

## Shire to Present Scientific Data Across a Range of Psychiatric Disorders at American Psychiatric Association Annual Meeting

*Research explores data on treatments for psychiatric disorders; health economics and outcomes research also to be presented*

**Philadelphia, PA, USA – May 17, 2013** – Shire plc (LSE: SHP, NASDAQ: SHPG), the global specialty biopharmaceutical company, announces that it will present scientific data in 7 poster presentations at the American Psychiatric Association (APA) 166th Annual Meeting in San Francisco, May 18-22. The data being presented represent Shire's ongoing commitment to the clinical research of Vyvanse® (lisdexamfetamine dimesylate) Capsules, (CII) and INTUNIV® (guanfacine) Extended-Release Tablets, its approved prescription medicines for Attention-Deficit/Hyperactivity Disorder (ADHD). Data being presented include post-hoc analyses from several of its phase 2 clinical studies investigating potential new psychiatric uses of Vyvanse for the adjunctive treatment for Major Depressive Disorder (MDD) and for the treatment of Binge Eating Disorder (BED). Shire also will present health economic data on INTUNIV and outcomes research in ADHD. Vyvanse and INTUNIV should only be used to treat ADHD.

“Shire is committed to research in the field of neuroscience and developing treatment options for conditions that have significant unmet patient need, such as MDD and BED,” said Arnaud Partiot, MD, PhD, Shire senior vice president, Research and Development.

Vyvanse is a once-daily prescription medication for patients ages 6 and above with Attention-Deficit/Hyperactivity disorder (ADHD) and may be used as part of a total treatment program that may include counseling or other therapies.

**Vyvanse is a Schedule II controlled substance. CNS stimulants (amphetamines and methylphenidate-containing products) have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence.**

INTUNIV is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to stimulant medications in children and adolescents ages 6 to 17. The effectiveness of INTUNIV for more than 8 weeks has not been systematically evaluated. The physician electing to use INTUNIV for extended periods should periodically reevaluate its long-term usefulness for the individual patient.

Patients with a history of hypersensitivity to INTUNIV, its inactive ingredients, or other products containing guanfacine should not take INTUNIV. Hypotension, bradycardia, and syncope were observed in clinical trials. Somnolence and sedation were commonly reported adverse reactions in clinical studies

The titles, dates, and times of the APA scientific presentations are noted below. Specific information about the data contained in these scientific presentations is embargoed until the respective presentation sessions have occurred at the meeting.

### **Lisdexamfetamine Dimesylate (Investigational New Uses)**

- **Sunday, May 19, 2013; 8:00am – 9:30am**

Poster #NR4-25: "Lisdexamfetamine Dimesylate Safety and Efficacy on Binge Eating Days/Episodes and Behavior in Adults With Moderate to Severe Binge Eating Disorder"

Presenter: Susan McElroy, MD

- **Monday, May 20, 2013; 2:00pm – 4:00pm**

Poster #NR9-20: "Effects of Lisdexamfetamine Dimesylate Augmentation on Sexual Function in Adults With Fully or Partially Remitted Major Depressive Disorder"

Presenter: Anita Clayton, MD

- **Monday, May 20, 2013; 2:00pm – 4:00pm**

Poster #NR9-41: "Response to Lisdexamfetamine Dimesylate Augmentation in Major Depression in People With or Without Baseline Executive Function Impairment"

Presenter: Andrew Cutler, MD

- **Monday, May 20, 2013; 2:00pm – 4:00pm**

Poster #NR9-30: "Lisdexamfetamine Dimesylate Augmentation Therapy in Anxious or Nonanxious Major Depressive Disorder"

Presenter: Bryan Dirks, MD

- **Monday, May 20, 2013; 2:00pm – 4:00pm**

Poster #NR9-38: "Post Hoc Analysis of Lisdexamfetamine Dimesylate Augmentation Therapy Effects on Sleep-Related Endpoints in Adults With Major Depressive Disorder"

Presenter: Angelo Sambunaris, MD

#### **Guanfacine Extended Release (Health Economics and Outcomes Research)**

- **Monday, May 20, 2013; 11:30pm – 1:00pm**

Poster #NR8-51: "Period Prevalence of Stimulant Augmentation Among Adolescents With ADHD in a U.S. Managed Care Population During 2009 and 2010"

