

## Press Release

### **Shire's DAYTRANA™ transdermal patch approved by FDA for treatment of ADHD**

**Philadelphia, PA, US and Basingstoke, UK – April 6, 2006** -- Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) announced today that the U.S. Food and Drug Administration (FDA) approved DAYTRANA (methylphenidate transdermal system), the first and only non-oral medication for the treatment of attention deficit hyperactivity disorder (ADHD). DAYTRANA, a once daily transdermal patch formulation of methylphenidate, will be available in 10 mg, 15 mg, 20 mg and 30 mg dosage strengths.

"The approval of DAYTRANA is important news for ADHD patients, their families and healthcare providers. In addition to being the only patch treatment for ADHD, it offers a convenient option to deliver medicine for those diagnosed with ADHD," said Shire Chief Executive Officer Matthew Emmens. "The addition of DAYTRANA to Shire's portfolio reaffirms our position as the market leader in ADHD."

Shire and Noven Pharmaceuticals, Inc. submitted an amended New Drug Application (NDA) for DAYTRANA to the FDA in June of last year. DAYTRANA is licensed globally to Shire by Noven and will be available in pharmacies in the U.S. in mid 2006.

The efficacy of DAYTRANA was established in two controlled clinical trials in children aged 6 to 12 years old with ADHD. DAYTRANA combines methylphenidate, a medication with a 50-year history of use, with Noven's patented DOT Matrix™ transdermal technology. This transdermal delivery system delivers medication directly through the skin into the bloodstream, and is designed to provide consistent, smooth drug release throughout the day. The patch is designed to stay on during the normal daily activities of a child, including swimming, exercising, and bathing. Because DAYTRANA is a patch, physicians can manage the duration of its effect and potential side effects by having the patient wear the patch for a shorter time period than the recommended 9 hour wear time on a given day. In clinical trials, wearing a DAYTRANA patch for 9 hours provided a duration of effect of 12 hours.

"The FDA's approval of DAYTRANA offers an important new option in the treatment of ADHD in children," said Robert Findling, MD, lead investigator and Professor of Psychiatry; Director, Division of Adolescent and Child Psychiatry, Case Western University. "DAYTRANA has been shown to be effective and generally well tolerated in clinical studies, and offers ADHD treatment in the convenient form of a patch."

As part of the agreement between Shire and Noven for DAYTRANA, Shire completed an upfront payment to Noven of \$25 million in 2003, and may make separate milestone payments up to \$125 million; \$50 million will be paid dictated by this FDA approval and \$75 million conditioned upon the achievement of certain sales targets.

## DAYTRANA Significantly Controls ADHD Symptoms

Data from phase II and phase III clinical trials demonstrated statistically significant improvements in the primary and secondary endpoints analyzed for children treated with DAYTRANA compared to children treated with placebo.

The phase II analog classroom study included 79 children with ADHD. The patch was worn for nine hours, and efficacy was assessed throughout the day for 12 hours. DAYTRANA demonstrated statistically significant improvement over placebo on the measures tested. Behavior, which was measured using the Swanson, Kotkin, Agler, M-Flynn, and Pelham-Department (SKAMP-D) scale, was improved with DAYTRANA overall (mean score 3.2 for DAYTRANA versus 8.0 for placebo) and at all time points assessed up to and including 12 hours post-application ( $P < .01$ ). The mean number of math problems attempted by children taking DAYTRANA on the Permanent Product Measure of Performance (PERMP) scale was significantly more than those taking placebo ( $P < .0001$ ) and this same group also completed more math problems correctly than did those taking placebo ( $P < .0001$ ).

In the phase III naturalistic trial with 270 participants, investigators found that DAYTRANA worn for nine hours reduced the children's overall symptoms of ADHD, compared to a placebo ( $P < .0001$ ), as measured by scores on the ADHD Rating Scale-IV (ADHD-RS-IV). By the study's end, mean ADHD-RS-IV scores declined 56% (24.2 points) from baseline for children treated with DAYTRANA versus a decline of 25 % (10.3) for those treated with placebo ( $P < .0001$ ). ADHD-RS assesses 18 individual symptoms of ADHD as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*®, a publication of the American Psychiatric Association.

In both studies, DAYTRANA was generally well tolerated during both the dose optimization and double-blind phases. Adverse events typically were mild to moderate, resolved with continued therapy and were consistent with known effects of methylphenidate. Common adverse events seen in clinical trials included: decreased appetite, insomnia, nausea, vomiting, weight loss, tic, and affect lability (mood swings).

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### Notes to editors

#### 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 - all being areas in which Shire has a commercial presence. 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 strategically aligned and relatively small-scale sales forces will deliver strong results. Shire's strategy is to develop and market products for specialty physicians. Shire's in-licensing and 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](http://www.shire.com).

## **About DAYTRANA**

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

DAYTRANA should not be used by children with allergies 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 rashes 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 additional information, please visit [www.DAYTRANA.com](http://www.DAYTRANA.com).

## **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.

## **"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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