Press Release

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Shire and NanoMedSyn Enter Into Research Agreement for Potential Lysosomal Storage Disorder Treatment

- *Research agreement focuses on evaluating a potential treatment for a lysosomal storage disorder using NanoMedSyn's proprietary AMFA technology*
- *Research reinforces Shire's genetic diseases franchise's leadership in rare diseases innovation*

Cambridge, MA and Montpellier, France – March 26, 2018 – Shire plc (LSE: SHP, NASDAQ: SHPG), the global biotechnology leader in rare diseases, and NanoMedSyn, a biotechnology company dedicated to innovation in enzyme replacement therapy (ERT), today announced that the companies have entered into a preclinical research collaboration to evaluate a potential ERT using NanoMedSyn's proprietary synthetic derivatives named AMFA.

"NanoMedSyn has demonstrated innovation in advancing the next generation of enzyme replacement therapy, and Shire is pleased to enter this research agreement with NanoMedSyn" said Andreas Busch, Ph.D., Head of Research and Development and Chief Scientific Officer at Shire. "The novel design of AMFA and the promising biological activity demonstrated in preclinical models makes this program an exciting opportunity for Shire to further expand its commitment to evaluating potential advancements in lysosomal storage disorder treatments."

"This agreement provides the opportunity to further evaluate molecules based on our proprietary AMFA technology, which may potentially benefit patients with lysosomal storage disorders that are currently treated with the traditional enzyme replacement therapies," said Henry-Vincent Charbonné, Chief Executive Officer and Chairman of NanoMedSyn. "As a global biotech leader in the development and commercialization of biologic therapeutics, Shire is an ideal research partner, particularly given their extensive expertise in the area of lysosomal storage disorders."

Lysosomal storage disorders are inherited metabolic disorders that are characterized by an abnormal build-up of various toxic materials in the body's cells as a result of enzyme deficiencies.[1] There are more than 50 of these disorders altogether, and they may affect different parts of the body, including the central nervous system.[1]

The AMFA compound is designed for the targeting of a specific membrane lectin, the mannose 6-phosphate (M6P) receptor, a major intracellular lysosomal trafficking pathway.[2,3,4] Preclinical data demonstrate that AMFA has a high affinity for binding to the M6P receptor.[4] Additionally, in preclinical models the AMFA compound leads to increased lysosomal exposure and enhanced activity of enzyme replacement therapy compared to a current available ERT.[4]

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[1] Bellettato CM et al. *Pediatr Clin North Am*. 2018 Apr;65(2):353-373. doi: 10.1016/j.pcl.2017.11.011.
[2] Coutinho MF, Prata MJ and Alves S. *Mol Gen Metab.* 2012 Apr;105(4):542-550. doi: 10.1016/j.ymgme.2011.12.012
[3] Staudt C, Puissant E and Boonen M. *Int J Mol Sci*. 2016 Dec;18(1). pii: E47. doi: 10.3390/ijms18010047.
[4] Cheikh et al. *Angew Chem Int Ed Engl*. 2016 Oct;55(47):14774-14777. doi: 10.1002/anie.201607824.

Under the terms of the agreement, the parties will perform preclinical evaluations of AMFA conjugated to recombinant enzyme. Shire will provide funding to NanoMedsyn under the agreement. Further terms of the agreement were not disclosed.

About NanoMedSyn and AMFA

NanoMedSyn is a private biotech company based in Montpellier (France) which was created to develop the innovative AMFA technology. NanoMedSyn holds the exclusive worldwide rights on the technology. The technological platform of AMFA compounds have the potential to target various proteins or drugs to tissues and cells expressing the mannose 6-phosphate receptors in order to facilitate their cellular entrance and eventual lysosomal uptake. In September 2016, the European Medicines Agency (EMA) granted orphan drug designation for NanoMedSyn's first compound, recombinant acid alpha-glucosidase conjugated with AMFA for the potential treatment of Pompe disease, a lysosomal storage disorder.

