Press Release

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Shire Announces Clear Regulatory Path Forward for SHP465, an Investigational Treatment for Adults with ADHD

- **Potential Launch of SHP465 Anticipated in Second Half of 2017**
- **Exclusivity for Shire's Overall ADHD Product Portfolio Extends to 2029**

Lexington, Mass., USA – April 7, 2015 – Shire plc (LSE: SHP, NASDAQ: SHPG) today announces that it has reached an agreement with the U.S. Food and Drug Administration (FDA) on a clear regulatory path for SHP465 (triple-bead mixed amphetamine salts - MAS), an investigational oral stimulant medication being evaluated as a potential treatment for Attention-Deficit/Hyperactivity Disorder (ADHD) in adults.

Shire has agreed with the FDA to conduct a short-term efficacy and safety study in pediatric patients with ADHD (ages 6-17). While Shire intends to pursue an adult indication, the FDA is requesting this additional pediatric data to better understand the potential effects of SHP465 on children with ADHD in the event of use in this population. The Company anticipates the clinical trial's first patient, first visit to take place in August 2015, with study completion targeted by the last quarter of 2016. Shire then expects to submit to the FDA by second quarter 2017 a Class 2 resubmission for approval of SHP465 as a treatment for ADHD in adults, which typically entails a 6-month review. Pending FDA approval, Shire anticipates launching the medicine in the second half of 2017. This update follows Shire's announcement on October 9, 2014, that it was engaging the FDA to determine the parameters of clinical data requirements in order to submit the Class 2 resubmission.

"We believe SHP465 has the potential to be an important treatment option for adults with ADHD, which is why we worked so diligently with the FDA to determine what additional clinical data would be necessary for Shire to finalize our resubmission plans for this medicine," said Philip J. Vickers, Ph.D., Head of Research and Development, Shire. "We're pleased that we now have a clear regulatory path to bring this investigational medicine forward as a potential treatment option for adults with ADHD."

Adult patients with ADHD represent the fastest growing segment of the overall ADHD patient population. Data from IMS Health (a global healthcare information and technology firm) suggest that about 10% of adult patients are adding an immediate release medicine to their extended release medicine, most often to gain a longer duration of treatment effect.

SHP465 demonstrated a statistically significant difference versus placebo at 16 hours post dosing, with onset of action starting 4 hours post dosing, as measured by the Permanent Product Measure of Performance (PERMP). Common adverse reactions in SHP465 registration trials (incidence ≥5% and at a rate twice placebo) in adults were: insomnia, decreased appetite, dry mouth, decreased weight, heart rate increased, and dysmenorrhea. These adverse events are generally known to be associated with the use of amphetamine products.

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Protection for Shire's ADHD Franchise Extends to 2029

There are patents supporting Shire's overall ADHD franchise in the U.S. that extend to 2029. With a launch planned for the second half of 2017, Shire expects that SHP465, following FDA approval, will have three years of Hatch-Waxman exclusivity and at least three patents listed in the FDA Orange Book expiring as late as May 2029.

Vyvanse® (lisdexamfetamine dimesylate), which has patents expiring in 2023, is a prescription medicine used for the treatment of ADHD in patients 6 years and above and for the treatment of moderate to severe Binge Eating Disorder (B.E.D.) in adults. Vyvanse is not for weight loss. It is not known if Vyvanse is safe and effective for the treatment of obesity. Shire announced on June 12, 2014 that it has agreed to a Written Request by the FDA to conduct pediatric clinical studies to investigate the potential use of Vyvanse for the treatment of ADHD in preschool-age children, ages 4 to 5. Upon FDA confirmation of a timely submission and review of data that adheres to the requirements of the Written Request, Shire will be entitled to the benefits of the Best Pharmaceuticals for Children Act, including a six-month extension to the exclusivity afforded by Shire's patents for Vyvanse.

Vyvanse is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep in a safe place to prevent misuse and abuse. Selling or sharing Vyvanse may harm others and is illegal.

About VYVANSE (lisdexamfetamine dimesylate)

Vyvanse is a prescription medicine currently only approved in the United States, Canada, Australia, several European countries (trade name: Elvanse®/Tyvense®) and Brazil (trade name: Venvanse™) for ADHD and in the United States for the treatment of moderate to severe B.E.D. in adults. Vyvanse should only be used in accordance with locally approved prescribing information.

INDICATION

Vyvanse is a prescription medicine used for the treatment of ADHD in patients 6 years and above and for the treatment of moderate to severe Binge Eating Disorder (B.E.D.) in adults.

Vyvanse is not for weight loss. It is not known if Vyvanse is safe and effective for the treatment of obesity.

IMPORTANT SAFETY INFORMATION

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Vyvanse is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep in a safe place to prevent misuse and abuse. Selling or sharing Vyvanse may harm others and is illegal.

- **Do not take Vyvanse if you or your child:**
  - is taking or has taken within the past 14 days an anti-depression medicine called a monoamine oxidase inhibitor or MAOI
  - is sensitive to, allergic to, or had a reaction to other stimulant medicines

- **Some people have had the following problems when taking stimulant medicines, such as Vyvanse:**

1. Heart-related problems including:

- **sudden death in people who have heart problems or heart defects**
- **sudden death, stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child has any heart problems, heart defects, high blood pressure, or a family history of these problems. The doctor should check your or your child's blood pressure and heart rate regularly during treatment.
Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking Vyvanse.

2. Mental (psychiatric) problems including:

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**

In Children and Teenagers

- **new psychotic symptoms such as:**
  - **seeing things or hearing voices that are not real**
  - **believing things that are not true**
  - **being suspicious**
- **new manic symptoms**

Tell your doctor about any drug abuse, alcohol abuse or mental problems that you or your child has had, or about a family history of suicide, bipolar illness, or depression.
Call your doctor right away if you or your child has any new or worsening mental symptoms or problems while taking Vyvanse.

3. Circulation problems in fingers and toes [Peripheral vasculopathy, including Raynaud's phenomenon]:

- **Fingers or toes may feel numb, cool, painful, sensitive to temperature and/or change color from pale, to blue, to red**

Call your doctor right away if you have or your child has any of these signs or symptoms or develops unexplained wounds on fingers or toes while taking Vyvanse.

- Tell the doctor if you or your child is pregnant, breast-feeding, or plans to become pregnant or breast-feed.

- **Vyvanse may cause serious side effects, including:**
  - slowing of growth (height and weight) in children. Your child should have his or her height and weight checked often while taking Vyvanse. The doctor may stop treatment if a problem is found during these check-ups.

- **The most common side effects reported in studies of Vyvanse in ADHD were:**
  - anxiety
  - decreased appetite
  - diarrhea
  - dizziness
  - dry mouth
  - irritability
  - loss of appetite
  - nausea
  - trouble sleeping
  - upper stomach pain
  - vomiting
  - weight loss

- **The most common side effects reported in studies of Vyvanse in B.E.D. were:**
  - dry mouth
  - trouble sleeping
  - decreased appetite
  - increased heart rate
  - Constipation
  - feeling jittery
  - anxiety

For additional safety information, click here for Prescribing Information and Medication Guide and discuss with your doctor.

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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 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.