Vyvanse® (lisdexamfetamine dimesylate) Capsules (CII) Becomes First and Only Treatment Approved by the FDA for Adults with Moderate to Severe Binge Eating Disorder

Lexington, MA – January 30, 2015 – Shire plc (LSE: SHP, NASDAQ: SHPG) announced today that the U.S. Food and Drug Administration (FDA) approved Vyvanse® (lisdexamfetamine dimesylate) Capsules (CII), the first and only medication for the treatment of moderate to severe binge eating disorder (B.E.D.) in adults, shown to significantly reduce the mean number of binge days per week. Vyvanse is not indicated or recommended for weight loss or the treatment of obesity. Other sympathomimetic drugs used for weight loss have been associated with serious cardiovascular reactions.

“Binge eating disorder is the most common adult eating disorder in the United States, and we are excited to provide the first FDA-approved treatment for moderate to severe B.E.D. in adults,” said Philip J. Vickers, Ph.D., Global Head of Research and Development at Shire. “This new indication for Vyvanse is a critical milestone in the treatment of this condition and reflects our ongoing commitment to address the needs of patients.”

“The management of B.E.D. is continuously being studied, and though advancements have been made to increase awareness and understanding of this real disorder, rates of diagnosis remain low,” said Susan L. McElroy, M.D., Professor of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine; and principal investigator of the B.E.D. clinical trials. “The development of new treatment options for adults with B.E.D. is important to the patients who continue to live with this complex disorder.”

The efficacy of Vyvanse in the treatment of B.E.D. was demonstrated in two 12-week randomized, double-blind, multi-center, parallel-group, placebo-controlled, dose-optimization studies in adults aged 18 to 55 years (Study 1: N=374, Study 2: N=350) with protocol-defined moderate to severe B.E.D. (severity was defined as having at least 3 binge days per week for 2 weeks prior to the baseline visit and a Clinical Global Impression Severity score of ≥4 at baseline). The primary efficacy outcome for the two studies was defined as the change from baseline at week 12 in the number of binge days per week. Baseline is defined as the weekly average of the number of binge days per week for the 14 days prior to the baseline visit.

Subjects from both studies on Vyvanse had a statistically significant greater reduction from baseline in mean number of binge days per week at Week 12. In study 1, Vyvanse reduced the mean number of binge days per week from 4.79 at baseline to 0.78 at study endpoint compared with 4.60 to 2.22 for placebo. The least squares mean change from baseline in binge days per week was –3.87 and –2.51 for Vyvanse and placebo, respectively. Similar results were seen in study 2.

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.
Greater improvement across key secondary outcomes was also observed in subjects treated with Vyvanse as compared to placebo, including a higher proportion of subjects rated improved on the Clinical Global Impressions-Improvement (CGI-I) rating scale, higher proportion of subjects with 4-week binge cessation, and greater reduction in the Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating (Y-BOCS-BE) total score in both studies.

Patients with current anorexia or bulimia nervosa; current comorbid psychiatric disorder; and cardiovascular risk factors other than obesity and smoking were excluded from the studies. In both studies, there were 4 patients each in the Vyvanse and placebo treated groups who reported serious adverse events (SAEs). There were no deaths in either of the studies. Of patients treated with Vyvanse, 5.1% (19/373) discontinued due to adverse reactions compared with 2.4% (9/372) of placebo-treated patients. The most common adverse reactions (incidence ≥ 5% and at least twice placebo) reported in adults with moderate to severe B.E.D. were dry mouth, insomnia, decreased appetite, increased heart rate, constipation, feeling jittery, and anxiety.

About B.E.D.

Binge eating disorder, now recognized as a distinct disorder, is defined as recurring episodes (≥ once weekly, for at least 3 months) of consuming a large amount of food in a short time, compared with others. Patients feel a lack of control during a binge eating episode and marked distress over their eating. They typically experience shame and guilt, among other symptoms, about their binge eating, and may conceal the symptoms. Unlike people with other eating disorders, adults with B.E.D. don’t routinely try to “undo” their excessive eating with extreme actions like purging or over-exercising.

B.E.D. is the most common eating disorder in the United States, affecting an estimated 2.8 million adults, according to a national survey. B.E.D. occurs in both men and women, and is more common than anorexia and bulimia combined. B.E.D. can occur in normal weight, overweight, and obese adults, and is seen across racial and ethnic groups. Medication is not appropriate for all adults with B.E.D.

More About Vyvanse (lisdexamfetamine dimesylate) B.E.D. Clinical Trials
In the two 12-week studies, patients were confirmed with a diagnosis of B.E.D. using DSM-IV-TR® criteria for B.E.D. For both studies, a binge day was defined as a day with at least 1 binge episode, as determined from the subject’s daily binge diary and confirmed by the clinician.

About VYVANSE (lisdexamfetamine dimesylate)

INDICATION

Vyvanse is a prescription medicine 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

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:
  • are taking or have taken within the past 14 days an anti-depression medicine called a monoamine oxidase inhibitor or MAOI
  • are 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 have any heart problems, heart defects, high blood pressure, or a family history of these problems. The doctor should check your blood pressure and heart rate regularly during treatment. Call your doctor right away if you have 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
     • 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 have had, or about a family history of suicide, bipolar illness, or depression. Call your doctor right away if you have 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 any of these signs or symptoms or develop unexplained wounds on fingers or toes while taking Vyvanse.

• Tell the doctor if you are pregnant, breast-feeding, or plan to become pregnant or breast-feed.

• The most common side effects of Vyvanse reported in studies of adults with moderate to severe 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.
Shire is committed to helping patients get the Shire medicines their physician has prescribed and is developing various programs to extend this commitment to adults with moderate to severe B.E.D. For more information, please visit [www.shire.com](http://www.shire.com).

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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 Neuroscience, Rare Diseases, and Gastrointestinal and Internal Medicine and are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas, such as Ophthalmology.

[www.shire.com](http://www.shire.com)

THE “SAFE HARBOR” STATEMENT UNDER THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995

Statements included in this communication 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 and INTUNIV are subject to generic erosion;
- 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

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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;
- Shire’s proposed acquisition of NPS Pharma may not be consummated due to the occurrence of an event, change or other circumstances that gives rise to the termination of the merger agreement;
- a governmental or regulatory approval required for the proposed acquisition of NPS Pharma may not obtained, or may be obtained subject to conditions that are not anticipated, or another condition to the closing of the proposed acquisition may not be satisfied;
- NPS Pharma may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners pending the consummation of the proposed acquisition by Shire, or NPS Pharma’s business may be disrupted by the proposed acquisition, including increased costs and diversion of management time and resources;
- difficulties in integrating NPS Pharma 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 or NPS Pharma’s filings with the U.S. Securities and Exchange Commission, including their respective most recent Annual Reports on Form 10-K.

Vyvanse® (lisdexamfetamine dimesylate) is a registered trademark of Shire LLC. Vyvanse is available in 10, 20, 30, 40, 50, 60 and 70 mg capsules.

DSM-5® is a registered trademark of the American Psychiatric Association.