to Zyprexa. *See* Rosenthal Decl. 37-31.

Dr. Rosenthal does not claim that Zyprexa's actual price would have been the same as the other medications had Lilly provided different information about side effects and effectiveness. Instead, she uses price as a proxy for the loss of value, or disappointment of consumer expectations, that occurred as a result of Lilly's alleged fraud. Evid. Hr'g Tr. 176. Her analysis may assist the jury in analyzing the overpricing claim.

The value of a product to patients relates to a manufacturer's strategic pricing decisions. A text on pharmaceutical pricing written by Lilly's own expert recognizes that drug launch prices reflect the value that customers can expect from the drug (as offset by possible adverse effects) compared to what is charged for competitive drugs. Lilly itself recognizes the interrelationship between pricing and comparative expected value to the consumer.

Using the loss-of-value approach, Dr. Rosenthal estimated damages for the putative 1996-2006 class period to range from $3.998 billion to $7.675 billion, i.e., approximately 25% of the total dollars spent by endpayers for Zyprexa over the class period. *See* Rosenthal Decl. 41-43. The below table shows a summary of total loss-of-value damages for Zyprexa.

Summary of "Loss-of-Value" Damages ($ millions)

	Lower Bound	Upper Bound
Using Seroquel as a Yardstick:		
Third-Party Payors	$3,541	$4,214
Cash Payors	$447	$529
Total	**$3,988**	**$4,743**
Using Perphenazine as a Yardstick:		
Third-Party Payors	$6,581	$6,822
Cash Payors	$821	$853
Total	**$7,403**	**$7,675**

Id. at 43.

Dr. Rosenthal's "Yardstick" Model Damages Estimate

	Off-Label Damages						On-Label Damages					
	Based on Seroquel Yardstick			Based on Perphenazine Yardstick			Based on Seroquel Yardstick			Based on Perphenazine Yardstick		
Year	Total Damages ($)	Total Damages to Private Third Party Payers ($)	Total Damages to Uninsured Cash Payers ($)	Total Damages ($)	Total Damages to Private Third Party Payers ($)	Total Damages to Uninsured Cash Payers ($)	Total Damages ($)	Total Damages to Private Third Party Payers ($)	Total Damages to Uninsured Cash Payers ($)	Total Damages ($)	Total Damages to Private Third Party Payers ($)	Total Damag to Uninsure Cash Payer ($)
1996	1,006,184	927,048	79,136	1,728,767	1,592,800	135,967	7,733,445	7,125,214	608,232	13,287,157	12,242,129	1,045,0
1997	22,687,319	20,144,439	2,542,880	39,183,032	34,789,572	4,393,460	74,325,149	65,859,674	8,465,476	128,489,453	113,849,697	14,639,7
1998	45,937,568	40,247,487	5,690,081	80,425,381	70,463,448	9,961,932	126,440,533	110,860,641	15,579,893	221,366,269	194,089,710	27,276,5
1999	76,777,025	67,474,258	9,302,767	135,515,252	119,095,408	16,419,844	162,210,718	142,362,499	19,848,219	286,309,952	251,276,862	35,033,0
2000	109,218,787	96,830,082	12,388,685	194,468,671	172,410,089	22,058,582	234,603,813	207,795,017	26,808,796	417,722,092	369,987,887	47,734,2
2001	124,720,221	109,839,902	14,880,319	239,141,506	210,600,455	28,541,050	274,516,477	241,788,595	32,727,882	522,138,861	459,871,005	62,267,8
2002	181,714,049	160,398,776	21,315,274	365,578,566	322,675,421	42,903,144	297,465,439	262,596,081	34,869,358	597,514,173	527,436,028	70,078,1
2003	188,987,462	166,726,301	22,261,161	347,344,247	306,430,888	40,913,360	342,819,173	302,594,099	40,225,075	629,433,106	555,571,318	73,861,7
2004	174,580,241	152,378,912	22,201,329	307,755,805	268,678,113	39,077,692	321,765,069	280,645,624	41,119,445	566,035,476	493,819,562	72,215,9
2005	137,790,267	119,829,652	17,960,615	257,242,455	223,707,643	33,534,811	304,878,016	265,197,303	39,680,713	568,895,637	494,838,829	74,056,8
2006	160,714,068	149,479,975	11,234,093	341,213,916	317,374,731	23,839,185	518,261,237	482,140,878	36,120,359	1,103,408,897	1,026,539,925	76,868,9
Total	1,224,133,171	1,084,276,832	139,856,339	2,309,597,597	2,047,818,569	261,779,028	2,665,019,071	2,366,965,623	296,053,447	5,054,601,073	4,499,522,952	555,078,1

Notes:

These calculations were derived using the following adjustments to the attachments from the Rebuttal Declaration of Meredith Rosenthal, April 5, 2007.

1. In Attachments E.4.a through E.5.b, all units "subject to off-label fraud" are set to zero.
2. For off-label damages, Columns C and E in Attachments E.4.a through E.5.b are multiplied by the quarterly off-label percentages found in Attachment C.3.b.
3. For on-label damages, Columns C and E in Attachments E.4.a through E.5.b are multiplied by the quarterly on-label percentages found in Attachment C.3.b.

The specific calculations used by Dr. Rosenthal in arriving at these figures are described in the Affidavit of Thomas M. Sobol in Connection with Damages Calculations, Apr. 24, 2008, Docket No. 05-CV-4115, Docket Entry No. 180.

Dr. Rosenthal also estimated unjust enrichment damages—with lower- and upper-bound estimates of $3.7 billion and $7.1 billion—over the class period. *See* Rosenthal Decl. 44-47. Her calculations are not discussed further here since the unjust enrichment cause of action has been rejected. Unjust enrichment is not available under civil RICO. *See* 18 U.S.C. § 1964(c) ("damages he sustains").

To refute her testimony, Lilly asserted that Dr. Rosenthal's "loss of value" theory failed because it was not based on sound economic models and theories. Dr. Rosenthal disputed this contention, asserting that her "analysis of the loss of value to the Class is based on standard microeconomic theories, including welfare theory and hedonic analysis." Rosenthal Second. Supp. Rep. 2. Lilly further noted that "loss of value" damages are impossible to quantify because the "value" itself of a drug, particularly an antipsychotic, cannot be measured. Dr. Rosenthal disagreed: "[v]alue is inherently subjective . . . this does not mean that it cannot be ascertained or measured. The theory of demand rests on the premise that consumers reveal their (inherently subjective) preferences through their purchasing behavior." *Id.* at 5.

Lilly also emphasized that the willingness to pay of different class members varies and thus is difficult or impossible to calculate. Dr. Rosenthal herself recognized the variation: "I don't contest that there's a range of willingness-to-pays among class members, that there's some variation and that while there's an effect over all class members, it will differ." Lilly Mem. 20-21 (quoting Rosenthal Dep. 229). But this variation in value among members of the class does not negate overpricing to all. Dr. Rosenthal convincingly testified that all class members experience

an effect. Even those who are still willing to pay the current price for Zyprexa experienced a loss of value because they did not receive what they had expected when they purchased Zyprexa:

> [T]o the extent that there have been adjustments in the market over the last several years, they have come in the form of reductions in quantity which could be expected to reflect the fact that those individuals who, once the information was revealed about the risks—the true risks and comparative effectiveness of Zyprexa, chose not to purchase it. And so those were individuals whose willingness-to-pay was substantially high enough to—to make it still worth their while. It's still true that those individuals in the past, what they thought they were getting out of the purchase was greater than what, in fact, they ended up getting, so those same individuals would still have had a loss-of-value in the past.

Rosenthal Dep. at 227-28. As she summarized: "again, the aggregate is the sum of the parts. It will reflect those specific differences, but I did not estimate any specific differences." *Id.* at 298-99.

3. Jeffrey E. Harris, M.D., Ph.D.

Dr. Harris is a professor of economics at the Massachusetts Institute of Technology and the Harvard Medical School-MIT Program in Health Sciences and Technology. Among other subjects, he teaches health economics and the economics of the pharmaceutical industry. He is also a practicing physician, now at the Providence Community Health Center, having previously spent almost thirty years as an attending doctor at the Massachusetts General Hospital. At the evidentiary hearing, he testified substantially as set forth in his previous reports, focusing on explaining his assumptions and damage calculations. *See* Expert Report Dr. Jeffrey Harris M.D., Ph.D., Feb. 20, 2007, Docket Entry No. 98 ("Harris Rep."); Rebuttal Expert Rep. of Jeffrey Harris, Apr. 4, 2007 ("Harris Rebuttal"). Dr. Harris offered no opinion on causation. Evid. Hr'g Tr. 304-05, 309-10; Harris Rebuttal 2. Lilly's *Daubert* motion to exclude Dr. Harris' testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

He was asked by plaintiffs' counsel to address the extent of aggregate economic damages, if any, suffered by the putative class as a result of defendant's alleged misconduct, during the proposed class period from 1996 to the present, under the following two assumptions:

> (1) But for Defendant Lilly's misconduct, the total nationwide number of Zyprexa prescriptions would not have exceeded its projected 2006 level.
> (2) But for its misconduct, Defendant Lilly would not have raised the price of a Zyprexa prescription beyond the average price per prescription charged for Seroquel, Risperdal, and Clozaril, which were its three principal competitors in the therapeutic category of atypical antipsychotics during the class period.

Harris Rep. 3-4; Harris Rebuttal 3; Evid. Hr'g Tr. 207. His damages estimate does not include any government (Medicaid or Medicare) payments. Harris Rep. 4. Dr. Harris worked independently from Dr. Rosenthal.

a. Damages Estimate

Dr. Harris first estimated the total nationwide increase in expenditures for Zyprexa attributable to defendant's alleged misconduct during 1996-2006 to be $11.342 billion. Excluding the government-paid fraction (estimated to be 56.5% of the total, *see* Harris Rep. App'x 3), Dr. Harris found total economic damages to be $4.926 billion during the class period, or somewhat less than 25% of what endpayers had paid for Zyprexa during the class period. Harris Rep. 4. His estimate accords with that of Dr. Rosenthal's loss-of-value approach. *See* Part XVIII.A.2, *supra*.

In calculating damages, he distinguished between two groups of consumers: (1) patients who, but for Lilly's alleged misconduct, would not have purchased Zyprexa at all ("Quantity" or "Excess Prescription Theory"); and (2) patients who, but for Lilly's alleged misconduct, would still have purchased Zyprexa, but at a lower price ("Excess Price Theory"). *Id.* at 5.

b. Data Sources

To quantify his theories, Dr. Harris acquired Zyprexa expenditure data from two different data sources (the National Prescription Audit ("NPA") and the National Disease and Therapeutic

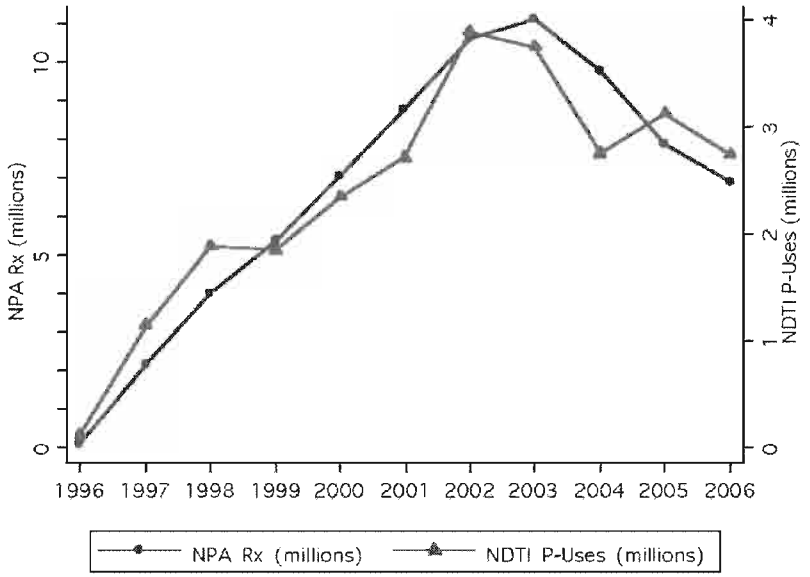
Index ("NDTI")). *Id.* at 6-7. Both data sources originated from IMS Health and are frequently used in scholarly analyses of the pharmaceutical industry. *Id.* at 7. Of defendant's two economic experts, Drs. Cockburn and Berndt, the former relied on IMS Health data for his own calculations and both have relied upon data from IMS Health in their published research. Harris Rebuttal 6.

The NPA is derived from prescription records of a large, representative panel of retail, chain, hospital, and mail-service pharmacies throughout the United States. The basic unit of analysis in the NPA is the prescription ("Rx"). Harris Rep. 7. The NDTI is derived from a large, representative panel of office-based physicians nationwide. The unit of analysis in the NDTI is a physician-reported drug use ("P-Use"), which includes patient encounters in which a drug was newly prescribed and encounters in which a previously ordered drug was continued. *Id.* The NDTI estimates of physician drug use were further broken down by widely-employed primary diagnostic codes, allowing Dr. Harris to track trends in Zyprexa use with respect to FDA-approved indications and off-label use. *Id.* at 11.

c. Prescription Trends

Although there is "sampling variability," the two sources of information present a consistent picture of the trends in Zyprexa use. The consumption of Zyprexa in the United States reached a peak in 2002-03, and then declined in 2004 and thereafter. *See also* charts in Part XI.E, *supra*. Based on NPA data, the number of Zyprexa prescriptions reached a maximum of 11.092 million in 2003; by 2004, Zyprexa prescriptions had fallen to 9.765 million; 2006 was projected to be 6.901 million, a 38% decrease from 2003. Harris Rep. 8.

Prescriptions



Harris Rep. fig. R1. The above graph shows trends in the quantity of Zyprexa consumed nationwide during 1996–2006. The circles, connected by lines and calibrated on the left axis, represent the estimated number of prescriptions written for Zyprexa nationwide, based upon the NPA. The triangles, connected by lines and calibrated on the right axis, represent the estimated number of physician uses of Zyprexa, based upon the NDTI.

Dr. Harris credited the 38% decline to the contemporaneous publication of information concerning the adverse effects of the drug, especially weight gain and the increased risk of diabetes. He noted that a warning for hyperglycemia and diabetes was first placed on Zyprexa's label in September 2003, followed by Lilly's "Dear Doctor" letter in March 2004. Harris Rep. 8; *see* Parts XI.D, XII.B, *infra*. Although the warning was required for all SGA labels, it negatively impacted Zyprexa in particular because of the perception of the drug's greater metabolic risks, reinforced by the February 2004 ADA consensus statement. *See* Harris Rep. 9 (noting that after

the ADA Consensus, prescriptions for all other SGAs except clozapine—identified with Zyprexa as having the worst metabolic side effects—increased).

Using the NDTI data broken down by diagnostic code, Dr. Harris was able to also determine the trends in Zyprexa's on- and off-label prescriptions. Dr. Rosenthal had found that overall, "unapproved uses represent an average of 31% of Zyprexa mentions" in the NDTI database, Rosenthal Decl. 26. Off-label use was particularly prevalent among conditions commonly diagnosed in children and for dementia, beginning with an upward trend beginning to accelerate around 2001. *Id.* at 26-27. In late 2002 and early 2003, there were increases in prescribing for pediatric conditions; off-label prescribing for dementia also experienced an increased trend beginning in 2001 to an apex in mid-2002. Use for dementia did not begin to decline until early 2006, many months after the FDA's decision in April 2005 to require a "black box" warning on all SGAs for elderly patients. *Id.* at 27.

Demonstrated by Dr. Harris was that the overall decline in Zyprexa sales since its peak in 2002-03 corresponds almost entirely to a decrease in prescriptions written for diagnoses other than the approved indications for schizophrenia and bipolar I disorder. *See* Graph, "Reasons for Prescriptions," at Part XI.E, *supra*; *see* Harris Rep.; *see also* Harris Rebuttal at Ex. 2 & 3.

Dr. Harris also examined trends in Zyprexa pricing during the class period. His analysis revealed that Zyprexa was consistently priced higher than the three other principal competitor antipsychotic drugs throughout the class period. The per-prescription price differential increased from $77 in 1996 to $150 in 2006. At the peak level of Zyprexa consumption in 2003, the difference in price per prescription was $113. *See* Graph, "Price Per Prescription," at Part XI.E, *supra*; Harris Rep. App'x B (explaining price-per-prescription calculations).

The "Price Per Prescription" graph of Dr. Harris is based on IMS Health data and shows trends in the estimated retail price per prescription of Zyprexa compared to the prices of the branded SGAs Risperdal, Clozaril, Seroquel, Geodon and Abilify during 1996–2006. Harris Rebuttal 16 fig. R3. Risperdal and Clozaril were already on the market in 1996 when Zyprexa was introduced. Seroquel, Geodon, and Abilify were introduced in 1997, 2001, and 2002, respectively. From its launch in 1996, Zyprexa was priced higher than Risperdal and Clozaril. During 1997–2000, Zyprexa remained at a consistently higher price than Risperdal, Clozaril and Seroquel, the three branded atypical antipsychotics that were on the market at the time. Price differentials between Zyprexa and its competitors remained the same over the class period; all prices increased at the same rate. *See* Harris Rep. 10 (noting the average price of a Zyprexa prescription rose by 26% between 2003 and 2006, while average price per prescription of all other brand-name atypical antipsychotics rose by 30% during the same period).

d. Damage Theory & Calculations

To calculate his "Quantity" or "Excess Prescription Theory" and identify those patients who, but for Lilly's alleged misconduct, would not have purchased Zyprexa at all, Dr. Harris assumed that sales of Zyprexa would not have exceeded the total for 2006. To calculate his "Excess Price Theory" and identify those patients who, but for Lilly's alleged misconduct, would still have purchased Zyprexa but at a lower price, Dr. Harris assumed that Zyprexa's price would not have exceeded the average price per prescription charged for Seroquel, Risperdal, and Clozaril.

The assumptions underlying both of Dr. Harris' theories include the following: (1) Lilly suppressed the truth about Zyprexa's side effects from the time of launch until the end of 2003, Evid. Hr'g Tr. 210, 260, 309-10, 320-21; (2) beginning in late 2003, the truth about these side-

effects was revealed to the market through the class-wide FDA label change, the ADA Panel Consensus Statement, and Lilly's "Dear Doctor" letter; (3) a reduction in Zyprexa prescriptions after 2003 was caused by these "revelations," *id.* at 254–55, 325; (4) therefore, in the years 2000 to 2005, the number of Zyprexa prescriptions per year would never have exceeded the projected total for 2006. *Id.* at 308. Finally, Dr. Harris assumed that plaintiffs were entitled to a 100% refund for the "excess scripts" written in 2000 to 2005. *Id.* at 312 ("Q: . . . [T]he basic theory there is that the people that paid for all of those so-called excess prescriptions should get their money back in full? A: Yes."). Dr. Harris supported his excess prescription theory by concluding that "those physicians who were using the drug for off-label purposes became the most influenced by the information about the side-effects" and that "the quantity effect is primarily an effect on off-label uses." *Id.* at 267.

For his Excess Price Theory, he assumed that but for Lilly's suppression, the price of Zyprexa "would have been the same as a combination or average of Risperdal, Seroquel, and Clozaril." *Id.* at 333. Taking the average price per prescription for these three medications, he subtracted that figure from the price per prescription for Zyprexa to estimate damages. *Id.* at 335.

e. Criticisms

The theory of Dr. Harris assumes that every one of the "excess" prescriptions from 2000-05 was written by a physician who was deceived by Lilly and who would not have written the prescription but for Lilly's alleged fraud. Dr. Harris claimed that 100% of the decline in Zyprexa prescriptions was due to the September 2003 class-wide label change and subsequent events. This assumption of 100% gullibility is contradicted by the many depositions read by the court showing that some doctors were not misled. *See* deposition exhibits attached to *In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007) (denying summary judgment). Nevertheless, the

analysis can be reduced in force by discounting the percentage of misled doctors without negating the theory and by permitting the jury to reduce the computed damages based on those doctors who were misled; recalculation for trial can be permitted.

Acknowledged by Dr. Harris himself was that "there was clearly information about potential risks [of Zyprexa] that was in the published referee literature" before the consensus statement was published." Evid. Hr'g Tr. 249 (noting the "accumulation of articles" on this very subject). Lilly's competitors would "very typical[ly]" have counter-detailed Zyprexa, serving as "another channel by which information about the side-effects of Zyprexa," *id.* at 328, would have been made known to prescribing physicians in advance of the supposedly watershed consensus statement. *Id.* at 249, 324 (knowledge previously available to prescribing physicians); *see also id.* at 835 ("The notion this was a bolt from the blue or a surprise or an earthshaking event or a watershed which suddenly started to have an impact with a publication of this ADA Consensus Statement is entirely unreasonable."). "Put differently, the ADA, American Diabetes Association, didn't invent for the first time the relationship between Zyprexa and these side-effects," *id.* at 249, nor would it have been the first time that most physicians had heard of that relationship.

Finding different damages for different class members will not be allowed at trial. It would complicate proof excessively. Plaintiffs as a class will be permitted to proceed only on a theory of an excessive computed price for all payors which may vary over time.

Dr. Harris's price theory results in recovery no matter what a payor or patient knew about Zyprexa, and does not depend on any deception of doctors by Lilly. *Id.* at 306, 310-11. It does not address reliance on either an individual or an aggregate basis nor examine individual prescribing decisions. *Id.* at 312. He used an average price-per-prescription to set a "but for"

aggregate price; plaintiffs had requested he make certain assumptions and calculate damages on an aggregate basis. *Id.*

Two of defendant's experts, Dr. Berndt and Dr. Cockburn, criticized the soundness of Dr. Harris's two main assumptions, deeming his report as having "no economic basis" and "no credible economic foundation." *See* Harris Rebuttal 3-4. Despite their criticisms, Dr. Harris insists that "as an economist and physician, [he] find[s] both assumptions to be entirely consistent with well-founded principles of economic analysis and to adhere to the methodological standards employed by scholarly and professional analysts of the pharmaceutical industry, including Professors Cockburn and Berndt themselves." *Id.* at 3. The assumptions "were not arbitrary and were in fact based on objective evidence of the kind normally relied upon by economists, physicians and other analysts of the pharmaceutical industry." *Id.* at 4. The jury will be in a position to assess the merits and deficiencies of Dr. Harris' analysis when computing the pricing overcharge for all class payors.

Defendant's two experts believe that Dr. Harris's model imputes the but-for changes in price and quantity and does not take "other factors" into account, although complex multivariate statistical methods—which Dr. Harris did not use—would. *Id.* Dr. Harris agrees that "[i]n principle, complex multivariate statistical methods, including hedonic price analysis, might be useful and reliable in computing damages," but that here "such statistical methods constitute a type of retrospective non-blinded analysis of the data and are highly susceptible to biases that may be difficult even for a professional audience to detect." *Id.* at 5-6.

Such "other factors" cited by Dr. Cockburn as possible explanations for the decline in Zyprexa use, including Abilify's introduction and attorney advertising for Zyprexa product liability suits, are not significant factors: Market shares of Risperdal and Seroquel, unlike

Zyprexa, continued to rise after Abilify and Geodon were introduced. Dr. Harris also estimated that the 20,000 individuals with pending Zyprexa personal injury claims against Lilly comprised only 1% of total Zyprexa prescriptions for non-governmentally covered patients since 1996. *Id.* at 9. These disagreements among competent experts are best left for jury resolution.

4. William Wirshing, M.D.

Dr. Wirshing is a professor of clinical psychiatry in the Department of Psychiatry and Behavioral Sciences at the University of California, Los Angeles, School of Medicine. For almost fifteen years, he was Chief of the Schizophrenia Treatment Unit at the West Los Angeles Veterans Affairs Medical Center, Brentwood Division, California, and Co-Chief of the Schizophrenia Outpatient Research Clinic for the last ten years. *See* Decl. of William Wirshing, M.D. ("Wirshing Decl."), Jan. 31, 2007, at 2-3. In those and his current position, he regularly treats patients with mental illnesses and conducts clinical trials of antipsychotic medications. *Id.* at 5; Evid. Hr'g Tr. 352-53 (Mar. 31 & Apr. 1, 2008: Wirshing). Dr. Wirshing has authored many articles, presentations, and other publications on schizophrenia, its effects, and the impact on the disease of various antipsychotic medications, including Zyprexa. *See* Wirshing Decl. 48.

His position in clinical research has allowed Dr. Wirshing to "test" potential medications in his patients under controlled protocol conditions before FDA approval. He has consulted and worked as a clinical investigator for various pharmaceutical companies, *id.* at 48, including Lilly, on every second-generation antipsychotic medication that has been approved—Risperdal, Geodon, Abilify, Seroquel, and Zyprexa. *Id.* at 4-5. His team worked "very closely" with top Lilly scientists. Evid. Hr'g Tr. 377.

In his expert reports, Dr. Wirshing supplied strong evidence supporting the plaintiffs' position. *See* Wirshing Decl.; Supp. Decl. of William Wirshing, M.D., Mar. 20, 2008, Docket

Entry No. 161 Ex. C ("Wirshing Supp. Decl."). His testimony is likely to be impressive to a jury on the key issue of fraud and damages. Lilly did not file a *Daubert* motion with respect to Dr. Wirshing.

