

REGENERON

FACT SHEET ON RILONACEPT (IL-1 TRAP) IN GOUT

ABOUT RILONACEPT

Rilonacept is being evaluated by Regeneron Pharmaceuticals, Inc. as a therapeutic drug candidate for the prevention of gout flares in patients who are initiating uric acid-lowering therapy.

Rilonacept is a fusion protein designed to attach to and neutralize interleukin-1 (IL-1) before IL-1 can bind to cell-surface receptors and generate signals that trigger inflammation.¹

ABOUT INTERLEUKIN-1 (IL-1)

IL-1 is a protein secreted by infection-fighting cells in the blood and tissues. It normally acts as a messenger to regulate inflammatory responses by attaching to surface receptors on cells that participate in the body's immune system.² In gout and certain other diseases, infection-fighting cells can generate excess levels of IL-1, transforming this normally helpful molecule into a key driver of inflammatory disease.³

CURRENT RILONACEPT PHASE 3 CLINICAL DEVELOPMENT PROGRAM IN GOUT

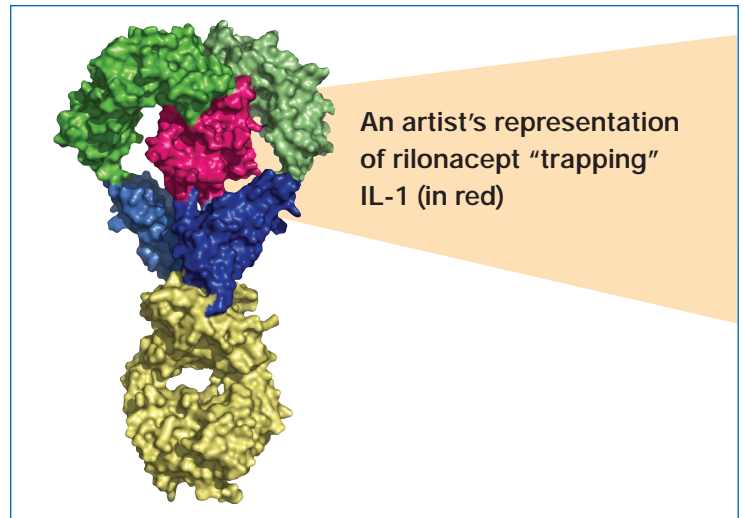
The current Regeneron Phase 3 rilonacept gout program includes two studies that are evaluating rilonacept for the prevention of gout flares in patients who are initiating uric acid-lowering therapy, and a separate safety study. The Phase 3 gout program was designed following discussions with the U.S. Food and Drug Administration. Descriptions of rilonacept clinical trials in gout may be found on www.clinicaltrials.gov by searching on the terms "rilonacept" and "gout".

The North American-based **PRE-SURGE 1 (PREventative Study against URate-lowering drug-induced Gout Exacerbations)** study and the global **PRE-SURGE 2** study are each evaluating, as the primary endpoint, the mean number of gout flares per patient over the first 16 weeks of initiation of allopurinol therapy. Approximately 240 patients are being randomized on a 1:1:1 basis in each study to receive one of the following treatment regimens:

- Rilonacept 160 milligrams (mg) as an initial loading dose, followed by weekly 80 mg subcutaneous injections
- Rilonacept 320 mg as an initial loading dose, followed by weekly 160 mg subcutaneous injections
- Weekly placebo injections

PRE-SURGE 2 data are expected in first half of 2011.

Preliminary results of the **PRE-SURGE 1** study were released on June 9, 2010.⁴ Patients who received rilonacept at a



weekly 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 rilonacept at a weekly dose of 80 mg had a 73% decrease compared to the placebo group (0.29 flares vs. 1.06 flares, $p < 0.0001$). All secondary endpoints of the study were highly positive ($p < 0.001$ vs. placebo). Adverse events that occurred at a frequency of at least 5% in any study group were: injection site reaction, upper respiratory tract infection, lower respiratory tract infection, musculoskeletal pain/discomfort, and headache.

The global **RE-SURGE (REview of Safety Using Rilonacept in preventing Gout Exacerbations)** study, is evaluating the safety of rilonacept versus placebo over 16 weeks in 1,200 patients at risk for gout flares from uric acid-lowering treatment, including allopurinol, febuxostat, probenecid, or sulfipyridone. Data are expected in the first half of 2011.

About 300 patients enrolled in **RE-SURGE** will receive placebo, and 900 patients will receive rilonacept as an initial 320 mg loading dose, followed by weekly 160 mg subcutaneous injections.

A recently completed Phase 3 study in a different gout setting, evaluating rilonacept 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 rilonacept, as measured by the primary endpoint of the average intensity of gout pain from 24-72 hours after initiation of treatment.⁴

