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Shire Reports Topline Results from First of Three Placebo-Controlled Phase 2 Studies of SHP625 (LUM001) in Children with Alagille Syndrome

Lexington, Mass. – April 09, 2015 – Shire plc (LSE: SHP, NASDAQ: SHPG) today announced that the 13-week Phase 2 IMAGO trial of its investigational compound SHP625 (LUM001) did not meet the primary or secondary endpoints in the study of 20 pediatric patients with Alagille syndrome (ALGS), a rare, life-threatening genetic disorder that presents with chronic cholestasis (accumulation of bile acids in the liver) and severe pruritus (itching). The primary endpoint was the change from baseline in serum bile acid levels as compared to placebo. The secondary endpoint of pruritus was assessed using the novel ItchRO™ instrument.

Mean serum bile acid levels and pruritus at the end of the study were lower in both SHP625 and placebo treated groups as compared to baseline. However, in a post-hoc analysis, a positive correlation between percent changes from baseline in serum bile acid levels and pruritis was observed in the SHP625 treated group. The number of patients in the placebo treated group was too small to make an accurate assessment of this relationship.

There were no treatment emergent serious adverse events in this study. As expected, the most common adverse events were diarrhea and abdominal pain, which were more frequent with SHP625 than with placebo.

“We have gained important insights from these first results from one of several phase 2 studies in the SHP625 development program,” said Philip J. Vickers, Ph.D., Head of Research and Development, Shire. “We remain committed to continuing the ongoing studies of SHP625 in ALGS and other indications.”

In addition to IMAGO, two larger placebo-controlled phase 2 studies in ALGS are in progress, one of which has pruritus as the primary endpoint. SHP625 is also being studied in progressive familial intrahepatic cholestasis, primary biliary cirrhosis and primary sclerosing cholangitis.

ABOUT THE IMAGO STUDY

IMAGO is a phase 2 multicenter, randomized, placebo-controlled study of children with ALGS, 1-18 years of age, conducted in the United Kingdom. Subjects (n=20) were randomized to receive oral, once-daily SHP625, 140 µg/kg/day (n=6) or 280 µg/kg/day (n=8) or placebo (n=6). The primary endpoint was change in fasting serum bile acid levels from baseline to Week 13. Serum bile acid level reductions from baseline were -66.1 µmol/L and -42.1 µmol/L (p=0.69) in

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the SHP625 and in the placebo treated groups, respectively. For the secondary endpoint of pruritus, the change from baseline for the ItchRO(Obs) scores was -0.61 and -0.59 (p=0.95) in the SHP625 and the placebo treated groups, respectively. Additional secondary endpoints included change in liver enzymes. The most common adverse events with SHP625 vs placebo were diarrhea (64.3% vs 33.3%) and abdominal pain (42.9% vs 16.7%).

ABOUT SHP625

SHP625 is being studied in several rare cholestatic liver diseases for both pediatric and adult populations. Preclinical models demonstrate that SHP625 is a potent, selective minimally absorbed inhibitor of the apical sodium-dependent bile acid transporter. It blocks bile acid reabsorption in the terminal ileum and increases fecal bile acid excretion, thereby reducing recirculation of bile acids to the liver.

ABOUT ALAGILLE SYNDROME

Alagille syndrome (ALGS) is a rare, life-threatening genetic disorder occurring in approximately one in 30,000 live births that affects the liver, heart, kidney and other systems of the body. Problems associated with the disorder generally become evident in infancy or early childhood. A person with Alagille syndrome has fewer than the normal number of bile ducts inside the liver. This causes bile to build up in the liver, a condition called cholestasis, and leads to liver damage. In addition, a buildup of bile acids in the blood also can cause pruritus, or itching, which can be severe. There are no approved medical therapies for ALGS, but some treatments can address its symptoms. Ten to 30 percent of people with ALGS will require a liver transplant.

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NOTES TO EDITORS

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

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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 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.