Based on his expert knowledge, Dr. Wirshing concluded, inter alia, that: (i) information released by pharmaceutical companies can substantially affect the decisions of treating doctors and their choice of drugs for the treatment of certain psychiatric disorders and in turn substantially affect the outcome of the treatment efforts; (ii) there is a direct and indirect causal connection between the administration of olanzapine and certain adverse effects including significant weight gain, hyperlipedemia, hyperglycemia, pancreatitis, and the development of diabetes, *id.* at 48; (iii) the degree of the adverse effect on some patients using Zyprexa is substantially greater than the adverse effects observed in patients on other atypical antipsychotic medications, *id.* at 49; (iv) there is no credible evidence that olanzapine is more efficacious than typical and other atypical antipsychotic medications, *id.*; (v) Lilly had a duty to notify health care providers and consumers when it knew or had reason to know of the clinically significant increase of weight gain to patients who had been prescribed Zyprexa, and to warn physicians that Zyprexa carries greater risk of diabetes than typical antipsychotics and all antipsychotic drugs other than clozapine, *id.*; (vi) Zyprexa should not be used as the first line drug of choice in the treatment of disorders for which it has been marketed, *id.*; (vii) had Lilly provided full disclosure to treating physicians of the actual potential consequences to their patients of the use of Zyprexa over other atypical antipsychotic medications, and of Zyprexa's lack of enhanced efficacy to justify the increased serious risk, a reasonably prudent doctor would not, given the fact that there are choices of typical antipsychotics and other atypical antipsychotics available to treat the illness for which Zyprexa is used, choose Zyprexa as the drug of first choice for treatment of any illness for which the drug has

been marketed, *id.* at 49-50; Wirshing Supp. Decl. 2-3; and (viii) Lilly was grossly negligent in allowing physicians to prescribe this drug without necessary and essential information about serious medical complications to a patient population already at an elevated risk for the development of diabetes or pancreatitis. Wirshing Decl. 50.

At the evidentiary hearing, Dr. Wirshing's testimony focused on two issues: 1) the clinical utility of Zyprexa and 2) what Lilly knew of Zyprexa's effects at time of launch.

a. Clinical Utility of Zyprexa

Dr. Wirshing was full of praise of Zyprexa's positive impact on a severely ill population: "Zyprexa . . . clearly is useful and indeed, for certain patients, life-altering to a positive degree." Evid. Hr'g Tr. 401. Using Zyprexa dramatically enhances some patients' quality of life. *Id.* at 430 ("[F]or that individual patient, it is potentially irreplaceable and crucial"). He preferred Zyprexa over Seroquel and perphenazine, believing them to be less effective, Evid. Hr'g Tr. 434 (conventional drugs); 436-37 (perphenazine); 436 (Seroquel), and because of perphenazine's more difficult-to-manage side effects. *Id.* at 432.

When a medication is working for a patient, Dr. Wirshing sticks with that treatment like "a pit bull with lockjaw," notwithstanding side effects. *Id.* at 391. It is "tantamount to malpractice," he believes, to stop using a medication which is successfully treating a patient's psychosis. *Id.* at 401; *id.* at 391 ("[T]here's almost on one hand I can tell you the side effects that I will stop a drug that's working because of toxicity . . . . I will stick with it because that's the right thing for that patient.").

Dr. Wirshing noted that not all patients benefit from Zyprexa. Because of the heterogeneity of mental illness, people respond differently to the different antipsychotics:

> I described to my students, I describe the selected serotonin reuptake inhibitors as slightly different shades of green of the same Chevy Caprice classic. I mean, okay,

> they are a little different, but it's not really anything to write home about. But for these, the antipsychotic drugs for a given patient, one drug can work magnificently and another drug not work at all. They aren't fungible . . . .

Id. 409-10. "Patients that are treated on olanzapine . . . . are not the same patients that are necessarily being treated with quetiapine [Seroquel] . . . . So, it's a bit like comparing apples and oranges." *Id.* at 407. For those patients successfully treated with Zyprexa, total cost savings may be more, despite the high cost of prescriptions:

> THE COURT: So, within the class then, of bi-polar and schizophrenic people, some would be better treated if they were using Zyprexa. Would have better results on a per-cost basis.
>
> THE WITNESS: Absolutely. Despite what's enormously expensive technology, I mean literally hundreds of times the cost of generic haloperidol, if it works, it will wipe out the other costs. And is a perfectly prudent and defensible thing to do.

Id. at 407-08.

While praising Zyprexa, Dr. Wirshing did describe at length its side effects of weight gain and associated morbidity, noting that some patients discontinued the medication for these reasons. Wirshing Decl. 8. Weight gain and obesity, connected to abnormal metabolic changes such as insulin resistance and dyslipidemia, are widely accepted as causal factors increasing the risk for hyperglycemia, diabetes, cardiovascular disease (heart attacks and strokes) and hypertension. *See id.* at 6-7. He highlighted research linking Zyprexa to these diseases:

> Coming together, the case reports, the vast majority of the retrospective database analyses, and controlled experimental studies including randomized clinical trials consistently demonstrate that olanzapine treatment increases the risk of significant weight gain, insulin resistance, hyperglycemia, and/or diabetes mellitus.

Id. at 28-29; Evid. Hr'g Tr. 363 (citing the "direct and indirect causal connection between the administration of olanzapine and [these] adverse effects"). In adults, substantial increases in risk are associated with "[w]eight gain of 5% or greater." Wirshing Decl. 10.

Dr. Wirshing confirmed that Zyprexa and clozapine are associated with greater weight gain than other antipsychotics. *See id.* (citing numerous studies). Zyprexa is "orexigenic; it causes people to eat more than they need." Evid. Hr'g Tr. 369. One study, for instance, found that over 10 weeks, patients on Zyprexa gained 9 pounds, an "astounding amount." Wirshing Decl. 10. On average, patients gain between one and two pounds per week during the first few weeks of treatment with Zyprexa; "they consume[] an excess of 3,500 to 7,000 kilocalories every week they were on the compound and that's a jaw dropping statistics [sic]." *Id.* at 366; *see id.* at 367 ("[I]t means you are consuming two-thirds more than you did the day before you took the drug."). Because of these side effects, Dr. Wirshing believes that "[o]lanzapine should not be used as a first-line drug of choice for the treatment of disorders for which it has been marketed." *Id.* at 364; 392.

As the chief of the Los Angeles VA's schizophrenia unit, Dr. Wirshing was in charge of the antipsychotic formulary for the entire medical center. *Id.* at 381. Because of Zyprexa's high cost—in 1998 it was the most expensive medication on the VA's formulary—and its associated weight gain (both approximately twice that of Risperdal, the next most expensive medication)—Dr. Wirshing, implementing his opinion that Zyprexa should not be used as first-line treatment, relegated Zyprexa to second-tier on the VA's formulary, requiring failure on risperidone first before olanzapine could be prescribed. *Id.* at 381-82.

b. Lilly's Knowledge of Zyprexa's Effects at Launch

Not only is olanzapine associated with weight gain and diabetes, but according to Dr. Wirshing, Lilly was aware of this link before Zyprexa's launch in 1996. Lilly knew that Clozapine and Risperdal, Zyprexa's predecessors and similar chemical agents, cause weight gain. As one of Zyprexa's own clinical trial investigators and former Lilly consultant, he opined that

"[t]he considerable risk of significant weight gain and its potential adverse effects on patients being given olanzapine was known to Lilly as early as 1995." *Id.* at 363, 396; Wirshing Decl. 49.

Dr. Wirshing himself had been "among the very first to report on the curious metabolic effects" of the new SGAs in the early to mid 1990s. Wirshing Decl. 5. During their clinical trials of atypical antipsychotics, his research group noticed that:

> {M]any of our patients gained weight when first begun on these drugs and at a rate that was, on occasion, singular in our experience. We also noted that these patients soon began to suffer the usual downstream consequences of gaining weight (e.g., glucose intolerance, frank diabetes . . . [W]e described our experience in the peer-reviewed literature, reported it at any number of scientific meetings, and discussed it with the manufacturers.

Id.; *see* Evid. Hr'g Tr. 451 (noting that a 1999 article about weight gain associated with Zyprexa only confirmed what "[t]hose of us in the field had been discussing . . . for years at that point.").

Lilly's own pre-FDA approval studies showed Zyprexa caused significant weight gain in many patients. "The controlled trials that Lilly had [prior to launch] suggested that [Dr. Wirshing's] numbers were pretty accurate: that there was weight shift on average of about 12 pounds in the . . . six to eight week" trials. Evid. Hr'g Tr. 368. Lilly's largest study to date, involving 1,996 patients with schizophrenia across the world, included 335 patients who took Zyprexa for a year and whose average weight shift was 24 pounds. *Id.* at 370-72; *see* Parts VI.A-B, *supra*. Despite knowing this information, Lilly only reported to the FDA the average weight shift at six months, which was approximately half of that observed at a year (5.8 kg vs. 24 lbs). Evid. Hr'g Tr. 379-80; *see also* Wirshing Slides at 2-12. In 1995, the company performed a review of its preclinical data, which showed that although Zyprexa seemed to lack neurotoxicity, it caused many patients to put on extra pounds. *See* Pfs.' Slides: Hr'g on Pfs.' Mot. for Class Cert.: William Wirshing M.D. at 7 [hereinafter "Wirshing Slides"]. The information made

available on the Zyprexa label in October 2007, opined Dr. Wirshing, consisted of the kind of data known to Lilly in 1996:

> It was completely in keeping with the work that we've talked about that we did dating back to 1994. So the drug has not changed in terms of the metabolic consequences it causes . . . .
> . . .
> [T]he information contained in the 2007 label could have been—I can go back to the 1996 data set and pull out those numbers and arrive at numbers that are within a fraction of a pound of the numbers that are listed in the current product labeling. There's been no evolution of [Lilly's] understanding about the temporal relationship between weight gain and the use of olanzapine. It's not like those data have been elaborated recently. Those data have been known since before the drug was marketed.

Evid. Hr'g Tr. 395-96.

Dr. Wirshing realized prior to Zyprexa's launch that "[t]here [was] no credible evidence that Olanzapine is more efficacious than typical or atypical psychotic medications." *Id.* at 363; *id.* at 385 ("The available evidence then . . . was that you can't demonstrate a clear superior efficacy for olanzapine."); *see also id.* at 362, 384-86. Lilly's own study, the largest to date, "failed to show superior efficacy." *Id.* at 385. It was Dr. Wirshing's view that "with the singular exception of clozapine, all of the other available antipsychotics, whether first or second generation, appeared to have . . . the same superiority or lack thereof in terms of efficacy or effectiveness." *Id.* at 363. It essentially becomes a "selection [of] toxicity, not . . . efficacies." *Id.* at 362.

c. Pricing of Zyprexa

Before Zyprexa was approved, Dr. Wirshing discussed the drug's launch price with Lilly officials. The only SGAs available on the market then were Clozaril and Risperdal; Zyprexa did offer some advantages over the two. Clozapine, while being the "most powerful antipsychotic on the planet earth," is "without question the most toxic," with "potentially fatal" side-effects. *Id.* at 442-43. "At the doses clinically used, Risperdal clearly has more incidence of EPS" than do the other SGAs. *Id.* at 443; *id.* at 369 ([Zyprexa] is not free of these [EPS] conditions but it is

substantially and measurably less than conventional drugs."). As a result, Dr. Wirshing opined, Lilly believed in "good faith" that Zyprexa justified a price premium over Risperdal:

> THE COURT: But was there at least, in your opinion, in your discussions with Lilly, a good faith marketing effort to price the drug at what they thought the value would be in the marketplace?
>
> THE WITNESS: In my opinion, absolutely. I mean, they were—were trying to price a drug which they felt, clearly felt, and I think they believed this, to be superior to the available technology at the time, which was risperidone. I didn't happen to share that opinion, but it's my belief that they had that opinion.

Id. at 402-03.

At the time, Dr. Wirshing advocated, as befitting his position overseeing the VA's formulary budget, that Lilly price the drug at a low cost on a per-patient, rather than per-dose, basis. A senior Lilly employee, he remembered, kept saying "premium drug, premium price," which to Dr. Wirshing suggested "they were gong to price it above risperidone." *Id.* at 389.

In Dr. Wirshing's opinion, olanzapine was "worth a premium by virtue of its toxicity above certain of the conventional drugs, but not as compared to risperidone." *Id.* at 389. He also noted that Seroquel in the dosages required cost more than Zyprexa for patients with schizophrenia. *See id.* at 407-08, 436 (Seroquel "is more expensive than clozapine," Risperdal, and Zyprexa, when it is dosed at high enough levels to "achieve an antipsychotic effect.").

5. Lon S. Schneider, M.D.

Dr. Schneider is a professor of psychiatry and behavioral sciences at the University of Southern California ("USC") Keck School of Medicine, where he has taught psychiatry and behavior sciences, neurology and gerontology for over twenty years. He is also a professor of gerontology at the USC Leonard Davis School of Gerontology. Decl. of Lon S. Schneider, M.D., at 3, Feb. 21, 2007, Docket Entry No. 100 ("Schneider Decl."). Dr. Schneider is a practicing geriatric psychiatrist; his clinical practice includes the diagnosis and treatment of patients with

dementia of various types, including Alzheimer's disease, behavior disorders, and psychosis. *Id.* He has published almost 200 peer-reviewed articles and many more academic writings. *Id.*

Dr. Schneider is presently the director of the psychiatry department at the Geriatric Studies Center; vice chief of psychiatry services at USC University Hospital; director and principal investigator of the USC Alzheimer's Disease Research and Clinical Center of California; and the clinical core director at USC Alzheimer's Disease Research Center. *Id.* He was the principal investigator in the Alzheimer's disease trial portion of CATIE ("CATIE-AD"), in which Zyprexa and other SGAs were evaluated for treatment of psychosis and agitation in Alzheimer's disease. *Id.* He has received consulting fees from Lilly and other manufacturers of antipsychotic medications. Schneider Decl. 6. Lilly paid him to participate in various meetings and advisory boards with respect to drugs in development for Alzheimer's disease, and to consult on design of and investigator training for two Zyprexa Alzheimer disease clinical trials. *Id.*

Dr. Schneider was asked by the plaintiffs to opine on the use of Zyprexa in elderly patients and efforts by Lilly to promote prescribing to elderly people and people with dementia. *Id.* at 2. At the evidentiary hearing, Dr. Schneider testified substantially as set forth in his previous report. *See id.* Lilly did not file a *Daubert* motion with respect to Dr. Schneider.

Based on his knowledge, experience, and review of the materials, Dr. Schneider opined that: (i) Lilly promoted evidence of efficacy and safety of Zyprexa for treating behavioral signs and symptoms in people with Alzheimer's disease and dementia that was misleading, *see* Schneider Decl. 14 ff.; (ii) despite knowing that its clinical trial results could not support a therapeutic claim in the FDA-approved label for efficacy for behavioral signs and symptoms associated with Alzheimer's disease, Lilly continued to advertise, promote and personally detail physicians that the drug was effective for such purposes, using the "Martha" patient profile toward

these efforts, *id.* at 21 ff.; (iii) between at least 1997 and 2003, Lilly published advertisements in geriatric medicine journals that advocated the use of Zyprexa, falsely and misleadingly implying its efficacy and safety for Alzheimer's disease, dementia, and behavioral symptoms in elderly patients, *see id.* at 30-38; and (iv) Lilly sponsored medical education meetings where the speakers were biased in favor of Zyprexa, touted its use for patients with dementia based on the results of a single positive trial, suppressed results of other negative trials, minimized adverse effects, and did not provide balance. *See id.* at 38-41; *see also* Abramson Rep. 62-66 (analyzing Lilly's marketing to the geriatric market).

Dr. Schneider also noted that he did not per se oppose off-label use of Zyprexa. But he emphasized that in order to properly prescribe off-label, physicians needed to be well informed—and that suppression or delay of related evidence or clinical trials could seriously mislead a doctor:

> Whether contemplating on- or off-label use, physicians also rely on personal experience, recommendations from colleagues and academics, educational seminars, and clinical trials evidence. This of course requires that they have access to that evidence. . . .

Schneider Decl. 11-12.

a. Use of Antipsychotics for Dementia and Alzheimer's

The majority of people with dementia, including Alzheimer's Disease, develop behavioral symptoms during the course of their illness, including agitation, aggression, delusions, and hallucinations. Schneider Decl. 7-8. Treatment of such people "is a difficult and challenging clinical problem for which there are no satisfactory pharmacological or non-pharmacological approaches that work for most people so afflicted." *Id.* at 8. Doctors use multiple medications to try to treat symptoms, including FGAs, SGAs, anti-anxiety, and anti-convulsants. *Id.* at 8. As Dr. Schneider noted,

> [That] so many medications have been used for this purpose demonstrates that there are no clearly good or universal choices. So does the fact that when these medications are used in attempts to treat behavioral signs and symptoms of dementia, they are being prescribed by physicians for "off-label" indications. If any of these medications could be shown to be safe and effective for this population of patients in adequate and well-controlled studies, then that medication's prescribing label most likely would contain that indication.

Id. at 8. Zyprexa's label currently carries a black box warning that it "is not approved for treatment of patients with dementia-related psychosis."

This is not for lack of trying; pharmaceutical companies, Lilly included, have sponsored trials intended to provide efficacy evidence for the FDA, but most results were not statistically significant. *Id.* at 11.

By 2000, Risperdal and Zyprexa became the dominant antipsychotics prescribed to nursing home patients, displacing FGAs, despite the limited efficacy. Schneider Decl. 12 (from July 1994 to March 2001, FGA market share dropped from 92% to 21%; in March 2001, SGAs had 79% market share). "The vast majority of nursing home residents prescribed these drugs did not have schizophrenia or bipolar disorder," and the vast majority—90%—of prescribing doctors were not psychiatrists, but generalists. *Id.* at 12-13.

b. Lilly's Misleading Marketing to Alzheimer's Patients

Dr. Schneider testified that "Lilly promoted misleading evidence of Zyprexa's efficacy and safety for treating behavioral signs and symptoms of Alzheimer's Disease by delaying or failing to publish results of clinical trials and through the Martha patient profile." Evid. Hr'g Tr. 484, 491; Schneider Decl. 15 ff.; *see also* Evid. Hr'g Tr. 493, 494, 495, 499, 505.

His opinions support Dr. Abramson's testimony; Dr. Abramson analyzed Lilly's internal marketing documents on geriatric use as supporting Dr. Schneider's conclusion about a program of Lilly to mislead. *See* Abramson Rep. 62-67; Part XVIII.A.6, *supra*.

At the evidentiary hearing, Dr. Schneider testified that at the time Zyprexa was launched "[t]here was no evidence known and I don't think there was evidence [that Zyprexa was effective in treating dementia]." Evid. Hr'g Tr. 484, 491; *see also id.* at 493, 494, 495, 499, 505. He further testified that despite a lack of evidence supporting the claim, "[Lilly] prepared materials suggesting that olanzapine was cognitively improving in, of patients with Alzheimer's disease." *Id.* at 501.

i. Delay of Clinical Trial Results

First, Dr. Schneider noted that although Lilly's HGAO study on use of olanzapine for Alzheimer's disease or dementia—apparently the first drug-company-sponsored trial of its kind—was completed in 1994, "[t]he results of that study still had yet to be published in the peer review journal" as of the writing of his report in early 2007, although a brief abstract had been published in a journal in 1995. *Id.* at 490; Schneider Decl. 14; *see* Abramson Rep. 64. In that trial, Zyprexa was not effective compared to a placebo. Schneider Decl. 15. Until 1999 there were no peer-reviewed published trials results available on the efficacy of SGAs in elderly people with dementia or Alzheimer's disease. *Id.* In October 2002, Lilly published the results of its HGEU Zyprexa trial for patients with Alzheimer's disease, with statistically significant results in favor of Zyprexa compared to a placebo. *Id.* at 15.

Because of the lack of availability of all clinical trial results, the geriatric community came to conclusions other than they would have had Lilly ensured full publication. As a member of the panel that drafted the 1997 *Practice Guidelines for the Treatment of Patients with Alzheimer's Disease and Other Dementias of Late Life*, Dr. Schneider declared that the recommendations were made without knowledge of Lilly's negative HGAO trial despite the trial having concluded in 1994:

Q: So if I understand it then, the negative HGAO study, at least the data for that, had been available for almost two years before this guideline was relegated, correct?
A: Yes.
Q: And the people, all of the people set forth in this practice guideline, none of them had available that data and that information for purposes of formulating guidelines that would be used for the treatment of those people, correct?
A: No—yes, we did not have that information . . .
. . .
Q: So if I understand it then . . . many doctors from around the country getting together, at least electronically, if not otherwise, trying to formulate guidelines for the treatment of Alzheimer's disease and other dementia items late-life seeking to get a hold of the best scientific information did not have access to the data from the HGAO study that had been around for two years at Lilly?
A: I believe that's the case.

Evid. Hr'g Tr. 548-49.

ii. Formation of "Martha" Patient Profile

The "Martha" patient profile was one of the ways that, according to Dr. Schneider, Lilly promoted misleading evidence of Zyprexa's efficacy and safety for treating behavioral signs and symptoms of Alzheimer's Disease. Schneider Decl. 21 ff. Lilly used "patient profiles" and gave them to their sales representatives for help detailing the product to doctors. *See* Zyprexa Patient Profiles, Pfs.' Ex. 480; Part XVIII.B.1.b, *infra* (describing the hypothetical patient profile of "Donna"). She is presented as a widow living independently, but at risk for nursing home placement because of agitation, restlessness and paranoia. *See* Zyprexa Patient Profiles 2.

> In sum, with the Martha spread, Lilly conflates various pieces of evidence—selected trials and evidence from patients with schizophrenia—to make up a story that Zyprexa is safe and effective for treating various behavioral symptoms in the elderly, including Alzheimer's disease, and improving the patients' cognitive function. In the spread, they show their intention to market this drug broadly to primary care physicians and elderly people generally. The primary care physician would interpret the Martha Spread as a claim that Zyprexa is effective for Alzheimer's disease and behavioral symptoms in old age.

Schneider Decl. 28-29.

iii. Ads in Geriatric Journals

During the late 1990s and early 2002, Lilly published Zyprexa advertisements in geriatric medical journals that, according to Dr. Schneider, were false and misleading, and which suggested that Zyprexa could be used for elderly people with dementia and people with behavioral signs and symptoms that have not been diagnosed. *Id.* at 30-38. Specifically, they "were intended to encourage geriatricians to prescribe Zyprexa for elderly patients with dementia and patients with undiagnosed behavior problems. The advertisements were not aimed at treating schizophrenia or bipolar illness." *Id.* at 30. He points to ten advertisements as examples, one of which being the following:

> Advertisement #3 states, "For your patients with SYMPTOMS and BEHAVIORS related to Psychotic Disorders . . . " and then follows with, "Goals of Therapy: symptoms and behaviors STABILIZE hostility, hallucinations, delusions; the Zyprexa Profile MAXIMIZE tolerability, ease of use, safety; on additional benefits CAPITALIZE benefits for depression, anxiety, social withdrawal, cognition." The front page goes on to say in small print, "In 6-week acute phase trials, the most common treatment emergent adverse events associated with Zyprexa was somnolence . . ." The second page with fine print on prescribing information under Indications and Uses is only that Zyprexa is "for the management of the manifestations of psychotic disorder." Advertisement #3 ran in *Journal of American Geriatrics Society Clinical Geriatrics* on a nearly monthly basis from July 1999 to August 2000. In October and November 1999, and July and August 2000, the advertisement appeared in *Annuals of Long-Term Care: Clinical Care and Aging.*

Schneider Rep. 31.

Dr. Schneider's conclusion was that:

> Taken together, these advertisements were meant to sell Zyprexa to nursing home physicians for nursing home patients and to encourage the prescribing of Zyprexa for elderly patients with nonspecific behavioral problems and dementia. The advertisements were important components of a "Long Term Care: Zyprexa Marketing Strategy7' (Plaintiffs' Exhibit No. 05843, Bates ZY1 00174845) that promoted Zyprexa for off-label uses in elderly people including a "wide range of symptoms, control of agitation and aggression, control of dangerous and inappropriate behaviors, does not impair cognition, [has] long term efficacy, . . . helps patients think more clearly (cognition story), patients interested in activities . . . ," and without scientific evidence for any of this.

Id. at 38.

This and other testimony and physical exhibits would support a finding that Lilly deliberately misled debtors and others, leading to overpayments by class members.

iv. Geriatric CMEs

Lilly-sponsored Continuing Medical Education ("CME") meetings, in Dr. Schneider's opinion, inappropriately promoted Zyprexa for use in the elderly to physicians and pharmacists by highlighting the drug, talking more about it and less about alternatives, and not providing fair balance. A physician attending these sessions would gain a misleading impression of Zyprexa's efficacy and safety. Schneider Decl. 38-41.

