REGENERON

FACT SHEET ON ARCALYST® (rilonacept) INJECTION

ABOUT ARCALYST

ARCALYST is under regulatory review 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]

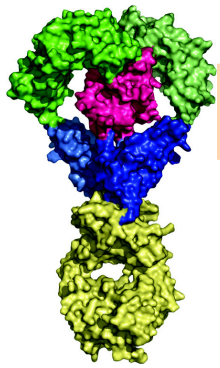
ABOUT INTERLEUKIN-1 (IL-1)

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]

RILONACEPT PHASE 3 CLINICAL DEVELOPMENT PROGRAM IN GOUT

Regeneron's Phase 3 rilonacept gout program included two studies that evaluated rilonacept for the prevention of gout flares in patients who are initiating urate-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** (**PRE**ventative Study against **UR**ate-lowering drug-induced Gout Exacerbations) study and the global **PRE-SURGE 2** study each evaluated, as the primary endpoint, the mean number of gout flares per patient over the first 16 weeks of initiation of allopurinol



An artist's representation of rilonacept "trapping" IL-1 (in red)

therapy. Approximately 240 patients were 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

The global **RE-SURGE** (**RE**view of **S**afety **U**sing **R**ilonacept in preventing **G**out **E**xacerbations) study, evaluated the safety of ARCALYST versus placebo over 16 weeks in 1,315 patients at risk for gout flares from urate-lowering treatment, including allopurinol, febuxostat, probenecid, or sulfinpyrizone. About 25 percent of patients received placebo, and 75 percent received rilonacept dosed at 320 mg as an initial 320 mg loading dose, followed by weekly 160 mg subcutaneous injections.

PRE-SURGE 1 data became available in June 2010. **PRE-SURGE 2** data became available in February 2011. The results of these studies were announced in press releases accessible at www.regeneron.com.

Note: ARCALYST is not approved for use in the prevention of gout flares in patients initiating uric acid lowering therapy.

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REGENERON

FACT SHEET ON ARCALYST® (rilonacept) INJECTION

ABOUT REGENERON PHARMACEUTICALS, INC.

Regeneron is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. Regeneron markets two products in the United States, ARCALYST® (rilonacept) Injection For Subcutaneous Use and EYLEA® (aflibercept) Injection, and has filed regulatory applications with the U.S. Food and Drug Administration (FDA) for second indications for each of these products. A regulatory application has also been submitted to the FDA for the product candidate ZALTRAP® (aflibercept) Concentrate for Intravenous Infusion. Phase 3 studies are in progress with EYLEA® in a third indication, and with product candidate sarilumab. Earlier-stage clinical programs are underway with nine additional monoclonal antibodies. Regeneron has active research and development programs in many disease areas, including ophthalmology, inflammation, cancer, and hypercholesterolemia. Additional information and recent news releases are available on the Regeneron web site at www.regeneron.com.

IMPORTANT INFORMATION ABOUT 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. 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.**

REFERENCES

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3. Dalbeth N and Haskard DO. Mechanisms of inflammation in gout. *Rheumatology* (Oxford). 2005;44:1090-96.

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