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SHIRE ANNOUNCES COMPLETION OF DECENTRALIZED PROCEDURE IN EUROPE FOR IMMUNOGLOBULIN TREATMENT CUVITRU

- *Cuvitru (IG 20mg/ml solution for subcutaneous injection) builds on company's broad portfolio of IG treatments gained through combination with Baxalta*
- *New option to treat primary and certain secondary immunodeficiencies can help meet patient needs related to number of infusion sites and infusion time*

Zug, Switzerland – June 10, 2016 – Shire plc (LSE: SHP, NASDAQ: SHPG) announced today the successful completion of a decentralized procedure (DCP) to support approval by 17 authorities in Europe for Cuvitru (IG 20mg/ml solution for subcutaneous injection), a treatment for pediatric and adult patients with primary and certain secondary immunodeficiency disorders, a group of disorders in which part of the body's immune system is missing or does not function properly.¹ It is estimated that as many as six million children and adults may be affected by primary immunodeficiencies (PI) worldwide.¹

With the addition of Cuvitru following the completion of the combination with Baxalta, Shire has the broadest immunoglobulin (IG) portfolio with intravenous, conventional and subcutaneous treatment options. Cuvitru is a new IG treatment that does not contain proline; it offers patients a new therapeutic option to meet their needs, particularly related to the number of infusion sites and infusion time. With the completion of the DCP, the 17 authorities mutually recognize approvability based on a scientific assessment of the product, and local marketing authorizations in Europe are expected to begin later in 2016.

Regulatory evaluation for Cuvitru was based on the positive results of a Phase 2/3 study that evaluated the efficacy, safety, tolerability and pharmacokinetics of IGSC 20% in European patients with PI. The study met its primary endpoint that measured the rate of validated acute serious bacterial infections.

“With the completion of the assessment procedure, we can move forward with seeking country approvals of Cuvitru in Europe as we continue to build a comprehensive portfolio of IG treatments that can address the distinct needs of people with PI around the world,” said Philip J. Vickers, Ph.D., Head of Research and Development, Shire.

Shire expects a regulatory decision for Cuvitru in the U.S. later this year in response to Baxalta's submission for licensing late in 2015 based on a separate Phase II/III study. The company expects to initiate additional global regulatory submissions in 2016.

About Primary Immunodeficiency

Primary immunodeficiencies (PI) are a group of more than 300 disorders in which part of the body's immune system is missing or does not function properly.² Normally, the immune system protects the body from pathogenic microorganisms like bacteria, viruses, and fungi, which can

cause infectious diseases. When any part of a person's immune system is absent or dysfunctional, the individuals are susceptible to infections, and it may take longer to recover from infections. When a defect in the immune system is genetically determined, it is called primary immune deficiency.³ It is estimated that as many as six million children and adults may be affected by PI worldwide.¹

About Cuvitru 20mg/ml solution for subcutaneous injection in Europe

After marketing authorization, Cuvitru 20mg/ml solution for subcutaneous injection will be indicated as a subcutaneous administration (SCIg) replacement therapy in adults, and children and adolescents (0 - 18 years) in:

- Primary immunodeficiency syndromes with impaired antibody production.
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (CLL), in whom prophylactic antibiotics have failed or are contra-indicated.
- Hypogammaglobulinaemia and recurrent bacterial infections in multiple myeloma (MM) patients.
- Hypogammaglobulinaemia in patients pre- and post- allogeneic haematopoietic stem cell transplantation (HSCT).

Detailed Important Risk Information

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

Severe IgA deficiency and a history of hypersensitivity to human immunoglobulin treatment.

Cuvitru must not be given intravascularly or intramuscularly.

WARNINGS and PRECAUTIONS

If Cuvitru is accidentally administered into a blood vessel patients could develop shock.

The recommended infusion rate must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.

Certain adverse reactions may occur more frequently in patients who receive human normal immunoglobulin for the first time or, in rare cases, when the human normal immunoglobulin product is switched or when there has been a long interval since the previous infusion.

Potential complications can often be avoided by:

- initially injecting the product slowly
- ensuring that patients are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human normal immunoglobulin, patients switched from an alternative immunoglobulin product or when there has been a long interval since the previous infusion should be monitored during the first infusion and for the first hour after the first infusion, in order to detect potential adverse signs.

All other patients should be observed for at least 20 minutes after administration.

In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. Suspicion of severe hypersensitivity or anaphylactic-type reactions requires immediate

discontinuation of the injection. The treatment required depends on the nature and severity of the adverse reaction.

In case of shock, standard medical treatment for shock should be implemented.