Dr. Abramson's report noted Lilly's marketing materials included "Strategy 1 in accomplishing this goal is to 'Establish Zyprexa as a first line choice in the treatment of the adult patient who is experiencing behavioral or cognitive symptoms-but is functioning well enough to live independently.' Handwritten on this document: 'Need to balance off label/symptoms and behaviors,' clearly showing that Lilly was aware that its 'Strategy l' involves active marketing of Zyprexa off-label." Abramson Rep. 63. Only "[t]wo studies [HGAO and HGEU] of the efficacy of Zyprexa in treating behavioral disorders in the elderly had been completed at that point." *Id.*

6. John Abramson, M.D.

Dr. Abramson is a medical doctor and clinical instructor at Harvard Medical School. He is board-certified in Family Medicine and also has a Master of Sciences degree in Family Practice. Pfs.' Witness Statements; Expert Rep. of John Abramson, M.D., Feb. 28, 2007, Docket Entry No. 97 ("Abramson Rep."), at 4. For twenty years he practiced family medicine, and from 1994 to 2001, he was Chair of the Department of Family Practice at the Lahey Clinic in Massachusetts. *Id.* Between 1986 and 1993, he served as Associate Medical Director of Pru-Care of Massachusetts, and is currently the Executive Director of Health Management for Acordia

Complete Health, a Wells Fargo Company, where he designs health benefits for self-insured companies. *Id.* at 5. Since 2002, Dr. Abramson has concentrated full time on his research, which focuses on how "the information and misinformation about drugs and other medical products available to practicing physicians impacts their medical decisions and the overall quality, effectiveness, and cost of American health care." He has published multiple works on the subject. *Id.* at 6.

He testified substantially as forth in his previous report. *See* Abramson Rep. Lilly's *Daubert* motion to exclude Dr. Abramson's report and testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007). He addressed the issue of how pharmaceutical-sponsored research and marketing affects doctors' decisions, patients' expectations and the overall quality and effectiveness of medical care. His opinion was that: (i) Lilly systematically maximized Zyprexa sales by influencing the sources of information that doctors are trained to trust, including scientific research, guidelines, continuing medical education, "thought leaders" and public advocacy groups, and marketing through drug representatives, (ii) much of Lilly's off-label marketing campaign was informed not by sound scientific studies of the benefits of Zyprexa, but by marketing studies designed to determine the most effective ways to convince doctors to prescribe Zyprexa rather than the most effective ways to treat patients, and (iii) Lilly influenced purchasers and policy makers with claims of clinical and economic superiority, neither of which have stood up to non-Lilly sponsored scrutiny. *See* Abramson Rep. *passim*.

In sum, it was Dr. Abramson's view that in the current commercially-dominated pharmaceutical arena, drug companies are able to turn medical data into brand messages. *See* Part IV.C, *supra* (describing drug company marketing influence over many sources of information).

Because medical education gets mixed with drug marketing, the scientific message is corrupted. Evid. Hr'g Tr. 740. Doctors themselves are often unaware of the extent of commercial influence on information they believe to be objective and subsequently find is biased and misleading.

a. Lilly's Influence over All Sources of Drug Information

Dr. Abramson testified that "Lilly systematically maximized Zyprexa sales by influencing the sources of information that doctors are trained to trust, including scientific research, guidelines, continuing medical education, 'thought leaders,' and public advocacy groups and marketing through drug representatives." *Id.* at 715; *see also* Pfs' Slides: Hr'g on Pfs.' Mot. for Class Cert.: John Abramson, M.D. at 2 ("Abramson Slides"). During direct questioning, he stated:

> Q: And you've identified here today the various channels of information that have been available to physicians to acquire information about the use of olanzapine, correct?
> A: Correct.
> Q: And didn't you reach an opinion that every area of information that might be available to physicians, whether they're psychiatrists or primary care physicians, . . . geriatric practitioners, was subject to the influence by Lilly?
> A: I did reach that opinion.

Evid. Hr'g Tr. 768-69.

Many sources of information contribute to the decision making of doctors. But over the past thirty years, the production and dissemination of medical knowledge about drugs and medical devices has been largely privatized. *Id.* at 716. Doctors should be, but often are not, aware of this commercial filter. *Id.* at 729. The system now depends on fair balance from, and truthfulness of, pharmaceutical companies themselves. *Id.* In sum, "[h]ealth policy decisions can be no better than the scientific evidence available to decision-makers. As shown above, it can no longer be assumed that the 'scientific evidence' is complete, unbiased, or represents the best possible information." Abramson Rep. 21.

b. Off-Label Promotion Informed by Marketing Studies

Dr. Abramson testified, "[m]uch of Lilly's off-label marketing campaign was informed not by sound scientific studies of the benefits of Zyprexa, but by marketing studies designed to determine the most effective ways to convince doctors to prescribe Zyprexa rather than the most effective ways to treat patients." *See* Abramson Slides at 2; *see also* Evid. Hr'g Tr. 715. In Dr. Abramson's opinion, Lilly engaged in a campaign of off-label marketing to primary care doctors, including Alzheimer's doctors, which was driven by marketing, not scientific research. Evid. Hr'g Tr. 749. Primary care doctors are particularly vulnerable to such marketing campaigns. *Id.* at 750. The marketing was designed to convince doctors that Zyprexa would enhance the doctor-patient relationship. *Id.* at 752. The marketing also targeted symptoms. *Id.*

In particular, Dr. Abramson analyzed Lilly's "Viva Zyprexa" marketing campaign targeted at primacy care doctors, which was launched at a national sales meeting in March 2001. *See* Part IX.A, *supra*; Evid. Hr'g Tr. 754. The focus of the campaign was to target symptoms, not diagnoses. *See id.* at 756 (quoting Lilly's "Zyprexa Implementation Guide" as stating that "in order to succeed in the primary care market we must focus on symptoms and behaviors that are found with mood, thought and behavioral disturbances."). After reviewing the marketing documents produced during discovery, including Zyprexa Implementation Guide, the "Zyprexa Surround Sound Marketing" document, Evid. Hr'g Tr. 738; Abramson Rep. 41, multi-page detail aids, Stat-Grams, and John Q. Public letters, Evid. Hr'g Tr. 747, he opined that the Viva Zyprexa drug detailers had been trained to provide information that is not honest and masked real risks. Evid. Hr'g Tr. 761. The campaign exploited doctors who desperately wanted to help patients in difficult circumstances for which there is no good solution and held out false hope. *Id.* at. 759.

Lilly first educated doctors on schizophrenia and bipolar treatment, and then switched to ordinary symptoms to enormously expand the potential range of customers for Zyprexa. *Id.* at 753-54.

On cross examination, Abramson said that for each new indication, the FDA must receive a supplemental NDA. *Id.* at 776. The dramatic expansion he referred to in 2000 occurred right after Zyprexa's indication for bipolar mania was approved. *Id.* at 777. According to Lilly's own market research, 100% of doctors associated Zyprexa with diabetes by 2001. *Id.* at 789. Lilly justified emphasis on prescribing for symptoms by its contention that it often takes seven to ten years for bipolar patients to be correctly diagnosed and that marketing to primary care doctors was required since psychiatrists are not always easily available to diagnose bipolar and schizophrenia diseases. *Id.* at 800.

c. Lilly's Claims of Zyprexa Superiority Have Been Proven False

Dr. Abramson's view was that Lilly influenced purchasers and policymakers with claims of clinical and economic superiority, neither of which have stood up to non-Lilly sponsored scrutiny. *Id.* at 715. He highlighted the fact that Lilly misrepresented information about Zyprexa for years despite warnings from the FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC"):

> And they describe three properties of atypicals including Zyprexa, of course. One is broad efficacy in treating negative as well as positive symptoms. DDMAC has said that they can't make comparative claims . . . . DDMAC has objected to comparative claims.
> One is greatly reduced risk of extrapyramidal side-effects and tardive dyskinesia. And DDMAC has taken exception to that claim.
> . . . the third point that's made in the primary care implementation guide is "neutral clinical impact on prolactin." And that claim is disallowed or not substantiated by the information about prolactin in the label.

Id. at 748.

It was Dr. Abramson's testimony that "Lilly created articles and marketing materials that made Zyprexa appear cost effective for managed care organizations and formularies." Abramson Slides at 5. In support of this opinion, he referred to two studies published in 1999 that "created a knowledge base that showed that using Zyprexa is cost effective compared to using first generation antipsychotics." *Id.* at 732. These two publications, based on the same study (Lilly's ICT study, *see* Rosenheck Decl. 8-9), suffered from methodological problems that were not known to the public until years later, in 2006, when a review article was published in the American Journal of Psychiatry. Evid. Hr'g Tr. 732-33. The 2006 article determined that "there is no clear evidence that atypical antipsychotics generate cost savings or are cost-effective in general use among all schizophrenia patients." *See* Abramson Slides at 30.

As of 2000, the "Zyprexa Product Team," with a "commercialization focus," had already published "over 125 full length manuscripts" in medical journals and in addition there were more than "100 recent manuscripts currently in play (i.e., under review ready for submission, etc) including proposed data mining papers." Abramson Rep. 30. 1999 Lilly studies had shown Zyprexa to be cost-effective. Evid. Hr'g Tr. 723. Formulary committees from 1999 to 2006 would have thought Zyprexa was cost-effective based on these reports. *Id.* at 733. "The three earliest studies of Zyprexa versus a first generation antipsychotic (FGA) [including the North American Double-Blind Olanzapine Trial and the International Collaborative Trial ("ICT")], all funded by Lilly, showed significant advantage of Zyprexa over haloperidol." Abramson Rep. 27. These studies were misleading according to plaintiffs' experts. *See* Rosenheck Decl. 8 ff.

B. Other Plaintiffs' Experts

1. Steven Klotz, M.D.

Dr. Klotz is a private practice psychiatrist, board-certified in Psychiatry, whose practice focuses on adult, child, and adolescent psychiatry. *See* Decl. of Steven Klotz, M.D. 4, Feb. 22, 2007, Docket Entry No. 99 ("Klotz Decl."). Lilly's *Daubert* motion to exclude Dr. Klotz as an expert was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007). Dr. Klotz reviewed the marketing materials and "diagnostic" instruments distributed by Lilly sales representatives to primary care doctors ("PCPs"). He then analyzed whether those materials conformed to and were appropriate diagnostic tools for Zyprexa's FDA-approved indications and found them misleading. *See* Klotz Decl. at 2.

Lilly marketed Zyprexa to PCPs as well as to psychiatrists to reach a greater number of potential prescription writers, *id.* at 5; many people, in fact, are given antipsychotic medications without a psychiatric examination. The accuracy of mental health diagnoses made by primary care doctors without the specialized training and experience of psychiatrists, however, often is questionable, as Dr. Klotz noted. Lilly's marketing documents took advantage of this lack of studied expertise, leading PCPs to prescribe Zyprexa to patients for whom the antipsychotic was not appropriate. *Id.* at 7.

In Dr. Klotz's opinion, Lilly's PCP marketing campaign was designed to encourage primary care physicians to overdiagnose bipolar disease and to prescribe Zyprexa for symptoms—not FDA-indicated diagnoses—while minimizing Zyprexa's severe side effects. *Id.* at 8. As examples, Dr. Klotz points to Lilly's Mood Disorder Questionnaire ("MDQ"), a screening instrument offered to PCPs, and to sales representatives' use of the "Donna" patient profile when detailing PCPs. *Id.* at 7; *see* Eli Lilly & Co., Mood Disorder Questionnaire.

a. Lilly's Mood Disorder Questionnaire ("MDQ")

To encourage prescriptions of Zyprexa, Lilly distributed the MDQ, originally designed by Dr. R. Hirschfeld, to primary care physicians. The hand-out contained a series of questions Lilly indicated were to help diagnose the person filling out the questionnaire. Eli Lilly & Co., Mood Disorder Questionnaire. The MDQ instructed physicians they "have a positive screen if the patient answers . . . 'Yes' to seven or more of the 13 items in question 1 AND . . . 'Yes' to question 2." *Id.* at 2.

In Dr. Klotz's view, Lilly's promotion of the MDQ as Zyprexa prescription aid was misleading: "Screening instruments are not diagnostic instruments. They suggest that a patient in a selection group should receive further evaluation or referral to a specialist if the diagnosis is outside the realm of expertise of the clinician. Screening instruments in no way suggest treatment." Klotz Decl. 11. The MDQ "does not discriminate between subtypes of bipolar disorder" and "is insufficient to differentially diagnose active bipolar mania from phenotypically similar illnesses." *Id.* at 10-12. Although Zyprexa is only FDA-approved for certain types of bipolar disorder, the MDQ implies that Zyprexa is appropriate for all bipolar types. Assuming Lilly's marketing materials promoted the message that if you have the disease, you need the medicine, that would be "unsupported in the literature and medically inappropriate." *Id.* at 12. Dr. Klotz went as far as calling use of the MDQ "dangerous." *See id.*

These limitations on the sensitivity and applicability of the MDQ did not stop Lilly from encouraging primary care physicians to diagnose serious psychiatric illnesses using this thumbnail questionnaire: of the 100,000 call notes produced in this litigation (0.7% or less of the total number of call notes Lilly has for Zyprexa), approximately 3,000 entries mention the MDQ.

b. Lilly's "Donna" Patient Profile

Lilly's marketing materials also present a patient profile of an abstract "Donna," which was constructed to exemplify and detail the symptoms and history of a hypothetical patient who was suffering from a mental illness that should be treated with Zyprexa. *See also* Part XVIII.A.5.b.ii, *supra* (describing the hypothetical older widow "Martha" profile used to market to the geriatric market). Lilly's marketing materials described "Donna" as a mother of two children in her early 30s who is "unable to focus," has "depressive symptoms" and cannot "get on with her life." She chiefly complained of sleeping too much and having trouble concentrating at work and home. Donna had been on SSRIs for depression in the past but has never been prescribed an antipsychotic. Primary care physicians were encouraged to prescribe Zyprexa to help people like Donna deal with symptoms of mood, anxiety, and disrupted sleep. Eli Lilly & Co., Primary Care Sales Force Resource Guide (June 2002).

In Dr. Klotz's opinion, Lilly's patient profiles, including Donna, "lack sufficient information to suggest a treatment trial that begins with Zyprexa." Klotz Decl. 13-14. Using only the information in the Donna profile would be "medically insufficient to determine that Zyprexa, or any antipsychotic, were indicated." *Id.* at 13. Moreover, there is no evidence that Zyprexa has any mood-stabilizing effects. *Id.* at 12. (A mood stabilizer is "a compound that when taken prevents both depressed mood and mania or euphoric mood elevations." *Id.*)

Dr. Klotz concluded that: (i) Lilly's marketing to primary care physicians fostered a variety of misconceptions which would have led to the inappropriate treatment by primary care physicians with Zyprexa; (ii) the promotion of Zyprexa for use in the bipolar depressed phase was not indicated and Lilly utilized a variety of misleading marketing materials that would have encouraged that use; and (iii) "the use of Zyprexa in children is not warranted, supported or

necessary," *see id.* at 16; moreover, the incidence of schizophrenia and bipolar in children is actually very low. *Id.* at 15.

2. Plaintiffs' Medical Experts

Plaintiffs also relied upon the following reports submitted in other phases of the Zyprexa litigation:

a. David B. Allison, Ph.D.

Plaintiffs' expert Dr. Allison is a professor in the department of biostatistics, head of the section of statistical genetics and director of the National Institute of Health-funded Clinical Nutrition Research Center at the University of Alabama in Birmingham, Alabama. In his report, Dr. Allison presented his opinion that: (i) antipsychotic drugs and especially the atypical agents generally induce significant weight gain after only a few months of treatment; (ii) among atypical antipsychotics, olanzapine produces more weight gain than all other drugs with the exception of clozapine; (iii) there are FDA-approved atypical antipsychotic drugs that cause little to no weight gain; (iv) the antipsychotic-induced or olanzapine-induced weight gain is at least as deleterious as other weight gain; and (v) it is a misapprehension to believe that weight gain response to olanzapine is correlated with a therapeutic response. *See* Expert Witness Rep. & Decl. of David Allison, Ph.D., Feb. 12, 2007 ("Allison Decl.").

Lilly did not file a *Daubert* motion with respect to Dr. Allison.

b. Fredrick Brancati, M.D., M.H.S.

Plaintiffs' expert Dr. Brancati is a professor of medicine and the director of the Division of General Internal Medicine at the John Hopkins School of Medicine, holding a joint appointment in epidemiology in the John Hopkins University Bloomberg School of Public Health. Dr. Brancati opines that: (i) the available peer-reviewed scientific evidence demonstrates that Zyprexa

and a number of other atypical antipsychotic medications are associated with an increased risk of type II diabetes; and (ii) the propensity of individual atypical antipsychotic agents to cause weight gain (in order: clozapine, Zyprexa, Risperdal, Seroquel, Abilify, Geodon) appears to mirror their risk for glucose dysregulation and type II diabetes. *See* Expert Witness Rep. & Decl. of Frederick Brancati, M.D., M.H.S., Feb. 12, 2007.

Lilly did not file a *Daubert* motion with respect to Dr. Brancati.

c. David Goff, Jr., M.D., Ph.D.

Plaintiff's expert Dr. Goff is a professor in the Division of Public Health Sciences, Department on Epidemiology and Prevention in the Department of Internal Medicine at Wake Forest University School of Medicine in Winston-Salem, North Carolina. He is also the director of the schizophrenia program at Massachusetts General Hospital. Dep. of Donald C. Goff at 9, Nov. 14, 2006 ("Goff Dep."). He is a clinician who prescribes atypical antipsychotics and testified that he prescribes a pharmaceutical every time he sees a patient. *Id.* at 11-12. Dr. Goff found that: (i) the use of olanzapine is specifically associated with an increased risk for diabetes; (ii) the strength and consistency of this evidence is striking; and (iii) there is evidence showing that correct temporality, a dose-response relationship and potential mechanisms of action demonstrate that olanzapine can cause diabetes mellitus. *See* Expert Report of David C. Goff, Jr., M.D., Ph.D., Feb. 12, 2007 ("Goff Rep.").

Lilly did not file a *Daubert* motion with respect to Dr. Goff.

d. John L. Guerigian, M.D.

Dr. Guerigian is a medical doctor, currently employed at PharmaGenesis, Inc., a pharmaceutical consultancy in which he works with pharmaceutical experts worldwide. Previously he was a medical officer for twenty years at the FDA assisting in the discovery,

development, and/or market introduction of a number of important drugs. In his report, Dr. Guerigian concludes that: (i) olanzapine can cause diabetes and its consequences or be a substantial contributing factor in the development of diabetes in some individuals; (ii) olanzapine increases the risk of diabetes and its consequences more than other atypical antipsychotics (other than clozapine) and thus the risk of diabetes with olanzapine is not "comparable" with other atypical antipsychotic drugs as claims by Lilly; (iii) internal Lilly documents demonstrate the company had credible scientific evidence in its possession since at least 1995 that the use of olanzapine was correlated with both weight gain and hyperglycemia; (iv) internal Lilly documents demonstrate the company had credible scientific evidence in its possession that weight gain and diabetes were inter-related and would thus act concurrently to increase the frequency of diabetes, its complications, and cardiovascular disease (which happens to be the number one cause of death in patients with diabetics); (v) Lilly's clinical studies were flawed by the use of imperfect methodologies, in particular the use of random blood glucose tests as opposed to the use of other more reliable methods of testing for hyperglycemia; (vi) internal Lilly documents demonstrate that the company delayed communicating essential data to regulatory agencies and resisted their requests to change the olanzapine label; (vii) internal Lilly documents demonstrate that the company did not act as a reasonably prudent manufacturer in that Lilly did not take the initiative of voluntarily adding to the label information needed by prescribers and indeed ignored internal and external expert advice to warn physicians about the risks of diabetes; (viii) internal Lilly documents demonstrate that the company trained its representatives to mislead prescribers about the risks and benefits of olanzapine; (ix) Lilly failed to adequately warn physicians of critically important information regarding the risks of olanzapine that were reflected in its own internal documents and in published medical literature; and (x) Lilly compounded the danger of failing to

adequately warn prescribing doctors about the risks of olanzapine by over-promoting the drug. *See* Rep. of John L. Gueriguian, Feb. 12, 2007.

Lilly's *Daubert* motion with respect to Dr. Guerigian was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

e. Laura Plunkett, Ph.D., D.A.B.D.

Plaintiffs' expert Dr. Plunkett is a pharmacologist, toxicologist, FDA regulatory specialist and principal of a consulting company known as Integrative BioStrategies, LLC. In her report, she declared that: (i) it is clear that Zyprexa use is associated with an increased risk of adverse metabolic effects that include clinically significant weight gain and diabetes; (ii) these effects of Zyprexa were predictable based on the pharmacological profile of the drug; (iii) adverse metabolic effects can be pronounced with both short and longer term use of the drug; and (iv) at the time that Lilly failed to change its labeling language to warn of risks it was aware of to patients for hyperglycemia and potentially diabetes, Lilly was widening its marketing of the drug from psychiatrists to general medicine physicians. *See* Expert Statement of Laura M. Plunkett, Ph.D., DABT.

Lilly's *Daubert* motion with respect to Dr. Plunkett was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

C. Defense Witnesses at Hearing

Defendant Lilly proffered two witnesses at the certification hearing: Dr. Eugene M. Kolassa, Evid. Hr'g Tr. 553-707 (Apr. 1, 2008), and Dr. Iain M. Cockburn, *id.* at 811-925 (Apr. 2, 2008). Both defendant's experts met *Daubert* and Rule 702 standards.

1. Eugene M. Kolassa, Ph.D.

Dr. Kolassa is a health economist with thirty years of experience in the field of pharmaceutical marketing and economics. He is the Chief Executive Officer and Managing Partner of Medical Marketing Economics, LLC, a consulting firm providing advice and training in the fields of pricing, marketing, and market analysis in health care markets. Dr. Kolassa also serves as Adjunct Professor of Pharmacy Administration at the University of Mississippi and as Adjunct Professor of Pharmaceutical Business at the University of the Sciences in Philadelphia. He has written and lectured extensively on the topics of pharmaceutical marketing and pricing, and the value of pharmaceuticals in the health care system, including authoring the book *Elements of Pharmaceutical Pricing* (1997), and coauthoring *Pharmaceutical Marketing: Principles, Environment, and Practice* (2002). *See* Kolassa Decl. 1.

In his declaration and at the evidentiary hearing, Dr. Kolassa presented his conclusions on several different issues, including: 1) the unusual nature of the pharmaceutical market; 2) the commonality of the proposed subclasses; 3) plaintiff's experts' determination of loss; 4) general rules of pharmaceutical pricing; and 5) pharmaceutical price elasticity.

a. Nature of the Pharmaceutical Market

Dr. Kolassa pointed out that the pharmaceutical market operates very differently from other markets and involves unique distribution and financial aspects. Typically, a consumer purchases a product from either the manufacturer itself or a distributor; in contrast, a consumer *cannot* purchase a prescription drug directly from the manufacturer. The patient must obtain the drug from a pharmacy or its equivalent and only then with a valid prescription from a licensed physician. Each physician makes clinical decisions regarding the appropriateness of a specific medicine based on a patient's individual needs and expected response to the agent selected, which varies considerably in the case of antipsychotic agents. *Id.* at 2.

b. The Commonality of the Proposed Subclasses

Dr. Kolassa also opined that the proposed consumer and third-party subclasses are lacking in commonality. Among third-party payors, access to and use of information about Zyprexa differs substantially, as does the degree to which they, individually, made any decisions regarding reimbursement for antipsychotics. *Id.* Patients also differ substantially and cannot be viewed as a group of similarly situated individuals. Differences in diagnoses, treatment history, insurance coverage, and co-payments make a common measure of "damages" impossible to quantity. In addition, prescribing physicians differ in knowledge levels and treatment approaches to mental illnesses. *Id.* at 2-3.

c. Plaintiff's Experts' Determination of "Loss"

Plaintiffs' methods for establishing "value," "actual worth" or "willingness to pay" were criticized by Dr. Kolassa. *See id.* at 3 ff. He believes that Dr. Rosenthal's determinations of loss of value for Zyprexa, computations of "excess sales" of Zyprexa caused by Lilly's alleged conduct, and calculation of damages "are neither consistent with marketplace realities nor the application of rigorous and accepted analytical techniques." *Id.* at 3. Her reliance on the CATIE study for comparative information "is totally inappropriate." Moreover, Dr. Kolassa takes issue with the plaintiffs' global approach to damages, opining that a "loss of value" approach requires individual damages assessment for each patient and payor.

d. General Rules of Pharmaceutical Pricing

Dr. Kolassa has established a set of pricing guidelines that have been widely adopted in the pharmaceutical marketplace. *Id.* at 4 (citing E.M. Kolassa, *The Elements of Pharmaceutical Pricing* (1997)). In setting the price for a prescription drug, manufacturers consider a variety of factors, including:

1. The existence and price of competitive products and the pricing behavior of the firms that sell them (i.e., how competitor respond to pricing actions).
2. The clinical, economic and social value offered by the medicine, both substantively and in economic terms.
3. Plaintiff population characteristics, such as age, common co-morbidities, and prescription drug coverage.
4. The factors that physicians will likely consider in determining whether to prescribe the medicine, and the degree to which the price may affect that decision.
5. Disease characteristics (e.g., chronic or acute; debilitating or cosmetic).
6. The reimbursement environment—how a product is likely to be reimbursed by payors— and issues in the specific market for the product.
7. Public relations and public policy concerns over pricing.
8. The needs and ability of the manufacturer, including overall corporate strategy, market positioning for future performance, and the availability of internal resources to support its pricing strategy.

