



October 18, 2013

Oral Selective JAK3 Inhibitor VX-509 Showed Statistically Significant Improvements in Signs and Symptoms of Rheumatoid Arthritis After 12 Weeks of Treatment in Phase 2b Study

-All doses of VX-509 showed statistically significant ACR20 and ACR50 responses compared to placebo and statistically significant improvement from baseline in DAS28 compared to placebo-

-Three highest doses of VX-509: ACR20 of 58% to 68% versus 18% for placebo; statistically significant ACR70 responses versus placebo-

-Results to be presented at American College of Rheumatology (ACR) Annual Meeting; late-breaker abstract published today on ACR website-

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- [Vertex Pharmaceuticals Incorporated](#) (Nasdaq: VRTX) today announced 12-week results from an ongoing Phase 2b study of VX-509, an investigational oral, selective Janus kinase 3 (JAK3) inhibitor, dosed once or twice daily in people with active rheumatoid arthritis (RA) taking methotrexate. The study met its primary endpoints of both the proportion of people who achieved at least a 20 percent improvement in signs and symptoms of RA, as measured by the ACR improvement criteria (ACR20), and the change from baseline in Disease Activity Score for 28 joints (DAS28). All doses of VX-509 showed statistically significant ACR20 and ACR50 responses versus placebo and statistically significant improvement from baseline in DAS28 versus placebo. The three highest dose groups showed ACR20 responses of between 58 percent and 68 percent, compared to 18 percent for placebo, and statistically significant ACR70 responses versus placebo.

In the study, the discontinuation rate due to adverse events was 6.6 percent for the pooled VX-509 treatment group and 8.5 percent for the placebo group. Overall, adverse event rates were 51.2 percent in the pooled VX-509 treatment groups compared to 38.0 percent for those who received placebo, and the majority of adverse events observed in the study were mild to moderate.

The results were published online today as part of a [late-breaker abstract](#) accepted for an oral presentation at the American College of Rheumatology (ACR) annual meeting. The study is ongoing, and Vertex expects 24-week data to be available in early 2014.

"These results are encouraging and provide further support for the development of VX-509 as a new approach to treating RA and potentially other immune-mediated and inflammatory diseases by selectively targeting JAK3," said Robert Kauffman, M.D. Ph.D., Senior Vice President and Chief Medical Officer at Vertex. "In this study, treatment with VX-509 showed good tolerability and resulted in significant improvements in the signs and symptoms of RA across all doses tested. We look forward to the presentation of these data at the ACR annual meeting later this month."

About the Phase 2b Study

This double-blind, randomized, placebo-controlled 24-week Phase 2b study of VX-509 enrolled and dosed 358 people with RA who had active disease despite methotrexate treatment. Patients continued to receive stable doses of methotrexate during the study. Up to 20 percent of people in the study could have previously been treated with a single tumor necrosis factor (TNF) inhibitor. People in the study were randomized to receive placebo or one of four doses of VX-509 (100 mg once daily (QD), 150 mg once daily, 200 mg once daily or 100 mg given twice daily (BID)) for 24 weeks. The data announced today reflect an analysis of the primary endpoints completed after 12 weeks of treatment, which was the pre-specified primary endpoint of the study.

Efficacy Data

The primary endpoints of the study were the proportion of people who achieved an ACR20 response at week 12 and the change from baseline in DAS28 at week 12. Additional secondary endpoints were used to evaluate the clinical activity of VX-509, including ACR50 and ACR70 responses at week 12. In all VX-509 treatment groups, the proportion of people achieving ACR20 and ACR50 and the decrease from baseline in DAS28 were significantly greater than in placebo. The three highest dose groups showed ACR20 responses of between 58 percent and 68 percent, compared to 18 percent for placebo, and

statistically significant ACR70 responses versus placebo. Efficacy results are provided below:

ACR Responses at Week 12:

	Placebo n=71	VX-509 100 mg QD n=71	VX-509 150 mg QD n=72	VX-509 200 mg QD n=72	VX-509 100 mg BID n=72
ACR20	13 (18.3%)	33 (46.5%) <i>p < 0.001</i>	48 (66.7%) <i>p < 0.001</i>	42 (58.3%) <i>p < 0.001</i>	49 (68.1%) <i>p < 0.001</i>
ACR50	5 (7.0%)	16 (22.5%) <i>p < 0.01</i>	28 (38.9%) <i>p < 0.001</i>	26 (36.1%) <i>p < 0.001</i>	28 (38.9%) <i>p < 0.001</i>
ACR70	2 (2.8%)	7 (9.9%) NS	8 (11.1%) <i>p < 0.05</i>	8 (11.1%) <i>p < 0.05</i>	16 (22.2%) <i>p < 0.001</i>

NS=not statistically significant

DAS28 at Week 12:

	Placebo n=71	VX-509 100 mg QD n=71	VX-509 150 mg QD n=72	VX-509 200 mg QD n=72	VX-509 100 mg BID n=72
DAS28 Improvement from Baseline	-0.70	-2.04 <i>p < 0.001</i>	-2.20 <i>p < 0.001</i>	-2.51 <i>p < 0.001</i>	-2.42 <i>p < 0.001</i>