About Shire's Genetic Disease Franchise

Shire is dedicated to helping patients with inherited illnesses. Shire's genetic disease franchise has a strong legacy in developing therapies for LSDs, with a portfolio that includes commercial products, late-stage investigational therapies, and pipeline candidates, as well as a robust R&D program. Therapeutic areas in which Shire is working include Hunter Syndrome, Type 1 Gaucher Disease and Fabry Disease.

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NOTES TO EDITORS

About Shire

Shire is the global leader in serving patients with rare diseases. We strive to develop best-in-class therapies across a core of rare disease areas including hematology, immunology, genetic diseases, neuroscience, and internal medicine with growing therapeutic areas in ophthalmics and oncology. Our diversified capabilities enable us to reach patients in more than 100 countries who are struggling to live their lives to the fullest.

We feel a strong sense of urgency to address unmet medical needs and work tirelessly to improve people's lives with medicines that have a meaningful impact on patients and all who support them on their journey.

Forward-Looking Statements

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, projected revenues, 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:

- Shire's products may not be a commercial success;
- increased pricing pressures and limits on patient access as a result of governmental regulations and market developments may affect Shire's future revenues, financial condition and results of operations;
- Shire depends on third parties to supply certain inputs and services critical to its operations including certain inputs, services and ingredients critical to its manufacturing processes. Any disruption to the supply chain for any of Shire's products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire's products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to, among other things, significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the nature of producing plasma-based therapies may prevent Shire from timely responding to market forces and effectively managing its production capacity;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products 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 Shire's ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire's revenues, financial conditions or results of operations;
- failure to comply with laws and regulations governing the sales and marketing of its products could materially impact Shire's revenues and profitability;
- Shire's products and product candidates face substantial competition in the product markets in which it operates, including competition from generics;
- Shire's patented products are subject to significant competition from generics;
- adverse outcomes in legal matters, tax audits and other disputes, including Shire's ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on the Shire's revenues, financial condition or results of operations;
- Shire may fail to obtain, maintain, enforce or defend the intellectual property rights required to conduct its business;
- Shire faces intense competition for highly qualified personnel from other companies and organizations;
- failure to successfully execute or attain strategic objectives from Shire's acquisitions and growth strategy may adversely affect the Shire's financial condition and results of operations;
- Shire's growth strategy depends in part upon its ability to expand its product portfolio through external collaborations, which, if unsuccessful, may adversely affect the development and sale of its products;
- a slowdown of global economic growth, or economic instability of countries in which Shire does business, could have negative consequences for Shire's business and increase the risk of non-payment by Shire's customers;
- changes in foreign currency exchange rates and interest rates could have a material adverse effect on Shire's operating results and liquidity;
- Shire is subject to evolving and complex tax laws, which may result in additional liabilities that may adversely affect the Shire's financial condition or results of operations;
- if a marketed product fails to work effectively or causes adverse side effects, this could result in damage to Shire's reputation, the withdrawal of the product and legal action against Shire;
- Shire 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 Shire's revenues, financial condition or results of operations;
- Shire faces risks relating to the expected exit of the United Kingdom from the European Union;
- Shire incurred substantial additional indebtedness to finance the Baxalta acquisition, which has increased its borrowing costs and may decrease its business flexibility;

- Shire's ongoing strategic review of its Neuroscience franchise may distract management and employees and may not lead to improved operating performance or financial results; there can be no guarantee that, once completed, Shire's strategic review will result in any additional strategic changes beyond those that have already been announced; and

a further list and description of risks, uncertainties and other matters can be found in Shire's most recent Annual Report on Form 10-K and in Shire's subsequent Quarterly Reports on Form 10-Q, in each case including those risks outlined in "ITEM1A: Risk Factors", and in Shire's subsequent reports on Form 8-K and other Securities and Exchange Commission filings, all of which are available on Shire's website.

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 update or revise forward-looking statements, whether as a result of new information, future events or otherwise.