This is a securities class action on behalf of all purchasers of the publicly traded securities of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company") between March 28, 2000 and March 30, 2003 (the "Class Period"), against Regeneron and certain of its officers and directors for violations of the Securities Exchange Act of 1934 (the "1934 Act").

2. Regeneron is a biopharmaceutical company that discovers, develops and intends to commercialize therapeutic drugs for the treatment of serious medical conditions. During the Class Period, Regeneron initiated Phase II clinical trials for its diet drug AXOKINE for use in obese patients. Defendants claimed that AXOKINE would help patients lose weight better than a placebo over a year. However, more than two-thirds of the 1,467 patients on the medicine in the clinical trials developed antibodies to it
after three months, which made the medicine less effective. The injected medicine, which would be Regeneron's first marketed product, stimulates an area of the brain regulating body weight. Before results were released, defendants had led the public to believe that AXOKINE would have more than $500 million in annual sales. Patients taking AXOKINE, including those who developed antibodies, lost an average 6.2 pounds, compared with 2.6 pounds for those on a placebo, which the Company admits is similar to results dieters get with already available pills.

3. On March 31, 2003, Regeneron admitted AXOKINE lost effectiveness in about 70% of patients in a study. On this news, the biotechnology company's shares plunged 57%. However, even defendants’ admission was false, as, in fact, defendants manipulated the results of the study. In truth, 73.5% of the patients developed antibodies to the drug.

4. On this news, the Company's shares plunged 57%, a market cap loss of more than $500 million.

5. The true facts which were known by each of the defendants, but concealed from the investing public during the Class Period, were as follows:

   (a) The Company's Phase III results were falsely spun to portray a favorable outcome. Since Regeneron was aware of its previous false and misleading statements regarding immunogenicity of AXOKINE, Regeneron misled investors by portraying Phase III results involving undesirable antibody formation in a highly positive manner. Since Regeneron has stated that in the design of AXOKINE immunogenic regions of the molecule were removed, Regeneron misled investors by using limited safety and tolerability data to allay concerns about antibody formation. Moreover, these statements are false and misleading for the following reasons:

   (i) Since Regeneron was aware of its previous false and misleading statements regarding immunogenicity of AXOKINE, it sought to portray Phase III study results involving detection of antibodies in a favorable manner. Regeneron knows that obese and diabetic patients are in a high-risk category. An anti-obesity drug in development that elicits an immune response in the majority of the population tested cannot be judged based on the available data as safe and effective for limited use, specifically, over a three month period, as Regeneron proposed in a recent article in the *Los Angeles Times*. In fact, in 73.5% of the patients tested with AXOKINE that completed one year of treatment, an
immune response occurred and has persisted. By Regeneron's own admission, this response persists for as long as one year. Regeneron has insufficient safety data showing that, in combination with other anti-obesity drugs or in combination with other conditions and health issues faced by a large segment of patients suffering from obesity, diabetes or the conditions in combination, the immune response elicited by AXOKINE can be ignored. Thus, the portrayal of the progress made through Phase III development ignores the dimensions of this immune response and is wholly false and misleading.

(ii) By stating in the November 2000 disclosure that Regeneron scientists had "deciphered" the mechanism by which ciliary neurotrophic factor ("CNTF") caused weight loss and then had synthesized a more potent version of CNTF, Regeneron represented that AXOKINE was designed based on a detailed understanding of the molecule and its mechanism of action. By stating that native human CNTF was intentionally altered to remove certain immunogenic regions of the molecule, Regeneron represented that it clearly understood what would make their more potent version of CNTF immunogenic and that it purposefully altered the molecule to "remove" those immunogenic regions, to yield the recombinant CNTF known as AXOKINE.

(iii) Regeneron claimed to have published a definitive account of the mechanism of action of AXOKINE in a Proceedings of the National Academy of Sciences ("PNAS") article in April of 2001. However, Regeneron in fact failed to provide a definitive account of the mechanism of action of the drug in this article, and in particular, if and how AXOKINE alters the hypothalamic body weight setpoint. The Regeneron supposition regarding this action of the drug is important support of its claim that the drug acts differently than forced dieting by preventing binge overeating and rapid rebound weight gain after termination of treatment. Moreover, since Regeneron failed to properly complete the study of the biomolecular action of CNTF in causing weight loss, the claim regarding removal of certain immunogenic regions as part of the overall design of the recombinant CNTF known as AXOKINE is also wholly false and misleading. Without a sophisticated and scientifically complete understanding of the mechanism of action of the recombinant CNTF known as AXOKINE, Regeneron scientists would not know how to design and alter the structure of the molecule.

(b) Moreover, the statements regarding immunogenicity were false for a multitude of reasons:
(i) By failing to report levels of antibodies in patients who were enrolled in the 12 week Phase II study at 24, 36 and 48 weeks, Regeneron purposefully withheld information regarding the immunogenicity of AXOKINE.

(ii) Regeneron misled and continues to mislead investors as to the sufficiency of preclinical and early clinical work on the immunogenicity of AXOKINE, despite existing FDA guidances on the undesirability of immunogenic properties of investigational new drugs, including recombinant biomolecules.

(iii) Since many recombinant cytokines possess immunogenic properties, resulting in the formation of both neutralizing and non-neutralizing antibodies, Regeneron scientists cannot claim that, absent clear and demonstrable evidence to the contrary, the recombinant CNTF known as AXOKINE would not be highly immunogenic.

(c) Regeneron sought to suppress immunogenicity of AXOKINE by pegylation. By failing to disclose the true purpose of pegylation of recombinant cytokines, including AXOKINE, Regeneron misled investors as to the nature and importance of antibody formation and into believing that AXOKINE, unlike many other cytokines, will not elicit neutralizing or non-neutralizing antibodies.

6. As a result of the defendants’ false statements, Regeneron's stock price traded at inflated levels during the Class Period, increasing to as high as $40 on December 18, 2000, whereby the Company and its top officers and directors sold more than $430 million worth of their own securities.

**JURISDICTION AND VENUE**

7. Jurisdiction is conferred by §27 of the 1934 Act. The claims asserted herein arise under §§10(b) and 20(a) of the 1934 Act and Rule 10b-5.

8. (a) Venue is proper in this District pursuant to §27 of the 1934 Act. Many of the false and misleading statements were made in or issued from this District.

(b) The Company's principal executive offices are in Dallas, Texas, where the day-to-day operations of the Company are directed and managed.
THE PARTIES

9. Plaintiff Maxine Phillips purchased Regeneron publicly traded securities as described in the attached certification and was damaged thereby.

10. Defendant Regeneron is a biopharmaceutical company that discovers, develops and intends to commercialize therapeutic drugs for the treatment of serious medical conditions. During the Class Period, the Individual Defendants caused the Company to issue $430 million worth of its own securities.

11. Defendant Leonard S. Schleifer ("Schleifer") was the President and CEO of Regeneron. During the Class Period, Schleifer sold more than $1.08 million worth (or close to half his shares) of Regeneron stock.