See id. at 4-5.

e. Pharmaceutical Price Elasticity

Dr. Kolassa described the wide discretion pharmaceutical companies have in the United States for setting and maintaining prices of their patented products. *See* Part IV.A, *supra*. Because most pharmaceutical markets, including the market for antipsychotic medications, are relatively inelastic (unit sales are not responsive to most price changes), manufacturers almost never lower a drug's wholesale price, even when new information, positive or negative, is

revealed; rather, they generally increase the prices of their products. *Id.* at 7 ("When a manufacturer learns that unexpected safety issues or other negative factors for their products emerge, the manufacturer does not lower the price to reflect a change in value. In fact, if such information is expected to result in a decrease in unit sales, the result is often more aggressive price increases, to compensate for that decrease and to protect revenue."). A change in value of a product does not usually result in a change in its price. Because medicines offer economic value considerably higher than the prices that are charged for them, Dr. Rosenthal's analysis, rooted in the hypothesis that the price of a medicine bears a direct and close correlation to its value, is "fundamentally unsound." *Id.* at 3.

The price of Zyprexa was set upon its launch into the marketplace and was increased regularly, according to Lilly's internal policies that were applied to the majority of its products. The price of Zyprexa increased more rapidly after the September 2003 label change and the publication of the CATIE study. *Id.* at 8.

Dr. Kolassa acknowledged, during questioning by the court, that

> A: . . . these products differ so much that generally the payor is going to say that I can't just automatically exclude one because the patients need that and, so, it really has to do with the therapeutic aspects and the clinical aspects of that market. Whereas in others, they're freer to [distinguish between drugs and impose restrictions].
> . . .
> The Court: In effect, these third-party payors are saying it's up to the doctor to decide with the patients we're just going to go along, right? . . .
> A: Yes, pretty much, because and, again, because they see the products as different and they don't want to deny that. I've actually spoken with P and T committee directors specifically about this in this category and he [sic] said our belief was every one of these products needs to be made available.

Evid. Hr'g Tr. 695.

As Dr. Kolassa explained, new indications for competitor drugs can create a 'halo effect;' a new indication can "signal to the marketplace that [doctors] might be comfortable in trying these products in other [off-label] areas as well." *Id.* at 601.

For Dr. Kolossa, "the primary principle that should guide every pricing decision is that the price should reflect the value of the product to the customer . . . The physical product itself should have clinical and economic value." E.M. Kolassa, *Pharmaceutical Pricing Principles*, *in* Pharmaceutical Marketing: Principles, Environment, and Practice (M.C. Smith & E.M. Kolassa, et al., eds. 2002). His chapter "Pharmaceutical Pricing Principles" in "Pharmaceutical Marketing: Principles, Environment, and Practice" then goes on to discuss "the factors that should be considered when making pricing decisions" which include "the economic and social value of the therapy itself." *Id.* at 189. And Dr. Kolassa acknowledges that simply because a product is new, or because it has some different mechanism of action, does not necessarily mean that the product has a greater value or should be priced at a higher level. Dr. Kolassa, a recent lecturer to Lilly's "senior pricing people," summarized the pricing issue well:

> But what the market values, and what should be priced, is not the mechanism of action or unique chemical structure, but the outcome of the therapy, the end result, and how that differs from competitive products. When a product delivers better outcomes, it deserves to be priced at a premium relative to competitors. Should the outcomes not differ from competitive products, a parity price is in order. Worse relative outcomes should be reflected by a price that is lower than prevailing levels.
>
> Setting the price according to the relative value of the product is pricing at its most basic and most logical.

Kolassa, *Pharmaceutical Pricing Principles*, at 211-12; *see also* Evid. Hr'g Tr. 649. Dr. Kolassa has made the same point elsewhere. *See, e.g.*, Slides of E.M. Kolassa "Eli Lilly Comprehensive Strategic Pricing" MME00861-2, Kolassa Dep. Ex. 5 ("Understanding Value . . . Value-based pricing is more than a buzzword; it is an important business tool and the most profitable method for reaching pricing decisions."); Slides of E.M. Kolassa "Eli Lilly Comprehensive Strategic

Pricing" MME00864, Kolassa Dep. Ex. 5 ("Value Comparisons . . . The value in which we should be most interested is the incremental value a new product will bring to the market"); E.M. Kolassa, Elements of Pharmaceutical Pricing 88 (1997) ("The economic value of the new product is the difference between the two treatment approaches: the cost of the original treatment minus the cost of treatment with the new product. Ideally, the treatment with the new product results in lower costs than treatment without it. The alternative, that treatment with the new product is more costly than treatment without, requires serious decisions about the launch of the product.").

In emphasizing value to the consumer as the basis for pricing, Dr. Kolassa joined issue with plaintiffs' experts who used this same assumption about principles but concluded that Lilly's estimate of value, compared to other drugs of the same class, was grossly excessive.

2. Iain M. Cockburn, Ph.D.

Defense expert Dr. Iain Cockburn is a Professor of Finance and Economics at the School of Management at Boston University and experienced in the field of pharmaceutical pricing and delivery. He has a Ph.D. in economics from Harvard University.

Dr. Cockburn was asked to review the work and analysis of plaintiff's economic experts, Dr. Rosenthal and Dr. Harris. Specifically, he addressed the question of the reasonableness of their analysis and conclusions. He did not himself conduct any econometric studies of the price and quantities in the antipsychotic market. Evid. Hr'g Tr. 814. He submitted an expert report, then supplemented it. *See* Cockburn Rep.; Cockburn Supp. Rep.; Evid. Hr'g Tr. 815.

Like Dr. Berndt, Dr. Cockburn agrees that the statistical and health economics methodologies used by Dr. Rosenthal and Dr. Harris are well-accepted in the field of health economics. Among other criteria, a "willingness to pay" approach is a proper method to perform damage calculations. Although Dr. Cockburn attempted to criticize the implementation of

econometrics by Dr. Rosenthal and Dr. Harris in their price analyses, Dr. Cockburn did not perform his own damage analysis. As a result, because he had been instructed not to perform any calculations in order to determine whether or not his criticisms of Dr. Rosenthal and Dr. Harris supported Lilly's position, his opinion (that different results might be reached with the tweaks he suggests) is speculative. Nevertheless, plaintiffs' *Daubert* motion to exclude Dr. Cockburn's expert report and testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

At the evidentiary hearing, Dr. Cockburn testified that he believed Dr. Harris and Dr. Rosenthal's price comparators are unreasonable and arbitrary, Evid. Hr'g Tr. 838; they did not model price setting behavior; manufacturers have wide latitude in setting price; and pricing of Zyprexa and Risperdal have not changed relative to each other since launch. *Id.* at 840. If Lilly had known of the adverse side effects in 1996, Zyprexa might have been priced even higher because of the smaller target group. *Id.* at 841. Dr. Cockburn summed up his view of why the market is so complex: the diseases it is designed for are hard-to-diagnose and treat, and the market has changed constantly with new entrants and new labels. *Id.* at 818.

Dr. Cockburn noted that any analysis of what was causing the change in Zyprexa off-label use would require studying not just other drugs in the antipsychotic class, but "what is going on in other drug classes" where there are alternatives (including on-label options) to off-label prescribing of an antipsychotic. *Id.* at 867.

a. Criticism of Dr. Rosenthal's Analysis

In criticizing Dr. Rosenthal's off-label quantity theory, Dr. Cockburn emphasized the impact of promotion on sales. Dr. Rosenthal is wrong to assume that all the promotional effort directed at, for example, primary care doctors were attempts to persuade them to write off-label

prescriptions, *id.* at 852, and that all the money in draft budget was actually spent; she assigns a value of zero for use of Zyprexa off-label, but off-label use is quite widespread since doctors prescribe off-label because they see some benefit in doing so, *id.* at 853-54; yardstick methodology or pricing is used only in a specific context relating to utility regulation, and he has never seen it used in a similar context to the instant case and believes it is unreliable, *id.* at 842; her yardstick comparators are very different products, which are not identical or interchangeable, *id.* at 843; she should not rely only on CATIE to establish equivalence of products, *id.* at 843-44; QALY is only one aspect of a drug's impact; dosing frequency is another, and very important, *id.* at 845; there is no evidence that prices have a clear relationship to QALYs, *id.*; and hedonic price analysis is a methodology that is being quite widely used in economics to try to understand differences in pricing, but notably neither Dr. Harris nor Dr. Rosenthal used hedonic price analysis. *Id.* at 846-47.

Also contended by Dr. Cockburn is that Dr. Rosenthal's loss of value theory did not use any standard tools of economic analysis, and included no detailed, quantitative empirical work. *Id.* at 847-48. Dr. Rosenthal used welfare analysis to capture the difference in consumer surplus were the demand curve to shift, but never measured the slope of the curve; the area of consumer surplus depends on the curve and the price elasticity, yet there is no way of knowing the slope of the curve or extent of the demand shift. *Id.* at 850-51.

b. Criticism of Dr. Harris' Analysis

Dr. Cockburn testified that Dr. Harris's assumptions are not reasonable. *Id.* at 817. He contended that the Harris opinion is not standard, but is "very different from the approach that would be normally taken by an economist which will be to look at a range of hypotheses, a full range of the factors that might affect pricing or sales, and then to conduct an statistical or

econometric testing of such hypotheses rather than to assume these factors away." *id.* at 820. Cockburn would draw a much steeper demand curve because of price inelasticity, *id.* at 822, and Harris did not try to calculate the slope of demand curve.

This defense expert asserted that Dr. Harris wrongly attributed 100% of the decline in sales post 2003 to revelation of weight information. *Id.* at 824. According to Dr. Cockburn, Dr. Harris's model is too simplistic—there are in fact many factors. He says that CATIE was not a watershed event. *Id.* at 835. The evidence of weight relationships had been building up to support a consensus statement over some time. *Id.* at 825 (2003 label change was for all SGAs, and weight gain on Zyprexa's label had existed for years). The 2003 label change did not mention weight, *id.* at 826, and other factors that should be considered in decline, including: 1) competition—of Geodon in March of 2001 and of Abilify in November of 2002, *id.* at 827; and 2) promotion effort differences among competing drugs. *Id.* at 830.

Dr. Cockburn stated that Zyprexa detailing fell in 2001, declining from $60 million per year to $30 million, while Abilify detailing went from $5 million to $40 million. *Id.* at 831. Other criticisms were based on the fact that direct-to-consumer advertising for Abilify was substantial during 2005—$40 million per quarter, *id.* at 832-33, while Zyprexa did not rely on direct advertising; personal injury litigation advertising began extensively in 2004 by personal injury lawyers, *id.* at 833; and reaction to information about metabolic issues may have caused doctors to change their prescribing behavior. *Id.* at 834. He would have modeled these five potential causes in analyzing the decline in Zyprexa sales. *Id.* at 834-35. Dr. Cockburn claims that Dr. Harris' assumption that sales in the years 2000 to 2005 would not have exceeded 2006 levels is invalid and unreasonable, *id.* at 836, since the weight issues were already known so they already had had an effect; Dr. Harris should have done empirical, quantitative investigation into

competing explanations. To Dr. Cockburn, plaintiffs were relying on "armchair economics" instead of field research. *Id.*

Dr. Cockburn emphasized that Lilly marketing documents from 2001 reported 100% doctors in a survey were aware of Zyprexa-related weight gain, metabolic issues, and diabetes. *Id.* at 835. He also explained that NDTI data is not reliable for measuring off-label prescriptions. *Id.* at 855 ff. NDTI data does not link individual prescriptions with a diagnosis code. *Id.* at 861. Most doctors who participate are primary care doctors. *Id.* at 862. NDTI data are reported quarterly with the possibility of substantial fluctuations within and between quarters, *id.* at 863, and what is on-label changes over time. *Id.* at 865. Off-label use could have fallen because the doctors were prescribing some other drug off-label. *Id.* at 867.

He noted that NDTI data does not track any individual prescriptions, but is based on "mentions" that certain office-based physicians enter on the survey form. *Id.* at 855-64. Linking the "mention" with the approved indication for the drug is an inexact science, and the substantial fluctuations in the data from quarter to quarter make NDTI a "noisy source." *Id.* at 863. "[T]here are multiple potential causative factors" that can drive NDTI data. *Id.* at 866. "You'd have to rule out a lot of other factors before you could necessarily attribute changes in prescribing these particular drugs to something such as, you know, these concerns about metabolic problems." *Id.* at 867. Any useful model of this market should look at market share. *Id.* at 868. There is a reliably fixed set of patients that have to be treated. Zyprexa fell and Abilify increased. *See also id.* at 866-67, 884, 889, 892, 897, 904, 926. As Dr. Cockburn testified, increased advertising by plaintiffs' attorneys about Zyprexa personal injury litigation might have frightened some number of physicians, as they moved away from using Zyprexa to other medications. *Id.* at 833.

Dr. Cockburn's Exhibit A showed that: "there were over 200 clinical trial studies published on antipsychotics between the period 1996 and 2005 . . . Approximately half of these were published prior to the label change in 2003." In rebuttal, plaintiffs point out that some publications may be far more influential than others, *see* Harris Rebuttal 8, and that many of these articles may have been written, produced, or influenced by Lilly, resulting in a positive, not negative, influence on Zyprexa. *Id.*

D. Other Defense Experts

Four of Lilly experts, upon whom Lilly relied during summary judgment proceedings, did not testify at the evidentiary hearing.

1. Ernest R. Berndt, Ph.D.

Defendant's expert, Dr. Ernest Berndt, is a professor of economics at the Massachusetts Institute of Technology. He has co-authored with Plaintiff's expert Dr. Rosenthal various articles that are a part of basic health economics literature applying accepted statistical and regression analysis quantifying the impact of various types of marketing efforts on pharmaceutical sales. He criticized Dr. Rosenthal's implementation of econometrics to estimate marketing impact on sales. Plaintiffs' *Daubert* motion to exclude Dr. Berndt's testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

2. David W. Feigal, Jr., M.D.

Defendant's Dr. Feigal is an employee with a pharmaceutical company although he once worked for the FDA. Dr. Feigal proffers the opinion that Lilly provided the FDA with comprehensive and appropriate information to evaluate the potential association between Zyprexa and glucose dysregulation and pancreatitis. He did not review Lilly's internal analysis of its own data or other available data or information concerning the safety profile of Zyprexa or any internal

Lilly correspondence on the subject. His opinions are based solely on his review of Lilly's final submission to the FDA. Plaintiffs' *Daubert* motion to exclude Dr. Feigal's testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

3. David Kahn, M.D.

Defendant's Dr. David Kahn is a clinical professor of psychiatry at the Columbia University College of Physicians and Surgeons. Dr. Kahn was a part of the "consensus" panel for the Texas Medication Algorithm Project, a project largely funded by the makers of psychotropic and atypical antipsychotics drugs. Dr. Kahn points out that results for Zyprexa in CATIE were not uniformly negative: "olanzapine had a statistically significant advantage over perphenazine for discontinuation due to lack of efficacy, and duration of successful treatment." Kahn Rep. 6

Dr. Kahn favors off-label use of medications, including Alzheimer's disease and especially in psychiatry. He proffered several opinions in an effort to rebut the sweeping cost-effectiveness studies, including CATIE, released in recent years. *See* Rosenheck Rebuttal Decl. (rebutting Dr. Kahn's comments on CATIE). In doing so Dr. Kahn contradicted another one of Lilly's proposed experts, Carol Tamminga, M.D. Plaintiffs' *Daubert* motion to exclude Dr. Kahn's testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

4. Jeffrey S. McCombs, Ph.D.

Defendant's expert Dr. McCombs is a professor at the School of Pharmacy at the University of Southern California. Dr. McCombs and his department have a long-standing relationship with Lilly; most of his grants are funded by the company. Dr. McCombs proffered an opinion that CATIE's results are inconsistent with his own Lilly-sponsored and unpublished retrospective findings based on underlying data and analysis Lilly has refused to produce. At the request of Lilly's counsel, Dr. McCombs did not undertake a review of all appropriate scientific

evidence regarding Zyprexa cost-effectiveness. *See* Pfs.' Fact Proffer at II. Plaintiffs' *Daubert* motion to exclude Dr. McCombs' testimony was denied. *See In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571, 580 (E.D.N.Y. 2007).

Dr. McCombs expressed concern about the loss of data in CATIE and the representativeness of CATIE's patient sample. He used an analysis of 2000-2002 data from the California Medicaid program. For purposes of the present analysis, the CATIE data suffices as a basis for opinion.

XIX. Proposed Class, Class Representatives, and Claims

A. Proposed Class

Plaintiffs propose one class, a Purchase Claim Plaintiff Class, with two subclasses: the Third-Party Payor Subclass and the Consumer or Direct Payor Subclass. These two subclasses could be further subdivided into classes for on-label purchases and off-label purchases. Plaintiffs seek class certification under two different legal causes of action: state consumer fraud statutes and the federal civil RICO statute.

Counsel for plaintiffs claim to represent the entirety of third-party payors. According to plaintiffs' counsel Mr. Sobol, "approximately 25,000 third party payers in the United States, i.e., for-profit and not-for-profit insurers, health and welfare funds, self-insured employers that routinely are that class." Sept. 21, 2006 Hr'g Tr. at 16.

As outlined in Plaintiffs' First Amended Complaint and the Memorandum of Law in Support of Purchase Claim Plaintiffs' Motion for Class Certification ("Plaintiffs' Class Certification Brief"), the Purchase Claim Plaintiff Class was then defined as:

> All individuals and entities in the United States and its territories who, for purposes other than resale, purchased, reimbursed, and/or paid for Zyprexa during the period from September 1996 through the present. For purposes of the Class definition,

individuals and entities "purchased" Zyprexa if they paid for some or all of the purchase price.

Pfs.' Corr. Supp. Post-Hr'g Mem. on Class Cert. 32.

1. Proposed Class Definitions

In Plaintiffs' Class Certification Brief, plaintiffs subdivided the Purchase Claim Plaintiff Class into the Third-Party Payor Class and the Consumer Class.

a. Third-Party Payor Subclass

The Third-Party Payor Subclass was proposed as:

> All private, non-government entities in the United States and its territories that are at risk, pursuant to a contract, policy, or plan, to pay or reimburse all or part of the cost of Zyprexa prescribed, provided, or administered to natural persons covered by such contract, policy, or plan during the period from January 1, 1996 to the present. Such entities include, but are not limited to, insurance companies, union health and welfare benefit plans, entities with self-funded plans that contract with a health insurance company or other entity to serve as a third-party claims administrator to administer their prescription drug benefits, private entities paid by any governmental entity (including a state Medicaid program), and other organizations that paid for all or part of a Zyprexa prescription since January 1, 1996.

Id. Alternatively, plaintiffs offered the following, slightly revised definition for the Third-Party Payor Subclass:

> All entities in the United States and its territories, except Medicare, Medicaid and the Veterans Administration, that are at risk, pursuant to a contract, policy, or plan, to pay or reimburse all or part of the cost of Zyprexa prescribed, provided, or administered to natural persons covered by such contract, policy, or plan during the period from January 1, 1996 to the present.

Id. at 32 n.90.

b. Direct Payor Subclass

The Direct Payor Subclass was proposed to be defined as:

> All individuals in the United States and its territories who, for purposes other than resale, purchased, reimbursed, or paid for some or all of the price of Zyprexa during the period from January 1, 1996 to the present.

Id. at 33. Alternatively, Plaintiffs suggested the following, slightly revised definition for the Direct Payor Subclass:

> All natural persons in the United States and its territories who paid, either in cash or as a percentage co-pay, all or part of the cost of Zyprexa prescribed, provided, or administered to natural persons during the period from September 30, 1996 to the present.

Id. Only consumers who paid for their entire prescriptions or whose insurance plans require variable co-payments are in the Direct Payor subclass. Individuals with flat co-pay plans are not included.

c. On-Label Sub-Subclass

Within the Direct Payor Subclass, Plaintiffs sought certification of two further subclasses based on individual class members' on-label and off-label use of Zyprexa. The proposed definition of the On-Label Direct Payor Subclass was as follows:

> All natural persons in the Consumer Class who paid for prescriptions of Zyprexa, as set forth in the Consumer Class definition, which were for diagnoses of schizophrenia, acute mixed or manic episodes associated with Bipolar I Disorder, or agitation associated with schizophrenia and bipolar I mania.

Id.

d. Off-Label Sub-Subclass

The proposed definition of the Off-Label Direct Payor Subclass was defined as:

> All natural persons in the Consumer Class who paid for prescriptions of Zyprexa, as set forth in the Consumer Class definition, which were for diagnoses other than schizophrenia, acute mixed or manic episodes associated with Bipolar I Disorder, or agitation associated with schizophrenia and bipolar I mania.

Id.

2. Proposed Multi-State Class

Plaintiffs request certification of these four classes/subclasses under a state law consumer fraud theory. Under that theory, the Direct Payor Class would consist of a class of consumers in

forty-one jurisdictions, including: Alaska, Arkansas, California, Colorado, Connecticut, Delaware, the District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oklahoma, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Vermont, Virginia, Washington, West Virginia, and Wisconsin. Ten states are not listed because they require individualized reliance, expressly preclude class actions, or have uniquely onerous elements that would make trial of class claims difficult. The third-party payor class would consist of a class of third-party payors in thirty-two jurisdictions, including: Alaska, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Idaho, Illinois, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Oregon, South Carolina, South Dakota, Tennessee, Texas, Vermont, Virginia, Washington, and Wisconsin. In addition to the ten states excluded from the Direct Payor Class, nine additional states have been removed from this class because their statutes prohibit standing by third-party payors.

Alternatively as to state law claims, Plaintiffs seek certification of an exemplar New York State-Only Class for each of the four subclasses. Six of the eight named class representatives are from New York, made their purchases in New York and invoke New York state substantive law for their claims. (The named plaintiffs' claims are governed by Pennsylvania (UFCW), Texas (Mid-West), and New York (SBA, Local 28, Teachers Fund, DC 37, Mr. Pronto and Mr. Vannello) law.) Certifying an exemplar New York State-Only Class would avoid, contend plaintiffs' counsel, arguments of complexity from multistate proceedings.

3. Proposed National Class

As to the federal RICO claim, Plaintiffs seek certification nationwide on behalf of all four subclasses on liability, causation and damages. They contend that *McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), *subsequently modified by Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008), does not bar this class action.

B. Proposed Class Representatives

Plaintiffs' counsel has selected as representative payor plaintiffs a few small entities that pay for prescription drugs under pharmacy benefit plans: Mid-West National Life Insurance Company of Tennessee; UFCW Local 1776 and Participating Employers Health and Welfare Fund; Local 28 Sheet Metal Workers; and Sergeants Benevolent Association Health and Welfare Fund, United Federation of Teachers Welfare Fund, and ASFCME District Council 37 Health and Security Fund. Five of the entities are Taft-Hartley or similar funds, and one is an insurance company. Additionally, Michael Pronto and Michael Vannello are co-lead plaintiff patients representing individual consumers who paid in part or in whole for their own individual Zyprexa prescriptions.

UFCW Local 1776

UFCW Local 1776 is a small labor union based in Philadelphia with over 20,000 active members. The union provides, through a trust fund, pharmacy benefits for employees and their family members. Payments for Zyprexa were $800,000, with estimated damages of $264,000.

Mid-West Life Insurance

Mid-West Life Insurance is a small life and health insurance company providing health and pharmacy benefits to beneficiaries throughout the United States, with payments for Zyprexa of $32,570 and estimated damages of $10,000.

Sheet Metal Workers Local 28

Sheet Metal Workers Local 28 operates its program through a Taft-Hartley trust fund. It provides coverage for members living in the five boroughs of New York as well as Nassau and Suffolk Counties in New York. Payments for Zyprexa were $200,000, with estimated damages of $66,000.

Sergeants Benevolent Association

Sergeants Benevolent Association has a Health and Welfare Fund. Provided are pharmaceutical benefits for approximately 33,000 individuals, including New York City police officers who have been promoted to the rank of Sergeant as well as line of duty widows, their dependents, and retiree sergeants. Its payments for Zyprexa were $87,869, with estimated damages of $28,996.

Michael Vannello

Michael Vannello is an individual payor and former messenger for the First Manhattan Company. He took Zyprexa from February 23, 2000 to October, 2002. His payments for Zyprexa were $5,932 out of pocket, with estimated damages of $1,957. As already noted, he cannot represent the class. *See* Part III.2.b.iv, *supra*.

Michael Pronto

Michael Pronto is an individual payor from New York who felt sad and depressed after breaking up with his girlfriend. He took Zyprexa from April 2003 through October 2006. His payments for Zyprexa were $500 in out-of-pocket copayments, with estimated damages of $165. As already noted, he cannot represent the class. *See* Part III.2.a.iv, *supra*. He is in the process of settling his claim for personal injuries due to Zyprexa. With the possibility of recovering for this use, Pronto would not be a suitable class representative.

