

## Press Release

### **Shire files Elaprase™ (idursulfase) with the FDA for the treatment of Hunter syndrome**

**Philadelphia, PA, US, and Basingstoke, UK – November 24, 2005** -- Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) announced today that it has submitted a Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA) for idursulfase under the tradename Elaprase™, formerly referred to as I2S. If approved, ELAPRASE would be the first human enzyme replacement therapy for the treatment of Hunter syndrome, also known as Mucopolysaccharidosis II (MPS II). Idursulfase has previously received Fast Track designation from FDA, and Shire has requested Priority Review of this submission, which would result in a six-month review. Submission to the European Medicines Agency (EMA) is anticipated before the end of 2005 and typically takes 12 months for review and approval.

“Our filing with the FDA is a milestone for Shire and our team, who have been steadfast in the research and development of this much needed treatment,” said Dr. David D. Pendergast, executive vice president and general manager of Shire Human Genetic Therapies, the Shire specialty unit focused specifically on genetic diseases. “We are now a significant step closer to helping patients and their families living with Hunter syndrome, and I am pleased that this application has been submitted on schedule and I look forward to approval and subsequent launch in 2006.”

The BLA contains data results of the pivotal AIM (Assessment of I2S in MPS II) study, which studied 96 patients over 52 weeks, and is the largest study ever conducted for a MPS disorder. The primary efficacy outcome assessments were distance walked during six minutes (6-minute walk test, or 6MWT) as a measure of endurance, and percent predicted Forced Vital Capacity (FVC) as a measure of pulmonary function. The primary endpoint combined these two components into a composite score. Patients who received 0.5mg/kg of ELAPRASE on a weekly basis showed a statistically significant difference ( $p=0.0049$ ) in the primary efficacy endpoint, compared to patients receiving placebo. Additional data demonstrated improvements in key secondary endpoints.

Treatment with ELAPRASE was generally well tolerated by patients in the trial. The most common adverse events observed were associated with the clinical manifestations of Hunter syndrome. Of the adverse events considered possibly related to ELAPRASE, infusion related reactions were the most common and were generally mild. There were two patient deaths during the study, both of which were considered to be unrelated to treatment with ELAPRASE. No patient withdrew from the trial due to an adverse event considered related to ELAPRASE, and to date all patients have agreed to continue in the extension study.

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The BLA also contains data from a randomized, placebo controlled, dose escalation Phase I/II clinical study. Safety data is derived from the two controlled trials, as well as from two extension trials in which some patients have been treated for up to 42 months. Ultimately, patients will be transitioned from the extension studies to the Hunter Outcome Survey (HOS) Registry, which will allow long term follow up of both safety and clinical outcomes.

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**Notes to editors**

**About Hunter Syndrome and ELAPRASE**

Hunter syndrome, also known as Mucopolysaccharidosis II (MPS II), is a rare, life threatening, genetic disorder with no available treatment. Individuals with Hunter syndrome lack the enzyme iduronate-2-sulfatase, which is essential in the continuous process of replacing and breaking down glycosaminoglycans (GAG). As a result, GAG remains stored in cells in the body causing progressive damage. The symptoms of Hunter syndrome are usually not visible at birth, but usually start to become noticeable after the first or second year of life. Often the first symptoms may include hernias, frequent ear infections, runny noses, reduced growth rate and abnormal facial appearance.

As the disease progresses, a variety of symptoms appear including enlarged liver and spleen, heart failure, decreased endurance, obstructive and restrictive airway disease, sleep apnea, joint stiffness, and, in some cases, central nervous system involvement. If central nervous system involvement exists, the life expectancy for patients with Hunter syndrome is typically 10-15 years of age, however, some patients can survive into the fifth or sixth decade of life. There is currently no effective therapy for Hunter syndrome.

ELAPRASE is a human iduronate-2-sulfatase produced by genetic engineering technology, developed to replace the missing enzyme in Hunter syndrome patients. ELAPRASE has been designated an orphan drug in both the United States and in the European Union.

Shire believes there are approximately 2,000 patients worldwide afflicted with Hunter syndrome in countries where reimbursement may be possible.

Shire is committed to helping patients and families with Hunter syndrome. Further information about Hunter syndrome is available at <http://www.hunterpatients.com>.

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## **Shire Pharmaceuticals Group plc**

Shire Pharmaceuticals Group plc (Shire) is a global specialty pharmaceutical company with a strategic focus on meeting the needs of the specialist physician and currently focuses on developing projects and marketing products in the areas of central nervous system (CNS), gastrointestinal (GI), renal diseases and human genetic therapies. Shire has operations in the world's key pharmaceutical markets (US, Canada, UK, France, Italy, Spain and Germany) as well as a specialist drug delivery unit in the US.

For further information on Shire, please visit the Company's website: [www.shire.com](http://www.shire.com).

### **"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 dates of DAYTRANA™ (MTS/METHYPATCH™) (ADHD), SPD503 (ADHD), SPD465 (ADHD), MESAVANCE™ (SPD476) (ulcerative colitis), I2S (iduronate-2-sulfatase) (Hunter syndrome), and NRP104 (ADHD), including its scheduling classification by the Drug Enforcement Administration in the United States; Shire's ability to benefit from its acquisition of Transkaryotic Therapies, Inc.; Shire's ability to secure new products for commercialization and/or development; and other risks and uncertainties detailed from time to time in Shire's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the year to December 31, 2004.

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