

Press Release

Significant ADHD Symptom Control With Shorter DAYTRANA™ (methylphenidate transdermal system) Wear Time

Shorter Wear Time Provides Shorter Duration of Effect, Offering Individualized ADHD Symptom Management

Philadelphia, US – May 25, 2006 – Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) announced that its methylphenidate transdermal system (MTS), DAYTRANA™, has significant efficacy in reducing the symptoms of Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 to 12 years during shorter wear times than the recommended nine hour wear time, and that the effect of the medication significantly decreased with patch removal, according to the results of a phase IIIb clinical trial reported at a major medical meeting in Toronto.

“For physicians and parents who want individualized control of a patient’s ADHD symptoms, our data show that ADHD symptoms still are significantly controlled when the ADHD patch is used for less than its recommended nine-hour wear time, but the effect of the medication decreases upon patch removal,” explained clinical trial principal investigator Timothy E. Wilens, M.D., director of Substance Abuse Services in the Clinical and Research Program in Pediatric Psychopharmacology at Massachusetts General Hospital. “Because the ADHD patch allows physicians to vary the duration of effect of the medication up to the recommended nine hours, this new treatment option adds an important dimension to the treatment of children with ADHD.”

The U.S. Food and Drug Administration (FDA) approved DAYTRANA for once-daily use to treat ADHD in children aged 6 to 12 years on April 6, 2006. DAYTRANA is the first and only patch medication for ADHD. Shire expects DAYTRANA to be available in pharmacies in mid-June in four dosage strengths – 10 mg, 15 mg, 20 mg and 30 mg – all designed for nine-hour wear times with 12-hour efficacy. Significant efficacy was demonstrated at the first time point measured in clinical trials, two hours after patch application.

DAYTRANA was developed by Noven Pharmaceuticals, Inc., and combines the active ingredient, methylphenidate, with Noven's patented DOT Matrix™ transdermal technology. This transdermal delivery system was designed to provide continuous medication release throughout the day. The patch is designed to stay on during the normal daily activities of a child such as swimming, exercising or bathing.

Significant Symptom Control With DAYTRANA When Worn for Four or Six Hours

In the study, DAYTRANA had a significant duration of effect when worn for four or six hours compared to a placebo patch, based on the children's scores on the primary study measure, the standard Swanson, Kotkin, Agler, M-Flynn, and Pelham-Department (SKAMP-D) scale. Higher SKAMP-D ratings reflect greater impairment.

SKAMP-D scores significantly declined two, four, and six hours after removing the patch when worn for four hours and two and four hours after removing the patch when worn for six hours, significantly lower at each time measured than placebo scores ($P < .05$ for all). Overall SKAMP-D scores averaged 5.7 points for the four-hour DAYTRANA wear time, and 5.9 points for the six-hour DAYTRANA wear time, both significantly lower than the overall average placebo score of 11.5 points ($P < .0001$ for both).

The children also demonstrated significant improvement, based on the Permanent Product Measure of Performance (PERMP) Derived Measures age-adjusted math test scores. PERMP is a 10-minute, age-adjusted collection of math problems that provides an accurate measure of a child's ability to pay attention and stay on task correlated by an increase in number of successfully completed problems.

For both the number of problems attempted and number correct, children using DAYTRANA for four- or six- hour wear times had significantly better scores than those using a placebo patch at the first time point measured (two hours after applying the patch) and at all time points through 10 hours ($P < .0001$ for both).

By the study's end, children wearing the DAYTRANA patch had significantly average declines from the study start as measured by the ADHD Rating Scale-IV (ADHD-RS-IV), in which higher scores reflect greater impairment. The ADHD-RS-IV assesses 18 individual symptoms of ADHD, in which each symptom is scored from a range of 0 (reflecting no symptoms) to 3 (reflecting severe symptoms). The symptoms are defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*®, a publication of the APA.

