REGENERON

ARCALYST(R) (rilonacept) Meets Primary and All Secondary Endpoints in Phase 3 Trial of Prevention of Gout Flares in Patients Initiating Allopurinol Therapy

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TARRYTOWN, N.Y., June 9, 2010 /PRNewswire via COMTEX News Network/ -- Regeneron Pharmaceuticals, Inc. (Nasdaq: REGN) today announced that a Phase 3 study in gout patients initiating allopurinol therapy to lower their uric acid levels showed that ARCALYST (rilonacept), also known as IL-1 Trap, prevented gout attacks, as measured by the primary endpoint of the number of gout flares per patient over the 16 week treatment period.

- **Primary Endpoint:**
  - Patients who received ARCALYST at a weekly, self-administered, subcutaneous dose of 160 milligrams (mg) had an 80% decrease in mean number of gout flares compared to the placebo group over the 16 week treatment period (0.21 flares vs. 1.06 flares, p<0.0001).
  - Patients who received ARCALYST at a weekly dose of 80 mg had a 73% decrease compared to the placebo group (0.29 flares vs. 1.06 flares, p<0.0001).
- **Key Secondary Endpoints**: All secondary endpoints of the study were highly positive (p<0.001 vs. placebo). These include:
  - Treatment with ARCALYST reduced the proportion of patients who experienced two or more flares during the study period by up to 88% (3.7% with ARCALYST 160 mg, 5.0% with ARCALYST 80 mg, and 31.6% with placebo, p<0.0001).
  - Treatment with ARCALYST reduced the proportion of patients who experienced at least one gout flare during the study period by up to 65% (16.3% with ARCALYST 160 mg, 18.8% with ARCALYST 80 mg, and 46.8% with placebo, p<0.001).

ARCALYST was generally well tolerated with no reported drug-related serious adverse events. Injection site reaction, generally considered mild, was the most commonly reported adverse event with ARCALYST.

"Gout is a very painful and common form of arthritis that results from high levels of uric acid. Uric acid-lowering therapy, most commonly with allopurinol, is a mainstay of treatment to reduce gout flares over the long term. Paradoxically, the initiation of uric acid-lowering therapy often triggers an increase in frequency of gout attacks in the first several months of treatment that may lead to discontinuation of therapy," stated George D. Yancopoulos, M.D., Ph.D., President of Regeneron Research Laboratories. "This positive pivotal study showed that ARCALYST(R) (rilonacept) markedly reduced the occurrence of painful gout attacks in patients initiating uric acid-lowering therapy. We look forward to data from our second efficacy study in this setting and our larger safety study. If these additional studies are successful, we plan to file for regulatory approval by mid-2011."

"Chronic urate-lowering therapy is critical to control the symptoms and the resulting consequences of gout in the joints. We in the rheumatology community have long recognized the challenge of adherence to uric acid-lowering therapies. Data suggest that many patients discontinue allopurinol within the first few months of therapy, in part due to increased flares," said H. Ralph Schumacher, M.D., Professor of Medicine, University of Pennsylvania, Philadelphia, PA. "Current therapies recommended to reduce the risk of gout flares in patients taking uric acid-lowering therapy are under-prescribed, especially outside of rheumatology practice. While additional Phase 3 data are needed, the results from this study suggest that concomitant use of rilonacept during the first several months of uric acid-lowering therapy may help avoid gout flares, which could, in turn, improve patient outcomes."

Results of a Phase 3 study in patients presenting with an ongoing acute gout flare showed that compared to indomethacin, a non-steroidal anti-inflammatory drug considered a standard of care, there was no significant benefit from combining indomethacin with ARCALYST, as measured by the primary endpoint of the average intensity of gout pain from 24 to 72 hours after initiation of treatment. Patients treated with indomethacin alone experienced an average reduction in patient-reported pain scores (0 to 4 Likert scale where 0 represents no pain and 4 represents extreme pain) of 1.40 points from baseline compared to an average reduction of 1.55 points from baseline in patients treated with both indomethacin and ARCALYST (p=0.33). Patients who received ARCALYST alone experienced an average pain reduction of 0.69 points. Treatment with ARCALYST was generally well tolerated with no reported drug-related serious adverse events. The most commonly reported adverse event with ARCALYST was headache.

