

## **Shionogi Concludes Licensing Agreements with Eddingpharm and EOC Pharma for Lusutrombopag, a Thrombopoietin Receptor Agonist and Epertinib, an HER2/EGFR Inhibitor**

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**OSAKA, Japan, June 24, 2019** - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; President and CEO: Isao Teshirogi, Ph.D.; hereafter "Shionogi" or "the Company") announces that the Company has concluded an agreement with Eddingpharm (Head Office: Shanghai, People's Republic of China; Chief Executive Officer: Ni Xin; hereafter "Eddingpharm") to license-out lusutrombopag, a thrombopoietin receptor agonist (brand name in Japan: MULPLETA<sup>®</sup>) and an agreement with EOC Pharma, (Chief Executive Office: Zou Xiaoming; hereafter "EOC") to license-out epertinib, an HER2 (human epidermal growth factor receptor 2)/EGFR (epidermal growth factor receptor) inhibitor for focused development to treat brain metastasis in advance metastatic breast cancer patients.

### **Licensing agreement of lusutrombopag with Eddingpharm**

In China, about 13.6<sup>1,2,3</sup> million adult patients have chronic liver disease and many of them are said to be planning to receive elective invasive therapy. On the other hand, the country faces a chronic shortage of blood for transfusions due to a growing demand for blood during advanced higher-level medical care, in addition to a lower rate of voluntary blood donation as compared to Europe, the U.S., and Japan. Additionally, it is also known that the current stored blood supply in China is at high risk of transfusion-transmitted infections. Under such circumstances, the application of lusutrombopag is a preferable mode of therapy versus platelet transfusion.

Eddingpharm is a pharmaceutical company with a broad-based sales network that covers hospitals nationwide specializing in liver disease, blood disorders, and infections where prescriptions of lusutrombopag are expected. Following product approval, it is anticipated that the two parties will further contribute to clinical treatment of patients in China by leveraging Eddingpharm's broad sales network and Shionogi's know-how in developing and marketing lusutrombopag globally. With the execution of this agreement, Eddingpharm will be granted with exclusive license rights of lusutrombopag in Mainland China, Hong Kong, and Macau while Shionogi will supply the product to Eddingpharm and receive an upfront payment as well as milestone payments according to post-launch sales periods. It is also agreed that the two companies will cooperate on the application for approval. The Company has been proceeding with preparations toward the application for approval of the product in China.

### **Licensing agreement of epertinib with EOC**

In these days, due to improved breast cancer therapy availability, the overall survival of patients with HER2 positive breast cancer is improving. Conversely, because of this, the incidence of brain metastasis

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in the breast cancer setting has been increasing among these patients<sup>4</sup>. Thus far, no drugs to date have demonstrated a clear effect on breast cancer metastatic tissue localized to the brain. Therefore, a therapeutic agent that focuses on and is efficacious on breast cancer metastatic brain tissue would address a major unmet medical need in the field. Epertinib, an HER2/EGFR inhibitor originated by Shionogi, is expected to demonstrate an anti-tumor effect on breast cancer brain metastasis because it has shown high permeability and distribution to the brain in non-clinical studies. In addition, it has been shown clinically to have anti-tumor effects on patients with breast cancer after HER2 molecular targeted therapy.

EOC is a specialty pharmaceutical company focusing on oncology. With the conclusion of the current licensing agreement, EOC will hold rights to develop, manufacture and market epertinib in mainland China, Hong Kong and Macau, and will start developing the product in mainland China, while Shionogi will receive an upfront payment as well as milestone payments according to the progress of the product development and royalties on the post-launch sales.

## **About Shionogi & Co., Ltd.**

Shionogi & Co., Ltd. is a major Japanese research-driven pharmaceutical company dedicated to bringing benefits to patients based on its corporate philosophy of “supplying the best possible medicine to protect the health and wellbeing of the patients we serve.” The company currently markets products in several therapeutic areas including anti-infectives, pain, cardiovascular diseases and gastroenterology. Our pipeline is focused on infectious disease, pain and CNS. For more information on Shionogi & Co., Ltd., please visit [www.shionogi.co.jp/en](http://www.shionogi.co.jp/en).

