

Shire and New River Pharmaceuticals Announce FDA Approval of the First and Only Stimulant Prodrug VYVANSE(TM) (lisdexamfetamine dimesylate) as a Novel Treatment for ADHD

BASINGSTOKE, England, PHILADELPHIA, Pennsylvania and Radford, VIRGINIA, February 23 /PRNewswire-FirstCall/ -- Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) and its collaborative partner New River Pharmaceuticals Inc. (NASDAQ: NRPH) announced today that the U.S. Food and Drug Administration (FDA) has granted marketing approval for VYVANSE (lisdexamfetamine dimesylate, formerly known as NRP104), for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

On February 20, 2007 Shire and New River announced an agreement whereby Shire will acquire New River for approximately \$2.6 billion in an all cash transaction unanimously recommended by the Boards of both companies. The transaction is the subject of another press release issued February 20, 2007.

VYVANSE is a prodrug that is therapeutically inactive until metabolized in the body. In clinical studies designed to measure duration of effect, VYVANSE provided significant efficacy compared to placebo for a full treatment day, up through and including 6:00 pm. Furthermore, when VYVANSE was administered orally and intravenously in two clinical human drug abuse studies, VYVANSE produced subjective responses on a scale of "Drug Liking Effects" (DLE) that were less than d-amphetamine at equivalent doses. DLE is used in clinical abuse studies to measure relative preference among known substance abusers.

"The FDA approval of VYVANSE is exciting news for Shire as well as for patients, their families, and healthcare providers as it's an important, novel approach for the treatment of ADHD," said Matthew Emmens, Shire Chief Executive Officer. "The label we received with the approval letter includes information about the extended duration of effect and abuse-related drug liking characteristics of VYVANSE which illustrate benefits that differentiate this compound from other ADHD medicines. The addition of VYVANSE to our ADHD portfolio reaffirms Shire's commitment to continue to address unmet medical needs and advance the science of ADHD treatment. Beginning with product launch in Q2 2007, Shire will make VYVANSE our top promotional priority within our ADHD portfolio."

Randal J. Kirk, New River's Chairman and Chief Executive Officer, remarked, "VYVANSE's approval signals a new era in the treatment of ADHD. Upon product launch, patients will have a novel treatment option combining the effectiveness of a stimulant - long considered the gold standard in ADHD medicines - with other potential benefits."

The FDA has proposed that VYVANSE be classified as a Schedule II controlled substance. This proposal was submitted to and accepted by the U.S. Drug Enforcement Administration (DEA). A final scheduling decision is expected from the DEA following a 30-day period for public comment. Once VYVANSE receives final scheduling designation, the label will be available. Pending final scheduling designation, product launch is anticipated in Q2 2007. VYVANSE will be available in three dosage strengths: 30 mg, 50 mg and 70 mg, all indicated for once-daily dosing.¹

New River developed VYVANSE as a new ADHD medication designed to provide lower potential for abuse, in which d-amphetamine is covalently linked to l-lysine, a naturally occurring amino acid. The combination is rapidly absorbed from the gastrointestinal tract and converted to d-amphetamine, which is responsible for VYVANSE's activity.

Joseph Biederman, MD, director of Pediatric Psychopharmacology at Massachusetts General Hospital, was lead investigator on the pivotal clinical studies testing lisdexamfetamine dimesylate for the treatment of

ADHD. These large multi-site studies showed that the drug significantly reduced ADHD symptoms throughout the day with a predictable tolerability profile. "Our studies showed that this next-generation stimulant medication's unique chemical profile offers an option for physicians and their patients in the treatment of ADHD, with outstanding efficacy and duration of action" said Dr. Biederman.

Additional information about VYVANSE and other Shire treatments for ADHD is available at <http://www.ShireADHDTreatments.com>.