C. Causes of Action

1. Federal Civil RICO Claim

Section 1964(c) of Title 18 ("civil RICO") gives private citizens a federal substantive cause of action under the Racketeer Influenced and Corrupt Organizations ("RICO") statute and the federal mail fraud statute. 18 U.S.C. §§ 1341 *et seq*. It provides that "[a]ny person injured in his business or property by reason of a violation of [RICO's substantive provisions] may sue therefor in any appropriate United States district court and shall recover threefold the damages he sustains and the cost of the suit, including a reasonable attorney's fee." 18 U.S.C. § 1964(c). To succeed on a civil RICO claim, a plaintiff must be able to prove (1) a RICO violation, (2) injury, and (3) transaction and loss causation. *McLaughlin*, 522 F.3d at 222; *Phoenix Bond*, 128 S. Ct. 2131 (holding that the persons injured by the fraud need not be the persons to whom the false statements were directed). *See also City of New York v. Smokes-Spirits.Com, Inc.*, 06-1665-CV (2d Cir. Sept. 2, 2008) (reducing proximate cause limitations on RICO fraud actions).

2. State Consumer Fraud Statutes

Plaintiffs have submitted an intellectually appealing proposed trial plan and analysis of relevant state laws. *See* Class Pfs.' Proposed Trial & Apportionment Plan & Statement of State Law in Support of Class Cert. ("Proposed Trial Plan"), Dec. 4, 2007, Docket Entry No. 144. In this court's opinion, it would place burdens on the court and jury trying the case that would make its execution almost impossible. (As a basis for settlement in which compromises on law and face are acceptable, it would be an appropriate basis for discussion.) *See* Part XXI.B, *infra*.

D. Proposed Class Damages Estimate the Total Out-of-Pocket Losses with Sufficient Precision

To certify a damages claim in this case (whether under RICO or state law), plaintiffs must propose one or more methods by which to reasonably estimate damages to class members in a

manner consistent with the flexibility and efficacy permitted by Rule 23 of the Federal Rules of Civil Procedure, and with appropriate consideration of defendant's and individual plaintiffs' due process rights. Plaintiffs claim to have done so; Lilly disagrees. In resolving factual disputes as to certification, the court "should be persuaded that [each] fact [relevant to Rule 23] at issue has been established." *In re Initial Public Offering Securities Litigation*, 483 F.3d 70 (2d Cir. 2007).

Assuming fraud leading to a price differential has been established, damages may be estimated based on the difference between what was paid for Zyprexa and the actual value of the product. The computation requires (i) estimating the total out-of-pocket expenditures for the class members and (ii) using well-accepted techniques in applied economics to determine the actual value or appropriate launch price (plus minor increases) of Zyprexa.

The evidence shows that reasonably accurate estimates can be made of the total out-of-pocket payments made by the class for Zyprexa over the class period. Lilly did not dispute at the evidentiary hearing or in its prior submissions that in the "data rich" pharmaceutical field, expenditure information by year, source of payment (e.g., third-party payors, government payors, insurance copay or cash consumers), and state are available. Plaintiffs' experts Drs. Rosenthal and Harris used widely available expenditure data to estimate expenditures by the class. Internal Lilly documents also show Lilly coming to similar estimates of expenditures by source of payment at various times. In short, the question of "what was paid?" for Zyprexa during the class period is readily determined.

The methodology for determining actual economic value, or true launch price of Zyprexa, is an issue a jury can determine. Evidence could be relied upon by a jury to determine that, but for Lilly's misconduct, the launch price of Zyprexa would have been set at markedly lower levels than its major competitors. Lilly's own experts both opined that pharmaceutical launch prices are in

large part set by the clinical attributes that distinguish the product. Better products suggest better launch prices. Internal Lilly documents confirm this methodology. And plaintiffs' experts persuasively testified that comparables with other competing pharmaceuticals are routinely used in applied microeconomics.

The implementation of comparative value is well-documented on this record. Two economists for plaintiffs, working independently, each chose and implemented a comparative methodology for determining the value of Zyprexa for damage purposes, both at launch and during the class period. The soundness of their comparative analysis was bolstered by the testimony of two of the nation's leading psychiatrists, along with the conclusions of an expansive clinical trial conducted by the NIMH. The CATIE study, bolstered by CUtLASS, the VA Cooperative Study, and many others, along with the testimony of Drs. Rosenheck and Schneider, supported the comparative use by Drs. Rosenthal and Harris of other, markedly less expensive, second-generation and even first-generation antipsychotics. Specific arguments raised by Lilly regarding the comparative analysis were rebutted by plaintiffs' experts, providing a jury issue.

McLaughlin does not bar the methodology for determining class members' damages here. Unlike plaintiffs' damages model used in the instant case, the plaintiffs in *McLaughlin* had not developed a manner by which a standardized overcharge based on the actual out-of-pocket losses caused by the defendants' conduct could be determined.

The plaintiffs in *McLaughlin* posited two methods of calculating damages: (i) the loss of value method, assuming that plaintiffs should have paid less for light cigarettes because they did not receive the benefit of their bargain over their out-of-pocket expenditures, to wit, healthier cigarettes, 522 F.3d at 228-29; and (ii) the price impact method, asserting that defendants would have been required to reduce their prices if the truth about their products had been known and the

concomitant demand had been reduced. *Id.* at 229-30. The *McLaughlin* court found that an unacceptable level of speculation was inherent in both proposed methodologies.

In the loss of value method, the *McLaughlin* plaintiffs would have had to estimate what a consumer would have paid for a healthy cigarette. According to the appellate court, plaintiffs' experts were, however, unable to quantify the purported loss of value. One expert asked consumers to make a comparison between a "genuine" light cigarette that reduced health risks and a "misrepresented" light cigarette that was no different than conventional cigarettes; survey respondents reported a "non-zero" loss in value, leading the appellate court to conclude that plaintiffs' theory was "pure speculation." *Id.* at 229.

In the price impact method of evaluating damages, the *McLaughlin* plaintiffs would have had to estimate how much class members would have been willing to pay for light cigarettes had the truth been known. But the plaintiffs had failed, according to the appellate court, to provide a reasonable means of estimating that price because (i) light cigarettes had always been priced the same as regular cigarettes, and (ii) no drop in demand or price for light cigarettes occurred once a monograph was published reporting that light cigarettes did not reduce the risks of smoking. *Id.* at 229-30.

In both proposed *McLaughlin* methodologies, the appellate court held that there was no method for determining an actual overcharge. It rejected the plaintiffs' proposed hypothetical overcharge method. Rejected as well was plaintiffs' method by which those with claims varying in strength might prove specific individual damages. They were concerned with the possibility that payment of damages would not reflect the defendants' actual liability or, worse, would "bear[] little or no relationship to the amount of economic harm actually caused by defendants." *Id.* at 231.

Contrary to the salient flaws found by the appellate court in the causation and damages model presented by the plaintiffs in *McLaughlin*, plaintiffs' Zyprexa model reflects actual overcharges and actual harm caused by defendant. A jury could find that Drs. Rosenthal and Harris's calculations of aggregate damages for the class are sufficiently reliable and appropriate based on the record.

The economic analyses undertaken in the instant case contain the features of reliability lacking in *McLaughlin.* For example, in *McLaughlin* there was a "lack of an appreciable drop in the demand . . . of light cigarettes after the truth about lights was revealed . . . . " *Id.* at 227. Here, however, there is a remarkable decline in the demand for Zyprexa after only some of the truth was revealed, despite Lilly's attempts to ameliorate its effects. *See* charts, Part XI.E, *supra*. Unlike the tobacco companies in *McLaughlin*, here Lilly itself ascribed the diminution in demand for Zyprexa to the disclosures of the American Diabetes Association's consensus statement in late 2003 and early 2004. And the decline occurred before further key revelations—e.g., (i) the lack of comparative cost effectiveness of Zyprexa to perphenazine or other antipsychotics, as revealed in CATIE and later trials; (ii) the FDA's eventual acquisition of data (previously undisclosed by Lilly) leading up to the label change in October 2007; and (iii) analyses regarding the lack of efficacy and safety issues posed by treating elderly persons with dementia by prescribing Zyprexa.

McLaughlin affirmatively ruled that in RICO cases the "acceptable measure of injury [is] out-of-pocket damages . . . ." *Id.* Unlike *McLaughlin* (where different types of cigarette purchasers might seek different levels of percentage recovery), in this case all purchasers seek the same level of recovery—the difference between what they paid and what the product should have been priced at.

Finally, in *McLaughlin*, the estimate of aggregate damages would "not accurately reflect the number of plaintiffs actually injured by defendants" and would bear "little or no relationship to the amount of economic harm actually caused by defendants." *Id.* at 231. But there is no rough estimation of gross damages proposed in the instant case. The present overcharge case may be likened to garden-variety antitrust claims. In this case even more so than in many such antitrust cases, a highly accurate estimation of the class members' damages can be determined for the class, given the "data rich" pharmaceutical environment.

It is important to note that the Supreme Court's ruling in *Phoenix Bond*, decided subsequent to *McLaughlin*, directly supports plaintiffs' theory of causation. The Court held that the person who suffered the loss need not be the one to whom the fraudulent words were directed. *Phoenix Bond*, 128 S. Ct. at 2145 ("[W]e hold that a plaintiff asserting a RICO claim predicated on mail fraud need not show, either as an element of its claim or as a prerequisite to establishing proximate causation, that it relied on the defendant's alleged misrepresentations."); *id.* at 2143-44 ("Petitioners' contention that proximate cause has traditionally incorporated a first-party reliance requirement for claims based on fraud cannot be reconciled with these authorities."); *id.* at 2144 ("Accordingly, it may well be that a RICO plaintiff alleging injury by reason of a pattern of mail fraud must establish at least third-party reliance in order to prove causation."); *id.* ("Proof that the plaintiff relied on the defendant's misrepresentations may in some cases be sufficient to establish proximate cause, but there is no sound reason to conclude that such proof is always necessary."). The instant case is a perfect example of that proposition. The fraud was directed to prescribing doctors. The overpayments were made by third-party and individual payors.

In *McLaughlin*, the Court of Appeals for the Second Circuit rejected the district court's proposal to allocate damages: "the plaintiffs could prove collective damages on a class-wide basis,

and individual plaintiffs would then claim shares of this fund." *McLaughlin*, 522 F.3d at 231. The appellate court based its decision on the fact that the circuit does not allow "fluid recovery" because it offends both the Rules Enabling Act ("REA") and the Due Process Clause. Damages that are too speculative and bear little relationship to the actual amount of economic harm offend the REA, which provides that Rule 23 (or any of the other civil rules) cannot be used to abridge, enlarge, or modify any substantive right. The defendants have a substantive right to pay damages reflective of their actual liability. *Id.* at 231. Even if individual damages are calculated accurately, distributing the balance of the monies not claimed through *cy pres* might result in overpayment by the defendant. "When fluid recovery is used to permit the mass aggregation of claims, the right of defendants to challenge the allegations of individual plaintiffs is lost, resulting in a due process violation." *Id. at* 232.

Assuming that this objection to fluid recovery of the Court of Appeals for the Second Circuit applies to some class actions, it has no bearing on the instant action. Each plaintiff can prove the amount it paid, the percentage overcharge can be computed by the jury, and an amount can be allocated to individuals with no need for the *cy pres* doctrine:

> Once fraud has been proven, the burden of proving specifics of damages by the claimant is reduced. "Where injury is established, damages need not be demonstrated with precision." *Schwab* [*v. Philip Morris*, 449 F. Supp. 2d 992,] 1065 (E.D.N.Y. 2006); *see Blue Cross* [*& Blue Shield of New Jersey, Inc. v. Philip Morris USA Inc.*, 344 F.3d 211, 224-25 (2d Cir. 2003)]; *cf. Lee v. Joseph E. Seagram & Sons, Inc.*, 552 F.2d 447, 456 (2d Cir.1977) ("When it is certain that damages have been caused by a breach of contract, and the only uncertainty is as to their amount, there can rarely be good reason for refusing, on account of such uncertainty, any damages whatever for the breach. A person violating his contract should not be permitted entirely to escape liability because the amount of damages which he has caused is uncertain.") (quotation and citation omitted).
>
> Both the individual and institutional plaintiffs have laid out their own money for Zyprexa. While it can be assumed for purposes of this motion that the drug was properly prescribed, payers may recover the difference between the price they paid for Zyprexa and the price they would have paid for Zyprexa but for Lilly's alleged fraud. *See, e.g., Schwab*, 449 F. Supp. 2d at 1065 (approving use of price impact model to

> calculate damages). The questions of damages and their allocation is in some respects simpler here than in *Schwab* since the institutional and individual claimants can probably trace their own payments through contemporaneous writings.

In re Zyprexa Prods. Liab. Litig., 493 F. Supp. 2d 571, 578 (E.D.N.Y. 2007) (denying summary judgment).

XX. Class Certification

A. Burden of Proof

As the party seeking certification of the class, plaintiffs bear the burden of proving that all of the Rule 23 requirements are met." *Amchem Prods., Inc. v. Windsor*, 521 U.S. 591, 614 (1997); *Caridad v. Metro-North Commuter R.R.*, 191 F.3d 283, 291 (2d Cir. 1999), *overruled on other grounds by In re Initial Public Offering Securities Litigation* ("*In re IPO*"), 471 F.3d 24, 42 (2d Cir. 2006). Thus, where disputed issues of fact implicate Rule 23 issues, it is the plaintiffs' burden to prove that those facts are established. *In re IPO*, 471 F.3d at 40. This is no *pro forma* burden. After *In re IPO*, it is no longer the case that "an expert's report will sustain a plaintiff's burden so long as it is not 'fatally flawed.'" *Id.* (quoting *In re Visa Check/MasterMoney*, 280 F.3d 124, 135 (2d Cir. 2001)). Instead, "the district judge must receive enough evidence by affidavits, documents, or testimony, to be satisfied that each Rule 23 requirement has been met." *Id.* at 41. Moreover, "[a] district judge is to assess *all* of the relevant evidence admitted at the class certification stage and determine whether each Rule 23 requirement has been met, just as the judge would resolve a dispute about any other threshold prerequisite for continuing a lawsuit." *Id.* at 42 (emphasis added). Thus, a court may not leave for the jury's consideration flaws in plaintiffs' experts' opinions that bear on Rule 23 considerations. *Id.* at 41.

As the Court of Appeals for the Second Circuit made clear in *In re IPO*, the time when plaintiffs seeking class certification can rely on the pleadings and unscrutinized expert reports

have passed. It is the plaintiffs' burden to produce sufficient evidence from which the court can conclude that all the requirements of Rule 23 have been met. The *In re IPO* court made three conclusions applicable to the instant case:

> We conclude (1) that a district judge may not certify a class without making a ruling that each Rule 23 requirement is met and that a lesser standard such as "some showing" for satisfying each requirement will not suffice, (2) that all of the evidence must be assessed as with any other threshold issue, (3) that the fact that a Rule 23 requirement might overlap with an issue on the merits does not avoid the court's obligation to make a ruling as to whether the requirement is met, although such a circumstance might appropriately limit the scope of the court's inquiry at the class certification stage.

In re IPO, 471 F.3d at 27 (rejecting former obtuse Rule 23 standards, such as "some showing" of the certification elements or the ability of an expert's report to sustain a plaintiff's burden so long as it is not "fatally flawed.").

But the Court of Appeals for the Second Circuit "resist[ed] saying that what are required are 'findings' because that word usually implies that a district judge is resolving a disputed issue of fact." *Id.* at 40. "The ultimate issue as to each requirement is really a mixed question of fact and law." Rule 23 requirements are threshold issues; a district court must make a ruling or a determination (not a finding) as to whether they are met. The Court of Appeals concluded that:

> (1) [A] district judge may certify a class only after making determinations that each of the Rule 23 requirements has been met; (2) such determinations can be made only if the judge resolves factual disputes relevant to each Rule 23 requirement and finds that whatever underlying facts are relevant to a particular Rule 23 requirement have been established and is persuaded to rule, based on the relevant facts and the applicable legal standard, that the requirement is met; (3) the obligation to make such determinations is not lessened by overlap between a Rule 23 requirement and a merits issue, even a merits issue that is identical with a Rule 23 requirement; (4) in making such determinations, a district judge should not assess any aspect of the merits unrelated to a Rule 23 requirement; and (5) a district judge has ample discretion to circumscribe both the extent of discovery concerning Rule 23 requirements and the extent of a hearing to determine whether such requirements are met in order to assure that a class certification motion does not become a pretext for a partial trial of the merits.

> In drawing these conclusions, we add three observations. First, our conclusions necessarily preclude the use of a "some showing" standard, and to whatever extent *Caridad* might have implied such a standard for a Rule 23 requirement, that implication is disavowed. Second, we also disavow the suggestion in *Visa Check* that an expert's testimony may establish a component of a Rule 23 requirement simply by being not fatally flawed. A district judge is to assess all of the relevant evidence admitted at the class certification stage and determine whether each Rule 23 requirement has been met, just as the judge would resolve a dispute about any other threshold prerequisite for continuing a lawsuit. Finally, we decline to follow the dictum in *Heerwagen* suggesting that a district judge may not weigh conflicting evidence and determine the existence of a Rule 23 requirement just because that requirement is identical to an issue on the merits.

Id. at 27. Following *In re IPO*, this court considered a huge amount of evidence in this and related Zyprexa cases on the viability issues, held extensive evidentiary hearings, and had briefed and argued all RICO and Rule 23 issues at great length.

B. RICO Claims

The Racketeer Influenced and Corrupt Organizations Act ("RICO"), 18 U.S.C. §§ 1961-1968, provides a private right of action for treble damages to "[a]ny person injured in his business or property by reason of a violation" of the Act's criminal prohibitions. § 1964(c). As the Supreme Court recently explained,

> RICO provides a private right of action for treble damages to any person injured in his business or property by reason of the conduct of a qualifying enterprise's affairs through a pattern of acts indictable as mail fraud. Mail fraud, in turn, occurs whenever a person, "having devised or intending to devise any scheme or artifice to defraud," uses the mail "for the purpose of executing such scheme or artifice or attempting so to do." § 1341. The gravamen of the offense is the scheme to defraud, and any "mailing that is incident to an essential part of the scheme satisfies the mailing element," even if the mailing itself "contain[s] no false information."

Phoenix Bond, 128 S. Ct. at 2138 (internal citations omitted). There is no requirement that a private action can proceed only against a defendant who has already been convicted of a predicate act or of a criminal RICO violation; neither is there a requirement that a plaintiff in a private action establish a "racketeering injury" as opposed to an injury resulting from the predicate acts

themselves. *Sedima, S.P.R.L. v. Imrex Co., Inc.*, 473 U.S. 479 (1985). To fulfill the statute's requirement that an injury occur "by reason of" a defendant's action, a plaintiff in a private RICO action as brought by present plaintiffs must establish: 1) reliance on defendant's misrepresentation; 2) injury; and 3) loss causation. *See McLaughlin,* 522 F.2d at 222.

1. Causation

a. Reliance

McLaughlin stated that where "mail or wire fraud is the predicate act for a civil RICO claim, the transaction or 'but for' causation element r*equires the plaintiff to demonstrate that he relied* on the defendant's misrepresentation." *Id.* (emphasis added). The first "half of the equation," involves proving widespread and uniform misrepresentation; the "other half" requires proving reliance on that misrepresentation. *Id.* As to this point, *McLaughlin* was subsequently placed in doubt by the Supreme Court's decision in *Phoenix Bond*, 128 S. Ct. 2131. The Court held "that a plaintiff asserting a RICO claim predicated on mail fraud need *not* show, either as an element of its claim or as a prerequisite to establishing proximate causation, that it relied on the defendant's alleged misrepresentations." 128 S. Ct. at 2145 (emphasis added). There is ample evidence that fraud was directed through mailings and otherwise at doctors who relied, causing damages in overpayments by plaintiffs.

b. Proof of Uniform Misrepresentation

The evidence showed misrepresentation leading to uniform overcharge per prescription paid for by plaintiffs.

c. Proof of Reliance on Misrepresentation

There is ample evidence that doctors' reliance on the misrepresentation in prescribing Zyprexa supported the excessive price. The Second Circuit Court of Appeals in *McLaughlin* held

that "reliance on the misrepresentation[] cannot be the subject of general proof. Individualized proof is needed to overcome the possibility that a member of the purported class purchased Lights for some reason other than the belief that Lights were a healthier alternative . . . ." *McLaughlin*, 522 F.3d at 223.

McLaughlin is distinguishable. In *McLaughlin*, the appellate court declared:

> Plaintiffs and the district court suggest that defendants distorted the body of public information and that, in purchasing Lights, plaintiffs relied upon the public's general sense that Lights were healthier than full-flavored cigarettes, whether or not individual plaintiffs were actually aware of defendants' alleged misrepresentation. *Cf. Falise v. Am. Tobacco Co.*, 94 F. Supp. 2d 316, 335 (E.D.N.Y. 2000) ("Where . . . the fraudulent scheme is targeted broadly at a large proportion of the American public[,] the requisite showing of reliance is less demanding. Such sophisticated, broad-based fraudulent schemes by their very nature are likely to be designed to distort the entire body of public knowledge . . . "). Their argument invokes the fraud-on-the-market presumption set forth in *Basic Inc. v. Levinson,* 485 U.S. 224 (1988), which concerned fraud claims in the securities context. "The fraud-on-the market doctrine . . . creates a rebuttable presumption that (1) misrepresentations by an issuer affect the price of securities traded in the open market, and (2) investors rely on the market price of securities as an accurate measure of their intrinsic value." *Hevesi v. Citigroup Inc.*, 366 F.3d 70, 77 (2d Cir. 2004). Thus, a plaintiff alleging securities fraud may establish reliance simply by virtue of the defendant's public dissemination of misleading information. *See Basic*, 485 U.S. at 241-42 (noting that because the price of stock in an efficient market reflects all publicly available information, "[m]isleading statements will . . . defraud purchasers of stock even if the purchasers do not directly rely on the misstatements").
>
> We do not think that the *Basic* presumption, or the district court's variation of it, applies in this case; we cannot assume that, regardless of whether individual smokers were aware of defendants' misrepresentation, the market at large internalized the misrepresentation to such an extent that all plaintiffs can be said to have relied on it. *Basic* involved an efficient market—the market in securities traded on the New York Stock Exchange—capable of rapidly assimilating public information into stock prices, *see id.* at 247, 249 n.29 (describing the securities market as "impersonal, well-developed," and "information-hungry"); the market for consumer goods, however, is anything but efficient, *cf. Sikes v. Teleline, Inc.*, 281 F.3d 1350, 1364 (5th Cir. 2002) ("[E]ach individual plaintiff is the only person with information about the content of the advertisement upon which he relied."). Indeed, the fact that the publication of Monograph 13 produced no change in either the sales or the price of Lights shows just how unresponsive the consumer market in Light cigarettes is to the advent of new information. *See In re IPO*, 471 F.3d at 43 ("Plaintiffs' own allegations as to how slow the market was to correct the alleged price inflation despite what they also allege was widespread knowledge of the scheme indicate the very antithesis of an efficient

> market."). As we stated in *In re IPO,* "[w]ithout the *Basic* presumption, individual questions of reliance would predominate over common questions." *Id.*; *see also Gunnells,* 348 F.3d at 435 (noting that *Basic's* presumption of actual reliance was based on the efficiency of capital markets, which did not apply to plaintiffs' purchase of health care plans, and that therefore actual reliance could not be presumed and individualized inquiry was required).

McLaughlin, 522 F.3d at 233-34 (footnote omitted); *see id.* at 226 ("Indeed, the fact that the market did not shift away from light cigarettes after the publication of Monograph 13 is compelling evidence that plaintiffs had other, non-health related reasons for purchasing Lights.").

Unlike *McLaughlin*, here the evidence supports a finding of an overcharge based on the fraud on doctors, third-party payors, and others. The overcharge resulted in specific damages to the plaintiffs who overpaid for Zyprexa.

McLaughlin found that "differences in plaintiffs' knowledge and levels of awareness also defeat the presumption of reliance" in cigarette cases. *Id.* at 226. Here the total fraud resulted in an increased price as in securities cases, so the fact that some doctors, patients or others were aware of the fraud is irrelevant. Without the fraud the price would have been lower to all payors.

2. Loss Causation

Loss causation means that the defendant's misrepresentations must have caused the plaintiff to "suffer economic loss." Did the alleged violation, in other words, lead directly to the plaintiff's injuries? *See Anza v. Ideal Steel Supply Corp.*, 126 S. Ct. 1991 (2006). In *McLaughlin*, the court noted,

> [P]laintiffs' theory is that they suffered an economic loss because they were overcharged for Lights. Plaintiffs argue that defendants' misrepresentation that Lights were healthier led to an increased market demand for light cigarettes, which drove up the price of Lights. Thus, plaintiffs contend that they paid more for Lights than they otherwise would have had the truth been known. As with reliance, plaintiffs claim that they can establish loss causation on a class-wide basis.

522 F.3d at 226. The Court of Appeals for the Second Circuit rejected this argument by holding that "the issue of loss causation, much like the issue of reliance, cannot be resolved by way of generalized proof." *Id.* Proof in the instant case is not generalized. The plaintiffs were directly injured by Lilly when each was overcharged a fixed computable amount for each prescription.

