Press Release

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This press release is intended for U.S. and EU audiences only.
A separate press release has been prepared for use in Japan.

Shire Partner, Shionogi, Submits New Drug Application in Japan for ADHD treatment for children

With submission, Shire continues to strengthen its presence in Japan

LEXINGTON, Mass. – February 10, 2016 – Shire plc (LSE: SHP, NASDAQ: SHPG) and Shionogi & Co., Ltd. recently announced that Shionogi submitted a New Drug Application (NDA) for the manufacturing and marketing in Japan of S-877503 (guanfacine hydrochloride prolonged release tablets),* for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children. The Japanese clinical studies were conducted in children 6 to 17 years old with this disorder.

Shire and Shionogi, under a co-development and commercialization licensing contract signed in 2011, have been developing S-877503 as an investigational pediatric ADHD candidate. Shionogi is a Japan-based pharmaceutical company focused on the research and development of treatments for various therapeutic areas, including central nervous system disorders and infectious diseases.

“This NDA is significant for patients, Shire and Shionogi. If approved, Shire will have another key product available in Japan, increasing patient access to more of our medicines in a market incredibly important on the world’s stage,” said Philip J. Vickers, Ph.D., Head of Research & Development, Shire. “Fortunately, we have a strong partner for our ADHD development and commercialization efforts in Shionogi, who has been central to our growth in Japan. Shire has a number of pipeline products, in addition to S-877503, intended for Japan, so we’re excited about the possibilities for addressing more unmet patient needs in this country.”

Shire Japan KK, Shire’s local operating company (LOC), also has investigational candidates in the pipeline for hereditary angioedema, short-bowel syndrome, convulsive seizures and hypoparathyroidism. The LOC offers two therapies of its own on the Japanese market – one for Gaucher disease and the other for thrombocythemia – and partners with several other companies to develop new products for the Japanese market.

New therapeutic options for ADHD are needed in Japan. Multiple medicines for the disorder are approved and sold in the United States and Europe. However, only two ADHD medicines have been approved in Japan, where the anticipated regulatory review process for an NDA is approximately 12 months.

About S-877503
The mode of action of S-877503 in ADHD is not fully established. Preclinical research suggests S-877503 modulates signalling in the prefrontal cortex and basal ganglia through direct modification of synaptic noradrenalin transmission at the alpha$_{2A}$-adrenergic receptors. This proposed mode of action is different than the other ADHD medicines currently available in Japan.

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*U.S. and EU brand name: INTUNIV® (guanfacine extended-release tablets in U.S.; guanfacine hydrochloride prolonged release tablets in EU). Canadian brand name: INTUNIV XR® (guanfacine hydrochloride extended-release tablets)

Guanfacine hydrochloride prolonged release tablets are marketed in the United States, EU and Canada. For more information on the product labelling in these markets, refer to the U.S. Prescribing Information, EU Summary of Product Characteristics (SmPC) and Canadian Product Monograph, respectively. In the United States, generic versions of guanfacine hydrochloride prolonged release tablets (or INTUNIV) are available for the treatment of ADHD.

About ADHD in children and adolescents

ADHD is a common psychiatric disorder in children and adolescents and is recognized by the World Health Organization (WHO). The core symptoms are inattention, hyperactivity and impulsivity. Worldwide, prevalence of ADHD is estimated to be between 5.29% and 7.1%, and just under 5% for children and adolescents (<18 years). While the exact origin of ADHD is unknown, it is recognized that the disorder may be caused by the interplay between genetic and environmental factors.

About Shionogi & Co., Ltd.

Shionogi & Co., Ltd. is a major research-driven pharmaceutical company dedicated to placing the highest value on patients based on its corporate philosophy of “supply the best possible medicine to protect the health and wellbeing of the patients we serve.” Shionogi’s research and development currently targets two therapeutic areas: infectious diseases and pain/CNS disorders. In addition, Shionogi is engaged in new research areas such as obesity/geriatric metabolic disease and oncology/immunology. Contributing to the health and QOL of patients around the world through development in these therapeutic areas is Shionogi’s primary goal.

For more information, please visit www.shionogi.co.jp/en/.

Important Safety Information for United States and EU

- INTUNIV is contraindicated in patients with a history of a hypersensitivity reaction to INTUNIV or its inactive ingredients. Rash and pruritus have been reported.