Presenter: Vanja Sikirica, PharmD, MPH

#### **ADHD Outcomes Research**

- **Monday, May 20, 2013; 11:30am – 1:00pm**

Poster #NR8-29: "Long-Term Outcomes in Attention-Deficit/Hyperactivity Disorder (ADHD): A Systematic Review of Self Esteem and Social Functioning"

Presenter: Paul Hodgkins, PhD

#### **ABOUT VYVANSE (lisdexamfetamine dimesylate)**

Vyvanse, which was introduced in the United States in July 2007 for the treatment of ADHD in children ages 6 to 12 years, approved in April 2008 to treat ADHD in adults, approved in November 2010 to treat ADHD in adolescents ages 13 to 17, approved in January 2012 for maintenance treatment in adults, and approved in April 2013 for maintenance treatment in children and adolescents, is currently available in the USA in six once-daily dosage strengths of 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, and 70 mg. In addition to being available in the USA and Canada, Vyvanse is approved in Brazil (brand name Venvanse), Ireland (brand name Tyvense), and Denmark, Germany, Norway, and the United Kingdom (brand name Elvanse). The efficacy and tolerability of Vyvanse have been studied in clinical trials in both the USA and Europe.

Vyvanse may be used as part of a total treatment program that may include counseling or other therapies.

## INDICATION

Vyvanse is indicated for the treatment of ADHD in patients ages 6 and above. Efficacy was established in short-term controlled studies in children aged 6 to 17 and in adults. Vyvanse is also approved as a maintenance treatment for patients ages 6 and above with ADHD based on one maintenance study in patients aged 6 to 17 and one maintenance study in adults.

## IMPORTANT SAFETY INFORMATION

### WARNING: ABUSE AND DEPENDENCE

- CNS stimulants (amphetamines and methylphenidate-containing products) have a high potential for abuse and dependence.
- Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy.

### Contraindications:

- Known hypersensitivity to amphetamines or other ingredients in Vyvanse. Anaphylactic reactions, Stevens - Johnson syndrome, angioedema, and urticaria have been observed in postmarketing reports.
  - Concurrent administration of monoamine oxidase inhibitors (MAOI) or administration of Vyvanse within 14 days of the last MAOI dose. Hypertensive crisis can occur.
  - Educate patients about abuse and periodically re-evaluate the need for Vyvanse.
- Sudden death, stroke and myocardial infarction have been reported in adults with CNS stimulant treatment at recommended doses. Sudden death has been reported in children and adolescents with structural cardiac abnormalities and other serious heart problems taking CNS stimulants at recommended doses for ADHD. Prior to treatment assess for the presence of cardiac disease. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmia, coronary artery disease, and other serious heart problems. Further evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during Vyvanse treatment.
- CNS stimulants cause an increase in blood pressure (mean increase about 2-4 mm Hg) and heart rate (mean increase about 3-6 bpm). Monitor all patients for tachycardia and hypertension.
- Use of stimulants may cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with preexisting psychosis. Clinical evaluation for bipolar disorder is recommended prior to stimulant use.
- CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Monitor weight and height in children during treatment with Vyvanse. Treatment may need to be interrupted in children not growing as expected.
- The most common adverse reactions ( $\geq 5\%$  and at least twice the rate of placebo) reported in clinical trials were:
  - Children aged 6 to 12: decreased appetite, insomnia, upper abdominal pain, irritability, vomiting, decreased weight, nausea, dry mouth and dizziness;
  - Adolescents aged 13 to 17: decreased appetite, insomnia, and decreased weight;
  - Adults: decreased appetite, insomnia, dry mouth, diarrhea, nausea, anxiety and anorexia.

**Please click here for [Full Prescribing Information](#) for Vyvanse, including **Boxed WARNING** regarding **Potential for Abuse and Dependence**.**

### **ABOUT INTUNIV (guanfacine)**

Once-daily INTUNIV is available in four doses—1 mg, 2 mg, 3 mg, and 4 mg. The active ingredient in INTUNIV is guanfacine. INTUNIV is not a central nervous system (CNS) stimulant or a controlled substance, and has no known potential for abuse or dependence. INTUNIV is a selective alpha-2A agonist. The mechanism of action of guanfacine in ADHD is not known.