3. Injury

"Only by showing that the plaintiffs paid more for [Zyprexa] than they would have but for defendant's misrepresentation can plaintiffs establish the requisite injury under civil RICO." *Id.* at 227. *McLaughlin* rejected the plaintiffs' two theories of injury: the loss of value theory and the price impact theory. The "acceptable measure of injury"—out-of-pocket damages—requires individualized proof. *Id.* As already indicated in Parts XVII.A.2-3, *supra*, plaintiffs have supported their theory of price impact sufficiently to go to the jury.

4. Claim Period

Damages sought are limited in this certification order to four years before filing of the suit. A four-year statute of limitations applies to civil RICO claims. *Agency Holding*, 483 U.S. 143. Here, accrual begins when payment for Zyprexa is made. Absent barring by equitable tolling, payments made before June 20, 2001 are barred because the case was filed on June 20, 2005. Moreover, as a matter of substantive equity it is not reasonable to permit the third-party payors, for the most part sophisticated institutions with sophisticated advisors, to recoup damages before 2001—to 1996, the earliest date the alleged fraud began. This decision is not dependent on the knowledge of third-party payors specifically. There are equitable considerations going beyond the actual knowledge or legitimate expectations of the third-party payors. The court is unwilling to allow the passivity of purchasers and payors to visit upon Lilly enormous potential exposure,

which could have been substantially limited had third-party payors exercised their responsibilities appropriately.

At the July 17, 2008 hearing on class certification, plaintiffs noted that although they would prefer the court to certify a longer time period, they accepted the proposed four-year certified time period, and noted they would not challenge it on appeal. *See* Hr'g Tr. 18, 21, July 17, 2008. Tolling is an equitable doctrine. The period fixed comports with both substantive and procedural equity. CATIE was published in 2005, and as a matter of law no damages should be allowed for purchases beyond its publication date.

No damages will be allowed beyond the initial filing date of June 20, 2005, since by then all potential third-party payors and prescribers of Zyprexa should have been sufficiently advised of alleged overpricing. This calculation results in a maximum period of June 20, 2001 to June 20, 2005 for recoverable overcharges. A jury may considerably reduce or eliminate this window on finding that the third-party payors knew or should have known of Zyprexa's alleged overpricing before they commenced suit on June 20, 2005—perhaps even before June 20, 2001.

Permitting recovery for overcharges before June 20, 2001 (four years before the suit was commenced) would be inappropriate. The specialists who are the third-party payors had a continuing duty to their clients to inquire. In these special circumstances, there are limits to awards that can be earned by violation of an affirmative duty to be alert to dangers to clients.

The chronological decision is not free from doubt as a matter of law. It is a pragmatic and seemingly fair solution to a complex, multifaceted set of rights and responsibilities.

a. Statute of Limitations

Although the RICO statute does not contain a statute of limitations for civil claims brought under its provisions, the Supreme Court has applied a four-year limit to such actions. *Agency*

Holding Corp. v. Malley-Duff & Associates, Inc., 483 U.S. 143 (1987). The Court has "not settle[d] upon a final rule" regarding when the statute begins to run, *Rotella v. Wood*, 528 U.S. 549, 554 n.2 (2000), but the Second Circuit Court of Appeals, along with the majority, if not all, of the appellate courts, now applies "an injury discovery accrual rule starting the clock when a plaintiff knew or should have known of his injury." *See McLaughlin*, 522 F.3d at 233; *In re Merrill Lynch Ltd. Partnerships Litig.*, 154 F.3d 56, 60 (2d Cir. 1998); *see also Rotella*, 528 U.S. 549 (rejecting the "injury and pattern discovery rule," under which a civil RICO claim accrued only when the claimant discovered, or should have discovered, *both* the injury and pattern of RICO activity).

A federal rule of equitable tolling may be applied in the case of fraudulent concealment in civil RICO actions as well as in litigation generally. *See Griffin v. McNiff*, 744 F. Supp. 1237 (S.D.N.Y. 1990), *aff'd*, 996 F.2d 303 (2d Cir. 1993); *Camotex, S.R.L. v. Hunt*, 741 F. Supp. 1086 (S.D.N.Y. 1990). Whatever efforts Lilly may have made to conceal its fraud, it was not in a position to have misled the class certified sufficiently to allow for the twelve-year class period claimed, or anything near that, in view of the third-party payors' expertise in merchandising of pharmaceuticals and fiduciary responsibilities to their clients.

There is no basis in the instant case for tolling a statute (or caselaw rule) limiting the time to commence this RICO action on equitable grounds. At some point sufficient information was available to put potential claimants on notice of a possible claim. Since the case was first filed on June 20, 2005, no damages for overpayment can be recovered for any purchases of Zyprexa prior to June 20, 2001. *See* Part I, *supra*.

b. End of Claim Period

At the latest, once the suit was first commenced on June 20, 2005, all members of the class (or their representatives and advisors) knew or should have known of the claimed overcharge. No damages can be recovered for any purchases after that date.

c. Certified Period

The temporal period for the class will be from June 20, 2001 to June 20, 2005. The jury may, on the present record, decide that plaintiffs should have known enough to sue before June 20, 2005. If it does, the temporal damage period will be shortened, or entirely eliminated.

C. Class Satisfies the Requirements Imposed by Rule 23(a)

To pursue their claims as a class action, plaintiffs must satisfy the four prerequisites of Federal Rule of Civil Procedure 23(a):

> (1) the class is so numerous that joinder of all members is impracticable; (2) there are questions of law or fact common to the class; (3) the claims or defenses of the representative parties are typical of the claims or defenses of the class; and (4) the representative parties will fairly and adequately protect the interests of the class.

Fed. R. Crim. P. 23(a).

1. Class Is So Numerous that Joinder of All Members Is Impracticable

Rule 23(a)(1) requires that the proposed class be so numerous that joinder of all members is impracticable. Fed. R. Civ. P. 23(a)(1). Impracticability does not mean impossibility of joinder, but refers to the difficulty of joinder. *Robidoux v. Celani*, 987 F.2d 931, 935 (2d Cir. 1993).

> Determination of practicability depends on all the circumstances surrounding a case, not on mere numbers. Relevant considerations include judicial economy arising from the avoidance of a multiplicity of actions, geographic dispersions of class members, financial resources of class members, the ability of claimants to institute individual suits, and requests for prospective injunctive relief which would involve future class members.

Id. at 936. Precise quantification of class members is not necessary, so long as plaintiffs reasonably estimate the number as substantial. *See id.* at 935; *McNeil v. New York City Hous. Auth.*, 719 F. Supp. 233, 252 (S.D.N.Y. 1989). The Court of Appeals for the Second Circuit has held that a prospective class of forty or more raises a presumption of numerosity. *See Consol. Rail Corp. v. Hyde Park*, 47 F.3d 473, 483 (2d Cir. 1995); *Trinidad v. Breakaway Courier Sys., Inc.*, 2007 U.S. Dist. LEXIS 2914 (S.D.N.Y. Jan. 12, 2007).

Numerosity of the class cannot reasonably be contested here. There are thousands of third-party payors in the United States. *See, e.g., In re Lupron Mktg. and Sales Practices Litig.*, 228 F.R.D. 75 (D. Mass. 2005) ("the class includes thousands of TPPs"). Given the overwhelming number of Zyprexa prescriptions during the class period, it stands to reason that most, if not all, TPPs have paid or reimbursed the cost of Zyprexa prescriptions. Accordingly, the numerosity requirement is easily satisfied.

2. Questions of Law and Fact Common to the Class

The single federal RICO statute and common factual background are common to each member of the class since each overpaid the same excess charge in each prescription. *See* Parts XVII.A.2-3, *supra*.

Because the federal RICO claim is certified, the court declines to rule on the issue of whether the state-law claims may be certified. *See* Part XXI, *infra*.

3. Claims of the Representative Parties Are Typical of the Claims of the Class

The claims of the third-party payors are typical of the claims of the class. *See* Part XIX.B, *supra*. The claims of the individual payors are not. *See id.* Only the Third-Party Payor class will be certified.

4. Representative Parties Will Fairly and Adequately Protect the Interests of the Class

Rule 23(a)(4) requires that "the representative parties will fairly and adequately protect the interests of the class." Fed. R. Civ. P. 23(a)(4). This requirement is satisfied when the class representatives have no interests conflicting with the class. *See Sosna v. Iowa*, 419 U.S. 393, 403 (1975); *Marisol A.*, 126 F.3d at 378. "The question of whether the named plaintiffs can fairly and adequately represent the class is one committed to the sound discretion of the district court." *County of Suffolk v. Long Island Lighting Co.*, 710 F. Supp. 1407, 1413 (E.D.N.Y. 1989) (internal quotation omitted), *aff'd* 907 F.2d 1295 (1990).

"Representative plaintiffs must not have interests that are antagonistic to or in conflict with those of the class as a whole," yet only a fundamental conflict will defeat the adequacy of representation requirement. *Schwab v. Philip Morris*, 449 F. Supp. 2d 992, 1107 (E.D.N.Y. 2006), *rev'd on other grounds by McLaughlin*, 522 F.3d 215; *see also In re Visa Check/MasterMoney*, 280 F.3d 124, 145 (2d Cir. 2001). The inquiry into adequacy "serves to uncover conflicts of interest between named parties and the class they seek to represent. A class representative must be part of the class and possess the same interest and suffer the same injury as the class members." *Amchem*, 521 U.S. at 625-26.

While some courts have considered the representative plaintiff's knowledge of the case, representative plaintiffs are only required to know enough about the case to "serve the interests of the class and ensure that they are not simply lending their names to a suit controlled entirely by the attorneys for the benefit of counsel." *Schwab*, 449 F. Supp. 2d at 1108; *see also Baffa v. Donaldson, Lufkin & Jenrette Sec. Corp.*, 222 F.3d 52, 61 (2d. Cir. 2000); *In re Frontier Ins. Group Secs. Litig.*, 172 F.R.D. 31 (E.D.N.Y. 1997). The Court of Appeals for the Second Circuit

has concluded: "The Supreme Court has expressly disapproved of attacks on the adequacy of a class representative based on the representative's ignorance." *Baffa*, 222 F.3d at 61 (2d. Cir. 2000) (citing *Surowitz v. Hilton Hotels Corp.*, 383 U.S. 363, 370-74 (1966)).

The credibility of the class representatives should only come into play during the class certification process if they "are so lacking in credibility that they are likely to harm their case." *In re Frontiers Ins. Group Secs. Litig.*, 172 F.R.D. 31 at 47. Courts have only held that class representatives were inadequate due to credibility concerns in extreme situations, including plaintiffs that gave inconsistent accounts of conversations or repeatedly changed their positions. *See Panzirer v. Wolf*, 663 F.2d 365, 368 (2d Cir. 1981) (plaintiff gave no less than four versions of her conversation with her broker). "Where the individual claims are not based on credibility of individual [plaintiffs], but on the characteristics of a universe to be determined with the aid of experts, the candor of one representative plaintiff among many is not decisive." *Schwab*, 449 F. Supp. 2d at 1109.

The named third-party plaintiffs are adequate representatives of the putative class. They are typical payors. There is no indication that their interests are antagonistic to the class, and they do not represent a fundamental conflict with other class members.

As to their knowledge about the case, the named plaintiffs have participated in the litigation to date, in part by answering interrogatories and having their depositions taken. Additionally, the third-party payors have informed members of the ongoing litigation (Sergeants Benevolence Association) and taken steps to require prior authorization of Zyprexa largely because of the same issues raised in this lawsuit (UFCW Local 1776). *See* Frontline Newsletter: Official Publication of the Sergeants Benevolent Association, Police Department, City of New York, Summer 2007. Plaintiffs are not merely lending their names to the case, but are aware of

the particular allegations involved in this litigation and have participated to the best of their ability. *See Baffa*, 222 F.3d at 61. There is no indication that the named plaintiffs are anything but credible.

The named individual plaintiffs cannot represent the class. *See* Part XIX.B, *supra*. An individual payors class will not be certified.

D. Class Satisfies the Requirements for Certification Under Rule 23(b)(3)

In addition to satisfying the four Rule 23(a) requirements, plaintiffs must satisfy one of the subsections of Rule 23(b). Fed. R. Crim. P. 23(b). Here, plaintiffs assert that their class is certifiable under Rule 23(b)(3), which requires that the court find that "the questions of law or fact common to class members predominate over any questions affecting only individual members, and that a class action is superior to other available methods for fairly and efficiently adjudicating the controversy." Fed. R. Crim. P. 23(b)(3). Also pertinent to the Rule 23(b)(3) inquiry are "the class members' interests in individually controlling the prosecution or defense of separate actions; the extent and nature of any litigation concerning the controversy already begun by or against class members; the desirability or undesirability of concentrating the litigation of the claims in the particular forum; and the likely difficulties in managing a class action." Fed. R. Crim. P. 23(b)(3)(A)-(D).

1. Questions of Law or Fact Common to Class Members Predominate over Questions Affecting Only Individual Members

Here both questions of law and fact are common to class members. *See* Part XX.C.2, *supra*. The only difference among class third-party payors is how much of the total overcharge each shall receive in damages. That can be readily computed based on available payment records of responsible entities. *See* Part XIX.D, *supra*.

2. Class Action Is Superior to Other Available Methods for Fairly and Efficiently Adjudicating the Controversy

Rule 23(b)(3) requires consideration of whether class action is superior to alternate methods of adjudication. Factors relevant to the inquiry include the interest of members of the class in individually controlling the prosecution or defense of separate actions, the extent and nature of any litigation concerning the controversy already commenced by or against members of the class, the desirability or undesirability of concentrating the litigation of the claims in the particular forum, and the difficulties likely to be encountered in the management of a class action. *See* Fed. R. Civ. P. 23(b)(3).

Class actions are a superior method of dealing with third-party payor claims. Denial of certification would constitute a death knell for third-party payor claims. The court takes note of the enormous amount of human and financial resources required of plaintiffs' counsel to arrive at this stage. To carry an individual burden of litigating individual actions, even for some of the largest funds, would be impractical. Individual litigation would constitute a waste of resources of the courts and the parties.

The difficulties likely to be encountered in the management of this RICO class action with respect to individual reliance and damages issues are not significant. Given the detailed evidence of payments by the class that is available, there should be no serious problems in administration. "[F]ailure to certify an action under Rule 23(b)(3) on the sole ground that it would be unmanageable is disfavored and should be the exception rather than the rule." *In re Visa Check*, 280 F.3d at 140.

In *Parker v. Time Warner Entertainment Co., L.P.*, the Court of Appeals for the Second Circuit held that the district court must revisit its refusal to certify a class under Rule 23(b)(3)

because it lacked sufficient information to determine if certification of a class would raise, among other things, issues of due process on account of the size of the class and its largely technical and statutory damage claims. 331 F.3d 13, 21-22 (2d Cir. 2003). "[T]he Court's conclusion that the size of the class would inevitably lead to 'the financial demise' of Time Warner, or even to significant manageability provisions, was speculative." *Id.* at 22. In the instant action, there is no risk that the size of any recovery or its distribution will put defendant's economic viability at issue or would create serious management problems.

"[T]he courts are arguably in the strongest position to effectively enforce appropriate standards protecting the public from fraudulent merchandising of drugs." Ct.'s Mem. & Order re Mot. for Summary J., July 3, 2007, Docket Entry No. 129. Without certification, this litigation could result in thousands of individual trials with overlap in scope, issues, testimony, and experts. Certifying a class provides an efficient and manageable means of litigating this matter.

3. Class Members' Interests in Individually Controlling the Prosecution Are Not Substantial and Can Be Fully Protected by Opt-Out Rights

Since the third-party payors are largely institutions with fiduciary obligations to manage resources and reduce costs, there is no reason to suggest that any will have due process qualms about recovery in the class litigation. Any of them may opt out. *See* the Proposed Notice Program, Part XXIII & Appendix A, *infra.*

4. Litigation Already Conducted on Behalf of the Class Is Substantial

The parties have thoroughly explored legal and factual issues and settlement. Dispositions of tens of thousands of other Zyprexa cases supply full assurance that little additional effort will be required to try the class action.

5. Desirable to Concentrate the Claims of the Class in One Forum

The fact that the Multidistrict Panel concentrated Zyprexa claims in one court, as well as procedures in related cases and extensive discovery, strongly suggest that third-party payor cases should be in one court.

6. No Substantial Difficulties in Managing Class Action

No substantial difficulties in managing this class action are likely. While the evidence is extensive, the legal and factual issues are of a garden-variety that have been thoroughly rehearsed in many federal courts.

E. Adequate Class Counsel Appointed

A court that certifies a class must ensure adequate class counsel. *See* Fed. R. Civ. P. 23(g). It "must consider:

> (i) the work counsel has done in identifying or investigating potential claims in the action;
> (ii) counsel's experience in handling class actions, other complex litigation, and the types of claims asserted in the action;
> (iii) counsel's knowledge of the applicable law; and
> (iv) the resources that counsel will commit to representing the class;

Fed. R. Civ. P. Rule 23(g)(1)(A)(i) - (iv). The court also "may consider any other matter pertinent to counsel's ability to fairly and adequately represent the interests of the class." Fed. R. Civ. P. Rule 23(g)(1)(B). "[The Adequacy of Counsel requirement] is satisfied where the class attorneys are experienced in the field or have demonstrated professional competence in other ways, such as by the quality of the briefs and the arguments during the early stages of the case." *Schwab*, 449 F. Supp. 2d at 1106 (E.D.N.Y. 2006), *rev'd on other grounds sub. nom, McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008) (citing *Klein v. A.G. Becker Paribus Inc.*, 109 F.R.D. 646 (S.D.N.Y. 1986) and *Bacon v. Toia*, 437 F. Supp. 1371 (S.D.N.Y. 1977)).

1. Class Counsel Is Adequate Under Rule 23(g)(1) & (2)

Thomas M. Sobol of Hagens Berman Sobol Shapiro, LLP and James Dugan, formerly with Dugan & Browne and now with the Murray Law Firm, were previously appointed interim class counsel in this matter. *See* Case Mgmt. Order 1, Feb. 1, 2006. Plaintiffs' counsel have fully demonstrated their competency during the progress of this now three-year-old case. Class counsel is adequate.

2. Class Counsel Will Fairly and Adequately Represent the Interests of Class Pursuant to Rule 23(g)(4)

Present class counsel can represent fairly and adequately the class as limited by the court, without the individual payors and state causes of action and for the abridged damages period only.

No potential attorney conflict of interest would result should there be settlement negotiations or trials for all or any of the Zyprexa overpricing cases or potential cases. *Cf. Ortiz v. Fibreboard Corp.*, 527 U.S. 815 (1999); *Amchem*, 521 U.S. 591. Rule 23 and other applicable law requires that there be "structural assurance of fair and adequate representation for the diverse groups and individuals affected." *Amchem*, 521 U.S. at 624-625; *accord Ortiz*, 524 U.S. at 853-4. Were there what may be considered three different plaintiff subclasses—third-party payors, individual patient payors, and state attorneys general—represented by the same counsel, it is conceivable that negotiation dynamics could potentially lead to favoring one group over another for a variety of reasons, such as difficulties in assessing damages to members of a group and providing for payment, or determining the total amounts available to each subgroup and the method of computation.

No such *Amchem* issues are raised here. Each of the proposed consumer and third-party payor class representatives has separate counsel. The court will ensure that counsel are independent. They have worked in coordination with interim class counsel and can be expected to

act ethically in connection with allocation or other issues under court, special master or magistrate judge supervision. Each state Attorney General involved in the litigation has attorneys who do not represent consumers or third-party payors. Moreover, the nature of the overpricing claims themselves "raises no apportionment difficulties because each [health benefit provider] and its patient co-payer has its own, segregable claim for economic harm to the extent of their respective co-pay." *Desiano v. Warner-Lambert Co.*, 326 F.3d 339, 350 (2d Cir. 2003), *as quoted in* Pfs.' Mem. in Response to the July 21, 2008 Order Regarding *Amchem* Issues 15-16, Aug. 4, 2008, Docket No. 05-CV-4115, Docket Entry No. 214.

F. Prosecuting Separate Actions Would Substantially Impede the Ability of Other Potential Claimants under Rule 23(b)(1)(B) to Protect Their Interests.

Were class certification granted, no potential plaintiff's ability to opt out and conduct an individual litigation would be impaired.

XXI. Conclusion as to Plaintiffs' Motion for Class Certification

Plaintiffs' motion for class certification is granted, subject to the limitations already outlined above and those stated below.

A. Limited Class Certified on RICO Claim

The certified class should be limited, as already described, to a single class of third-party payors for Zyprexa under RICO for the period June 20, 2001 to June 20, 2005. *See* Part XXIV, *infra*. Overpayments will be computed for all purchases, whether on- or off-label.

The parties have attempted to agree on a class definition following the analysis in this memorandum. Submission of a proposal does not constitute agreement with any findings now being made.

B. State Consumer Protection Claims Not Certified at this Time

State consumer protection laws vary on a range of fundamental substantive and procedural issues. The application of various state laws to a class, which would be required here, presents both predominance and manageability issues. *See, e.g.*, *Schwab*, 449 F. Supp. 2d at 1019, *rev'd on other grounds sub. nom, McLaughlin*, 522 F.3d 215 ("[T]he tort law in the fifty states is not uniform" and creates commonality, typicality, and predominance "difficulties"); *In re Pharmaceutical Industry Average Wholesale Price Litigation*, 230 F.R.D. 61, 82-86 (D. Mass. 2005) (refusing to certify a nationwide class of third-party payors and consumers because varying state laws preclude a finding of commonality, typicality, and predominance).

Plaintiffs claim that multi-state classes are manageable and that there are no material differences among the majority of state laws. They point out that most state consumer fraud statutes draw on language from the Federal Trade Commission, so that nearly all of them proscribe conduct in somewhat the same terms: "unfair practices," "deceptive practices," "unconscionable practices," using generally the same common definitions. In support of these claims, plaintiffs have submitted an ingenious Trial Plan and Statement of State Law organized around broad statutory language and propose to argue their case to the jury using "broad" jury instructions that sweep together the law of up to forty-one states. *See* Class Pfs.' Proposed Trial & Apportionment Plan & Statement of State Law in Support of Class Cert., Dec. 4, 2007, Docket Entry No. 144. The proposed state law trial plan is not adopted.

Suggestions during the course of litigation as to the impracticability of a class action based upon multiple state substantive laws were dicta, not holdings. *See* Transcript of Hearing, September, 4 2008. In view of the ease of administering a class action based upon a single national law, RICO, it would be inexpedient and wasteful of court and litigant energy to attempt to shape the present case to conform to fifty separate state substantive-procedural rules. In the

absence of a federal conflicts of law rule, or other solution, the court prefers to avoid engaging in such a daunting enterprise. Solutions required under the Class Action Fairness Act of 2005, providing for removal of state-substantive-law-based cases, can be put off for the future. *See* 28 U.S.C. § 1332(d) (expansion of diversity jurisdiction in national class action lawsuits); 28 U.S.C. §§ 1711-15 (procedures on removal of class actions).

The court declines to certify plaintiffs' state consumer fraud claims. In light of this court's ruling on the RICO claims, certification of the state claims is not necessary to afford substantially complete reimbursement for any loss due to fraud.

XXII. Administration, Damages, and Fees

A. Administration

Administration of this class litigation should be simple. A single substantive rule—RICO—applies. There are no subclasses.

Plaintiffs should have written receipts or other data indicating what was prescribed and the sales price. The available data is sufficiently accurate and complete to go to the jury. *See Schwab*, 449 F. Supp. 2d at 1065, *rev'd on other grounds by McLaughlin*, 522 F.3d 215 ("Where injury is established, damages need not be demonstrated with precision."); *see Blue Cross & Blue Shield of New Jersey, Inc. v. Philip Morris USA Inc.*, 344 F.3d 211, 224-25 (2d Cir. 2003); *cf. Lee v. Joseph E. Seagram & Sons, Inc.*, 552 F.2d 447, 456 (2d Cir. 1977) ("When it is certain that damages have been caused by a breach of contract, and the only uncertainty is as to their amount, there can rarely be good reason for refusing, on account of such uncertainty, any damages whatever for the breach. A person violating his contract should not be permitted entirely to escape liability because the amount of damages which he has caused is uncertain.") (quotation and citation omitted).

The evidence, including that of experts suffices to prove a cause of action for the class.

A simple method of computing individual class action members' damages will be available. Distribution of damages to individual payors should present no serious problem. A special master or magistrate judge will be appointed to determine whether damages have been proven with sufficient testimony, affidavits and supporting documentation as to each claimant's payments and overpayments.

B. Notice and Claims Procedures

The agreed-upon notification procedures to be used under Rule 23(c)(2), including opt-out provisions and the like, are attached as Appendix A, *infra*.

Examples of notice and claims procedures undertaken in other pharmaceutical matters, including participation rates of consumers and third-party payors and efforts taken to increase such rates, have been furnished by plaintiffs' counsel and are set forth below for litigations involving ten different pharmaceuticals. Notice and claims procedures are available to ensure widespread class participation. *See* Todd B. Hilsee, *Notice Expert Shines a Light on (Another) Bad Nationwide Class Action Notice*, 36(14) Prod. Safety & Liab. Rep. 346 (2008). The fact that a class action is settled does not detract from its relevance as to practicality. The instances relied upon by plaintiffs demonstrate that distribution of funds and allocation of damages would not present substantial problems in an action tried by a jury.

