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AstraZeneca Announces Top-Line Results of OSKIRA-4 Phase IIb Study of Fostamatinib as a Monotherapy for Rheumatoid Arthritis

SOUTH SAN FRANCISCO, Calif., Dec. 13, 2012 /PRNewswire/ -- AstraZeneca today announced top-line results of OSKIRA-4, a Phase IIb monotherapy study of fostamatinib, the first kinase inhibitor with selectivity for SYK (spleen tyrosine kinase) in development as an oral treatment for rheumatoid arthritis (RA).

OSKIRA-4 was a six month study evaluating improvements in signs and symptoms of RA in 280 patients who had never previously used a disease-modifying anti-rheumatic drug (DMARD), were DMARD intolerant or had an inadequate response to DMARDs and were randomised to receive fostamatinib as a monotherapy, adalimumab as a monotherapy, or placebo. Three dose regimens of fostamatinib were evaluated in OSKIRA-4: 100mg twice daily, 100mg twice daily for a month followed by 150mg once daily, and 100mg twice daily for a month followed by 100mg once daily.

OSKIRA-4 had two primary objectives – a superiority comparison to placebo at 6 weeks and a non-inferiority analysis against adalimumab monotherapy at 24 weeks as measured by change from baseline in DAS28 score (a composite endpoint assessing signs and symptoms of RA).

In the OSKIRA-4 study, fostamatinib as a monotherapy met the first primary objective, showing a statistically significant superior DAS28 score change from baseline compared to placebo at 6 weeks at the 100mg twice daily dose and the 100mg twice daily for a month followed by 150mg once daily dose, but not at the 100mg twice daily for a month followed by 100mg once daily dose.

The OSKIRA-4 study did not meet its second primary objective as all fostamatinib monotherapy doses were inferior to adalimumab monotherapy at week 24 based on DAS28. The adalimumab monotherapy ACR20 result at the 24 week endpoint was 59%.

The safety and tolerability findings for fostamatinib as reported in the OSKIRA-4 study were generally consistent with that previously observed in the TASKi Phase II programme.

Martin Mackay, President of AstraZeneca Research and Development said: "This Phase IIb dose finding study was designed to evaluate the effect of fostamatinib independent of methotrexate and to inform the further development of fostamatinib as a monotherapy treatment for RA. A more comprehensive assessment of the benefit/risk profile of fostamatinib used in combination with a DMARD is being undertaken in the pivotal studies that form the OSKIRA Phase III programme which are on track to report in the first half of 2013, and would form the basis of regulatory submissions."

Regulatory filings in the US and EU for use in combination with a DMARD based on the OSKIRA Phase III programme, are expected in the second half of 2013.

A more detailed analysis of the OSKIRA-4 findings will be published in due course.

About the OSKIRA programme
Ongoing Phase III trials in the OSKIRA (Oral Syk Inhibition in Rheumatoid Arthritis) programme, include three pivotal studies assessing the efficacy and safety of fostamatinib; two 12-month studies examining the effect of fostamatinib on patients responding inadequately to DMARDs including methotrexate (OSKIRA-1, OSKIRA-2); a six-month study assessing the effect of fostamatinib on patients who have previously responded inadequately to an anti-TNF therapy (OSKIRA-3); and a long-term extension study looking at the ongoing safety and tolerability of fostamatinib (OSKIRA-X). The three pivotal studies have as their primary endpoint the proportion of patients with ACR20 compared to placebo (ACR20 = American College of Rheumatology 20% response criteria). The OSKIRA-1 study also has a co-primary endpoint of change from baseline to week 24 in modified total Sharp score (mTSS), an x-ray endpoint assessing structural progression.

These Phase III studies are expected to be completed in the first half of 2013.

For more information about OSKIRA-4 visit: http://clinicaltrials.gov/ct2/show/NCT01264770

About Fostamatinib
Fostamatinib (previously referred to as R788), is the first kinase inhibitor with selectivity for SYK in development as an oral treatment for rheumatoid arthritis. Fostamatinib blocks signalling in multiple cell types involved in inflammation and tissue degradation in rheumatoid arthritis and it is hypothesized that it may hinder key steps in the progression of the disease. In February 2010, AstraZeneca and Rigel Pharmaceuticals announced a worldwide license agreement whereby AstraZeneca will develop and commercialise fostamatinib.

About Rheumatoid Arthritis (RA)
RA is a painful, systemic, chronic inflamatory disease which can cause damage to the joints and vital organs as well as affecting other parts of the musculoskeletal system such as connective tissues, muscles and tendons. The disease affects approximately one in 100 people worldwide.

If not adequately treated, RA is a major cause of disability and is associated with reduced life expectancy. In the US alone the total annual societal cost of RA is estimated to amount to $39.2 billion, with even greater indirect costs to individuals and society including costs from diminished work capacity, loss of productivity, loss in earnings and loss in tax contributions.

About Rigel Pharmaceuticals
Rigel Pharmaceuticals, Inc. (Nasdaq:RIGL) is a clinical-stage drug development company that discovers and develops novel, small-molecule drugs for the treatment of inflammatory and autoimmune diseases, as well as muscle disorders. Rigel's pioneering research focuses on intracellular signaling pathways and related targets that are critical to disease mechanisms. Rigel's productivity has resulted in strategic collaborations with large pharmaceutical partners to develop and market its product candidates. Current product development programs include fostamatinib, an oral SYK inhibitor that is in Phase III clinical trials for rheumatoid arthritis with its partner AstraZeneca; R343, an inhaled SYK inhibitor for asthma and R333, a topical JAK/SYK inhibitor for discoid lupus – both of which have commenced Phase II clinical trials; and R548, an oral JAK3 inhibitor for the treatment of transplant rejection and other immune disorders. Visit www.rigel.com.

About AstraZeneca
AstraZeneca is a global, innovation-driven biopharmaceutical business with a primary focus on the discovery, development and commercialisation of prescription medicines for gastrointestinal, cardiovascular, neuroscience, respiratory and inflammation, oncology and infectious disease. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.com

Rigel Pharmaceuticals Forward Looking Statement
This press release contains "forward-looking" statements, including, without limitation, statements related to the progress of the development of fostamatinib, partnered with AstraZeneca, and the results of OSKIRA-4, as well as statements related to dates for clinical filings and publications. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "hypothesized," "will," "may," "expect," and similar expressions are intended to identify these forward-looking statements. These forward-looking statements are based upon Rigel's current expectations and involve risks and uncertainties. There are a number of important factors that could cause Rigel's results to differ materially from those indicated by these forward-looking statements, including, without limitation, the timing and success of clinical trials and the potential problems that may arise in the development and approval process, market competition, risks associated with Rigel's corporate partnerships, as well as other risks detailed from time to time in Rigel's reports with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2012. Rigel does not undertake any obligation to update forward-looking statements and expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein.

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