### **INDICATION**

- INTUNIV is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to stimulant medications in children and adolescents ages 6 to 17. The effectiveness of INTUNIV for more than 8 weeks has not been systematically evaluated. The physician electing to use INTUNIV for extended periods should periodically reevaluate its long-term usefulness for the individual patient.

### **IMPORTANT SAFETY INFORMATION**

- Patients with a history of hypersensitivity to INTUNIV, its inactive ingredients, or other products containing guanfacine should not take INTUNIV.
- Hypotension, bradycardia, and syncope were observed in clinical trials. Decreases in blood pressure and heart rate were dose-dependent and were less pronounced over time of treatment. Heart rate and blood pressure should be measured prior to initiation of therapy, following dose increases, and periodically while on therapy. Use INTUNIV with caution in patients with a history of hypotension, heart block, bradycardia, cardiovascular disease, or syncope, or who may have a condition that predisposes them to syncope; are treated concomitantly with antihypertensives or other drugs that can reduce blood pressure or heart rate or increase the risk of syncope. Advise patients to avoid becoming dehydrated or overheated.
- Somnolence and sedation were commonly reported adverse reactions in clinical studies. The potential for additive sedative effects with CNS depressant drugs should be considered. Caution patients against operating heavy equipment or driving until they know how they respond to INTUNIV. Advise patients to avoid use with alcohol.
- The most common adverse reactions (incidence  $\geq 5\%$  and at least twice the rate for placebo) in the monotherapy trials with INTUNIV were somnolence, fatigue, nausea, lethargy, and hypotension, and in the adjunctive trial with INTUNIV were somnolence, fatigue, insomnia, dizziness, and abdominal pain.

**Please see [Full Prescribing Information](#), including **Patient Information**.**

### **About ADHD**

Attention-Deficit/Hyperactivity Disorder is a neurobehavioral disorder that manifests as a persistent pattern of inattention and/or hyperactivity-impulsivity and is more frequent and severe than is typically observed in individuals at a comparable level of development.

ADHD is one of the most common childhood psychiatric disorders. Although many people tend to think of ADHD as a childhood problem, 60% to 85% of children with ADHD may continue to meet the criteria for the disorder during their teenage years. Nearly 50% of children with ADHD may continue to meet the criteria for the disorder in adulthood, based on parent-report. The disorder is estimated to affect 4.4 percent of US adults aged 18 to 44 based on results from the National Comorbidity Survey Replication. When this percentage is

extrapolated to the full US population aged 18 and over, approximately 10 million adults are estimated to have ADHD. Drug treatment may not be appropriate for all patients with ADHD.

The specific etiology of ADHD is unknown, and there is no single diagnostic test for this disorder. Adequate diagnosis requires the use of medical and special psychological, educational, and social resources, utilizing diagnostic criteria specified in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition, Text Revision (*DSM-IV-TR*®) or *International Classification of Diseases*, 10<sup>th</sup> revision (*ICD-10*).

Although there is no cure for ADHD, there are accepted treatments that have been demonstrated to improve symptoms. Standard treatments include educational approaches, psychological therapies which may include behavioral modification, and/or medication.

**For further information please contact:**

**Investor Relations**

Eric Rojas	<a href="mailto:erojas@shire.com">erojas@shire.com</a>	+1 781 482 0999
Sarah Elton-Farr	<a href="mailto:seltonfarr@shire.com">seltonfarr@shire.com</a>	+44 1256 894157

**Media**

Jessica Mann	<a href="mailto:jmann@shire.com">jmann@shire.com</a>	+44 1256 894 280
Gwen Fisher	<a href="mailto:gfisher@shire.com">gfisher@shire.com</a>	+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, Internal Medicine and Regenerative Medicine and we are developing treatments for symptomatic conditions treated by specialist physicians in other targeted therapeutic areas.

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

## **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;
- 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 and earnings;
- Shire relies on a single source for manufacture of certain of its products and a disruption to the supply chain for those 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;
- Shire uses third party manufacturers to manufacture many of its products and is reliant upon third party contractors for certain goods and services, and any inability of these third party manufacturers to manufacture products, or any failure of these third party contractors to provide these goods and services, in each case in accordance with its respective contractual obligations, could adversely affect Shire's ability to manage its manufacturing processes or to operate its business;
- 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 and fluctuations in buying or distribution patterns by such customers could 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 obtain, maintain, 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;

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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