Press Release

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Shire Reports Top-Line Results on OPUS-2, a Phase 3 Study Investigating the Use of Lifitegrast (5.0% Ophthalmic Solution) in Adults With Dry Eye Disease

December 5, 2013 –– Shire plc (LSE: SHP, NASDAQ: SHPG), the global specialty biopharmaceutical company, today announced top-line results from OPUS-2, a Phase 3 efficacy and safety study of 5.0% lifitegrast ophthalmic solution. OPUS-2 compared lifitegrast to placebo administered twice daily for 84 days (12 weeks) in dry eye patients with history of active artificial tear use within 30 days prior to screening. Lifitegrast met the prespecified co-primary endpoint for the patient-reported symptom of eye dryness (change in Eye Dryness Score from baseline to week 12) (p-value<0.0001). Lifitegrast did not meet the prespecified co-primary endpoint for the sign of inferior corneal staining score (change from baseline to Week 12) using fluorescein staining compared with placebo (p-value=0.6186).

"In this clinical trial, we note that lifitegrast showed a statistically significant improvement in the prespecified symptoms of dry eye disease and is the first drug to do so in a phase 3 clinical trial," said Flemming Ornskov, M.D., Chief Executive Officer, Shire. "We will be examining the totality of the data for lifitegrast in OPUS-2, as well as OPUS-1 and across the entire clinical trial program. We look forward to discussing the lifitegrast program with regulatory authorities."

The study also evaluated the safety and tolerability of lifitegrast based on occurrence of treatment-emergent adverse events (TEAEs). The most commonly reported TEAEs associated with lifitegrast were dysgeusia (altered sense of taste) (16.2% vs 0.3% for placebo), instillation site irritation (7.8% vs 1.4% for placebo), instillation site reaction (7.0% vs 1.1% for placebo) and visual acuity reduced (5.0% vs 6.4% for placebo). There were no ocular serious TEAEs or drug-related serious TEAEs. 93.2% of patients enrolled in the study remained for the entire duration of the 12-week clinical trial.

ABOUT THE LIFITEGRAST PHASE 3 CLINICAL DEVELOPMENT PROGRAM

OPUS-1, OPUS-2 and SONATA currently make up the phase 3 clinical development program for lifitegrast.

OPUS-1 was a multicenter, placebo-controlled trial conducted in a controlled adverse environment with 588 dry eye subjects to investigate the efficacy and safety of lifitegrast (5.0% solution) versus placebo twice daily for 84 days.

- In OPUS-1, the pre-specified co-primary endpoints were: 1) mean change from baseline to Day 84 in the inferior corneal fluorescein staining score (i.e., "sign"); and 2) the mean change from baseline to Day 84 in the Visual Related (VR) function subscale of the Ocular Surface Disease Index (OSDI) (i.e., "symptom"). In this study, lifitegrast demonstrated superiority over placebo on the sign endpoint of improvement of the inferior corneal fluorescein staining score (P=0.0007). Ocular surface damage, which is a hallmark of chronic inflammation from dry eye disease, is often detected using this staining parameter. However, the co-primary symptom endpoint, the VR function subscale of the OSDI, did not achieve statistical significance.

- There were no serious ocular adverse events. The most commonly reported ocular adverse events were irritation and pain upon initial instillation, and were generally mild in severity.

OPUS-2, initiated in December 2012, was conducted in the natural environment and compared lifitegrast to placebo administered twice daily for 84 days (12 weeks) in dry eye patients with history of active artificial tear use within 30 days prior to screening.

OPUS-2 was a multicenter, randomized, double-masked, placebo-controlled, parallel-arm study with a 14-day open-label placebo screening run-in period. Patients randomized into the study were not allowed to use artificial tears during the study. Overall, 718 patients were randomized at 31 US sites. The study consisted of 5 visits over 98 days: screening visits Day -14 (Visit 1) to Day 0 (Visit 2), and treatment visits at Day 0 (Visit 2), Day 14 (Visit 3), Day 42 (Visit 4), and Day 84 (Visit 5).

SONATA, which was initiated in December 2012, is a prospective, randomized, double-masked, placebo-controlled trial in 300 dry eye subjects to evaluate the safety of lifitegrast for 1 year. This trial is scheduled for completion in mid 2014.

ABOUT LIFITEGRAST

Lifitegrast, a small-molecule integrin antagonist, was designed in order to treat dry eye disease, and is a preservative-free topical eye solution. Lifitegrast is believed to work by reducing inflammation through inhibition of lymphocyte function-associated antigen 1 (LFA-1) and preventing its binding to intercellular adhesion molecule-1 (ICAM-1) that influences T-cell activation and cytokine (protein) release. The interaction between these two proteins plays a key role in the chronic inflammation associated with dry eye. T-cells are important components of the immune system that help control the body's response to a foreign or harmful substance or stimuli.

ABOUT DRY EYE DISEASE

As defined by the International Dry Eye Workshop in 2007, dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

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NOTES TO EDITORS

Shire enables people with life-altering conditions to lead better lives.

Our strategy is to focus on developing and marketing innovative specialty medicines to meet significant unmet patient needs.

We provide treatments in Neuroscience, Rare Diseases, Gastrointestinal, Internal Medicine and Regenerative Medicine and we are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas.

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FORWARD - LOOKING STATEMENTS - "SAFE HARBOR" STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

Statements included in this announcement that are not historical facts are forward-looking statements. Forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, Shire's results could be materially adversely affected. The risks and uncertainties include, but are not limited to, that:

- Shire's products may not be a commercial success;
- revenues from ADDERALL XR are subject to generic erosion;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payors in a timely manner for Shire's products may impact future revenues and earnings;
- Shire relies on a single source for manufacture of certain of its products and a disruption to the supply chain for those products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis;
- Shire uses third party manufacturers to manufacture many of its products and is reliant upon third party contractors for certain goods and services, and any inability of these third party manufacturers to manufacture products, or any failure of these third party contractors to provide these goods and services, in each case in accordance with its respective contractual obligations, could adversely affect Shire's ability to manage its manufacturing processes or to operate its business;
- the development, approval and manufacturing of Shire's products is subject to extensive oversight by various regulatory agencies and regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the actions of certain customers could affect Shire 's ability to sell or market products profitably and fluctuations in buying or distribution patterns by such customers could adversely impact Shire's revenues, financial conditions or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to Shire's activities in the highly regulated markets in which it operates may result in the distraction of senior management, significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire's ability to obtain, maintain, enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire's revenues, financial condition or results of operations;and other risks and uncertainties detailed from time to time in Shire's filings with the U.S. Securities and Exchange Commission, including its most recent Annual Report on Form 10-K.