- Treatment with INTUNIV can cause dose-dependent decreases in blood pressure and heart rate. Orthostatic hypotension and syncope have been reported. Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. In patients with a history of syncope or a condition that predisposes them to syncope, advise against becoming dehydrated or overheated.

- Somnolence and sedation were commonly reported adverse reactions in clinical studies. Caution patients against operating heavy equipment or driving until they know how they respond to INTUNIV. Advise patients to avoid use with alcohol.

- Cardiac Conduction Abnormalities: May worsen sinus node dysfunction and atrioventricular (AV) block, especially in patients taking other sympatholytic drugs.

- Side effects – very common (frequency ≥ 1/10): Somnolence, headache, abdominal pain and fatigue. Please consult the U.S. Prescribing Information or the EU SPC for additional information on adverse reactions.

Please click here for the INTUNIV U.S. Prescribing Information or the EU Summary of Product Characteristics.

In the U.S., INTUNIV (guanfacine extended-release tablets) is available in 1 mg, 2 mg, 3 mg and 4 mg. The same strengths are licensed in the EU.

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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.

For more information, please visit www.shire.com. Follow Shire on Social Media: @Shireplc, LinkedIn and YouTube.

FORWARD-LOOKING STATEMENTS

Statements included herein that are not historical facts, including without limitation statements concerning our proposed business combination with Baxalta Incorporated ("Baxalta") and the timing and financial and strategic benefits thereof, our 20x20 ambition that targets $20 billion in combined product sales by 2020, as well as other targets for future financial results, capital structure, performance and sustainability of the combined company, the combined company's future strategy, plans, objectives, expectations and intentions, the anticipated timing of clinical trials and approvals for, and the commercial potential of, inline or pipeline products 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, the following:

- the proposed combination with Baxalta may not be completed due to a failure to satisfy certain closing conditions, including any shareholder or regulatory approvals or the receipt of applicable tax opinions;
- disruption from the proposed transaction with Baxalta may make it more difficult to conduct business as usual or maintain relationships with patients, physicians, employees or suppliers;
- the combined company may not achieve some or all of the anticipated benefits of Baxalta's spin-off from Baxter International, Inc. ("Baxter") and the proposed transaction may have an adverse impact on Baxalta's existing arrangements with Baxter, including those related to transition, manufacturing and supply services and tax matters;
- the failure to achieve the strategic objectives with respect to the proposed combination with Baxalta may adversely affect the combined company's financial condition and results of operations;
- products and product candidates may not achieve commercial success;

- product sales from ADDERALL XR and INTUNIV are subject to generic competition in the United States; this does not apply to markets where the product is currently not licensed (i.e., Japan);
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for the combined company's products may affect future revenues, financial condition and results of operations, particularly if there is pressure on pricing of products to treat rare diseases;
- supply chain or manufacturing disruptions may result in declines in revenue for affected products and commercial traction from competitors; regulatory actions associated with product approvals or 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;
- the successful development of products in various stages of research and development 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 the combined company's ability to sell or market products profitably, and fluctuations in buying or distribution patterns by such customers can adversely affect the combined company's revenues, financial condition or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to the combined company'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 the combined company's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the combined company's revenues, financial condition or results of operations;
- Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect the combined company's ability to attract and/or retain the highly skilled personnel needed to meet its strategic objectives;
- failure to achieve the strategic objectives with respect to Shire's acquisition of NPS Pharmaceuticals Inc. or Dyax Corp. ("Dyax") may adversely affect the combined company's financial condition and results of operations;
- the combined company will be dependent on information technology and its systems and infrastructure face certain risks, including from service disruptions, the loss of sensitive or confidential information, cyber-attacks and other security breaches or data leakages that could have a material adverse effect on the combined company's revenues, financial condition or results of operations;
- the combined company may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners;
- difficulties in integrating Dyax or Baxalta into Shire may lead to the combined company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all; and

other risks and uncertainties detailed from time to time in Shire's, Dyax's or Baxalta's filings with the Securities and Exchange Commission ("SEC"), including those risks outlined in Baxalta's current Registration Statement on Form S-1, as amended, and in "Item 1A: Risk Factors" in Shire's Annual Report on Form 10-K for the year ended December 31, 2014.

All forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date

hereof. Except to the extent otherwise required by applicable law, we do not undertake any obligation to republish revised forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.