VYVANSE Significantly Controls ADHD Symptoms

Data from phase II and phase III clinical trials demonstrated statistically significant improvements in ADHD symptoms for patients aged 6 to 12 years treated with VYVANSE compared to patients treated with placebo. These studies demonstrated that all doses of VYVANSE (30 mg, 50 mg and 70 mg) provided significant efficacy at all time points tested, including 6pm.²

In the phase II, analog classroom study, patients demonstrated significantly improved behavior when receiving either VYVANSE or ADDERALL XR(R) (mixed salts of a single-entity amphetamine product) as measured by the Swanson, Kotkin, Agler, M. Flynn and Pelham (SKAMP) department rating scale, a standardized, validated classroom assessment tool used for evaluating the behavioral symptoms of ADHD.³ Both treatments resulted in significantly improved behavior versus a placebo ($P < .0001$, for both).⁴ Patients also demonstrated significantly improved academic productivity with both treatments, compared to placebo ($P < .0001$ for both medications) as measured by Permanent Product Measure of Performance (PERMP), an age-adjusted collection of math problems that measures a child's ability to pay attention and stay on task as demonstrated by an increase in the number of attempted and successfully completed problems.⁴

In the phase III, randomized, double-blind placebo-controlled study, all three doses of VYVANSE demonstrated significant improvements in ADHD Rating Scale (ADHD-RS-IV) scores compared with placebo ($P < .0001$) after four weeks of once-daily treatment. ⁵ ADHD-RS-IV is a standardized, validated test for assessing symptoms of ADHD in children and for assessing their response to treatment.^{6,7} This scale, which contains 18 items, is based on the ADHD diagnostic criteria as defined in the APA's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision(R), a publication of the American Psychiatric Association. ⁸

Additionally, in a study presented in October at a major scientific meeting, VYVANSE yielded a 60 percent improvement in the primary rating scale scores for symptoms of ADHD in children aged 6 to 12 years who received six months of treatment in an open-label phase III study. Results also demonstrated that at 6 months, 95 percent of children taking VYVANSE produced a "much improved" or "very much improved" rating on the Clinical Global Impressions - Improvement score.⁹

About VYVANSE and ADDERALL XR

Tell your doctor about any heart conditions, including structural abnormalities, that you, your child, or a family member, may have. Inform your doctor immediately if you or your child develops symptoms that suggest heart problems, such as chest pain or fainting.

VYVANSE or Adderall XR should not be taken by patients who have advanced disease of the blood vessels (arteriosclerosis); symptomatic heart disease; moderate to severe high blood pressure; overactive thyroid gland (hyperthyroidism); known allergy or unusual reactions to drugs called sympathomimetic amines (for example, pseudoephedrine); seizures; glaucoma; a history of problems with alcohol or drugs; agitated states; taken a monoamine oxidase inhibitor (MAOI) within the last 14 days.

Tell your doctor before using VYVANSE or Adderall XR if you or your

child are being treated for or have symptoms of depression (sadness, worthlessness, or hopelessness) or bipolar disorder; have abnormal thoughts or visions, hear abnormal sounds, or have been diagnosed with psychosis; have had seizures or abnormal EEGs; have or have had high blood pressure; exhibit aggressive behavior or hostility. Tell your doctor immediately if any of these conditions or symptoms develop while using VYVANSE or Adderall XR.

Abuse of amphetamines may lead to dependence. Misuse of amphetamine may cause sudden death and serious cardiovascular adverse events. These events have also been reported rarely with amphetamine use.

VYVANSE and Adderall XR were generally well tolerated in clinical studies. The most common side effects in studies of VYVANSE included: children - decreased appetite, difficulty falling asleep, stomachache, and irritability. The most common side effects in studies of Adderall XR included: children - decreased appetite, difficulty falling asleep, stomachache, and emotional lability; adolescents - loss of appetite, difficulty falling asleep, stomachache, and weight loss; adults - dry mouth, loss of appetite, difficulty falling asleep, headache, and weight loss.

Aggression, new abnormal thoughts/behaviors, mania, growth suppression, worsening of motion or verbal tics and Tourette's syndrome have been associated with use of drugs of this type. Tell your doctor if you or your child have blurred vision while taking VYVANSE or Adderall XR.

The Collaboration Agreement

In January 2005, New River Pharmaceuticals signed a collaborative agreement with Shire to develop and commercialize VYVANSE. Details on the collaboration agreement are available in previous filings with the U.S. Securities and Exchange Commission.