12. Defendant George D. Yancopoulos ("Yancopoulos") was the Chief Scientific Officer of Regeneron. During the Class Period and just prior to the Company making its March 31, 2003 disclosure, Yancopoulos sold more than $2.6 million worth (or more than half his shares) of Regeneron stock.

13. Defendant Hans-Peter Guler ("Guler") was the Vice President of Clinical Studies of Regeneron. During the Class Period, Guler sold more than $212,000 worth (or more than half his shares) of Regeneron stock.

14. Defendant Neil Stahl ("Stahl") was Vice President of Regeneron. During the Class Period, Stahl sold more than $557,000 worth (or more than half his shares) of Regeneron stock.

15. Defendant Murray A. Goldberg ("Goldberg") was the Chief Financial Officer of Regeneron. During the Class Period, Goldberg sold more than $1.5 million worth (or more than half his shares) of Regeneron stock.

16. The individuals named as defendants in ¶¶11-15 are referred to herein as the "Individual Defendants." The Individual Defendants, because of their positions with the Company, possessed the power and authority to control the contents of Regeneron's quarterly reports, press releases and presentations to securities analysts, money and portfolio managers and institutional investors, i.e., the market. Each defendant was provided with copies of the Company's reports and press releases alleged herein to be misleading prior to or shortly after their issuance and had the ability and opportunity to prevent their issuance or cause them to be corrected. Because of their positions and access to material non-public information available to them but not to the public, each of these defendants knew that the adverse facts
specified herein had not been disclosed to and were being concealed from the public and that the positive representations which were being made were then materially false and misleading. The Individual Defendants are liable for the false statements pleaded herein at ¶¶26-29, 31-36 and 38, as those statements were each "group-published" information, the result of the collective actions of the Individual Defendants.

SCIENTER

17. In addition to the above-described involvement, each Individual Defendant had knowledge of Regeneron's problems and was motivated to conceal such problems. Moreover, the expertise of collaborative partners and knowledge of the scientific literature and reports within the areas of Regeneron research interests must be imputed to Regeneron. Regeneron knew that pegylation is an effective strategy in minimizing the occurrence of anti-drug antibodies. Clinical trial data indicated during the Class Period that AXOKINE did not otherwise have severe potency issues. The antibody issue was the real reason for embarking on this parallel development program. Since Regeneron was aware of its previous false and misleading statements regarding immunogenicity of AXOKINE, Regeneron purposefully failed to disclose the rationale for mounting this program. The internal reports showing Regeneron's forecasted growth were premised on false statements concerning its drugs. Defendants, as top officers, directors and scientists, were responsible for the financial results and press releases issued by the Company. Each Individual Defendant sought to demonstrate that he could lead the Company successfully and generate the growth expected by the market.

FRAUDULENT SCHEME AND COURSE OF BUSINESS

18. Each defendant is liable for (i) making false statements, or (ii) failing to disclose adverse facts known to him about Regeneron. Defendants' fraudulent scheme and course of business that operated as a fraud or deceit on purchasers of Regeneron publicly traded securities was a success, as it (i) deceived the investing public regarding Regeneron's prospects and business; (ii) artificially inflated the prices of Regeneron's publicly traded securities; (iii) allowed defendants to obtain larger bonuses which were directly tied to the performance of Regeneron shares; (iv) allowed defendants to arrange to sell and actually sell in excess of $430 million worth of Regeneron securities at artificially inflated prices; and (v) caused plaintiff and other members of the Class to purchase Regeneron publicly traded securities at inflated prices.

BACKGROUND

-6-
19. FDA guidance for industry documents serves as a roadmap for drug development. These documents also serve as an assurance to investors of how firms are expected to manage development risks anticipated by regulators. A 1997 FDA guidance dealing with preclinical development requirements was available to Regeneron. Per the guidance, the AXOKINE anti-drug antibody issue should have been understood at an earlier stage of development.

20. AXOKINE is a genetically engineered version of ciliary neurotrophic factor ("CNTF"). CNTF is a cytokine, associated with central, peripheral, and sensory neurons. Cytokines are soluble glycoproteins released by cells of the immune system, which act nonenzymatically through specific receptors to regulate immune responses. Regeneron genetically modified CNTF based on implication of the factor in mechanisms important for metabolism and weight loss.

21. Regeneron recognized CNTF for its beneficial effects on motor neurons. The neurotropic factor was initially evaluated in patients suffering from a motor neuron disease known as amyotrophic lateral sclerosis ("ALS"). In a trial in over 750 patients suffering from ALS, CNTF caused significant weight loss. Using animal models of diet-induced obesity, Regeneron determined the mechanism of action for induction of weight loss and dosages that caused weight loss without other side effects, such as cachexia or wasting. Regeneron then synthesized a new more potent version of CNTF, termed AXOKINE, from which certain immunogenic regions of the molecule were removed.

22. Regeneron was therefore aware of the immunogenicity of CNTF and worked to remove this potential from the molecule. The communications between the Company and the FDA concerning antibody formation and other indications of immunoreactivity through the course of the clinical studies provide a framework to understand the defendants' individual knowledge.

23. In July of 1997, the FDA issued a Guidance to Industry entitled "S6 Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals." This guidance was endorsed both by the Center for Drug Evaluation and Research ("CBER") and Center for Biologics Evaluation and Research ("CDER") divisions and was harmonized under the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("ICH"). The scope of the guidance is clear:

1.3 Scope
This guidance is intended primarily to recommend a basic framework for the preclinical safety evaluation of biotechnology-derived pharmaceuticals. It applies to products derived from characterized cells through the use of a variety of expression systems including bacteria, yeast, insect, plant, and mammalian cells. The intended indications may include in vivo diagnostic, therapeutic, or prophylactic uses. The active substances include proteins and peptides, their derivatives, and products of which they are components; they could be derived from cell cultures or produced using recombinant deoxyribonucleic acid (DNA) technology, including production by transgenic plants and animals. Examples include but are not limited to: Cytokines, plasminogen activators, recombinant plasma factors, growth factors, fusion proteins, enzymes, receptors, hormones, and monoclonal antibodies.

24. **AXOKINE preclinical research conducted by Regeneron was governed by the recommendations in this guidance.** The immunogenic properties of CNTF were known to Regeneron at a very early stage of development. Genetic engineering was necessary to remove certain immunogenic regions from the molecule. Again, the guidance is clear as to the preclinical study requirements. The following recommendations are noteworthy, when considered in relation to any biotechnology-derived investigational drug experiencing immunogenicity issues during Phase III studies, absent sufficient investigation at the preclinical development stage:

3.6 Immunogenicity

Many biotechnology-derived pharmaceuticals intended for humans are immunogenic in animals. Therefore, measurement of antibodies associated with administration of these types of products should be performed when conducting repeated dose toxicity studies in order to aid in the interpretation of these studies. Antibody responses should be characterized (e.g., titer, number of responding animals, neutralizing or non-neutralizing) and their appearance should be correlated with any pharmacological and/or toxicological changes. Specifically, the effects of antibody formation on pharmacokinetic/pharmacodynamic parameters, incidence and/or severity of adverse effects, complement activation, or the emergence of new toxic effects should be considered when interpreting the data. Attention should also be paid to the evaluation of possible pathological changes related to immune complex formation and deposition.