Thromboembolic events (e.g. myocardial infarction, cerebral vascular accident, deep vein thrombosis, and pulmonary embolism), renal dysfunction/failure, aseptic meningitis syndrome, hemolysis and interference with serological testing have been observed with IG administered intravenously and cannot be excluded with use of Cuvitru. Thrombotic events and hemolysis have also been reported in association with the subcutaneous administration of immunoglobulin products.

Human normal immunoglobulin is produced from human plasma and may carry a risk of transmitting infectious agents.

Shire, Baxalta and Cuvitru are trademarks of Shire plc, its subsidiaries or affiliates.

References

1. Bousfiha AA et al. Primary immunodeficiency diseases worldwide: more common than generally thought. J Clin Immunol. 2013 Jan;33(1):1-7.
2. Picard C, Al-Herz W, et al. Primary Immunodeficiency Diseases: an Update on the Classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency. J Clin Immunol. 2015 Nov;35(8):696-726.
3. IDF Patient & Family Handbook for Primary Immunodeficiency Diseases. 5th edition. Blaese. 2013.

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NOTES TO EDITORS

About Shire

Shire is the leading global biotechnology company focused on serving people with rare diseases and other highly specialized conditions. We have best-in-class products available in more than 100 countries across core therapeutic areas including Hematology, Immunology, Neuroscience, Lysosomal Storage Disorders, Gastrointestinal / Internal Medicine / Endocrine and Hereditary Angioedema; a growing franchise in Oncology; and an emerging, innovative pipeline in Ophthalmics.

Our employees come to work every day with a shared mission: to develop and deliver breakthrough therapies for the hundreds of millions of people in the world affected by rare diseases and other high-need conditions, and who lack effective therapies to live their lives to the fullest.

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Forward-Looking Statements

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, the anticipated timing of clinical trials and approvals for, and the commercial potential of, inline or pipeline products 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 adversely affected. The risks and uncertainties include, but are not limited to, the following:

- disruption from the acquisition and integration of Baxalta Incorporated ("Baxalta") may make it more difficult to conduct business as usual or maintain relationships with patients, physicians, employees or suppliers;
- the company may not achieve some or all of the anticipated benefits of Baxalta's spin-off from Baxter International, Inc. ("Baxter") and the acquisition may have an adverse impact on Baxalta's existing arrangements with Baxter, including those related to transition, manufacturing and supply services and tax matters;
- the failure to achieve the strategic objectives with respect to the acquisition of Baxalta may adversely affect the company's financial condition and results of operations;
- products and product candidates may not achieve commercial success;
- product sales from ADDERALL XR and INTUNIV are subject to generic competition;
- the failure to obtain and maintain reimbursement, or an adequate level of reimbursement, by third-party payers in a timely manner for the company's products may affect future revenues, financial condition and results of operations, particularly if there is pressure on pricing of products to treat rare diseases;
- supply chain or manufacturing disruptions may result in declines in revenue for affected products and commercial traction from competitors; regulatory actions associated with product approvals or changes to manufacturing sites, ingredients or manufacturing processes could lead to significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the successful development of products in various stages of research and development is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect the company's ability to sell or market products profitably, and fluctuations in buying or distribution patterns by such customers can adversely affect the company's revenues, financial condition or results of operations;
- investigations or enforcement action by regulatory authorities or law enforcement agencies relating to the company's activities in the highly regulated markets in which it operates may result in significant legal costs and the payment of substantial compensation or fines;
- adverse outcomes in legal matters, tax audits and other disputes, including the company's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the company's revenues, financial condition or results of operations;
- Shire is undergoing a corporate reorganization and was the subject of an unsuccessful acquisition proposal and the consequent uncertainty could adversely affect the company's ability to attract and/or retain the highly skilled personnel needed to meet its strategic objectives;
- failure to achieve the strategic objectives with respect to Shire's acquisition of NPS Pharmaceuticals Inc. or Dyax Corp. ("Dyax") may adversely affect the company's financial condition and results of operations;
- the company is dependent on information technology and its systems and infrastructure face certain risks, including from service disruptions, the loss of sensitive or confidential information, cyber-attacks and other security breaches or data leakages that could have a material adverse effect on the company's revenues, financial condition or results of operations;
- the company may be unable to retain and hire key personnel and/or maintain its relationships with customers, suppliers and other business partners;
- difficulties in integrating Dyax or Baxalta into Shire may lead to the company not being able to realize the expected operating efficiencies, cost savings, revenue enhancements, synergies or other benefits at the time anticipated or at all; and

other risks and uncertainties detailed from time to time in Shire's, Dyax's or Baxalta's filings with the Securities and Exchange Commission, including those risks outlined in "ITEM 1A: Risk Factors" in Shire's and Baxalta's Annual Reports on Form 10-K for the year ended December 31, 2015.

All forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Except to the extent otherwise required by applicable law, we do not undertake any obligation to republish revised forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.