Press Release

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Shire R&D Day Profiles Innovative Pipeline Expected to Contribute $3 Billion in Product Sales by 2020

Lexington, MA – December 10, 2014 – Shire plc (LSE: SHP, NASDAQ: SHPG) is hosting a Research and Development (R&D) Day for the investment community focused on the Company's pipeline of innovative medicines being developed to treat rare diseases and other specialty conditions. Shire also announced a collaboration with Cystic Fibrosis Foundation Therapeutics Inc. (CFFT), the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation, to support the Company's Messenger RNA Technology platform for cystic fibrosis (CF), and Fast Track designation from the U.S. Food and Drug Administration (FDA) for SHP607, a protein replacement therapy being developed for the prevention of Retinopathy of Prematurity (ROP).

"Shire's clear and focused strategy has enabled us to transform our pipeline with 22 programs in the clinic, the most in Shire's history," said Flemming Ornskov, M.D., MPH, Chief Executive Officer.

"Our clinical and scientific capabilities in discovering new therapies for rare diseases are focused on new indications and therapeutic areas," said Philip J. Vickers, Ph.D., Global Head of Research & Development. "We have a number of significant clinical milestones anticipated over the next 18 months, and aim to accelerate delivery of therapies to patients from a highly productive internal pipeline, complemented by the acquisition of external assets and innovative collaborations."

CFFT Investment/Messenger RNA Technology Platform

Messenger RNA (mRNA) is a natural material produced by living organisms to convey coded genetic information from a gene (DNA) to the ribosome, which translates the coded genetic information into protein. In many diseases, the underlying cause is the lack of sufficient levels of functional protein.

Shire is investigating therapies in its preclinical pipeline which would deliver mRNA to sites in the body where it can be used by the body's own cellular mechanisms to produce normal working copies of the protein.

CFFT has committed to up to $15 million to support Shire's mRNA technology platform for CF. In CF, mutations in the CFTR gene (Cystic Fibrosis Transmembrane Conductance Regulator) lead to a disruption of the normal regulation of fluids in the lung that cause the secretions to thicken, thereby restricting lung function and leading to recurrent lung infections.

Shire's goal is to deliver mRNA that codes for a fully functional (wild type) version of the CFTR protein to the lungs of CF patients. If high enough levels of functional CFTR protein can be produced, lung function may be improved, thereby reducing the frequency and severity of infections.

Shire is also investigating other diseases that are caused by a lack of sufficient levels of a functional protein and where the Company may be able to leverage its mRNA Technology platform. Shire will highlight its mRNA platform at today's R&D Day.

Fast Track Designation for SHP607

Shire has received Fast Track designation from the FDA for SHP607, a protein replacement therapy for the prevention of Retinopathy of Prematurity (ROP), which is a potentially blinding proliferative retinopathy unique to prematurely born infants.

Fast Track designation is an FDA-approved process that facilitates the development and expedites the review of drugs to treat serious diseases that fill an unmet medical need with the goal of delivering important new treatments to patients earlier.

SHP607 is currently in a Phase 2 study that aims to compare the severity of ROP among treated patients versus an untreated control population matched for gestational age. Topline data from this study are expected in the second half of 2015.

Recent R&D Highlights

Lifitegrast (SHP606)
Shire expects to file an NDA for Lifitegrast for the treatment of signs and symptoms of Dry Eye Disease in Q1 2015. The Company is also conducting a Phase 3 safety and efficacy study (OPUS-3) in support of a potential label in the U.S. and international markets. The study will run concurrent to the U.S. NDA review.

SHP625 (LUM001)
Shire has completed enrollment of a Phase 2 registration study in pediatric patients with Alagille Syndrome (ALGS). ALGS is a rare genetic disorder that affects the liver, heart, kidney, and other systems of the body. The Company expects to report top-line results in the first half of 2015. There are also four other Phase 2/3 pediatric studies ongoing in ALGS.

Shire is also conducting a Phase 2 pediatric study in patients with Progressive Familial Intrahepatic Cholestasis (PFIC). PFIC is a rare inherited condition in which children are unable to drain bile from the liver.

Shire has also completed enrollment of a Phase 2 study in adult patients with Primary Biliary Cirrhosis, a rare disease that causes progressive destruction to the small bile ducts of the liver that can lead to scarring, fibrosis, and cirrhosis. The Company expects to report top-line results in the first half of 2015.

SHP626 (LUM002)
An IND for SHP626 in patients with Non-Alcoholic Steatohepatitis (NASH) has been submitted in November and following FDA permission to proceed we plan to initiate a Phase 1b multiple-dose study in Q1 2015. NASH is a condition characterized by fat deposits in the liver, leading to inflammation and, in a subset of patients, significant fibrosis.

Vyvanse for BED
The FDA has granted priority review for Shire's sNDA of Lisdexamfetamine dimesylate (active ingredient in VYVANSE) in Binge Eating Disorder (BED). BED is characterized by recurring episodes of eating large amounts of food in a discrete period of time, consistent loss of control while binging and remorse in the aftermath of a binge. Those with BED binge on food at least once a week over a period of three months or more. The PDUFA date is February 1, 2015.

Further details of these, and the remainder of Shire's portfolio, will be discussed at today's R&D Day.

Meeting Webcast

These presentations will be broadcast via a live webcast that can be accessed under the "Presentations & Webcasts" tab in the Investor Relations section of the Company's website at www.shire.com. A replay of the webcast will be archived on the website following the presentation.

The details of the Conference Call are as follows:

UK Toll-Free Number: 08082370033

UK and International Number: +44 (0) 2034262889

US Toll Number: +16467224897

US Toll-Free Number: 18778414559

For further information please contact:

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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 focus on providing treatments in Rare Diseases, Neuroscience, Gastrointestinal, and Internal Medicine and we 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 herein 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;
- revenues from ADDERALL XR are subject to generic erosion and revenues from INTUNIV will become subject to generic competition starting in December 2014;
- 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, 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 Shire's products or ingredients are only available from a single approved source for manufacture. Any disruption to the supply chain for any of 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 development, approval and manufacturing of Shire's products is subject to extensive oversight by various regulatory agencies. Submission of an application for regulatory approval of any of our product candidates, such as our planned submission of a New Drug Application to the FDA for Lifitegrast, may be delayed for any number of reasons and, once submitted, may be subjected to lengthy review and ultimately rejected. Moreover, 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. Fluctuations in buying or distribution patterns by such customers can adversely impact Shire's revenues, financial condition 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, academic institutions, government entities and other organizations. Shire is undergoing a corporate reorganization and the consequent uncertainty could adversely impact 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 ViroPharma Incorporated 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 Securities and Exchange Commission, including those risks outlined in "Item 1A: Risk Factors" in Shire's Annual Report on Form 10-K for the year ended December 31, 2013.