The detection of antibodies should not be the sole criterion for the early termination of a preclinical safety study or modification in the duration of the study design unless the immune response neutralizes the pharmacological and/or toxicological effects of the biopharmaceutical in a large proportion of the animals. In most cases, the immune response to biopharmaceuticals is variable, like that observed in humans. If the interpretation of the data from the safety study is not compromised by these issues, then no special significance should be ascribed to the antibody response.

25. The principles of preclinical investigation outlined in the guidance apply to the AXOKINE development program. Significant deviation from these principles increases the risk of failure at later stages of the program. Since the FDA had issued this guidance in July of 1997, it is clear that the type of concern
now facing the AXOKINE development program should have been addressed and was known to the defendants prior to the beginning of the Class Period.

FALSE AND MISLEADING STATEMENTS

26. On March 28, 2000, the Company issued a press release entitled, "Regeneron Initiates Phase II Obesity Clinical Trial." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced that it has initiated a Phase II dose-ranging trial to study the safety and efficacy of AXOKINE® second generation ciliary neurotrophic factor in obese patients. AXOKINE is being developed for the treatment of obesity and complications of obesity such as Type II diabetes. The double-blind, placebo-controlled multicenter clinical trial will be conducted in approximately 175 severely obese patients who will be treated for 90 days at doses up to 2 micrograms per kilogram per day administered subcutaneously.

The Phase II study follows a two-week Phase I study completed in late 1999, in which mildly to moderately obese subjects treated with AXOKINE lost weight and had reduced food intake compared to those on placebo.

In the Phase I study, some patients who received higher doses of AXOKINE and who had previously contracted herpes simplex virus (HSV) experienced "cold sores" related to reactivation of their HSV infection. The Phase II study will be conducted at doses that were associated with weight loss, generally well tolerated, and not associated with herpes cold sores in the Phase I study; there will be no restrictions as to a subject's prior history of herpes cold sores. The Phase II study is designed to confirm the weight loss observed in the Phase I study in a trial of longer duration and to determine the lowest effective well-tolerated dose.

27. On March 30, 2000, just two days after the Company announced its initiation of Phase II trials, the Company issued a press release entitled, "Regeneron Announces Pricing of Public Offering of Shares of Common Stock." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced that its public offering of 2,600,000 shares of common stock was priced yesterday at $29.75 per share, for gross proceeds to the Company of $77,350,000. The offering is expected to close on April 4, 2000.

A shareholder of the Company has granted a 30-day option to the underwriters of the offering to purchase up to an additional 390,000 shares of Regeneron common stock at the public offering price to cover over-allotments, if any. Regeneron will not receive any of the proceeds from shares sold by the selling shareholder.

The net proceeds of the offering received by Regeneron, totaling approximately $72,952,000 after underwriting discounts and estimated expenses, will be used for working capital and general corporate purposes, including research and development.

28. On June 13, 2000, the Company issued a press release entitled, "Regeneron Expands AXOKINE Clinical Program for Obesity by Initiating a Study in Type 2 Diabetics." The press release stated in part:
Regeneron Pharmaceuticals, Inc. today announced the initiation of a clinical trial to assess the safety and efficacy of AXOKINE® in overweight and obese individuals with type 2 diabetes mellitus.

This is the fourth clinical trial to be initiated as part of Regeneron's Phase III clinical program of AXOKINE for the treatment of obesity. This is the first of two planned studies that will measure the weight loss effects of AXOKINE in people who have type 2 diabetes mellitus.

"More than 15 million people in the United States suffer from diabetes, and each year another 800,000 Americans are newly diagnosed. The medical costs of treating diabetes exceed $45 billion annually," noted Leonard S. Schleifer, M.D., Ph.D., President and Chief Executive Officer of Regeneron. "Excess weight has been linked to type 2 diabetes and is associated with many of its chronic side effects. With this trial, we want to begin evaluating weight loss with AXOKINE in people who have type 2 diabetes to see if it may reduce some of the negative effects of this growing healthcare problem."

Summary of Clinical Study in Patients with Type 2 Diabetes Mellitus.

This AXOKINE study is double-blind and placebo-controlled. Participants will be randomized into three treatment groups and given placebo or one of two AXOKINE doses (0.5 or 1.0 mcg/kg/day) for 12 weeks. At the end of the initial phase, all participants, in two separate dose groups, will receive AXOKINE for a 12-week extension period. This trial will measure weight loss and explore the short-term effects of weight loss with AXOKINE on blood levels of insulin, glucose, and other glycemic parameters.

The study will involve approximately 180 overweight and obese subjects with type 2 diabetes. The study will be conducted at approximately 12 sites within the United States. Study participants will be adults who have a body mass index (BMI) of 27 to 45 kg/m2 (kilograms per meter of height squared).

29. On July 10, 2000, the Company issued a press release entitled, "Regeneron Completes Enrollment for Phase II Obesity Clinical Trial." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced that it has completed enrollment for its Phase II dose-ranging trial to study the safety and efficacy of AXOKINE® second generation ciliary neurotrophic factor in obese patients. AXOKINE is being developed for the treatment of obesity and complications of obesity such as Type II diabetes.

The double-blind, placebo-controlled multicenter clinical trial is being conducted in approximately 175 severely obese patients who will be treated for 3 months at doses up to 2 micrograms per kilogram per day administered subcutaneously.

The Phase II study follows a two-week Phase I study completed in late 1999, in which mildly to moderately obese subjects treated with AXOKINE lost weight and had reduced food intake compared to those on placebo. The Phase II study is being conducted at doses that were associated with weight loss and generally well tolerated in the Phase I study. The Phase II study is designed to confirm the weight loss observed in the Phase I study in a trial of longer duration and to determine the lowest effective well-tolerated dose.

Hans-Peter Guler, M.D., Regeneron's Vice President, Clinical Sciences, commented: "We are pleased that enrollment has progressed so rapidly, and we
expect to have the results of this trial by around the end of this year. Obesity is a serious and growing medical problem in all developed countries, and obesity-related conditions rank second only to smoking as a cause of preventable death. There is a real need for a drug that can safely and effectively treat medically serious obesity."


31. On November 28, 2000, the Company issued a press release entitled, "Regeneron's Obesity Drug Demonstrates Medically Significant Weight Loss in Phase II Clinical Trial; Phase III Study Planned for 2001." The press release stated in part:

Regeneron Pharmaceuticals, Inc. today announced results of a Phase II dose-ranging trial to study the safety and efficacy of AXOKINE® in severely obese patients.

