# SECURITIES AND EXCHANGE COMMISSION

Washington, D. C. 20549

# FORM 8-K

Current Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report: March 28, 2003 (Date of earliest event reported)

# **REGENERON PHARMACEUTICALS, INC.**

(Exact name of Registrant as specified in its charter)

New York (State or Other Jurisdiction of Incorporation) 0-19034 (Commission File Number) 13-3444607 (IRS Employer Identification No.)

777 Old Saw Mill River Road Tarrytown, NY 10591-6707

(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (914) 347-7000

# **ITEM 5. OTHER EVENTS**

On March 28, 2003, the Company issued a press release announcing its Collaboration, License and Option Agreement with Novartis Pharma AG, a copy of which is attached to this filing.

On March 31, 2003, the Company issued a press release announcing the results of its Phase III obesity study. This release as issued contained a statement that AXOKINE treatment achieved statistically significant results in all secondary endpoints of the study. A corrected press release is attached to this filing, which clarifies that AXOKINE treatment achieved statistically significant results in two of the three secondary endpoints.

# ITEM 7. FINANCIAL STATEMENTS, PRO FORMA FINANCIAL INFORMATION AND EXHIBITS

- (c) Exhibits.
  - 99a Press Release dated March 28, 2003
  - 99b Press Release dated March 31, 2003 (As Corrected)

# SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REGENERON PHARMACEUTICALS, INC.

By: /s/ Stuart Kolinski

Name: Stuart Kolinski Title: Vice President & General Counsel

Date: April 1, 2003

## FOR IMMEDIATE RELEASE

# REGENERON AND NOVARTIS FORM STRATEGIC COLLABORATION TO DEVELOP AND COMMERCIALIZE THE IL-1 TRAP IN RHEUMATOID ARTHRITIS AND OTHER INDICATIONS

Novartis to Pay Regeneron \$27 Million and Will Make \$48 Million Equity Investment in Regeneron

Novartis to Provide 100% Funding for Clinical Development and Provide Manufacturing Facility for Commercial Product Needs

Companies Will Have Co-promotion Rights and Will Share Profits Equally in Europe and North America

Companies May Broaden the Collaboration to Additional Pre-Clinical or Early Development IL-1 Antagonists

Tarrytown, NY – March 28, 2003 – Regeneron Pharmaceuticals, Inc. (Nasdaq: **REGN**) announced today that it has signed a development and commercialization agreement with Novartis AG covering Regeneron's IL-1 Trap, a novel therapeutic candidate that blocks the activity of Interleukin-1 (IL-1). The IL-1 Trap is currently in Phase II clinical development for the treatment of rheumatoid arthritis.

"We are delighted to embark on this collaboration with Novartis," noted Leonard S. Schleifer, M.D., Ph.D., Regeneron's President and Chief Executive Officer. "With their exceptionally strong skills in development, manufacturing, and marketing, they are ideal collaborators with us. We believe that combining the capabilities of our two organizations gives us an opportunity to accelerate development of the IL-1 Trap and increase its commercial potential, dramatically enhancing our ability to create value for our shareholders."

#### The Agreement

Under the terms of the agreement, Novartis will purchase \$48 million of newly issued Regeneron common stock. In addition, Novartis will pay Regeneron \$27 million upon closing for its

development activities. The price per share will be determined based on the average closing price of the common stock for the 20 consecutive trading days ending May 9, 2003. The initial focus of development will be rheumatoid arthritis; however, other indications will also be explored. Development expenses incurred during 2003 will be shared equally by the companies. Regeneron's potion will be financed by a loan from Novartis that will be forgiven should certain preclinical and clinical milestones be reached.

After 2003, Novartis will be responsible for any additional pre-Phase III development expenses. Phase III development expenses and pre-launch expenses will be shared equally by the companies. Novartis will provide a loan to finance Regeneron's share of these expenses. The loan and accrued interest are repayable in full five years after the initial product launch of the IL-1 Trap or five years after termination of Novartis' rights to the IL-1 Trap under the agreement, whichever occurs first.

Novartis will be responsible for providing commercial scale manufacturing capacity for the IL-1 Trap. Regeneron will continue to manufacture clinical supplies of the IL-1 Trap at its plant in Rensselaer, New York.

The two companies will share co-promotion rights and profits, including an equal profit sharing agreement in Europe and North America. Regeneron retains full rights to Japan. In other markets, both companies will have co-promotion rights, and Novartis will receive 75 percent of the profits from revenues in those regions.

Novartis will also pay Regeneron certain milestones, up to \$275 million, related to the receipt of marketing approval in Europe and the United States for the IL-1 Trap and to achieving certain subsequent product revenue targets.

Under the agreement, each company also has the right to elect to collaborate on the development and commercialization of other pre-clinical / early development IL-1 antagonists that Regeneron and Novartis are currently developing independently.