1. Paxil

In *Nichols v. SmithKline Beecham*, Docket No. 00-CV-622 (E.D. Pa.), class plaintiffs brought suit against GlaxoSmithKline, alleging the company violated antitrust and consumer protection laws by unlawfully seeking to keep lower cost generic versions of Paxil off the market. The Eastern District of Pennsylvania certified a national settlement class of all

consumers and third-party payors who purchased and paid for Paxil or its general equivalent during a six-year period. *See* Ct.'s Order Cert. Settlement Class & Prelim. Approving Settlement, Oct. 18, 2004; Order, Apr. 22, 2005.

The parties and the court distributed notice of the proposed settlement class through national consumer publications focusing on the appropriate target demographic, first class mailings to ascertainable potential class members, and a website. In order to facilitate consumer claims, the widely published summary notice even included a simple claim form that could be detached and returned by consumers. *See* Paxil Summary Notice Form 2. Although several settlements have adopted this method of notice publishing since then, the inclusion of a simple claim form in the widely published summary notice forms in the Paxil litigation was a first at that time. In total, administrators received 65,088 consumer claims and paid out more than 61,000 claims.

YOUR LEGAL RIGHTS AND OPTIONS IN THIS SETTLEMENT:	
SUBMIT A CLAIM FORM	The only way to get a payment.
EXCLUDE YOURSELF	Get no payment. This is the only option that allows you to be part of any other lawsuit against GlaxoSmithKline about the legal claims in this case.
OBJECT	Write to the Court about why you don't like the settlement.
GO TO A HEARING	Ask to speak in Court about the settlement.
DO NOTHING	Get no payment. Give up rights to be part of any other lawsuit against GlaxoSmithKline about the legal claims in this case.

2. Relafen

In re Relafen Antitrust Litigation, Docket No. 01-CV-12239 (D. Mass.), involved antitrust claims brought by putative classes of consumers and third-party payors against GlaxoSmithKline, manufacturer of the drug Relafen (nabumatone), on behalf of purchasers of

Relafen or its generic equivalent. The District Court of Massachusetts certified an exemplar litigation class of consumers and the parties thereafter entered into a nationwide settlement for $75 million. Order Approving Settlement, 231 F.R.D. 52 (D. Mass. 2005).

The notice program to consumers involved many traditional avenues, including publication in many national newspapers and magazines as well as the use of a settlement website. *Id.* Yet plaintiffs' counsel also subpoenaed data from ten of the largest retail chain pharmacies as well as the five largest pharmacy benefit managers in the United States to get contact and payment information for individual consumers for whom the entities had filled a prescription. Because of the reliability of the data, checks were sent to consumers without the need for a claims process. Thus, in addition to paying the claims of individuals who submitted traditional claim forms as a result of seeing a notice publication, the claims administrator mailed unsolicited checks, totaling more than $14 million, to more than 250,000 consumers whose information appeared in the subpoenaed data.

3. AWP

The *In re Pharmaceutical Industry Average Wholesale Price Litigation*, Docket No. MDL 1456 (D. Mass), involves RICO and state law claims against seventeen of the largest pharmaceutical manufacturers in the United States. Claims against five defendants were "fast-tracked" and three initial classes certified: a national subclass of Medicaid recipients who made or incurred an obligation to make percentage co-payments for drugs at issue, a national subclass of third-party payors who provided supplemental Medicare insurance, and a Massachusetts state-wide subclass of third-party payors and consumers who made payments for the same drugs based on AWP but outside the Medicare context. Order Certifying Class, Jan. 30, 2006.

Claims against several of the "fast-tracked" defendants culminated in a nine week bench trial in late 2006 and a finding of liability against three of those defendants. Many of the claims against many of the defendants have settled, however, and the notice and claims provisions are described briefly below.

GlaxoSmithKline Settlement: The parties settled claims against GlaxoSmithKline prior to trial for $75 million. *See* Order Approving GSK Settlement, Aug. 7, 2007. The notice program for third-party payors used traditional direct mail but the consumer notice program involved an extensive national publication program, claims website, press releases, and a direct mail notice program directed at Medicare enrollees. Plaintiffs' counsel subpoenaed electronic data from the Centers for Medicare and Medicaid Services ("CMS") and generated a list of all individual consumers who incurred an obligation to make a percentage co-payment for the drugs at issue in the settlement for the entire class period. As a result, more than two million notices were sent via first class mail to potential Medicare consumer class members. No claims have yet been paid due to the pending appeal of the court's final approval order.

AstraZeneca Settlement: The District of Massachusetts preliminarily approved a settlement between AstraZeneca and the plaintiffs in 2007. *See* Order Approving AstraZeneca Settlement, Nov. 1, 2007. Because this settlement involves only the Medicare subclass and a single drug, the parties accomplished notice of the settlement primarily through direct mail using data from CMS like that used in the GlaxoSmithKline settlement. As a result of this data, approximately 450,000 consumers received mailed notice of the settlement. In addition, as a supplement to direct mailing, the notice program also included publication of notice in a number of national publications and the creation of a settlement website.

"Track Two" Settlement: Finally, the court preliminarily approved a $125 million settlement with eleven remaining defendants, including all three subclasses. The proposed notice program in this settlement built on that approved in the GlaxoSmithKline Settlement, including mailed notice to third-party payors, mailed notice to Medicare recipients through data obtained from CMS, and an extensive national publication program. Like the AstraZeneca settlement, this data will be used not just to send direct mail notice, but to calculate Medicare consumers' potential claim amounts, thus making it easier for consumers to collect from the settlement.

In addition, the notice program also included outreach to potential consumer class members through various consumer organizations, use of television cable advertisement, and internet banner advertisement directed to health-related websites. Further, in order to try to increase participation of consumers who made payments for the drugs at issue through private insurance, plaintiffs' counsel have been working with counsel representing most of the largest third-party payors in the United States to provide data identifying consumer class members from their active membership databases. These third-party payors will provide this data to the claims administrator, who will use it to send direct mail notice to consumers who paid outside of the Medicare context.

4. Lorazepam-Clorazepate

In *State of Connecticut v. Mylan Laboratories, Inc.*, class plaintiffs brought suit against Mylan Laboratories, alleging violations of antitrust and consumer protection laws related to an exclusive agreement entered into by the defendants pertaining to the drugs lorazepam and clorazepate. *See Connecticut v. Mylan Laboratories, Inc.*, MDL No. 1290, Docket No. 99-MISC-276 (D.D.C.). The court certified a national settlement class of consumers and, in 2002, approved the settlement for $100 million. *See* Ct.'s Order, 205 F.R.D. 369 (D.D.C. 2002).

The notice program for the proposed settlement utilized national consumer publications, targeting the appropriate demographic and a website that included answers to commonly asked questions, allowed consumers to download the claim form, and contained an email link for consumers to ask additional questions. In order to facilitate consumer claims, fifteen national pharmacy chains agreed to mail settlement notices directly to over 1,000,000 consumers who purchased lorazepam and/or clorazepate, thus ensuring confidentiality of prescription data. All told, nearly 251,000 consumers received reimbursements totaling over $42 million.

5. Synthroid

In *In re Synthroid Marketing Litigation*, class plaintiffs brought suit against the various manufacturers of Synthroid, alleging violations of antitrust, RICO, and consumer protection statutes. *In re Synthroid Marketing Litig.*, MDL No. 1182, Docket No. 97-CV-6017 (N.D. Il. 1999). The Northern District of Illinois certified two national settlement classes—one for consumers and one for third-party payors—of those who purchased or paid for Synthroid. Notice of the proposed settlement included publication of ads (often full-page in size) in hundreds of newspapers and magazines and a website maintained on the internet.

6. Sereno

In the *Serono* litigation, plaintiffs claimed that defendants violated both RICO and consumer protection statutes by encouraging doctors to prescribe Serostim, a growth hormone approved by the FDA to treat HIV/AIDS patients, based on diagnostic criteria that were not approved by the FDA and for purposes other than those indicated. *Government Employees Hospital Association v. Serono,* Docket No. 05-CV-11935 (D. Mass.), and *Eugene Francis v. Serono Laboratories, Inc.,* Docket No. 06-CV-10613 (D. Mass.). There was a proposed settlement, and the court certified a national settlement class of all consumers and third-party

payors who purchased or paid for Serostim during the ten-year class period and approved a settlement in the amount of $24 million. *See* Order Granting Prelim. Approval of Settlement, Feb. 13, 2007.

Because an estimated 70% of third-party payors that had paid for Serostim were represented in the litigation, mass mailings were relied on to reach the remaining third-party payors. Notice to consumers included the traditional aspects, such as publication in newspapers and magazines and a HIV+ website. In order to better facilitate consumer claims, the parties used three novel notice techniques. First, every physician that had prescribed Serostim received direct mailings, in the hopes that they would pass the notice along to their patients. (This information was in the defendant's possession.) Second, the claims administrator reached out to various activist and charitable groups so that they might provide notice to the potential claimants they worked with. Third, counsel for plaintiffs subpoenaed certain pharmacies with the highest dispensing rates of Serostim for the names, last known addresses, and amounts paid by consumers who had purchased Serostim. The court and attorneys were extremely cognizant of privacy concerns, particularly in light of the fact that potential claimants all suffered from HIV and/or AIDS. Privacy issues were addressed through the use of appropriate protective orders, as well as having the names, addresses, and amounts paid sent directly to the claims administrator, forbidding the claims administrator to share that information with anyone (including the attorneys), and ensuring that all such information will be destroyed as soon as the consumer claims are paid. *See* Order Requiring Class Counsel to Serve Subpoenas in Furtherance of Class Claims, May 18, 2007, Docket No. 05-CV-11935, Docket Entry No. 89.

7. Buspar

In *In re Buspirone Antitrust Litigation*, class plaintiffs brought an antitrust suit against Bristol Myers Squibb, alleging that the defendant acted illegally in order to prevent the availability of less expensive, generic brands of BuSpar from coming to market. *In re Buspirone Antitrust Litig.*, Docket No. 01-MDL-1413 (S.D.N.Y. 2001). The court certified a nationwide class of approximately 119-169 million consumers who had purchased or paid for Buspar and approved a $42 million settlement.

The notice program for the proposed settlement used national consumer publications focusing on the appropriate target demographic, nearly 200 thirty-second spots aired on broadcast and cable networks, press releases, as well as audio and video news releases that were distributed to news outlets, and a website with claims information. In order to facilitate consumer claims, notice also included the involvement of certain advocacy groups: several organizations with relationships with the target audience assisted in disseminating notice of the claim through articles and providing links to the claims website.

8. Lupron

In *In re Lupron Marketing and Sales Practices Litigation*, class plaintiffs brought a suit against TAP, Abbott Laboratories, and Takeda Pharmaceuticals, alleging that they manipulated the average wholesale price of the drug Lupron and actively marketed the resulting profit doctors could make, thus increasing the price paid by consumers and third-party payors. *In re Lupron Marketing & Sales Practices Litig.*, MDL No. 1430, Docket No. No. 01-CV-10861 (D. Mass.). The court approved a proposed settlement of $150 million and certified a national settlement class of all consumers and third-party payors who purchased and paid for Lupron during a twenty-year time period. *See* Order Granting Prelim. Approval of Settlement, Cert. Class For

Purposes of Settlement, Directing Notice to the Class and Scheduling Fairness Hr'g, Nov. 24, 2004; Mem. & Order Approving Settlement & Cert. the Class, May 12, 2005.

"TPP Notice Packets" were mailed to 235,480 potential third-party payor class members. For consumers, individual notice was given where practicable, but the notice program also included nationwide publication notice, solicitation of public service radio announcements and mainstream news coverage, the posting of court-approved notices on Lupron-related websites, establishment of an interactive claims information website, and a toll-free telephone number to take questions from class members. In order to increase consumer claims, notice also included a court-approved informational release issued to news wires reaching more than 450 health and medical publications, as well as 4,200 press outlets throughout the country. The informational release was also sent to sixty-eight support groups for the diseases treated by Lupron in the hopes that the groups would inform their members.

9. Remeron

In *In re Remeron End-Payor Antitrust Litigation*, class plaintiffs brought an antitrust suit against Organon USA Inc. and Akzo Nobel N.V., alleging the companies had improperly monopolized the United States market for Remeron® and mirtazapine. *In re Remeron End-Payor Antitrust Litigation*, Master File No. 02-CV-2007 (D.N.J. 2002). The court approved a proposed settlement in the amount of $36 million and certified a nationwide class of consumers and third-party purchasers that had purchased or paid for Remeron or its generic equivalents. *See* Order Conditionally Certifying Settlement Class, Approving Representation of Attorneys General and Preliminarily Approving Proposed Settlement, June 25, 2005; Final J. & Order Certifying Settlement Class, Approving Proposed Settlement and Dismissing Actions, Aug. 31, 2005.

The parties used traditional measures of notifying class members of the settlement—such as press releases and Radio public service announcements—but also utilized additional types of notice. First, website banner advertising brought individuals to the settlement website, where they could submit a claim. (The target demographic for these class members was known to be heavy with Internet users.) The claims administrator and state attorneys general also solicited the help of chain pharmacies, third-party payors, senior citizen organizations, mental health organizations, psychiatrists, and women's organizations in spreading word to the target demographic for consumer class members. *See* Letter from The Kroger Family of Pharmacies, to Customer (Apr. 20, 2005); Letter from Claims Administrator, Complete Claims Solutions, Inc., to Doctor (Mar. 14, 2005). Nearly 70,000 consumer claims were paid out.

10. Hytrin

In *In re Terazosin Hydrochloride Antitrust Litigation*, plaintiffs brought suit against Abbott Laboratories and Geneva Pharmaceuticals, alleging defendants had violated antitrust and consumer protection laws in marketing Terazosin products (including Hytrin). *In re Terazosin Hydrochloride Antitrust Litig.*, Docket No. 99-MDL-1317 (S.D. Fla.). The court approved a settlement in the amount of $30.7 million and certified a class of all consumers and TPPs in eighteen states who paid for all or part of the purchase price of Hytrin or its generic equivalents over a ten year period. *See* Order Prelim. Approving the Indirect Purchaser Pf. Settlement, May 7, 2005.

Notice to third-party payor class members included direct mailing and publication. Notice to consumers included direct mailings to chain pharmacies asking them to display Point of Sale ("POS") placards on their counters, which demonstrably increased the number of claims filed. *See* Order Approving Form & Language of Point-Of-Sale Placard, July 8, 2005; Letter from

Settlement Administrator, Complete Claims Solutions, Inc., to Pharmacy Manager (undated); Aff. of Thomas R. Glenn re: Consumer Claim Submissions as a Result of the Point-Of-Sale Placard Project.

C. Damages

Damages in the present case will not be speculative. They will be based on proven payments by plaintiffs. Fluid recovery will not be relied upon. It has no bearing on the instant case. *See McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), *subsequently placed in doubt by Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008). Because of Lilly's patent monopoly for Zyprexa, while sales have decreased, the price has remained essentially the same, increasing slightly in parallel with competing drugs. A price differential can be validly determined by the jury year by year for the few years in which damages are permitted under the temporal definition of the class.

Since under plaintiffs' theory a single amount of overcharge is attributable to each prescription, a subclass for an award for off-label use is not required. No other subclass is required.

XXIII. Interlocutory Appeal

When denying summary judgment in *In re Zyprexa Prods. Liab. Litig.*, 493 F. Supp. 2d 571 (E.D.N.Y. 2007), this court noted that:

> Section 1292(b)'s requirements are not met in this case, even though both the substantive and procedural law relied upon by the parties are in a state of flux and not free from doubt. An immediate appeal might save considerable costs in discovery, preparation for trial, and trial. But an interlocutory appeal should await a decision on the critical question of class certification—an issue not yet considered by the court. When that question is decided by this court, the Court of Appeals can in its discretion decide the class certification issue under Rule 23(f) of the Federal Rules of Civil Procedure. For this reason, upon deciding on class certification this court plans to certify an interlocutory appeal under [18 U.S.C.] § 1292(b) so the class-procedural and substantive merits can be considered together by the appellate court.

493 F. Supp. 2d at 580-81.

Now that the critical question of class certification has been decided, the court continues to be of the opinion that its Order of June 28, 2007, denying Lilly's motion for summary judgment, involves a controlling question of law as to which there is substantial ground for difference of opinion and that an immediate appeal from the Order may materially advance the ultimate termination of the litigation. An interlocutory appeal is certified on this court's order denying summary judgment. The requirements of 18 U.S.C. § 1292(b) have been met. *See* 18 U.S.C. § 1292(b) (providing that a district court judge may certify an order to the Court of Appeals that is "not otherwise appealable" if the judge is "of the opinion that such order involves [1] a controlling question of law [2] as to which there is a substantial ground for difference of opinion and [3] that an immediate appeal from the order may materially advance the ultimate termination of the litigation . . . "). A delay in certification of the interlocutory appeal was designed to avoid unnecessary separate applications to the Court of Appeals for the Second Circuit.

Primarily that question is whether Lilly is entitled to summary judgment on the ground that plaintiffs cannot satisfy essential elements of their RICO and state law claims, particularly computation of damages. As noted in the court's summary judgment opinion, the law controlling this litigation is in a state of flux. Recent appellate decisions may call into question some aspects of the decision. *See, e.g., McLaughlin v. American Tobacco Co.*, 522 F.3d 215 (2d Cir. 2008), and *Bridge v. Phoenix Bond & Indemnity Co.*, 128 S. Ct. 2131 (2008). Because the court has now entered this Order on Plaintiffs' Motion for Class Certification—which is subject to interlocutory appeal pursuant to Rule 23(f) of the Federal Rules of Civil Procedure—certification of the Order of June 28, 2007 at this time will allow the Court of Appeals for the Second Circuit

to consider, at its discretion, the interrelated issues involved in the rulings on summary judgment and class certification.

In accordance with 28 U.S.C. § 1292(b) and Rule 5(a)(3) of the Federal Rules of Appellate Procedure, the Court's Order of June 28, 2007, is incorporated, amended, and resettled herein, and Lilly's time to petition for appeal from that Order should begin to run from the entry of today's order. *See Al-Jundi v. Estate of Rockefeller*, 757 F. Supp. 206 (W.D.N.Y. 1990) (certifying an order after it was originally entered); *see also Marisol A. by Forbes v. Giuliani*, 104 F.3d 524, 528 (2d Cir. 1996) (permitting the recertification of an order even where the would-be petitioner failed, through its own negligence, to timely appeal the original certified order). Having carefully evaluated all circumstances surrounding the certification for interlocutory review of the Order of June 28, 2007, in relation to the ultimate efficiency goals of § 1292(b), this court determines that certification at this time is proper.

Interlocutory appeal provisions of Rule 23(f) of the Federal Rules of Civil Procedure on certification of the class also apply. *See* Fed. R. Civ. P. 23(f) ("A court of appeals may permit an appeal from an order granting or denying class-action certification"). Further proceedings in this court are stayed pending any possible remand by the Court of Appeals for the Second Circuit or refusal to hear an interlocutory appeal under section 1292(b) or Rule 23(f). *See id.* ("An appeal does not stay proceedings in the district court unless the district court of appeals so orders.").

XXIV. Conclusion

A. Unsealed Documents

Plaintiffs' motion for an order under Rule 23(d) permitting publication of approximately 350 documents previously designated confidential is granted. *See* Pfs.' Notice of Mot. & Mem. in Support, Aug. 4, 2008, Docket No. 05-CV-4115, Docket Entry Nos. 215-16; *see* Part II.C,

supra. All documents, reports, depositions, arguments, and transcripts referred to in the First Amended Complaint, the motions to dismiss, motions for summary judgment (including plaintiffs' Fact Proffer), and certification motions are unsealed. Also unsealed are the all materials cited in this court's summary judgment order and the present opinion and memorandum. The protective order embodied in Case Management Order 3 will no longer apply to these documents after the special master acts. *See Gambale*, 377 F.3d at 141("[A] district court can modify a protective order when a third party requests judicial documents"); *State of Alaska v. Eli Lilly & Co.*, Docket No. 3AN-06-5630 CI (Alaska Sup. Ct. 3d Dist., June 13, 2008) (granting Bloomberg, LLC's motion to intervene and unseal certain documents that had been confidentially filed with the Alaska court pursuant to its blanket protective order).

Unsealing accords with this country's general policy of public accessibility of court records. *See Nixon v. Warner Communication*, 435 U.S. 589, 597 (1978) (recognizing a "general right to inspect and copy public records and documents, including judicial records and documents."). Documents may be protected under Rule 26(c) of the Federal Rules of Civil Procedure if the court finds that there is "good cause . . . to protect a party or person from annoyance, embarrassment, oppression, or undue burden or expense, including . . . requiring that a trade secret or other confidential research, development, or commercial information not be revealed or be revealed only in a specified way . . . ." Fed. R. Civ. P. 26(c)(1)(G). But "[d]ocuments that are properly protected under Rule 26(c)(7) should nonetheless be declassified unless defendant demonstrates an extraordinary reason to keep them under seal." Order 7-8, Mar. 30, 2007, Docket No. 04-MD-1956, Docket Entry No. 1227. Lilly's legitimate interest in confidentiality does not outweigh the public interest in disclosure at this stage of the litigation. *Gambale v. Deutsche Bank AG*, 377 F.3d 133, 142 (2d Cir. 2004) ("A district court that

concludes that there is a public right of access to judicial documents . . . acts within its jurisdiction when it modifies or vacates a protective order to allow that access"). The documents are now so outdated that unsealing will not significantly harm Lilly.

Public access is now advisable because this litigation involves issues of great public interest, the health of hundreds of thousands of people, fundamental questions about our system of approval and monitoring of pharmaceutical products, and the funding for many health and insurance benefit plans. Public and private agencies and organizations have a right to be informed. At this stage public disclosure, congruent with our long tradition of open courts, is desirable. *See In re Zyprexa Injunction*, 474 F. Supp. 2d 385, 394-95 (E.D.N.Y. 2007); *see, e.g.*, *In re Agent Orange Prods. Liab. Litig.*, 104 F.R.D. 559, 572 (E.D.N.Y. 1985), *aff'd* 821 F.2d 139 (2d Cir. 1987) (declassifying documents upon a showing "that the need for disclosure outweighs the need for further protection"); *see also In re Agent Orange Prods. Liab. Litig.*, 821 F.2d 139, 145 (2d Cir.1987) ("It is undisputed that a district court retains the power to modify or lift protective orders that it has entered."); Monograph, Individual Justice in Mass Tort Litigation 66-72 (1995); Aaron Twerski, et al., *Secrecy and the Civil Justice System*, 9 J. of L. & Pol'y, 51, 51-107 (2000); Note, *Secrecy in Civil Trials: Some Tentative Views*, 9 J. of L. & Pol'y 53 (2000); Catherine Wimberly et al., *Secrecy in Law and Science*, 23 Cardozo L. Rev. 1 (2001). Some documents have already been released. *See In re Zyprexa Injunction*, 474 F. Supp. 2d 385 (E.D.N.Y. 2007). Most are so old as to be unlikely to reveal current secrets.

Release of these documents is also appropriate under Federal Rule of Civil Procedure 23(d)(1)(B)(iii), which provides for the issues of orders that:

> [P]rotect class members and fairly conduct the action—giving appropriate notice to some or all class members of . . . (iii) the members' opportunity to signify whether they consider the representation fair and adequate, to intervene and present claims or defenses, or to otherwise come into the action . . . .

Fed. R. Civ. P. 23(d)(1)(B)(iii). Due process and fundamental fairness dictate that class members be allowed to view these documents and make informed decisions about whether to participate in the litigation. Plaintiffs' plan to post these documents and the unredacted pleadings on a website is appropriate since this method will make them available at the least possible cost to those most likely to be interested. *See* Notice Plan, Appendix A, *infra*. The public and interested parties should know the evidence upon which the parties relied in view of the significance of the case.

The matter is referred to the special master to supervise the unsealing so as to avoid unnecessary embarrassment or damage to any party. In the course of that supervision, the special master may order specific items redacted or to be sealed in part or whole. Names of individual plaintiffs shall be redacted and referred to by number, to permit later identification if that becomes necessary. This court's umbrella protective order, Case Management Order 3, still applies to the vast majority of Lilly documents produced in discovery; only those documents specified above are unsealed.

Reference to the special master will permit time for an application for a stay to the Court of Appeals for the Second Circuit. Until the special master rules, the unsealing is stayed.

B. Class Certification Order

Upon consideration of plaintiffs' motion for class certification, and for the reasons set forth in this memorandum and order, the motion is granted in part and denied in part as follows.

1. The court finds that the requirements of Rules 23(a) and 23(b)(3) of the Federal Rules of Civil Procedure are satisfied.

2. Pursuant to Rule 23(c)(1) of the Federal Rules of Civil Procedure, the court certifies a Class, defined as follows:

> All private, non-governmental, entities in the United States and its territories that are at risk, pursuant to a contract, policy

> or plan, to pay or reimburse all or part of the cost of Zyprexa prescribed, provided, or administered to natural persons covered by such contract, policy or plan during the period from June 20, 2001 to June 20, 2005.