About the Phase 3 Gout Flare Prevention Study

The North American-based **PRE-SURGE 1** (**PRE**ventative **S**tudy against **UR**ate-lowering drug-induced **G**out **E**xacerbations) study was a double-blind, placebo-controlled study which evaluated the number of gout flares per patient over the first 16 weeks following initiation of allopurinol therapy. In the trial, a gout flare was defined as patient-reported acute articular pain typical of a gout attack that is deemed (by patient and/or investigator) to require treatment with an anti-inflammatory therapeutic; presence of at least three of the following four signs/symptoms: joint swelling, redness, tenderness and pain, and at least one of the following: rapid onset of pain, decreased range of motion, joint warmth or other symptoms similar to a prior gout flare. A total of 241 patients were randomized on a 1:1:1 basis to receive one of the following treatment regimens:

- ARCALYST 160 mg as an initial subcutaneous loading dose, followed by weekly 80 mg subcutaneous injections (n=80)
- ARCALYST 320 mg as an initial subcutaneous loading dose, followed by weekly 160 mg subcutaneous injections (n=81)
- Subcutaneous weekly placebo injections (n=80)

Adverse event that occurred at a frequency of at least 5% in any study group were: injection site reaction (19.8% with ARCALYST(R) (rilonacept) 160 mg, 8.8% with ARCALYST 80 mg, and 1.3% with placebo), upper respiratory tract infection (9.9% with ARCALYST 160 mg, 8.8% with ARCALYST 80 mg, and 7.6% with placebo), lower respiratory tract infection (0% with ARCALYST 160 mg, 5.0% with ARCALYST 80 mg, and 2.5% with placebo), musculoskeletal pain/ discomfort (6.2% with ARCALYST 160 mg, 7.5% with ARCALYST 80 mg, and 8.9% with placebo), and headache, (3.7% with ARCALYST 160 mg, 6.3% with ARCALYST 80 mg, and 1.3% with placebo).

Detailed data from this study will be presented at future scientific conferences.

About the Acute Gout Flare Treatment Study

The North-American-based **SURGE** (**S**tudy **U**tilizing **R**ilonacept in **G**out **E**xacerbations) study was a double blind, placebo-controlled, Phase 3 study that evaluated pain during the initial 72 hours of treatment in patients experiencing an acute gout attack. A total of 225 patients were randomized on a 1:1:1 basis to receive one of the following treatment regimens:

- ARCALYST 320 mg administered by subcutaneous injection on day 1 plus oral placebo taken for 3 days or more (n=76)
- ARCALYST 320 mg administered by subcutaneous injection on day 1 plus oral indomethacin (an anti-inflammatory drug currently indicated for the treatment of gout) taken for 3 days or more (n=74)
- Placebo administered by subcutaneous injection on day 1 plus oral indomethacin taken for 3 days or more (n=75)

Adverse events reported at an incidence of at least 5% in any group were headache (7.8% indomethacin alone, 5.5% with indomethacin plus ARCALYST, and 10.8% with ARCALYST alone) and neurological signs and symptoms (dizziness; 5.2% with indomethacin alone, 4.1% with indomethacin plus ARCALYST, and 2.7% with ARCALYST alone).

Detailed data from this study will be presented at future scientific conferences.

About the Additional Phase 3 Gout Studies

The ongoing studies in the Phase 3 program with ARCALYST in gout include:

- The global **PRE-SURGE 2** (**PRE**ventative **S**tudy against **UR**ate-lowering drug-induced **G**out **E**xacerbations) study evaluating the number of gout flares per patient over the first 16 weeks of initiation of allopurinol therapy. PRE-SURGE 2, which has a similar trial design as PRE-SURGE 1, is over 80% enrolled and data is expected in early 2011. A total of 240 patients will be randomized on a 1:1:1 basis to receive one of the following treatment regimens:
  - ARCALYST 160 mg as an initial loading dose, followed by weekly 80 mg subcutaneous injections
  - ARCALYST 320 mg as an initial loading dose, followed by weekly 160 mg subcutaneous injections
  - Weekly placebo injections
- The global **RE-SURGE** (**RE**view of **S**afety **U**sing **R**ilonacept in preventing **G**out **E**xacerbations) study, evaluating the safety of ARCALYST(R) (rilonacept) versus placebo over 16 weeks in patients who are at risk for gout flares because they are taking uric acid-lowering drug treatment. RE-SURGE is over 80% enrolled and data is expected in early 2011. Over 1000 patients will be randomly allocated in a 1:3 ratio to receive weekly placebo or ARCALYST dosed at 320 mg as an initial loading dose, followed by weekly 160 mg subcutaneous injections. Patients can be taking any of four uric acid-lowering drugs, allopurinol, febuxostat, probenecid, or sulfinpyrazone, with no requirements in the study design as to the total number of patients taking each.

Conference Call

Regeneron will host a webcast conference call to discuss these results today, **June 9, 2010, at 8:30 a.m., Eastern Time**. The dial-in information is:

Domestic Dial-in Number: (877) 390-5538

International Dial-in Number: (408) 940-3843

Participant Passcode: 80129194

The live conference call is being webcast and it, and slides for the conference call, can be accessed on the "Newsroom" page of the Company's website, www.regeneron.com. The webcast will be available for 30 days following the call.