Planned Acquisition Additional Information

The tender offer described in this press release has not yet commenced, and this press release is neither an offer to purchase nor a solicitation of an offer to sell New River common stock. Investors and security holders are urged to read both the tender offer statement and the solicitation/recommendation statement regarding the tender offer described in this report when they become available because they will contain important information. The tender offer statement will be filed by a subsidiary of Shire with the Securities and Exchange Commission (SEC), and the solicitation/recommendation statement will be filed by New River with the SEC. Investors and security holders may obtain a free copy of these statements (when available) and other documents filed by Shire or New River with the SEC at the website maintained by the SEC at <http://www.sec.gov>. The tender offer statement and related materials may be obtained for free by directing such requests to Shire at Hampshire International Business Park, Chineham, Basingstoke, Hampshire, England, RG24 8EP, attention: Investor Relations. The solicitation/recommendation statement and such other documents may be obtained by directing such requests to New River at 1881 Grove Avenue, Radford, Virginia 24141, attention: Director of Corporate Communications.

About ADHD

Approximately 7.8 percent of all school-age children, or about 4.4 million U.S. children aged 4 to 17 years, have been diagnosed with ADHD at some point in their lives, according to the U.S. Centers for Disease Control and Prevention (CDC). 10 ADHD is one of the most common psychiatric disorders in children and adolescents. 11 ADHD is a neurobiological disorder that manifests as a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically observed in individuals at a comparable level of development.8 To

be properly diagnosed with ADHD, a child needs to demonstrate at least six of nine symptoms of inattention; at least six of nine symptoms of hyperactivity/impulsivity; the onset of such symptoms before age 7 years; that some impairment from the symptoms is present in two or more settings (e.g., at school and home); that the symptoms continue for at least six months; and that there is clinically significant impairment in social, academic or occupational functioning.⁸

Although there is no "cure" for ADHD, there are accepted treatments that specifically target its symptoms. The most common standard treatments include educational approaches, psychological or behavioral modification, and medication.¹²

New River

New River Pharmaceuticals Inc. is a specialty pharmaceutical company developing novel pharmaceuticals that are generational improvements of widely prescribed drugs in large and growing markets. For further information on New River, please visit the Company's Web site at <http://www.nrpharma.com>.

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

This press release contains certain forward-looking information that is intended to be covered by the safe harbor for "forward-looking statements" provided by the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts. Words such as "expect(s)," "feel(s)," "believe(s)," "will," "may," "anticipate(s)" and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, financial projections and estimates and their underlying assumptions; statements regarding plans, objectives and expectations with respect to future operations, products and services; and statements regarding future performance. Such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond the control of New River Pharmaceuticals, that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include: those discussed and identified in the New River Pharmaceuticals Inc. annual report on Form 10-K, filed with the SEC on March 15, 2006, as well as other public filings with the SEC; the timing, progress and likelihood of success of our product research and development programs; the timing and status of our preclinical and clinical development of potential drugs; the likelihood of success of our drug products in clinical trials and the regulatory approval process; our drug products' efficacy, abuse and tamper resistance, resistance to intravenous abuse, onset and duration of drug action, ability to provide protection from overdose, ability to improve patients' symptoms, incidence of adverse events, ability to reduce opioid tolerance, ability to reduce therapeutic variability, and ability to reduce the risks associated with certain therapies; the ability to develop, manufacture, launch and market our drug products; our projections for future revenues, profitability and ability to achieve certain threshold sales targets; our estimates regarding our capital requirements and our needs for additional financing; the likelihood of obtaining favorable scheduling and labeling of our drug products; the likelihood of regulatory approval under the Federal Food, Drug, and Cosmetic Act without having to conduct long and costly trials to generate all of the data which are often required in connection with a traditional new chemical entity; our ability to develop safer and improved versions of widely prescribed drugs using our Carrierwave (TM) technology; our success in developing our own sales and marketing capabilities for our lead product candidate; and our ability to obtain favorable patent claims. Readers are

cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. New River Pharmaceuticals does 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. Readers are also urged to carefully review and consider the various disclosures in New River Pharmaceuticals' annual report on Form 10-K, filed with the SEC on March 15, 2006, as well as other public filings with the SEC.

Shire plc

Shire's strategic goal is to become the leading specialty pharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on attention deficit and hyperactivity disorder (ADHD), human genetic therapies (HGT), gastrointestinal (GI) and renal diseases. The structure is sufficiently flexible to allow Shire to target new therapeutic areas to the extent opportunities arise through acquisitions. Shire believes that a carefully selected portfolio of products with a strategically aligned and relatively small-scale sales force will deliver strong results.