Patients treated with AXOKINE showed medically meaningful and statistically significant weight loss compared to those receiving a placebo in a dose-dependent manner (p less than 0.0001). Patients who received the optimal dose of AXOKINE over the 12 week treatment period averaged 10 pounds more weight loss than patients on placebo (p less than 0.0001) and continued to lose weight over the entire treatment period. Moreover, 46% of these treated patients lost at least 10 pounds, compared with just 5% of those on placebo. The drug was generally well tolerated and was not associated with any serious adverse events.

"Everyone at Regeneron is pleased with these results, which indicate that AXOKINE has the potential to help address a growing health crisis. Millions of people in the United States suffer from obesity, and the problem is especially serious for the approximately 12 million people with clinically severe obesity. The prevalence and severity of obesity has risen sharply in recent years in many developed nations, and that trend shows no signs of easing," said Leonard S. Schleifer, M.D., Ph.D., President and Chief Executive Officer of Regeneron. "Subject to discussions with regulatory authorities, we plan on initiating Phase III testing of AXOKINE as quickly as possible to gather information about the safety and efficacy of the drug in larger numbers of patients over longer periods of time."

"Pending confirmation of these results and obtaining further safety and efficacy data in additional clinical studies, AXOKINE appears to be one of the most promising potential treatments for obesity. Weight loss in this trial was at a medically desirable rate," said Steven B. Heymsfield, M.D., Deputy Director of the New York Obesity Research Center, Professor of Medicine at Columbia University's College of Physicians and Surgeons, and an investigator in the Phase II clinical study. "Physicians and patients desperately need new treatment approaches for obesity, which substantially increases the risk of morbidity and mortality from Type 2 diabetes, hypertension, coronary heart disease, stroke, gallbladder disease, certain cancers, and many other medical conditions."
**Trial Design and Results**

The Phase II trial was a randomized, double-blind, placebo-controlled, out-patient study conducted at seven clinical sites in the United States. Patients participating in the study were severely or morbidly obese, with an average baseline weight of 240 pounds and a body mass index (BMI) between 35 and 50 kg/square meter. Following an initial two-week "run-in period" in which all subjects received a placebo, 170 patients were randomized into five groups who received 12 weeks of daily treatment, administered under the skin by patient self–injection. Four of the groups were part of the pre–specified primary analyses and consisted of a group receiving placebo, a second group receiving a daily dose of 0.3 micrograms (mcg) per kilogram (kg) of AXOKINE, a third group receiving a daily dose of 1.0 mcg/kg, and a fourth group receiving a daily dose of 2.0 mcg/kg. The fifth group consisted of patients who received a daily dose of 1.0 mcg/kg for eight weeks, followed by a blinded withdrawal period in which they received placebo for four weeks.

The pre-specified co-primary endpoints of the study were change in weight for the patients who completed the full 12 weeks of treatment ("Completer Analysis"), as well as change in weight for all patients, whether or not they completed the full 12 weeks of treatment ("Last Observed Value Analysis"). All AXOKINE-treated groups showed statistically significant weight loss compared to placebo, as summarized below:

### Completer Analysis

**Mean Weight Change from Baseline (pounds)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Weight Change</th>
<th>p value (relative to placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=19)</td>
<td>+1.3</td>
<td>---</td>
</tr>
<tr>
<td>0.3 mcg/kg (n=23)</td>
<td>–3.4</td>
<td>p = 0.01</td>
</tr>
<tr>
<td>1.0 mcg/kg (n=26)</td>
<td>–8.9</td>
<td>p less than 0.0001</td>
</tr>
<tr>
<td>2.0 mcg/kg (n=19)</td>
<td>–7.5</td>
<td>p less than 0.0001</td>
</tr>
</tbody>
</table>

### Last Observed Value Analysis

**Mean Weight Change from Baseline (pounds)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Weight Change</th>
<th>p value (relative to placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=31)</td>
<td>+0.6</td>
<td>---</td>
</tr>
<tr>
<td>0.3 mcg/kg (n=31)</td>
<td>–2.4</td>
<td>p = 0.04</td>
</tr>
<tr>
<td>1.0 mcg/kg (n=37)</td>
<td>–7.5</td>
<td>p less than 0.0001</td>
</tr>
<tr>
<td>2.0 mcg/kg (n=33)</td>
<td>–5.8</td>
<td>p less than 0.0001</td>
</tr>
</tbody>
</table>
Patients in the fifth group who received 1 mcg/kg of daily AXOKINE for eight weeks, followed by the four week blinded withdrawal period, lost weight during the treatment period and did not appear to regain weight while taking placebo.

Safety and Tolerability

No serious adverse events associated with the drug were reported during the trial. The most common side effect was dose-dependent injection site reactions (skin redness), which occurred in all patient groups, including placebo, and were generally mild. Other side effects associated with the drug included cough, which was notable only in the highest dose group, and nausea, which occurred most frequently in the highest dose group. There was no increase compared to placebo in the incidence of herpes simplex virus infections in patients taking AXOKINE. Neutralizing antibodies, based on a laboratory test, were not dose-related and occurred in less than 10% of all patients receiving AXOKINE. Further evidence of the tolerability of the drug was demonstrated by the ratio of patients in each dose group completing the full 12 weeks of treatment: placebo, 61%; 0.3 mcg/kg, 74%; 1.0 mcg/kg, 70%; and 2.0 mcg/kg, 58%.

Hans-Peter Guler, M.D., Regeneron's Vice President of Clinical Sciences, stated: "We are pleased that the trial accomplished its major objectives. We established an optimal dose of AXOKINE of 1 mcg/kg and demonstrated that this dose causes medically significant weight loss and is generally well-tolerated in a short-term study of 12 weeks. We look forward to gathering further safety and efficacy data for AXOKINE in the Phase III clinical trial that we plan to initiate in 2001."

AXOKINE: Scientific Rationale in Obesity

AXOKINE is a genetically re-engineered version of a naturally occurring human protein known as ciliary neurotrophic factor (CNTF). Preclinical studies have shown that injected AXOKINE travels through the bloodstream to reach a critical area of the brain, known as the hypothalamus, that regulates body weight. AXOKINE binds to specific receptors and activates key signaling pathways in the hypothalamus that suppress appetite and reduce body weight. Both the site and mechanism of action of AXOKINE are similar to those of leptin, a natural hormone regulator of body weight that is released by fat cells. However, in animal models of the most common form of obesity (diet-induced obesity), animals are resistant to administration of leptin, while AXOKINE is able to cause substantial weight loss.

In animal studies, AXOKINE caused weight loss, produced selective loss of fat (as opposed to lean body mass), and had beneficial effects on obesity-associated comorbidities such as diabetes. In addition, unlike forced dieting, cessation of AXOKINE treatment did not lead to an immediate rebound in weight.

"It's very satisfying that animal models of diet-induced obesity seem to have correctly predicted AXOKINE's ability to cause weight loss in common human obesity," commented George D. Yancopoulos, M.D., Ph.D., the Chief Scientific Officer and Senior Vice President of Research at Regeneron.