"The IL-1 Trap, like our other Traps, involves innovative molecular engineering in which two separate genetic structures are combined to provide a product candidate with potentially important therapeutic benefit," said Neil Stahl, Ph.D., Regeneron's Senior Vice President, Preclinical Development and Biomolecular Science. "Novartis and Regeneron have a shared vision of the vital role that excellence in scientific discovery and clinical development play in reducing the risk of bringing innovative new pharmaceuticals to market. We firmly believe that together we have the best possible chance of successfully bringing the IL-1 Trap to market."

#### About the IL-1 Trap

IL-1 is a soluble protein secreted by the certain cells in the body. In many cases, IL-1 acts as a messenger to help regulate immune and inflammatory responses by attaching to cell-surface receptors, or docking stations, in cells that participate in the body's immune system. In excess, it can be harmful and has been linked to a variety of inflammatory diseases. Blocking IL-1 is a proven therapeutic approach in rheumatoid arthritis, and IL-1 represents an important target for pharmaceutical development in other inflammatory conditions.

In a Nature Medicine paper published in January 2003, Regeneron described a general approach to blocking the activity of cytokines using its proprietary Trap technology. The Traps have the ability to attach to and "trap" target cytokines in the blood stream before the cytokines can attach to cell-surface receptors, or docking stations, and generate signals that can trigger disease activity in body tissue. For most cytokines, two distinct receptor components cooperate to bind the cytokine very tightly. Regeneron's proprietary Traps incorporate both of these receptors components in one soluble blocker, thereby mimicking the cell's natural receptors. Once attached to the Trap, the cytokines cannot bind to the cell surface receptors and, together with the Trap, are flushed from the body. Traps have the benefit of very long circulation in the body, potentially allowing for weekly or less frequent dosing in patients. Regeneron has three issued United States patents that broadly cover the design and production of its Cytokine Traps.

In July 2002, Regeneron initiated a dose-ranging, placebo-controlled Phase II clinical trial to study the safety and efficacy of the IL-1 Trap in patients with rheumatoid arthritis. Subjects are receiving weekly self-injections of one of three fixed doses of IL-1 Trap or placebo for 12 weeks

followed by 10 weeks of open-label follow-up. The 200 patient study is fully enrolled and results of the initial treatment period are expected in the third quarter of 2003.

## **About Regeneron**

Regeneron is a biopharmaceutical company that discovers, develops, and intends to commercialize therapeutic medicines for the treatment of serious medical conditions. Regeneron has therapeutic candidates for the potential treatment of obesity, rheumatoid arthritis, cancer, and asthma and has preclinical programs in other diseases and disorders.

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This news release discusses historical information and includes forward-looking statements about Regeneron and its products, programs, finances, and business, all of which involve a number of risks and uncertainties, such as risks associated with preclinical and clinical development of drugs and biologics, determinations by regulatory and administrative governmental authorities, competitive factors, technological developments, the availability and cost of capital, the costs of developing, producing, and selling products, the potential for any collaboration agreement to be canceled or to terminate without any product success, and other material risks. A more complete description of these risks can be found in Regeneron's filings with the United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2001 and the Form 10-Q for the quarter ended September 30, 2002. Regeneron does not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, unless required by law.

Investor Relations Contact:	Charles Poole
	Vice President, Investor Relations
	Regeneron Pharmaceuticals, Inc.
	charles.poole@regn.com
	(914) 345-7641

Additional information about Regeneron and recent news releases are available on Regeneron's Worldwide Web Home Page at www.regn.com.

# FOR IMMEDIATE RELEASE

#### Regeneron Announces Results of Phase III Obesity Study

Tarrytown, New York (March 31, 2003) — Regeneron Pharmaceuticals, Inc. (Nasdaq: **REGN**) 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:
  - o 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)
  - o 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:
  - o Achieved greater average weight loss (12.6 lbs vs. 4.5 lbs, p<.001)
  - o Resulted in a higher proportion of subjects who lost at least 5% of initial body weight (46% vs. 24%, p<.001)
  - o Resulted in a higher proportion of subjects who lost at least 10% of initial body weight (24% vs. 6.6%, p<.001)
  - o 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
- Greater than 5% weight loss in both the AXOKINE-treated and placebo populations was associated with expected trends in improvements in obesityrelated parameters such as blood pressure, blood glucose and lipids

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"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."

#### Trial Design

The double-blind, randomized, placebo-controlled trial included 501 placebo-treated and 1467 AXOKINE-treated participants from 65 study sites across the United States. The average baseline weight for all participants was approximately 235 lbs. For 12 months, subjects received daily subcutaneous injections of either placebo or AXOKINE at a dose of 1.0 microgram per kilogram of body weight. To be included in the study, participants could not have diabetes, and had to have a body mass index (BMI) of 30 to 55 without obesity-related risk factors, or 27 to 55 if they had obesity-related risk factors such as high blood pressure or high blood lipids.

