Press Release

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Shire submits INTUNIV® (guanfacine extended release) Marketing Authorisation Application to EMA

Nyon, Switzerland – March 27, 2014 – Shire plc (LSE: SHP, NASDAQ: SHPG) today announced the acceptance of submission of a Marketing Authorisation Application (MAA) by the European Medicines Agency (EMA) for their once-daily, non-stimulant guanfacine extended release for the treatment of Attention Deficit/Hyperactivity Disorder (ADHD) in children/adolescents aged 6-17 years.

"The regulatory submission of guanfacine extended release brings Shire one step closer to providing an alternative to stimulant medication for the treatment of ADHD," said Perry Sternberg, Senior Vice President of the Neuroscience Business Unit at Shire. "Every patient has different needs and we hope to be able to extend our range of treatment options which will help the physician to offer personalised management of ADHD."

Evidence for the submission is based on three pivotal studies investigating the short and long-term safety and efficacy profile of guanfacine extended release.[1-3]

About guanfacine extended release
Guanfacine extended release is a long-acting, once daily, non-stimulant medicine, which contains the active substance guanfacine hydrochloride – a selective alpha$_2$A-adrenergic receptor agonist. Guanfacine extended release is currently approved for use in the US (as INTUNIV®) and Canada (as INTUNIV XR™) as a monotherapy in children aged 6-17 and adjunctively with a stimulant medication for ADHD in children/adolescents aged 6 -17 in the US and aged 6-12 in Canada. For more information please see full prescribing information.

US Important Safety Information

- Patients should not take INTUNIV if they are allergic to guanfacine or other ingredients in INTUNIV, or other medicines containing guanfacine. Tell the doctor about all medicines, vitamins, and herbal supplements your child is taking.
- INTUNIV may cause serious side effects including low blood pressure, low heart rate, fainting, and sleepiness.
- Before starting INTUNIV, tell the doctor if your child has low blood pressure, low heart rate, heart problems, has fainted, has liver or kidney problems, or has any other medical condition. You should also tell the doctor if your child is pregnant, breast-feeding, or plans to become pregnant or breast-feed.
- Patients should drink plenty of water and not get overheated while taking INTUNIV.
- Patients should not drive or use machinery like lawn mowers or power tools until they know how INTUNIV affects them. INTUNIV can slow thinking and motor skills. While taking INTUNIV, patients should not drink alcohol or take other medicines that can cause sleepiness or dizziness because these symptoms may get worse.
- The most common side effects of INTUNIV include sleepiness, tiredness, trouble sleeping, low blood pressure, nausea, stomach pain, and dizziness.

- INTUNIV should be swallowed whole without crushing, chewing, or breaking the tablet. INTUNIV should not be taken with a high-fat meal. Do not change the dose or stop INTUNIV without talking with the doctor. The doctor will regularly check your child's blood pressure and heart rate.

About ADHD
ADHD is a common psychiatric disorder[4-6] and is recognised by the World Health Organization (WHO).[7] Worldwide prevalence is estimated at 5.3 percent for children/adolescents.[8] While the exact causes of ADHD are not fully understood, it is thought to result from complex interactions between genetic and environmental factors, with studies estimating that genetic factors explain 60 – 75% of the aetiology of ADHD.[9-12] Environmental factors which may increase the risk of developing ADHD include low birth weight/prematurity and maternal smoking during pregnancy.[11,13]

For further information please contact:

Media

Nicole Barraud	nbarraud@shire.com	+41 22 419 40 56
Gwen Fisher	gfisher@shire.com	+1 484 595 9836

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, and Internal 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 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 Rare Diseases products and is reliant on third party contractors 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 the 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 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. Fluctuations in buying or distribution patterns by such customers can 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 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 U.S. Securities and Exchange Commission, including its most recent Annual Report on Form 10-K.

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