Previous Trials of AXOKINE and CNTF

CNTF was first recognized for its beneficial effects on motor neurons, and initially it was evaluated in patients suffering from a motor neuron disease known as amyotrophic lateral sclerosis (ALS). In a trial in over 750 patients suffering from ALS, CNTF caused significant weight loss. Using animal models of diet-induced obesity, Regeneron scientists deciphered the mechanism by which CNTF
induced weight loss and identified doses of CNTF that caused weight loss without other side effects, such as cachexia or wasting. They then synthesized a new more potent version of CNTF, termed AXOKINE, from which certain immunogenic regions of the molecule were removed.

In 1999, Regeneron conducted a Phase I study of AXOKINE in mildly to moderately obese healthy volunteers. In this 14-day in-patient study, subjects treated with AXOKINE lost weight and had reduced food intake compared to those on placebo. Dose ranges that appeared well-tolerated were identified and evaluated in the current Phase II.

32. On March 20, 2001, the Company issued a press release entitled, "Regeneron Announces Pricing of Public Offering of Shares of Common Stock." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced that its public offering of 7,000,000 shares of the Company's common stock was priced at $25.00 per share.

The Company is selling 6,500,000 shares and a shareholder is selling 500,000 shares. Gross proceeds to Regeneron will be $162,500,000. The Company will not receive any of the proceeds from shares sold by the selling shareholder. The offering is expected to close on March 23, 2001.

The net proceeds of the offering received by Regeneron, totaling approximately $153,625,000 after underwriting discounts and estimated expenses, will be used for preclinical and clinical development, research, working capital, and general corporate purposes.

33. On July 31, 2001, Regeneron reported 24-week follow-up data from the Phase II clinical trial (12 weeks post-treatment with AXOKINE). In this news release, Regeneron made no mention of (a) the removal of immunogenic regions from the more potent version of CNTF known as AXOKINE, (b) further discussion of the observation of antibodies as observed after 12 weeks of treatment, or (c) any positive or negative comments regarding observation of antibodies at 24 weeks (12 weeks post-treatment with AXOKINE). These omissions were highly material, since any further report of neutralizing antibodies post 12 weeks would impact judgment as to the risks inherent in the development program.

34. On September 11, 2001, Regeneron reported 36 and 48 week (24 and 36 weeks post-treatment) follow-up data from this same Phase II clinical trial. Again, Regeneron makes no mention of (a) the removal of immunogenic regions from the more potent version of CNTF known as AXOKINE, (b) further discussion of the observation of antibodies as observed after 12 weeks of treatment, or (c) any positive or negative comments regarding observation of antibodies at 36 and 48 weeks (24 and 36 weeks post-treatment with AXOKINE). These omissions rendered the report incomplete at best, since it represented the final account of results for the Phase II trial.
35. On October 12, 2001, the Company issued a press release entitled, "Regeneron Sells $200 Million of Convertible Senior Subordinated Notes." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced today that it has entered into a purchase agreement providing for the sale of $200 million aggregate principal amount of convertible senior subordinated notes due 2008, reflecting an increase in the size of the offering from $150 million. In addition, the company has granted the initial purchasers an option to purchase an additional $50 million in principal amount of notes. The notes will accrue interest at a rate of 5.50% per year and will be convertible into shares of Regeneron common stock at a conversion price of $30.25. The notes are redeemable by the company at any time if certain conditions are satisfied. The offering will be made by means of an offering memorandum to qualified institutional buyers pursuant to Rule 144A of the Securities Act of 1933, as amended, and is expected to close on or about October 17, 2001. Regeneron expects to use the net proceeds from this offering for development of its drug candidates, expansion of its manufacturing facilities, research, working capital, and general corporate purposes.

36. On January 9, 2002, the Company issued a press release entitled, "Regeneron Completes Enrollment for AXOKINE Phase III Obesity Clinical Trial." The press release stated in part:

Regeneron Pharmaceuticals, Inc. announced today at the JP Morgan H&Q Healthcare Conference that it has completed enrollment for a [sic] initial pivotal trial in its Phase III program for the treatment of obesity.

The program will assess the safety and efficacy of AXOKINE® in obese patients. The double-blind, randomized, placebo-controlled study has enrolled approximately 2,000 patients at 65 study sites across the United States.

"We are extremely pleased by the enthusiastic response from the physicians and patients participating in this clinical program. The rate of enrollment was rapid, and thus far the dropout rate is low. To date, we have seen an overall dropout rate of 4%, with an average patient time in the study of 2 months," remarked Hans-Peter Guler, M.D., Regenerons Vice President, Clinical Sciences.

The AXOKINE Phase III Program

This pivotal trial will have a 12-month treatment period, in which patients will receive daily subcutaneous self-injections of placebo or AXOKINE at a dose of 1.0 microgram (mcg) per kilogram (kg) of body weight. The treatment period will be followed by a 12-month open-label safety extension phase, during which all patients will receive AXOKINE. Endpoints of the study are based on changes in body weight versus baseline during the treatment period.

To be included in the initial study, patients must have a body mass index (BMI) of 30 to 55 if they do not have obesity-related risk factors and 27 to 55 if they have obesity-related risk factors, such as elevated blood pressure or increased blood lipids. People are classified as overweight if they have a BMI between 25 and 30, and obese if they have a BMI of 30 or greater. BMI is a medical measure of obesity. It measures weight in relation to height and is calculated as weight in kilograms divided by height measured in meters, squared. For example, a person 5'8" tall weighing 174 pounds would have a BMI of 27 and be considered overweight. The same 5'8" adult weighing 258 pounds would have a BMI of 40 and be considered extremely obese.
As part of the overall Phase III program, Regeneron will conduct additional confirmatory and ancillary studies of AXOKINE in obese and obese diabetic patients. These studies will vary in duration and size. The Phase III program is expected to enroll approximately 4,000 subjects in total.


38. On June 13, 2002, Regeneron reported that it initiated a Phase I study for "pegylated AXOKINE." In this announcement, Regeneron reported that (a) this chemically modified version of AXOKINE is a potentially more potent and longer-lasting molecule, and (b) that the molecule will be prepared using chemistries devised by Shearwater Corporation, a division of Inhale Therapeutics Systems.

Regeneron Pharmaceuticals, Inc. announced that it has initiated a Phase I clinical trial to assess the safety and pharmacokinetics of the Company's pegylated version of AXOKINE (PegAXOKINE) for the treatment of obesity. Regeneron developed this chemically modified version of AXOKINE as a potentially more potent and longer-lasting molecule. AXOKINE is currently being evaluated in a large Phase III program for overweight and obese patients. The PegAXOKINE Phase I trial is a placebo-controlled, double-blind, single-dose, dose-escalation study.

*     *     *

Pegylated AXOKINE is a second-generation molecule designed to remain in the bloodstream longer. Pegylation achieves that goal by attaching polyethylene glycol polymer chains to therapeutic molecules. Shearwater Corporation, a division of Inhale Therapeutic Systems, Inc., will supply the pegylated reagent that, with other chemical modifications to AXOKINE, results in a potentially more potent and longer acting therapeutic candidate, called PegAXOKINE. AXOKINE is a protein that is taken daily by a self-administered subcutaneous injection. Regeneron will evaluate alternative dosing regimens with PegAXOKINE to take advantage of the potentially extended time in which this modified molecule circulates in the bloodstream.