## **About Eddingpharm**

Established in 2001, Eddingpharm’s vision and mission has always been to become China's leading supplier of patented drugs and branded drugs, bridge the gap between Chinese patients and global high quality medicines. Eddingpharm has nearly 1,000 professional representatives in 30 provinces across the country, with coverage of 19,000+ hospitals and 20,000+ pharmacies. Eddingpharm has collaborated with various multinational pharmaceutical companies, specialty pharmaceutical companies and leading R&D institutions to enrich its product portfolio by acquisitions, in-licensing, joint ventures, exclusive distribution and strategic alliances. Over the past few years, Eddingpharm rapidly expanded its business and strategically deployed resources in various fields, and is now upgrading to a whole-industry-chain entity from sole in-licensing R&D and commercialization. For more information on Eddingpharm, please visit [www.eddingpharm.com](http://www.eddingpharm.com).

## **About EOC Pharma**

EOC Pharma is an integrated biopharmaceutical company that is focused on the manufacturing, development and commercialization of innovative global oncology products in China. EOC has adopted a licensing model in order to build EOC’s innovative pipeline by plugging our partner’s molecule into EOC’s “core engine” of local manufacturing, clinical development, regulatory filing, and

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commercialization. The company now has a pipeline of seven novel products from global biopharmaceutical partners that are potentially first- and best-in-class. Until now, EOC has obtained four Class I innovative drug CTA approvals and initiated clinical studies of four lead products in China. EOC has a team of entrepreneurs and consultants with overseas background that boasts of first-class pharmaceutical R&D expertise as well as rich industry experience. The company owns an 8,000 square meter cGMP manufacturing facility in Taizhou, China Medical City and has offices in Shanghai, Beijing, Hong Kong and Los Angeles. For more information on EOC Pharma, please visit [www.eocpharma.com](http://www.eocpharma.com).

## **About Lustrombopag**

Lusutrombopag, which has already been approved for routine use in the US, EU, and Japan, is an orally active, small molecule agonist of the human thrombopoietin receptor that triggers the production of endogenous platelets.

## **About Thrombocytopenia in Chronic Liver Disease**

Thrombocytopenia is a common complication of chronic liver disease (CLD) and may be caused by multiple mechanisms including splenic sequestration and decreased production of thrombopoietin<sup>3</sup>. There is evidence that the annual health care cost of a CLD patient with thrombocytopenia is more than three times that of a CLD patient without thrombocytopenia<sup>5</sup>. In addition to the potential of thrombocytopenia, especially severe thrombocytopenia, to aggravate procedural or traumatic bleeding, it may also significantly complicate routine diagnostic procedures and patient care, such as liver biopsy and medically indicated or elective procedures for cirrhotic patients, resulting in delayed or cancelled curative treatment<sup>6</sup>.

## **About Epertinib (S-222611)**

HER2 is a receptor of cancer growth factors which are specifically expressed in carcinoma cells and mainly found in breast and stomach cancers. Studies conducted so far have demonstrated that epertinib possesses favorable anti-tumor effect on patients with breast cancer after HER2 molecular targeted therapy. In addition, non-clinical studies have revealed that migration of the drug to the brain was superior to that of lapatinib that is also a molecular targeted agent. Thus, epertinib is anticipated to exert the anti-tumor effect on brain metastasis. In China, the number of new patients with metastatic HER2 positive breast cancer is estimated to be approximately 17,600<sup>7</sup>, about three times greater than that of Japan. New onset of metastasis is reported to be found in 30 - 55%<sup>8</sup> of these patients.

## **References**

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7. Global Data HER2 positive breast cancer global drug forecast and market analysis to 2025
8. Chronic Diseases and Translational Medicine 3 (2017) 21-32.

## **Forward-Looking Statements**

*This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.*

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