3. The Class is certified for pretrial and trial purposes only for Counts I and II in the First Amended Class Action Complaint asserted under the Racketeering Influenced and Corrupt Organization Act ("RICO"), 18 U.S.C. § 1864, that are predicated on the alleged overpricing of Zyprexa, limited to the period June 20, 2001, to June 20, 2005, and all defenses to those counts.

4. Plaintiffs' request to certify a class for consideration of any claim under RICO that is predicated on theories other than the alleged overpricing of Zyprexa or for any claim for the period before June 20, 2001 or after June 20, 2005 is denied.

5. A decision on plaintiffs' request to certify a class for consideration of Counts III, IV and V (state law claims) is deferred in light of this court's ruling on the RICO claims.

6. Plaintiffs' request to certify a class comprising of individuals who paid for Zyprexa is denied.

7. The following entities are designated as representatives of the class:

   UFCW Local 1776 and Participating Employers Health and Welfare Fund;

   Mid-West National Life Insurance Company of Tennessee;

   Local 28 Sheet Metal Workers;

   Sergeants Benevolent Association Health and Welfare Fund;

   United Federation of Teachers Welfare Fund; and

   AFSCME District Council 37 Health and Security Fund.

Fed. R. Civ. P. 23(d)(1)(B)(iii). Due process and fundamental fairness dictate that class members be allowed to view these documents and make informed decisions about whether to participate in the litigation. Plaintiffs' plan to post these documents and the unredacted pleadings on a website is appropriate since this method will make them available at the least possible cost to those most likely to be interested. *See* Notice Plan, Appendix A, *infra*. The public and interested parties should know the evidence upon which the parties relied in view of the significance of the case.

The matter is referred to the special master to supervise the unsealing so as to avoid unnecessary embarrassment or damage to any party. In the course of that supervision, the special master may order specific items redacted or to be sealed in part or whole. Names of individual plaintiffs shall be redacted and referred to by number, to permit later identification if that becomes necessary. This court's umbrella protective order, Case Management Order 3, still applies to the vast majority of Lilly documents produced in discovery; only those documents specified above are unsealed.

Reference to the special master will permit time for an application for a stay to the Court of Appeals for the Second Circuit. Until the special master rules, the unsealing is stayed.

B. Class Certification Order

Upon consideration of plaintiffs' motion for class certification, and for the reasons set forth in this memorandum and order, the motion is granted in part and denied in part as follows.

1. The court finds that the requirements of Rules 23(a) and 23(b)(3) of the Federal Rules of Civil Procedure are satisfied.

2. Pursuant to Rule 23(c)(1) of the Federal Rules of Civil Procedure, the court certifies a Class, defined as follows:

> All private, non-governmental, entities in the United States and its territories that are at risk, pursuant to a contract, policy

8. Pursuant to Rule 23(g) of the Federal Rules of Civil Procedure, Thomas M. Sobol of Hagens Berman Sobol Shapiro LLP and James R. Dugan, II, of the Murray Law Firm are appointed as co-lead class counsel. Co-lead class counsel may, as they have to date, associate other lawyers and firms to provide services for the Class.

9. The Notice Program proposed by the parties and attached as Appendix A, *infra*, meets the requirements of Rule 23(c)(2)(B) of the Federal Rules of Civil Procedure. It is approved. Notice to the class shall not be given at this time, pending possible review by the Court of Appeals of the Second Circuit of this memorandum and order pursuant to Rule 23(f) of the Federal Rules of Civil Procedure.

SO ORDERED.

Jack B. Weinstein
Senior United States District Judge

Date: September 5, 2008
Brooklyn, New York

Appendix A: Notice Plan Agreed Upon by Parties

Notice Program

UCFW Local 1776 and Participating Employers Health and Welfare Fund, et al vs. Eli Lilly and Company

No. 05-CV-41115

United States District Court for the
Eastern District of New York

Table of Contents

Firm Overviews

Complete Claim Solutions, LLC
Headquartered in Palm Beach Gardens, Florida, Complete Claim Solutions, LLC ("CCS") is an administration firm specializing in consumer, insurance, employment, securities and antitrust class action settlements. The CCS team is made up of professionals with backgrounds in, but not limited to, claims administration, legal, imaging, quality assurance, insurance, financial and management information systems. Our experience, talent and technology allow us to provide powerful support and simple solutions for even the most complex settlements.

CCS has a significant amount of combined experience in legal, claims administration including notice dissemination and settlement implementation. This experience includes administering numerous settlements and notice plans; implementing low to high-volume settlements, both complex and simple; building, customizing and maintaining database systems designed to receive, process, and track claims, prepare letters and labels, create reports and payout distributions; receiving and scrubbing millions of records in a variety of data formats and media submissions; working with a number of search vendors, based on settlement requirements, who assist in locating Class members and beneficiaries; disseminating related pieces of correspondence on various settlements, including notices of pendency, settlement notices, claim forms, benefit statements or refund forms, deficiency and rejection letters, coupons, vouchers and checks; coordinating small to multi-million dollar media campaigns including identifying Class or industry specific publications, reach and demographic analysis, placement of summary notices, and website development to target certain classes or consumer populations; managing call center activities including maintenance of toll-free numbers, oversight of customer service representatives, with bilingual and hearing-impaired (TTY/TDD) capabilities, customized scripts, training and 24-hour support; scanning/imaging of hardcopy correspondence including the configuration of scanning software to work with proprietary systems and setup of optical character recognition (OCR) of key data and bar-coded information; conducting operational reviews, including testing and auditing services for troubled settlements; and performing distribution functions including disbursement of settlements, coupons, vouchers and checks, accounting and reconciliation of monthly bank statements, and tax reporting.

To minimize costs, CCS utilizes several service providers for printing and mailing of various Notices and Proofs of Claim to Class members. In addition to providing professional services at reasonable rates, our service providers are familiar with the class action process and understand the deadlines imposed by the Courts. Together, we have been able to produce small and large volume mailings from simple to complex forms, in a variety of design formats and color combinations.

Kinsella/Novak Communications, LLC

Kinsella/Novak Communications, LLC ("KNC") is a nationally recognized legal notification firm specializing in media-based class action and bankruptcy notification programs in the antitrust, consumer, mass tort and product liability arenas. Specific cases have involved, among others, asbestos, breast implants, home siding and roofing products, infant formula, pharmaceuticals, polybutylene plumbing, tobacco and Holocaust claims. KNC has directed some of the largest and most complex national notification programs in the country. The firm has developed or consulted on over 325 notification programs and has placed over $175 million in media notice.

KNC develops advertisements, press materials, websites and other notice materials that bridge the gap between litigation complexities and the need for a clear and simple explanation of legal rights. In addition to designing and producing notices in "plain language," all KNC notice programs are fully compliant with Rule 23 of the Federal Rules of Civil Procedure and comparable state guidelines. The firm employs industry-recognized tools of media measurement to quantify the adequacy of the notice for the court.

Situation Analysis

There is a pending class action lawsuit involving Third-Party Payors ("TPPs") and Eli Lilly and Company ("Lilly"). The lawsuit alleges that Lilly improperly marketed Zyprexa and, as a result, TPPs over-paid for the drug. Lilly denies these claims.

The Class includes all private, non-governmental TPPs, such as insurance companies, union health and welfare benefit plans and other entities in the United States and its territories that paid or were obligated to pay, either directly or indirectly, for all or part of the purchase price of a Zyprexa prescription for persons covered during the period from June 20, 2001 to June 20, 2005. TPPs that paid a fixed co-payment are not included in the Class.

Direct Mail notice will be provided to all identifiable TPPs. To supplement the extensive Direct Mail notice, supplemental notice will be provided in the form of published notice.

Notice Program Overview

This Notice Program is submitted by KNC in connection with *UCFW Local 1776 and Participating Employers Health and Welfare Fund, et al., vs. Eli Lilly and Company*, No. 05-CV-4115, pending in the United States District Court for the Eastern District of New York. The Notice Program outlines procedures to provide notice of the certification of the Class in this case, consistent with the requirements set forth in Rule 23 of the Federal Rules of Civil Procedure.

The following three-part Notice Program is recommended.

- Direct notice by First-class mail to all identifiable TPPs and to all persons who request the *Notice of Class Certification* (the "Notice") as a result of seeing the published form of notice ("Publication Notice").

- Supplemental published notice to TPPs through the use of trade publications and newspapers in the U.S. Territories and Possessions.

- Electronic notice through a dedicated website.

DIRECT NOTICE

Direct Mail notice to TPPs will consist of mailing the Notice, attached as Exhibit 1 to all identifiable TPP Class Members informing them of their legal rights and how they may exclude themselves from the class action, if they wish.

The Notice will be sent to all entities likely to be Class Members contained in the proprietary TPP Database compiled by CCS. The Database includes insurance companies, healthcare and welfare funds, employee benefit funds, third-party administrators, pharmacy benefit managers and other record keepers for noticing purposes in TPP class actions. The Database was compiled by contacting, researching and accessing the records of various databases and listings of affiliations, group insurance plans, self-insureds, ERISA funds, pharmacy benefit manager listings, etc. as follows:

- Pharmacy Benefit Management Institute;
- Benefits SourceBook;
- Managed Care Information Centers;
- Judy Diamond Associates;
- AM Best Company;
- Association of Managed Care Providers;
- Society of Professional Benefit Administrators;
- American's Health Insurance Plans;
- Self-Insurance Institute of America; and
- National Association of Insurance Commissioners.

Included in the Database, among others, are:

- Approximately 29,000 companies with 100 or more employees that have self-funded (fully or partially) plans, derived from Form 5500 filings;
- 1,356 Third-Party Claim Administrators; and
- 1,300 member companies of American Health Insurance Plans that provide or administer health insurance benefits to over 200 million Americans which

represent 90 percent of the managed care market (HMOs, PPOs and POSs, etc.).

The Database has been used in numerous class actions targeting TPPs and is regularly updated with new entries from the above sources as well as TPPs identified through other class action settlements.

The Notice will also be sent to all persons who call the toll-free number as a result of seeing the Publication Notice.

PUBLISHED NOTICE

To supplement the extensive direct mail, KNC will cause the Publication Notice to appear in national trade publications and newspapers in the U.S. Territories and Possessions.

TRADE PUBLICATIONS

HRMagazine

- A full-page ad (7-1/2" x 10-3/8") will appear once in *HR Magazine* with an estimated circulation of 213,141.

- *HR Magazine* is the official publication of the Society for Human Resource Management. It is written for human resources professionals and executives and to further the professional aims of both the Society and the human resource management profession. The publication features new approaches and innovative best practices in all areas of HR management and informs on new models of ways of thinking. It is designed as a forum for trends and legal issues as well as new concepts used by human resources management professionals. It has the highest readership of any human resources publication.

National Underwriter LIFE & HEALTH

- A full-page ad (7" x 10") will appear once in *National Underwriter Life and Health* with an estimated circulation of 50,206.

- *National Underwriter Life and Health* is the only weekly magazine serving the life, health and financial services market. It contains news and feature articles to help agents better understand products and markets, and insurance company executives identify new business opportunities. Topics covered include agency management, taxes, legislation, executive benefits, retirement planning and profitable sales ideas.

NEWSPAPERS

To provide notice in U.S. Territories and Possessions, KNC selected newspaper advertising. The Publication Notice will be translated, when necessary, and appropriately sized for placement in the following newspapers in Puerto Rico and in the U.S. Territories and Possessions:

U.S. TERRITORY/POSSESSION	NEWSPAPER	CIRCULATION
American Samoa	*Samoa News*	2,500
Guam	*Agana Pacific News*	22,451
Northern Mariana Islands	*Saipan Tribune*	4,000
Puerto Rico	*El Nuevo Dia*	204,772
Puerto Rico	*El Vocero*	185,613
Puerto Rico	*San Juan Star*	105,597
St. Croix (United States Virgin Islands)	*St. Croix Avis*	11,000
St. John (United States Virgin Islands)	*St. John Trade Winds*	3,000
St. Thomas (United States Virgin Islands)	*St. Thomas News*	16,362

Notice Design

Recent revisions to Rule 23(c)(2) of the Federal Rules of Civil Procedure as well as most state rules of civil procedure require class action notices to be written in "plain, easily understood language." KNC applies the plain language requirement when drafting notices in federal and state class actions. The firm maintains a strong commitment to adhering to the plain language requirement while drawing on its experience and expertise to draft notices that effectively transmit the necessary information to Class Members.

The plain language Publication Notice, attached as Exhibit 2, is designed to alert Class Members to the litigation through the use of a bold headline. This headline will enable Class Members to quickly determine if they are potentially affected by the litigation. Plain language text provides important information regarding the subject of the litigation, the Class definition and the legal rights available to Class Members.

Each advertisement will prominently feature a toll-free number and website address for Class Members to obtain the Notice and other information.

Website Design

An informational interactive website is a critical component of the Notice Program. A website is a constant information source instantly accessible to millions. The site will utilize the Internet's ability to serve as a key distribution channel and customer service bureau. Internet banner ads will help direct Class Members to the website.

Combining clean site design, consistent site navigation cues and search engine optimization, the website will provide Class Members with easy access to the details of the litigation.

EXHIBIT 1

UNITED STATES DISTRICT COURT – EASTERN DISTRICT OF NEW YORK

If You are a Third-Party Payor That Paid or Reimbursed for Zyprexa® for Persons Covered from June 20, 2001 to June 20, 2005

A Class Action May Affect Your Rights

A federal court authorized this Notice. This is not a solicitation from a lawyer.

- There is a pending class action lawsuit involving Third-Party Payors ("TPPs") and Eli Lilly and Company ("Lilly"). The lawsuit alleges that Lilly improperly marketed Zyprexa® and, as a result, TPPs over-paid for the medication. Lilly denies these allegations. TPPs in the United States and its territories are included.

- There is no money available at this time and no guarantee there will be. However, your legal rights are affected by the Court's decision to certify a Class, and you must decide whether to remain in the lawsuit or exclude yourself.

- The name of the lawsuit is *UCFW Local 1776 and Participating Employers Health and Welfare Fund, et al, vs. Eli Lilly and Company,* No. 05-CV-4115. This case is pending in the U.S. District Court for the Eastern District of New York.

A Summary of Your Rights and Choices:
Your Legal Rights Are Affected Even If You Do Not Act.
Read This Notice Carefully.

You May:		**Due Date:**
Remain in the Class	If you wish to stay in the Class, you do not need to do anything. You will not be able to file your own lawsuit against Lilly for the claims in this lawsuit and you will also be bound by the Court's decisions concerning the case, including any trial. **See Question 5.**	***N/A***
Exclude Yourself	You can write and ask to get out of the Class and keep your right to sue Lilly on your own about the claims in the lawsuits. **See Questions 7 and 8.**	***Postmarked or E-Mailed by Month Date 2008***

WHAT THIS NOTICE CONTAINS

BASIC INFORMATION

1. Why did I get this Notice?

You received this Notice because you are a Third-Party Payor that might have made payments or reimbursements for Zyprexa® prescriptions pursuant to a contract, policy or plan for persons covered by such contract, policy or plan between June 20, 2001 to June 20, 2005 ("Class Period").

You may also have requested this Notice after seeing the Summary Notice in a publication. If so, the lawsuit may affect you.

This Notice explains:

- What the lawsuit is about.
- What the lawsuit claims and what Lilly says about the claims.
- Who is affected by the Class Action.
- Who represents the Class in the lawsuit.
- What your legal rights and choices are.
- How and by when you need to act.

2. What is the lawsuit about?

The lawsuit alleges that Lilly overcharged for and over-promoted the medication Zyprexa®, and that, as a result, TPPs overpaid for the drug. Specifically, the lawsuit alleges that:

a) Lilly understated the dangers of weight gain, Hypercholesterolemia, and Diabetes related to taking Zyprexa®;
b) Lilly overstated the efficacy of Zyprexa® in treating several psychiatric disorders and conditions;
c) Lilly promoted Zyprexa® as superior to other similar medications used to treat psychiatric disorders and conditions;
d) Lilly engaged in wrongful marketing efforts to increase total sales of Zyprexa®, including for uses not approved by the FDA; and
e) Lilly conspired with other parties to accomplish its marketing plans.

Lilly denies these allegations. Specifically, Lilly says that its conduct has been lawful and that it has defenses to all of the claims. Lilly also says that Plaintiffs' claims fail as a matter of law and that Plaintiffs are not entitled to any recovery.

The fact that the Court has certified this case as a class action does not mean Plaintiffs have won or that the dispute has been resolved. The Court has not decided whether the Plaintiffs or Lilly are right. Rather, the Court has simply certified part of the case against Lilly for trial as a class action.

3. Why is this lawsuit a class action?

In a class action lawsuit, one or more parties called "class representatives" sue on behalf of people or entities that have similar claims. The people or entities together are a "class" or "class members." The court can determine if it will allow a lawsuit to proceed as a class action. If it does, the Court then decides the lawsuit for everyone in the class, or the parties may settle without a decision by the Court.

4. Who are the Class Members?

The Class includes:

All private, non-governmental entities in the United States and its territories that are at risk, pursuant to a contract, policy, or plan, to pay or reimburse all or part of the cost of Zyprexa® prescribed, provided, or administered to natural persons covered by such contract, policy, or plan during the period from June 20, 2001 to June 20, 2005. An entity is "at risk" when it is obligated to pay or reimburse without any reimbursement to it from another source.

Such entities may include, but are not limited to, insurance companies, union health and welfare benefit plans, entities with self-funded plans that contract with a health insurance company or other entity to serve as a third-party claims administrator to administer their prescription drug benefits, private entities paid by any governmental entity (including a state Medicaid program), and other organizations that paid for all or part of a Zyprexa® prescription from June 20, 2001 to June 20, 2005.

Not included in the Class are:

a) Lilly and its present or former, direct and indirect, parents, subsidiaries, divisions, partners and affiliates;
b) The United States government, its officers, agents, agencies and departments;
c) The States of the United States and their respective officers, agents, agencies and departments;
d) All other local governments and their officers, agents, agencies and departments; and
e) Those who contract with ultimate TPPs of a prescription drug benefit to perform certain services in the administration and management of that prescription drug benefit for those ultimate TPPs.

REMAINING IN THE CLASS

5. What happens if I do nothing and stay in the Class?

If you do nothing, you will be included in the Class. You will be bound by the outcome of the proceedings. If you stay in the Class and the Plaintiffs obtain money or benefits, either as a result of a trial or a settlement, you will be notified about how to participate (or how to ask to be excluded from any settlement).

6. If I remain in the Class, what am I giving up?

Keep in mind that if you remain in the Class, regardless of whether the Plaintiffs win or lose the trial, you will not be able to sue Lilly on your own in the future for claims like those asserted in this lawsuit.

EXCLUDING YOURSELF FROM THE CLASS

7. Why would I want to be excluded from the Class?

If you wish to keep the right to sue Lilly on your own for the claims in this lawsuit, you need to ask to be **excluded** from the Class. If you exclude yourself from the Class, you will not get any money or benefits from this lawsuit. However, you may then be able to sue Lilly for damages that relate to the purchase of Zyprexa® on your own. If you exclude yourself, you will not be legally bound by the Court's judgments in this class action.

If you start your own lawsuit against Lilly after you exclude yourself, you'll have to hire and pay your own lawyer for that lawsuit, and you'll have to prove your claims. If you are considering excluding yourself from the class so that you can start your own lawsuit against Lilly, you should talk to your own lawyer soon, because exclusion from the class may affect the statute of limitations.

8. How do I exclude myself from the Class?

If you are a TPP and wish to be excluded from the Class, send a written request that indicates the following:

- The name, address and telephone number of the TPP;
- The name and number of this class action: *UCFW Local 1776 and Participating Employers Health and Welfare Fund, et al, vs. Eli Lilly and Company* No. 05-CV-4115.
- The tax identification number for the TPP;
- A statement that the individual signing the letter is authorized to act on behalf of the TPP; and
- A statement that you want to be excluded from the Class.

If a TPP seeks to act on behalf of other TPPs for which it administers prescription drug benefits, the exclusion request must also include the tax identification numbers for each entity seeking to be excluded. It must also include a statement that the individual signing the letter has the authority to act on behalf of such entity either expressly or by contract.

All exclusion requests must either be mailed first class, **postmarked on or before [Month Date,] 2008,** to:

Zyprexa® TPP Litigation Administrator
P.O. Box xxx
City, State Zip code

Or must be **emailed on or before [Month Date,] 2008,** to:

Zyprexa® TPP Litigation Administrator
[email address]

Please remember that you can't exclude yourself by phone.

THE LAWYERS REPRESENTING THE CLASS

9. Do I have a lawyer representing my interests in this case?

Yes. The Court has appointed the following law firms to represent you and other Class Members:

Thomas M. Sobol
Hagens Berman Sobol Shapiro LLP
www.hagens-berman.com
One Main Street, 4th Floor
Cambridge, MA 02142

James R. Dugan, II
Murray Law Firm
www.murray-lawfirm.com
650 Poydras Street, Suite 2150
New Orleans, LA 70130

These lawyers are called Class Counsel. You will not be charged personally for these lawyers, but they will ask the Court to award them a fee that will be paid from any award or recovery that may be established in the lawsuit. More information about Class Counsel and their experience is available at the websites listed above.

You may hire your own attorney, if you wish. However, you will be responsible for that attorney's fees and expenses.

THE TRIAL

10. How and when will the Court decide who is right?

The Court will issue a Scheduling Order, including the trial date, which will be posted at www.xxxxxxx.gov. The Court's address is xxxxxxxxxxxxxx. If a trial takes place, a Jury will hear all evidence to help them reach a decision about whether the Plaintiffs or Defendant are right about the claims in the lawsuit. There is no guarantee that the Plaintiffs will win, or that they will get any money for the Class.

11. Do I have to come to the trial?

You do not need to attend the trial unless you receive notice to attend, as a witness for example. Class Counsel will present the case for the Plaintiffs, and Lilly will present the defenses. You and/or your own lawyer are welcome to come at your own expense.

12. Will I get money after the trial?

If the Plaintiffs obtain money or benefits as a result of the trial or a settlement, you will be notified about how to participate. We do not know if this will happen, or how long this will take.

GETTING MORE INFORMATION

13. Where do I obtain more information?

More details are available in the legal documents that have been filed with the Court. You can look at and copy these documents at any time during regular office hours at the Office of the Clerk of Court, xxxxxxxxxxxxxxxxxxxxx.

- These documents will also be available on the Zyprexa® TPP Litigation Web site at www.xxxxxxx.com,
- You can call 1-800-xxx-xxxx
- You can write and request specific information form the Zyprexa® TPP Litigation Administrator, PO Box xxxx, City, State Zip.

[date]

EXHIBIT 2

If You are a Third-Party Payor That Paid or Reimbursed for Zyprexa® for Persons Covered from June 20, 2001 to June 20, 2005

A Class Action May Affect Your Rights

There is a pending class action lawsuit involving Third-Party Payors ("TPPs") and Eli Lilly and Company ("Lilly"). The lawsuit alleges that Lilly improperly marketed Zyprexa®. The name of the lawsuit is *UCFW Local 1776 and Participating Employers Health and Wellfare Fund, et al, vs. Eli Lilly and Company,* No. 05-CV-4115. This case is pending in the U.S. District Court for the Eastern District of New York.

This Notice is only a summary. For complete information, you should read the complete Notice available by visiting the website or calling the toll-free number listed below.

What is This Lawsuit About?

Lilly is the manufacturer of Zyprexa®. The lawsuit claims that Lilly overcharged for and over-promoted Zyprexa®, and as a result, TPPs overpaid for the drug. Lilly denies that it did anything wrong. The Court has not made a decision about the claims; it has only decided that the case can move forward as a class action.

Who is Affected?

The Class is made up of TPPs that paid or were obligated to pay, either directly or indirectly, for all or part of a the purchase price of a Zyprexa® prescription for persons covered during the period from June 20, 2001 to June 20, 2005. TPPs in the United States and its territories are included.

What Are My Legal Rights?

You have a choice of whether to stay in the Class or not, and you **must decide this now**.

Remain in the Class

You do not have to do anything to remain in the Class. However, if you stay in the Class, you will be bound by any decision in this lawsuit. You won't be able to bring your own separate lawsuit against Lilly for the same claims that are the subject of this lawsuit now or in the future. If benefits become available in the future, you will be notified about how to participate.

Exclude Yourself from the Class

If you do not want to remain in the Class, you must exclude yourself in writing, postmarked on or before **Month Date Year.** If you exclude yourself, you cannot get any money or benefits from this lawsuit if they are awarded. However, you will keep the right to bring your own separate lawsuit against Lilly for these claims, and you will not be bound by any orders or judgments of the Court.

Who Represents the Class?

The Court has appointed attorneys to represent the Class. These lawyers are called Class Counsel. You will not be charged personally for these lawyers, but they will ask the Court to award them fees and expenses. You may hire your own attorney, if you wish. However, you will be responsible for that attorney's fees and expenses.

For More Information and a Copy of the Complete Notice,

Visit: www.xxxxxxxxx.com Call: 1-8xx-xxx-xxxx

Or Write: Zyprexa® TPP Litigation Administrator
P.O. Box xxxx, City, State Zip