



## Press Release

### **Shire's ELAPRASE™ (idursulfase) Approved by the Food and Drug Administration (FDA) for Hunter Syndrome**

**Basingstoke, UK and Philadelphia, US – July 24, 2006** – Shire plc (LSE: SHP, NASDAQ: SHPGY, TSX: SHQ) today announced that the FDA has granted marketing approval for ELAPRASE, a human enzyme replacement therapy for the treatment of Hunter syndrome, also known as Mucopolysaccharidosis II (MPS II). Hunter syndrome is a rare, life-threatening genetic condition that results from the absence or insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. Without this enzyme, cellular waste products accumulate in tissues and organs, which then begin to malfunction.

ELAPRASE is the first and only treatment approved for people suffering from Hunter syndrome. The product, which is given as weekly infusions, replaces the missing enzyme that Hunter syndrome patients fail to produce in sufficient quantities.

Shire expects to launch ELAPRASE in the United States within the next 30 days.

“The FDA approval of ELAPRASE marks a significant milestone in Shire's effort to provide meaningful treatments for patients suffering from genetic diseases,” said Matthew Emmens, chief executive officer of Shire. “A hallmark of the ELAPRASE program is the commitment demonstrated by patients and families, investigators and Shire employees involved in the development effort. We look forward to making ELAPRASE available to patients in the coming weeks.”

“Regulatory approval of ELAPRASE will enable physicians to move needy patients beyond palliative care and make Hunter syndrome a treatable disease,” said Joseph Muenzer, MD., Ph.D, of the University of North Carolina at Chapel Hill. “Until today, there were no options for addressing the underlying cause of this devastating disease.”

Shire submitted a Marketing Authorization Application (MAA) for ELAPRASE to the European Medicines Agency (EMA) on December 1, 2005. Based on average evaluation times, Shire anticipates completion of the EMA review by year end. In European countries that have mechanisms for pre-approval access, Shire has also submitted applications.

## **Clinical Trial Results**

A 53-week, randomized, double-blind, placebo-controlled Phase II/III trial demonstrated that ELAPRASE provides clinically important benefits to Hunter syndrome patients. The primary efficacy endpoint of the trial was a composite analysis of changes from baseline in two clinical measures: a 6-minute walk test and percent predicted forced vital capacity. Shire is pleased to report that this endpoint achieved statistical significance compared to placebo. After one year of treatment, patients receiving weekly infusions of ELAPRASE experienced a mean increase in the distance walked in six minutes of 35 meters compared to patients receiving placebo.

## **Safety Data**

Treatment with ELAPRASE was generally well-tolerated by patients in the Phase II/III trial. Adverse reactions were commonly reported in association with infusions, and were generally mild to moderate.

The ELAPRASE label includes a boxed warning with information on the potential for hypersensitivity reactions. The boxed warning states that “Anaphylactoid reactions, which may be life threatening, have been observed in some patients during ELAPRASE infusions. Therefore, appropriate medical support should be readily available when ELAPRASE is administered. Patients with compromised respiratory function or acute respiratory disease may be at risk of serious acute exacerbation of their respiratory compromise due to infusion reactions, and require additional monitoring.”

In all phases of clinical study for ELAPRASE, 11 patients experienced significant hypersensitivity reactions during 19 of 8,274 infusions (0.2%) and no patients discontinued treatment permanently as a result of a hypersensitivity reaction. The most common adverse events observed in >30% of patients during the Phase II/III trial were pyrexia, headache and arthralgia.

Fifty-one percent (32 of 63) of patients in the weekly ELAPRASE treatment arm in the pivotal clinical study (53-week placebo-controlled study with an open-label extension) developed anti-idursulfase IgG antibodies.

## **About ELAPRASE**

ELAPRASE is a purified form of the lysosomal enzyme iduronate-2-sulfatase and is produced by recombinant DNA technology in a human cell line.

In conjunction with the market approval of ELAPRASE, Shire Human Genetic Therapies (the Shire business unit focused on genetic diseases) has introduced a new product support center called OnePath<sup>SM</sup> for the U.S market. OnePath<sup>SM</sup> is a single source of product support for healthcare providers, patients and their families, where personalized, comprehensive information about ELAPRASE is available from a case manager. Case managers can provide information about coding, reimbursement and insurance verification, authorization letters, product access and treatment center locations. OnePath<sup>SM</sup> also offers

education about Hunter syndrome and can refer patients to additional support services, if needed.

Shire Human Genetic Therapies is actively tracking health data among individuals affected by Hunter syndrome as part of the company's long-term outcome survey, called the Hunter Outcome Survey (HOS). HOS is designed to support the gathering, analysis, reporting and sharing of data from around the world about Hunter syndrome. Shire believes that the inclusion of all people affected by Hunter syndrome and the analysis and dissemination of this information will allow for further understanding of Hunter syndrome and disease education on a global scale.

More information about ELAPRASE and Hunter syndrome is available at <http://www.elaprased.com>, [www.hunterpatients.com](http://www.hunterpatients.com), or through OnePath<sup>SM</sup> at 1 (866) 888-0660.

### **About Hunter Syndrome**

Hunter syndrome (MPS II) is a serious genetic disorder mainly affecting males that interferes with the body's ability to break down and recycle waste substances called mucopolysaccharides, also known as glycosaminoglycans or GAG. Hunter syndrome is one of several related lysosomal storage diseases.

In Hunter syndrome, cumulative buildup of GAG in cells throughout the body interferes with the way certain tissues and organs function, leading to severe clinical complications and early mortality. Physical manifestations for some people with Hunter syndrome may include distinct facial features, a large head and an enlarged abdomen. People with Hunter syndrome may also experience hearing loss, thickening of the heart valves leading to a decline in cardiac function, obstructive airway disease, sleep apnea, and enlargement of the liver and spleen. In some cases, central nervous system involvement leads to progressive neurologic decline.

Shire estimates that there are approximately 2,000 patients worldwide afflicted with Hunter syndrome in areas where reimbursement may be possible. Shires estimates that the U.S. accounts for approximately 25% of the global market for Hunter syndrome.

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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 attention deficit and hyperactivity disorder, gastrointestinal, renal diseases 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](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 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) 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.