41. On December 2, 2002, defendant Guler sold 10,000 shares of Regeneron stock at $21.27.

42. On December 16, 2002, defendant Goldberg sold 14,000 shares of Regeneron stock at $20.35.


46. On January 9, 2003, defendant Goldberg sold 1,428 shares of Regeneron stock at $19.05.


49. On February 12, 2003, defendant Yancopoulos sold 25,000 shares of Regeneron stock at $17.06.


52. On March 31, 2003, before the market opened, Regeneron announced results of a Phase III study evaluating AXOKINE for the treatment of obesity. In this announcement, Regeneron reported that (a) while the results of this Phase III study were statistically significant, the overall magnitude of the weight loss was small, (b) more than 60% of the total 1,467 subjects treated with AXOKINE began to develop antibodies to the drug after 12 weeks of treatment, and (c) the drug had a favorable safety and tolerability profile whether or not subjects developed antibodies. The release stated:

Regeneron Pharmaceuticals, Inc. today announced preliminary results of its initial Phase III study evaluating AXOKINE® in the treatment of obesity. After one year of treatment, the placebo-controlled study of 1467 AXOKINE- treated subjects and 501 placebo- treated subjects demonstrated that:

• AXOKINE treatment, when compared with placebo, achieved statistical significance with regard to both primary endpoints of the study:

  " A greater proportion of AXOKINE-treated patients lost at least 5% of their initial body weight compared with placebo-treated patients (25.1% vs. 17.6%, p<.001)

  " Participants receiving AXOKINE experienced a greater average weight loss than those receiving placebo (6.2 lbs vs. 2.6 lbs, p<.001)

• AXOKINE treatment achieved statistically significant results in two of the three secondary endpoints, such as proportion of subjects losing at least 10% of their initial body weight (11.3% vs. 4.2%, p <.001)
• AXOKINE treatment was generally well-tolerated. Adverse events were generally characterized as mild to moderate and no pattern of serious or severe adverse events emerged. The most notable adverse effects as compared with placebo were injection site reactions, nausea and cough, which were largely characterized as mild.

• **AXOKINE-associated weight loss was limited by the development of antibodies beginning after about three months of AXOKINE treatment. However, more than 30% of the total 1467 subjects treated with AXOKINE did not develop antibodies by the end of one year.**

• In comparison with placebo subjects who completed one year of treatment, AXOKINE-treated participants who completed one year without developing antibodies:

  "Achieved greater average weight loss (12.6 lbs vs. 4.5 lbs, p<.001).

  "Resulted in a higher proportion of subjects who lost at least 5% of initial body weight (46% vs. 24%, p<.001)

  "Resulted in a higher proportion of subjects who lost at least 10% of initial body weight (24% vs. 6.6%, p<.001)

  "Included more than 50% who were early responders (i.e., those who lost at least 4 lbs in the first month of treatment), and who experienced average weight loss of 19.4 lbs.

"Although the results of this Phase III study were statistically significant, the overall magnitude of the weight loss was small. However, in patients who did not become resistant to treatment through the development of antibodies, the effect appears in line with currently available treatments for obesity. **Further, AXOKINE showed a favorable safety and tolerability profile whether or not subjects developed antibodies," said Leonard S. Schleifer, M.D., Ph.D., President and CEO of Regeneron Pharmaceuticals. **"In the very near future, we will finish the analysis of our recently concluded pilot study in obese individuals with type 2 diabetes, and complete our on-going AXOKINE short-term treatment studies. Subsequently, we will discuss all of this data with regulatory authorities. At that time, we will be able to discuss our plans for the further development of AXOKINE for the treatment of obesity."

Dr. Louis Aronne, Clinical Associate Professor at Weill-Cornell University Medical College, and Director of the Comprehensive Weight Control Program at New York Presbyterian Hospital said, "**AXOKINE appears to be generally well-tolerated, and in the 30% of AXOKINE-treated patients who did not develop antibodies, the efficacy was comparable to currently available drugs.** Given the epidemic proportions of obesity, the group of potential responders is very large." Dr. Aronne continued, "Obesity is a complex metabolic disease similar to type 2 diabetes, and like diabetes will probably require combination therapies to achieve optimal efficacy and the dramatic weight losses that people have been hoping for. Its unique and well-defined mechanism of action makes AXOKINE a potentially attractive candidate as part of an obesity regimen."
53. On this news, Regeneron's shares plunged 57%. However, even defendants' admission was false as, in fact, defendants manipulated the results of the study. In truth, 73.5% of the patients developed antibodies to the drug.

**POST CLASS PERIOD STATEMENTS**

54. On April 21, 2003, the _Los Angeles Times_ reported the following after interviewing the Company:

Today, the drug, AXOKINE, is poised to become the next prescription weight-loss medication. In January, the Food and Drug Administration gave it "fast track" status because, by facilitating weight loss, it could reduce the risk for heart attack, stroke and diabetes in obese people. The designation means the agency will expedite the drug's review.

Studies on AXOKINE indicate that most people taking the drug experience weight loss for a few months. Over a longer period of time, only about one-third of people taking the drug continue to experience weight loss, but for them, the loss can be dramatic.

Although AXOKINE is still under investigation and is probably a few years from the marketplace, it would offer a new approach to treating obesity. AXOKINE is a modified form of a naturally occurring protein, called ciliary neurotrophic factor, that acts in the brain to inhibit hunger signals. Initially, scientists believed that patients with Lou Gehrig's disease might be helped because ciliary neurotrophic factor promotes the survival of nerve cells.

"The hypothalamus, the master gland of the brain, is the Grand Central Station where information on energy intake, expenditure and reserves all converge," said Dr. Leonard S. Schleifer, president and chief executive of Regeneron Pharmaceuticals, which developed the drug. "Our protein acts by telling the brain that it has enough food and to eat less."

AXOKINE also seems to prevent the overeating that occurs when the brain responds to a restricted food intake -- the well-known rebound effect many dieters experience, said Schleifer.

Two-thirds of people who take the drug, however, become resistant to it. Regeneron has a blood test that, Schleifer said, can show who will continue to benefit from taking the drug.

"Overall, everyone appears to benefit for a few months," he said. "But thereafter, some people continue to benefit and others don't. In two-thirds of people, their immune system seems to reject this treatment."

