

## Press Release

### **Shire Receives Approvable Letter from FDA for INTUNIV™ (guanfacine) Extended Release, a Nonstimulant for the Treatment of ADHD**

**Basingstoke, U.K., and Philadelphia, U.S. – June 21, 2007** – Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) announced today that it has received an approvable letter from the U.S. Food and Drug Administration (FDA) for INTUNIV (guanfacine) extended release tablets (previously referred to as SPD503), a nonstimulant selective alpha-2A-receptor agonist, which has been studied in children and adolescents with Attention-Deficit/Hyperactivity Disorder (ADHD). Unlike some other ADHD treatments, INTUNIV, a nonstimulant, is not a controlled substance and does not have a known mechanism for potential abuse or dependence. The information requested by the FDA was not unexpected, and Shire is working with the FDA to provide a full and timely response to the agency's request.

"The FDA's approvable letter for INTUNIV is positive news, and Shire will be working closely with the agency to address its questions," said Matthew Emmens, CEO of Shire. "When approved, INTUNIV will be the first medication indicated to treat ADHD symptoms by selectively targeting alpha-2A-receptors in the prefrontal cortex, an area of the brain that is thought to manage executive functioning tasks. Shire is looking forward to further strengthening our broad portfolio of ADHD medications by adding a nonstimulant treatment option with a novel mechanism of action and demonstrated clinical efficacy, which may be ideal for those patients who have not benefited from currently available ADHD medications."

#### **About INTUNIV (guanfacine) Extended Release Tablets**

Shire is seeking approval of INTUNIV as monotherapy for the treatment of ADHD symptoms throughout the day in children aged 6 to 17 years, with dosage strengths of 1 mg to 4 mg daily. The INTUNIV New Drug Application (NDA) includes data from two placebo-controlled trials in children and adolescents ages 6 to 17 evaluating the compound's safety and efficacy in controlling ADHD symptoms evaluated on a once-weekly basis using the ADHD Rating Scale (ADHD-RS-IV), which included both hyperactive/impulsive and inattentive subscales. ADHD-RS-IV is a standardized, validated test for assessing symptoms of ADHD in children and for assessing their response to treatment. 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*®. In these two clinical trials, treatment related adverse events greater than 10 percent included somnolence, fatigue, upper abdominal pain, sedation and headache.

INTUNIV, a once-daily formulation of guanfacine, provides a controlled, steady delivery of drug throughout the day and evening with a delivery system that minimizes the fluctuations between peak and trough concentrations as seen with immediate-release guanfacine. It has been shown that guanfacine, the active ingredient in INTUNIV, binds selectively to alpha 2A adrenergic cell receptors located in the part of the brain called the prefrontal cortex. The

prefrontal cortex is an area of the brain associated with executive functioning, i.e., working memory, behavioral inhibition, regulation of attention, distractibility, impulsivity, and frustration tolerance. The selective alpha-2A agonist strengthens working memory and prefrontal cortex neuronal firing. This research supports the use of guanfacine for the treatment of ADHD.

### **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 CDC. ADHD is one of the most common psychiatric disorders in children and adolescents. The disorder is also estimated to affect approximately 9.8 million adults across the U.S. based on a retrospective survey of adults aged 18 to 44, projected to the full U.S. adult population. 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 level of development. To be properly diagnosed with ADHD, a child needs to demonstrate at least six of nine symptoms of inattention; and/or at least six of nine symptoms of hyperactivity/impulsivity; the onset of which appears 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 and the symptoms cannot be better explained by another psychiatric disorder.

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.

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### **SHIRE PLC**

Shire’s strategic goal is to become the leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on 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: [www.shire.com](http://www.shire.com).

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

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 date of INTUNIV™ (guanfacine) extended release (ADHD); Shire's ability to secure new products for commercialization and/or development; Shire's ability to benefit from its acquisition of New River Pharmaceuticals Inc.; the successful development of JUVISTA®, and other risks and uncertainties detailed from time to time in Shire 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, 2006.

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