BMI is calculated as the weight of an individual in kilograms divided by the square of their height in meters. Normal weight is designated by BMIs of 18.5-24.9, overweight by BMIs of 25-29.9 and obesity by BMIs of 30 and above.

The 12-month treatment period is being followed by a 12-month open-label safety extension phase during which all participants receive AXOKINE and are further monitored for side effects.

#### Preliminary Trial Results

The preliminary data from the study are summarized below. The Intent-to-Treat Analysis includes all randomized subjects whether or not they completed the full twelve months of treatment. The Completer Analysis includes only those subjects who completed the full twelve months of treatment.

#### **Comparison of Placebo versus Total AXOKINE-Treated Participants**

Average Weight Loss vs. Baseline:

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	Placebo	AXOKINE	p-value
Intent-to-Treat Analysis	2.6 lbs n=501	6.2 lbs n=1467	<.001
Completer Analysis	4.5 lbs n= 304 (61%)	7.9 lbs n= 979 (67%)	<.001

• Percentage of Patients Losing at Least 5% of Body Weight (i.e., > ~12 lbs on average):

	Placebo	AXOKINE	p-value
Intent-to-Treat Analysis	17.6% n=88/501	25.1% n=368/1467	<.001
Completer Analysis	24.0% n=73/304	32.4% n=317/979	=.005

• Percentage of Patients Losing at Least 10% of Body Weight (i.e., > ~24 lbs on average):

	Placebo	AXOKINE	p-value
Intent-to-Treat Analysis	4.2% n=21/501	11.3% n=166/1467	<.001
Completer Analysis	6.6% n=20/304	15.5% n=152/979	<.001

# Comparison of Participants Completing One-Year of Treatment: Placebo-Treated (Pbo) vs. AXOKINE-Treated Who Developed Antibodies (Ab-Pos) and AXOKINE-Treated Who Did Not Develop Antibodies (Ab-Neg)

• Average Weight Loss vs. Baseline:

Placebo	AXOKINE (Ab-Pos)	AXOKINE (Ab-Neg)	p-value (Ab-Neg vs. Pbo)
n=304	n=720	n=259	
4.5 lbs	6.4 lbs	12.6 lbs	<.001

Average Weight Loss in Early Responders (Participants who lost at least 4 lbs in the first month):

Placebo n=94	AXOKINE (Ab-Pos) n=383	AXOKINE (Ab-Neg) n=135	p-value (Ab-Neg vs. Pbo)
12.2 lbs	10.6 lbs	19.4 lbs	<.001

• Percentage of Patients Losing at Least 5% of Body Weight (i.e., > ~12 lbs on average):

Placebo	AXOKINE	AXOKINE	p-value
	(Ab-Pos)	(Ab-Neg)	(Ab-Neg vs. Pbo)
24.0%	27.4%	46.3%	<.001
n=73/304	n=197/720	n=120/259	

#### • Percentage of Patients Losing at Least 10% of Body Weight (i.e., > ~24 lbs on average):

Placebo	AXOKINE	AXOKINE	p-value
	(Ab-Pos)	(Ab-Neg)	(Ab-Neg vs. Pbo)
6.6%	12.5%	23.9%	<.001
n=20/304	n=90/720	n=62/259	

## Conference Call/Web Cast Information

To more fully discuss the AXOKINE Phase III preliminary results, management of Regeneron will host a conference call and PowerPoint presentation at 10:00 a.m. ET today, March 31, 2003. The conference call will be available by web cast at www.regeneron.com. To access the PowerPoint presentation, go to www.presentonline.com, click on participant and use access number x1261432.

You must have a Java-enabled web browser to access the web cast presentation, i.e., Microsoft Internet Explorer<sup>™</sup> 4.0 or higher or Netscape Communicator<sup>™</sup> 4.0 or higher. To test browser compatibility, go to and click on Browser Check. If you are having difficulties, please contact Technical Support at 800-291-4047 or 706-645-6040. Furthermore, an audio replay of the call will be available from noon ET March 31, 2003 until midnight ET April 14, 2003. For domestic access to the replay, please dial 1-800-642-1687 and enter Reservation Number 9464121. For international access to the replay, please dial 1-706-645-9291 and enter Reservation Number 9464121.

#### About Regeneron

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description of these risks can be found in Regeneron's filings with the United States Securities and Exchange Commission, including its Form 10-K for the year ended December 31, 2001 and the Form 10-Q for the quarter ended September 30, 2002. Regeneron does not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, unless required by law.

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Contact: Miriam Weber Biosector 2 mweber@biosector2.com (212) 414-5630

For non-media inquiry call (914) 509-7000.

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