A small study published earlier this month in the Journal of the American Medical Assn. showed that most AXOKINE users experienced continuous weight loss during 12 weeks of use. A preliminary report on a larger study -- more than 1,400 people taking the drug for one year -- found that among the 30% of people who did not develop resistance to the drug, half lost 5% of their body weight and one-quarter lost 10% of their body weight. This result is similar to the effects of prescription obesity drugs already on the market.
55. The true facts which were known by each of the defendants, but concealed from the investing public during the Class Period, were as follows:

(a) The Company's Phase III results were falsely spun to portray a favorable outcome. Since Regeneron was aware of its previous false and misleading statements regarding immunogenicity of AXOKINE, Regeneron misled investors by portraying Phase III results involving undesirable antibody formation in as positive a manner as possible. Since Regeneron stated that in the design of AXOKINE immunogenic regions of the molecule were removed, Regeneron misled investors by using limited safety and tolerability data to allay concerns about antibody formation. Moreover, these statements are false and misleading for the following reasons:

(i) Regeneron misled investors by stating in the March 31st press release that, "more than 30% of the total 1467 subjects treated with AXOKINE did not develop antibodies by the end of one year." A closer look at the data demonstrates that this statement is false. In fact, out of the 1283 patients completing one year of treatment, and of the 979 of these patients treated with AXOKINE, a total of 720, or nearly three-quarters of those subjects treated with AXOKINE, developed antibodies. Thus, only 26.5% of the patients completing one year of treatment with AXOKINE did not develop antibodies.

(ii) Since Regeneron was aware of its previous false and misleading statements regarding immunogenicity of AXOKINE, it sought to portray Phase III study results involving detection of antibodies in a favorable manner. Regeneron knows that obese and diabetic patients are in a high-risk category. An anti-obesity drug in development that elicits an immune response in the majority of the population tested cannot be judged on the basis of the available data, as safe and effective for limited use, specifically over a three month period. In fact, in nearly three-quarters of the patients completing one year of treatment with AXOKINE, an immune response has occurred and persisted. By Regeneron's own admission, this response persists for as long as one year.

(iii) Regeneron has no safety data showing that, in combination with other anti-obesity drugs or in combination with other conditions and health issues faced by a large segment of patients suffering from obesity, diabetes or the conditions in combination, the immune response elicited by AXOKINE can be ignored. Thus, the portrayal of the progress made through Phase III development ignores the dimensions of this immune response and is wholly false and misleading.
(b) AXOKINE was not a more potent CNTF with certain immunogenic regions removed. Since an understanding of the precise mechanism of action of AXOKINE is lacking, the claim that Regeneron scientists had "deciphered" the mechanism by which CNTF caused weight loss and used this knowledge to design a more potent recombinant CNTF known as AXOKINE is wholly false and misleading.

(i) Since Regeneron's studies omitted relevant scientific data of the precise biomolecular action of CNTF in causing weight loss, the further claim regarding removal of certain immunogenic regions as part of the design of the more potent recombinant CNTF known as AXOKINE is wholly false and misleading.

(ii) By stating in the November 2000 disclosure that Regeneron scientists had "deciphered" the mechanism by which CNTF caused weight loss and then synthesized a more potent version of CNTF, Regeneron represented that AXOKINE was designed by them based on a detailed understanding of the molecule and its mechanism of action. By stating that native human CNTF was intentionally altered to remove certain immunogenic regions of the molecule, Regeneron represented that it would make the more potent version of CNTF immunogenic and purposefully altered the molecule to "remove" those immunogenic regions, to yield a recombinant CNTF known as AXOKINE.

(iii) These representations are also false and misleading for the following reasons. First, Regeneron does not even yet understand the mechanism by which AXOKINE works to cause weight loss. Since an understanding of the precise mechanism of action of AXOKINE is lacking, the claim that Regeneron scientists had "deciphered" the mechanism by which CNTF caused weight loss and used this knowledge to design a more potent recombinant CNTF known as AXOKINE is wholly false and misleading. Regeneron published a groundbreaking account exploring various possible modalities for the drug in a PNAS article published in 2001. However, Regeneron has yet to publish a definitive account of the mechanism of action of the drug, in particular, if and how AXOKINE alters the hypothalamic body weight setpoint. The Regeneron supposition regarding this action of the drug is important support of its claim that the drug acts differently than forced dieting by preventing binge overeating and rapid rebound weight gain after termination of treatment. Second, since Regeneron lacks a thorough and complete understanding of the biomolecular action of CNTF in causing weight loss, the claim regarding removal of
certain immunogenic regions as part of the overall design of the recombinant CNTF known as AXOKINE is also wholly false and misleading. Without a clear and complete understanding of the mechanism of action of the recombinant CNTF known as AXOKINE, Regeneron scientists would not know how to alter the structure of the molecule.

(c) The statements regarding immunogenicity were false and misleading for the following reasons:

(i) By failing to report levels of antibodies in patients who were enrolled in the 12 week Phase II study at 24, 36 and 48 weeks, Regeneron purposefully withheld information regarding the immunogenicity of AXOKINE.

(ii) Regeneron misled and continues to mislead investors to this date as to the sufficiency of preclinical and early clinical work on the immunogenicity of AXOKINE, despite existing FDA guidance on the undesirability of immunogenic properties of recombinant biomolecules.

(iii) Since many recombinant cytokines possess immunogenic properties, resulting in the formation of both neutralizing and non-neutralizing antibodies, Regeneron scientists cannot claim that, absent clear and demonstrable evidence to the contrary, the recombinant CNTF known as AXOKINE would not be highly immunogenic.

(iv) By reporting in the November 2000 disclosure that less than 10% of patients formed neutralizing antibodies in the Phase II study, and by failing to report results of any antibody levels in patients at the 24, 36 and 48 week timepoints in the July and September 2001 disclosures, Regeneron represented that it had validated the design of a more potent and low immunogenic recombinant CNTF, known as AXOKINE. By reporting together the success of the Phase II study, the limited immunogenicity of AXOKINE and the efforts made to design the molecule for potency and removal of immunogenic regions from the molecule, defendants represented that they had limited the risks of immunogenicity inherent in the development of many recombinant cytokine biopharmaceuticals.

(v) By failing to publicly report levels of antibodies in patients who were enrolled in the 12 week Phase II study at 24, 36 and 48 weeks, Regeneron purposefully withheld information regarding the immunogenicity of AXOKINE. It was not until the conference call of March 31,
2003 that Regeneron had further evidence of antibody formation at these later timepoints, when defendant Schleifer made the following remarks:

"We know from the Phase II that when – if you – even if you have an antibody respond, we probably match a year, the antibodies disappear over time. So, we're not concerned that you would have a prolonged antibody response once you're off the drug."

(vi) Defendants knew that further observation of neutralizing antibodies made at the end of the 12-week dosing period would raise questions about the formation of neutralizing antibodies and the safety and efficacy of AXOKINE. By failing to disclose further observations of antibodies in Phase II trial patients, Regeneron sought to avoid these questions, so that it could initiate the Phase III trial.

