Press Release

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U.S. FDA Grants Priority Review to Lifitegrast NDA for the Treatment of Dry Eye Disease in Adults

Lexington, Mass. – April 9, 2015 – Shire plc (LSE: SHP, NASDAQ: SHPG) today announced that the United States Food and Drug Administration (FDA) has accepted for filing the New Drug Application (NDA) for lifitegrast and granted a Priority Review designation. Lifitegrast is an investigational treatment for dry eye disease in adults and, if approved, has the potential to be the first treatment indicated to address both signs and symptoms of the disease. The FDA is expected to provide a decision on October 25, 2015, based on the Prescription Drug User Fee Act V action date.

The FDA grants Priority Review designation to drugs that have the potential to provide significant improvements in the safety or effectiveness for the treatment, diagnosis or prevention of a serious disease. Drugs with Priority Review designation have an accelerated review target of eight months, instead of the standard of 12 months

"Our NDA filing for lifitegrast represents an important regulatory milestone, exemplifying Shire's ability to forge new paths in therapeutic areas aligned with our focus in rare and specialty conditions," said Philip J. Vickers, Ph.D., Head of Research and Development, Shire. "Our commitment to moving lifitegrast forward reflects our intent to grow in the Ophthalmics therapeutic category in areas of unmet patient need. We look forward to working closely with the FDA throughout the review process."

The NDA filing is supported by the totality of evidence from four clinical trials with more than 1,800 patients. These include one Phase 2 study, two Phase 3 efficacy and safety studies, and one long-term Phase 3 safety study.

"The symptoms of dry eye are one of the most common complaints from patients, yet there remains a tremendous unmet need," said Stephen C. Pflugfelder, M.D., Professor of Ophthalmology at Baylor College of Medicine, Houston, Texas. "It's encouraging to see Shire moving the program for lifitegrast forward."

About Lifitegrast

Lifitegrast is a novel small-molecule integrin inhibitor. It binds to the integrin LFA-1 (lymphocyte function-associated antigen-1), a cell surface protein found on leukocytes, and blocks the interaction of LFA-1 with its cognate ligand ICAM-1 (intercellular adhesion molecule-1). ICAM-1 is over-expressed in corneal and conjunctival tissues in dry eye disease. LFA-1/ICAM-1 interaction contributes to the formation of immunological synapses resulting in T-cell activation and migration to target tissues.

About Dry Eye Disease

As defined by the 2007 Dry Eye WorkShop ("DEWS"), sponsored by the Tear Film & Ocular Surface Society (TFOS), 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. Dry eye, an often chronic and progressive ocular disease, is one of the most common complaints to eye care professionals, and represents a significant unmet need. [1,2]

About Shire

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 focus on providing treatments in Rare Diseases, Neuroscience, Gastrointestinal and Internal Medicine and are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas, such as Ophthalmics.

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THE "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. Such 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;
- product sales from ADDERALL XR and INTUNIV are subject to generic competition;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for Shire's products may affect future revenues, financial condition and results of operations;
- Shire conducts its own manufacturing operations for certain of its products and is reliant on third party contract manufacturers to manufacture other products and to provide goods and services.
- Some of the Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of the Shire's 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 for some period of time;

- the manufacture of Shire's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect 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 significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters and other disputes, including Shire's ability to 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;
- Shire faces intense competition for highly qualified personnel from other companies and organizations. Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect Shire's ability to attract and/or retain the highly skilled personnel needed for Shire to meet its strategic objectives;
- failure to achieve Shire's strategic objectives with respect to the acquisition of NPS Pharmaceuticals, Inc. may adversely affect Shire's financial condition and results of operations;

and other risks and uncertainties detailed from time to time in Shire's filings with the US Securities and Exchange Commission, including its most recent Annual Report on Form 10-K.

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[1] Schaumberg DA, Sullivan DA, Buring JE et al. Prevalence of dry eye syndrome among US women. *Am J Ophthalmol*. 2003 Aug;136(2):318-26.

[2] Schaumberg DA, Dana R, Buring JE et al. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. *Arch Ophthalmol.* 2009 Jun;127(6):763-8.