About Gout

Gout is a condition that occurs when the bodily waste product, uric acid, is deposited in the joints and/or soft tissues. In the joints, these uric acid crystals cause inflammation, which leads to pain, swelling, redness, heat, and stiffness in the joints. Treatment guidelines recommend that patients with elevated uric acid levels who experience multiple gout attacks each year should receive chronic uric acid-lowering therapy, such as allopurinol. Allopurinol reduces the production of uric acid in the body to prevent the occurrence of gout attacks with long-term use. Approximately 750,000 gout patients initiate allopurinol therapy each year. During the first months of allopurinol therapy while uric acid blood levels are being reduced, the break up of the uric acid crystals can result in stimulation of inflammatory mediators, including interleukin-1 (IL-1), resulting in acute flares of joint pain and inflammation. Anti-inflammatory therapy with colchicine is sometimes used to help prevent these flares. However, the side effects associated with colchicine, which include diarrhea, abdominal cramps, nausea, and vomiting, can limit patients' adherence to both colchicine and allopurinol treatment.

Rationale for the Clinical Exploration of Use of ARCALYST in the Treatment of Gout

Interleukin-1 (IL-1) is a protein secreted by infection-fighting cells in the blood and tissues. In many cases, IL-1 acts as a messenger to help regulate immune and inflammatory responses by attaching to cell-surface receptors in cells that participate in the body's immune system. In excess, it can be

harmful and has been shown to be a key driver of inflammation in a variety of diseases, including gout. In gout, uric acid crystals stimulate the production of IL-1, which causes an inflammatory response in the joints and surrounding tissues.

Rilonacept is an agent that inhibits IL-1. It is designed to attach to and neutralize IL-1 in the blood stream before the IL-1 can attach to cell-surface receptors and generate signals that can trigger disease activity in body tissue. Once attached to rilonacept, IL-1 cannot bind to the cell-surface receptors and is eventually eliminated from the body.

Important Information About ARCALYST(R) (rilonacept)

Rilonacept, marketed as ARCALYST, is currently indicated in the U.S. for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older. Rilonacept is also approved, but not marketed, in the E.U. for the same patient population. The safety and efficacy of ARCALYST in the gout setting have not been evaluated by the Food and Drug Administration. ARCALYST is not approved for use in gout.

IL-1 blockade may interfere with immune response to infections. Serious, life-threatening infections have been reported in patients taking rilonacept. Rilonacept should be discontinued if a patient develops a serious infection. Taking rilonacept with tumor necrosis factor inhibitors is not recommended because this may increase the risk of serious infections. Treatment with rilonacept should not be initiated in patients with active or chronic infections. Patients should not receive a live vaccine while taking rilonacept. It is recommended that patients receive all recommended vaccinations prior to initiation of treatment with rilonacept. Patients should be monitored for changes in their lipid profiles and provided with medical treatment if warranted. Hypersensitivity reactions associated with rilonacept administration have been rare. Please see the full Prescribing Information for ARCALYST, available online at www.regeneron.com/ARCALYST-fpi.pdf.

About Regeneron Pharmaceuticals

Regeneron is a fully integrated biopharmaceutical company that discovers, develops, and commercializes medicines for the treatment of serious medical conditions. In addition to ARCALYST(R) (rilonacept) Injection for Subcutaneous Use, its first commercialized product, Regeneron has therapeutic candidates in Phase 3 clinical trials for the potential treatment of gout, diseases of the eye (wet age-related macular degeneration and central retinal vein occlusion), and certain cancers. Additional therapeutic candidates are in earlier stage development programs in rheumatoid arthritis and other inflammatory conditions, pain, cholesterol reduction, allergic and immune conditions, and cancer. Additional information about Regeneron and recent news releases are available on Regeneron's web site at www.regeneron.com.

Forward Looking Statement

This news release discusses historical information and includes forward-looking statements about Regeneron and its products, development programs, finances, and business, all of which involve a number of risks and uncertainties. These include, among others, risks and timing associated with preclinical and clinical development of ARCALYST(R), determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize ARCALYST, competing drugs that are superior to ARCALYST, risks associated with the ability to market and sell ARCALYST, uncertainty of market acceptance of ARCALYST, uncertainty concerning the ability of Regeneron to obtain third party coverage and reimbursement for ARCALYST, unanticipated expenses, the availability and cost of capital, the costs of developing, producing, and selling products, and risks associated with third party intellectual property. A more complete description of these and other material risks can be found in Regeneron's filings with the United States Securities and Exchange Commission (SEC), including its Form 10-K for the year ended December 31, 2009 and Form 10-Q for the quarter ended March 31, 2010. 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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