(vii) Defendants knew that many recombinant-derived biopharmaceuticals have immunogenic properties. In response to these concerns FDA issued a Guidance to Industry in July of 1997 entitled "S6 Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals." This guidance was endorsed both by the CBER and CDER divisions and is harmonized under the ICH. The scope for the guidance includes cytokines:

1.3 Scope

This guidance is intended primarily to recommend a basic framework for the preclinical safety evaluation of biotechnology-derived pharmaceuticals. It applies to products derived from characterized cells through the use of a variety of expression systems including bacteria, yeast, insect, plant, and mammalian cells. The intended indications may include in vivo diagnostic, therapeutic, or prophylactic uses. The active substances include proteins and peptides, their derivatives, and products of which they are components; they could be derived from cell cultures or produced using recombinant deoxyribonucleic acid (DNA) technology, including production by transgenic plants and animals. Examples include but are not limited to: Cytokines, plasminogen activators, recombinant plasma factors, growth factors, fusion proteins, enzymes, receptors, hormones, and monoclonal antibodies."

All AXOKINE research conducted by Regeneron is subject to the recommendations in this guidance. The guidance was intended to assist manufacturers, amongst other things, in finding out about immunogenic properties of drugs at the preclinical development stage. The principles of preclinical investigation outlined apply to the AXOKINE development program. Significant deviation from the recommendations in the guidance increases the risk of failure at later stages of any drug development program. FDA had issued this guidance in July of 1997. Had Regeneron applied the principles of this guidance document to the
AXOKINE development program, the immunogenicity issue should have been addressed at an earlier stage of development.

(d) Regeneron sought to suppress immunogenicity of AXOKINE by pegylation. By failing to disclose the true purpose of pegylation of recombinant cytokines, Regeneron misled investors as to the nature and importance of antibody formation.

(i) By failing to discuss the true purpose of pegylation of AXOKINE, Regeneron misled investors into believing that AXOKINE, unlike many other cytokines will not elicit neutralizing or non-neutralizing antibodies.

(ii) Defendants also knew of a previous study involving patients treated with recombinant human interleukin-2. The recombinant cytokine used in these Phase I clinical trials lacked the N-terminal alanine of the native molecule, was not glycosylated and possessed a serine-cysteine substitution at position 125. The parties developed sensitive specific assays for anti-IL-2 antibodies. From the study, defendants knew or should have known that eleven of seventeen patients had developed serum anti-IL-2 antibodies.

(iii) Defendants knew of cytokine-induced formation of both neutralizing and non-neutralizing antibodies. This phenomenon is of considerable concern to the FDA. While neutralizing antibodies act by direct interference with the mechanism of action of the drug, non-neutralizing antibodies act to impact the pharmacokinetics of the drug, lowering potency. Taken separately or together, formations of both types of antibodies have a negative impact on drug action. The FDA currently refers to this formation using the generic term "anti-drug antibodies."

(iv) Defendants knew about the need to monitor and carefully study any observed immune response elicited during clinical trials of recombinant human cytokines, as well as the importance in accounting for both neutralizing and non-neutralizing antibodies.

(v) However, prior to the Class Period, defendants had become seriously concerned with the formation of anti-AXOKINE antibodies. The use of pegylation to remove immunogenicity from cytokines was known to defendants. Defendants knew of a study which pegylated a highly immunogenic form of recombinant IL-2. They knew that this chemically altered form of human
recombinant IL-2 had enhanced solubility and extended in vivo circulation. Furthermore, the pegylation sharply reduced the immunogenicity of the molecule when tested in rabbits and mice.

**FIRST CLAIM FOR RELIEF**

*For Violation of §10(b) of the 1934 Act and Rule 10b-5 Against All Defendants*

56. Plaintiff incorporates ¶¶1-55 by reference.

57. During the Class Period, defendants disseminated or approved the false statements specified above, which they knew or deliberately disregarded were misleading in that they contained misrepresentations and failed to disclose material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading.

58. Defendants violated §10(b) of the 1934 Act and Rule 10b-5 in that they:
   
   (a) Employed devices, schemes, and artifices to defraud;
   
   (b) Made untrue statements of material facts or omitted to state material facts necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading; or
   
   (c) Engaged in acts, practices, and a course of business that operated as a fraud or deceit upon plaintiff and others similarly situated in connection with their purchases of Regeneron publicly traded securities during the Class Period.

59. Plaintiff and the Class have suffered damages in that, in reliance on the integrity of the market, they paid artificially inflated prices for Regeneron publicly traded securities. Plaintiff and the Class would not have purchased Regeneron publicly traded securities at the prices they paid, or at all, if they had been aware that the market prices had been artificially and falsely inflated by defendants' misleading statements.

60. As a direct and proximate result of these defendants' wrongful conduct, plaintiff and the other members of the Class suffered damages in connection with their purchases of Regeneron publicly traded securities during the Class Period.
SECOND CLAIM FOR RELIEF 
For Violation of §20(a) of the 1934 Act 
Against All Defendants

61. Plaintiff incorporates ¶¶1-60 by reference.

62. The Individual Defendants acted as controlling persons of Regeneron within the meaning of §20(a) of the 1934 Act. By reason of their positions as officers and/or directors of Regeneron, and their ownership of Regeneron stock, the Individual Defendants had the power and authority to cause Regeneron to engage in the wrongful conduct complained of herein. Regeneron controlled each of the Individual Defendants and all of its employees. By reason of such conduct, the Individual Defendants and Regeneron are liable pursuant to §20(a) of the 1934 Act.

CLASS ACTION ALLEGATIONS

63. Plaintiff brings this action as a class action pursuant to Rule 23 of the Federal Rules of Civil Procedure on behalf of all persons who purchased Regeneron publicly traded securities (the "Class") on the open market during the Class Period. Excluded from the Class are defendants.

64. The members of the Class are so numerous that joinder of all members is impracticable. The disposition of their claims in a class action will provide substantial benefits to the parties and the Court. Regeneron had more than 44 million shares of stock outstanding, owned by hundreds if not thousands of persons.

65. There is a well-defined community of interest in the questions of law and fact involved in this case. Questions of law and fact common to the members of the Class which predominate over questions which may affect individual Class members include:

(a) Whether the 1934 Act was violated by defendants;

(b) Whether defendants omitted and/or misrepresented material facts;

(c) Whether defendants’ statements omitted material facts necessary to make the statements made, in light of the circumstances under which they were made, not misleading;

(d) Whether defendants knew or deliberately disregarded that their statements were false and misleading;
(e) Whether the prices of Regeneron’s publicly traded securities were artificially inflated; and  

(f) The extent of damage sustained by Class members and the appropriate measure of damages.

66. Plaintiff’s claims are typical of those of the Class because plaintiff and the Class sustained damages from defendants’ wrongful conduct.

67. Plaintiff will adequately protect the interests of the Class and has retained counsel who are experienced in class action securities litigation. Plaintiff has no interests which conflict with those of the Class.

68. A class action is superior to other available methods for the fair and efficient adjudication of this controversy.

PRAYER FOR RELIEF

WHEREFORE, plaintiff prays for judgment as follows:

A. Declaring this action to be a proper class action pursuant to FRCP 23;

B. Awarding plaintiff and the members of the Class damages, interest and costs; and

C. Awarding such equitable/injunctive or other relief as the Court may deem just and proper.

JURY DEMAND

Plaintiff demands a trial by jury.

DATED: May 2, 2003

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