When the study began, the average score on the ADHD-RS IV scale was 44.6. By week eight, ADHD-RS-IV scores declined significantly, with participants averaging 13.8 across all four DAYTRANA doses ($P < .0001$).

In the three-way cross-over study, 117 children aged 6 to 12 years diagnosed with ADHD were titrated to their optimal DAYTRANA dose, beginning with the 10 mg patch, during a five-week period. Then, on the three laboratory classroom days only, the researchers randomized the children to treatment sequences of a placebo or DAYTRANA, either four- or six-hour wear-times, but neither the investigators nor the children knew which treatment was received until study end. On classroom days, the children received two patches of the same size of their optimized dose, one DAYTRANA and one placebo or two placebo patches, and one patch was removed after four hours, and the second, after six hours. In between classroom sessions, all children, including those randomized to placebo, remained on their optimized daily dose of DAYTRANA with a nine-hour wear-time.

DAYTRANA was generally well tolerated during the dose optimization and double-blind phases and for 30 days after the last dosing. Adverse events typically were mild to moderate, resolved with continued therapy and were consistent with known effects of methylphenidate. The most common adverse events seen in the trial included: decreased appetite, insomnia, headache and abdominal pain.

The study was supported by funding from Shire.

About DAYTRANA

DAYTRANA is a Schedule II controlled substance. DAYTRANA was generally well tolerated in clinical studies. As with other products containing methylphenidate (the active ingredient in methylphenidate transdermal system), common side effects reported in children who received DAYTRANA were decreased appetite, insomnia, nausea, vomiting, weight loss, tics, and affect lability (mood swings).

DAYTRANA should not be used by children allergic to methylphenidate or other ingredients in DAYTRANA. The patch should be applied daily to clean, dry skin, which is free of any cuts or irritation. Avoid applying external heat to the patch. Skin irritation or allergic skin rash may occur.

Methylphenidate should not be taken by children with significant anxiety, tension, or agitation; glaucoma; tics, Tourette's syndrome, or family history of Tourette's syndrome; or

current/recent use of MAO inhibitors (a type of antidepressant). Abuse of methylphenidate may lead to dependence. Tell your healthcare professional if your child has had problems with alcohol or drugs or has had depression, abnormal thoughts/behaviors, visual disturbances, seizures, high blood pressure, or heart conditions including structural abnormalities.

For Full Prescribing Information on DAYTRANA system, please visit www.ADHDsupport.com or call Shire Medical Affairs at 1-800-828-2088, option 4.

About ADHD

ADHD affects approximately 7.8 percent of all school-age children, more than 4 million in the United States. ADHD is considered the most commonly diagnosed psychiatric disorder in children and adolescents. ADHD is a neurological brain 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 age and maturity. If untreated, ADHD can acutely affect a child's life, leading to problems with family members, friends, sports, after-school activities and academics.

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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 central nervous system, gastrointestinal, general products and human genetic therapies. 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: www.shire.com.

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

Statements included herein that are not historical facts are forwarding-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 plc'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 plc's Attention Deficit and Hyperactivity Disorder ("ADHD") franchise; patents, including but not limited to, legal challenges relating to Shire plc's ADHD franchise; government regulation and approval, including but not limited to the expected product approval dates of SPD503 (ADHD), SPD465 (ADHD), MESAVANCE™ (SPD476) (ulcerative colitis), ELAPRASE™ (I2S) (Hunter syndrome) and NRP104 (ADHD), including its scheduling classification by the Drug Enforcement Administration in the United States; Shire plc's ability to benefit from the acquisition of Transkaryotic Therapies Inc.; Shire plc's ability to secure new products for commercialization and/or development; and other risks and uncertainties detailed from time to time in Shire plc's and its predecessor registrant Shire Pharmaceuticals Group plc's filings with the US Securities and Exchange Commission, including Shire plc's Annual Report on Form 10-K for the year ended December 31, 2005.

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Diagnostic and Statistical Manual of Mental Disorders is a registered trademark of the American Psychiatric Association.

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