Shire's focused strategy is to develop and market products for specialty physicians. Shire's in-licensing, merger and acquisition efforts are focused on products in niche markets with strong intellectual property protection either in the US or Europe.

For further information on Shire, please visit the Company's website: <http://www.shire.com>.

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Statements included herein 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 affected. The risks and uncertainties include, but are not limited to, risks associated with: the inherent uncertainty of pharmaceutical research, product development, manufacturing and commercialization; the impact of competitive products, including, but not limited to the impact of those on Shire's Attention Deficit and Hyperactivity Disorder (ADHD) franchise; patents, including but not limited to, legal challenges relating to Shire's ADHD franchise; government regulation and approval, including but not limited to the expected product approval dates of SPD503 (guanfacine extended release) (ADHD), SPD465 (extended release triple-bead mixed amphetamine salts) (ADHD); Shire's ability to secure new products for commercialization and/or development; Shire's planned acquisition of New River Pharmaceuticals announced February 20, 2007; and other risks and uncertainties detailed from time to time in Shire's and its predecessor registrant Shire Pharmaceuticals Group plc's filings with the Securities and Exchange Commission, particularly Shire plc's Annual Report on Form 10-K for the year ended December 31, 2005.

1 data on file

2 New River Pharmaceuticals Inc. CONFIDENTIAL CLINICAL STUDY REPORT PROTOCOL NO.; LDX.301 "A Phase 3, Randomized, Multi-Center, Double-Blind, Parallel-Group, Placebo-Controlled Study of LDX in Children Aged 6-12 Years with Attention Deficit Hyperactivity Disorder (ADHD)," Final (4.0), 02 November 2005.

3 Wigal SB, Gupta S, Guinta S, Swanson JM. Reliability and Validity of the SKAMP Rating Scale in a Laboratory School Setting. *Psychopharmacol Bull.* 1998; 34 (1): 47-53.

4 "Improvements in Symptoms of Attention-Deficit/Hyperactivity Disorder in School-aged Children with Lisdexamfetamine (NRP104) and Mixed Amphetamine Salts, Extended-Release Versus Placebo," presented at the American Psychiatric Association, Toronto, Ontario, Canada, May 24, 2006.

5 "Efficacy and Safety of Lisdexamfetamine (NRP104) in Children Aged 6 to 12 Years With Attention-Deficit/Hyperactivity Disorder (ADHD)," presented at the American Psychiatric Association, Toronto, Ontario, Canada, May 24, 2006.

6 DuPaul G. Parent and Teacher Ratings of ADHD Symptoms: Psychometric Properties in a Community-Based Sample. *Journal of Clinical Child Psychology.* 1991; 20(3): 245-53.

7 Collett BR, Ohan JL, Meyers KM. Ten Year Review of Rating Scales. V: Scales Assessing Attention-Deficit/Hyperactivity Disorder. *Journal of American Academic Child Adolescent Psychiatry.* 2003; 42(9): 1015-37.

8 Diagnostic and Statistical Manual of Mental Disorders: Fourth Edition, Text Revision. DSM-TR-IV(R). Washington, DC: American Psychiatric Association; 2000: 85.

9 Childress AC, Krishnan S, McGough JJ, Findling RL. Interim Analysis of a Long-Term, Open-Label, Single-Arm Study of Lisdexamfetamine (LDX), an Amphetamine Prodrug, in children with ADHD. *American Academy of Child and Adolescent Psychiatry Annual Meeting;* 2006 Oct. 27; San Diego, CA: American Academy of Child and Adolescent Psychiatry; 2006.

10 Mental health in the United States: Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder, United States, 2003. *MMWR*, September 2, 2005;54(34):842-847. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5434a2.htm>. Accessed September 27, 2005.

11 "Introduction," *Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder.* NIH Consensus Statement 1998 Nov 16-18; 16(2): 1-37. Available at: http://consensus.nih.gov/cons/110/110_statement.htm#0_Abstract. Accessed on June 8, 2005.

12 Baumgartel A, et al. Practice guideline for the diagnosis and management of attention deficit hyperactivity disorder. *Ambulatory Child Health.* 1998;4:51.

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