Least squares mean change from baseline

Safety Data

In the study, adverse events led to discontinuation in 6.6 percent and 8.5 percent of people in the VX-509 and placebo groups, respectively. Through 12 weeks, adverse event rates were 51.2 percent for the pooled VX-509 treatment group compared to 38.0 percent for those who received placebo, and the majority of adverse events observed in the study were mild to moderate. The most common adverse events in the pooled VX-509 treatment group were headache (8.0 percent), hypercholesterolemia (3.8 percent) and nasopharyngitis (3.5 percent). The safety profile of VX-509 was comparable across all treatment groups. Serious adverse events occurred in equal proportions of people across the pooled VX-509 and placebo treatment groups (5.6 percent). Infections occurred in 22.0 percent of people in the pooled VX-509 treatment group compared to 15.5 percent in the placebo group, and serious infections occurred in 2.8 percent of people in the VX-509 group compared to 1.4 percent for placebo. One death, deemed unrelated to study drug, occurred in the VX-509 100 mg BID group and was due to cardiac failure. Elevations in transaminase levels and decreases in median neutrophil and lymphocyte counts were observed in the VX-509 groups and were generally mild.

Presentation at ACR Annual Meeting

These results were accepted for presentation at the ACR annual meeting, being held October 25-30 in San Diego, CA. The presentation of the results will take place in the "ACR Late-Breaking Abstract Oral Session" on October 29 from 2:30 — 4:00 p.m. PT. The abstract presentation number is "L3."

About VX-509

VX-509 is an oral, selective Janus kinase 3 (JAK3) inhibitor being developed by Vertex. VX-509 may represent a new approach to treating an underlying disease mechanism that triggers inflammation in a number of debilitating diseases, including RA. In immune-mediated diseases, JAK3 is an essential component of the immune signaling cascade. This cascade ultimately contributes to abnormal immune response that results in chronic inflammation and, in the case of RA, irreversible damage to cartilage and bones. Based on *in vitro* data, VX-509 has demonstrated a high level of selectivity for inhibition of JAK3 compared to JAK1- and JAK2-dependent assays, and this high level of selectivity was confirmed in clinical studies where dose-related inhibition of a JAK3-dependent biomarker was observed while little to no effect was shown against a JAK2/JAK1-dependent biomarker.

About Rheumatoid Arthritis

RA is a chronic, progressive, inflammatory disease that affects almost 1 percent of the world's population¹, including at least 1.3 million adults in the United States. The disease causes destruction of joint cartilage and erosion of adjacent bone, resulting in pain, swelling, stiffness and limited motion and function of joints. People with RA may also have a higher risk for heart disease and stroke² and suffer from progressive disability over time leading to premature death.³ RA can also result in substantial health care costs.⁴

The treatment of RA focuses on reducing symptoms and inhibiting progression of the disease. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids may reduce swelling, pain and fever, but they do not alter the natural course of the disease. Disease-modifying anti-rheumatic drugs (DMARDs) have shown effects in slowing the progression of joint damage and thus altering the natural history of RA. While recently approved medicines are effective in a portion of patients, there is still no cure for RA and many patients must change their treatment at least once in their lifetime, creating a significant need for new approaches to RA treatment.²

About Endpoints in RA: ACR Responses and DAS28

The most common measures of improvement in RA clinical studies are ACR responses and DAS28. An ACR response is defined as at least a pre-specified percent improvement in the signs and symptoms of RA in a patient, as measured by tender and swollen joint counts and five other criteria (patient's assessment of pain, patient's assessment of disease activity, physician's assessment of disease activity, patient's assessment of physical function and levels of an acute phase reactant (either the C-reactive protein (CRP) level or the erythrocyte sedimentation rate (ESR))). Thus, an ACR20 response is defined as at least 20 percent improvement in both the tender and swollen joint counts, and at least 20 percent improvement in three of the five other criteria. DAS28 scores are derived from an assessment of tender and swollen joints, CRP or ESR, and a patient's assessment of general health.

About Vertex

Vertex creates new possibilities in medicine. Our team discovers, develops and commercializes innovative therapies so people with serious diseases can lead better lives.

Vertex scientists and our collaborators are working on new medicines to cure or significantly advance the treatment of hepatitis C, cystic fibrosis, rheumatoid arthritis and other life-threatening diseases.

Founded more than 20 years ago in Cambridge, Mass., we now have ongoing worldwide research programs and sites in the U.S., U.K. and Canada. Today, Vertex has more than 2,000 employees around the world, and for three years in a row, *Science* magazine has named Vertex one of its Top Employers in the life sciences.

Special Note Regarding Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, Dr. Kauffman's statements in the fourth paragraph of this press release and statements regarding (i) Vertex's expectation that 24-week data from the study will be available in early 2014 and (ii) VX-509 potentially representing a new approach to treating an underlying disease mechanism that triggers inflammation in a number of debilitating diseases. While Vertex believes the forward-looking statements contained in this press release are accurate, there are a number of factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include, among other things, that the 24-week data or outcomes from any future studies of VX-509 may not be favorable, and the other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

References:

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Source: Vertex Pharmaceuticals Incorporated

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