

News Release

Otsuka and Takeda Announce a Co-promotion Agreement in Japan of TAK-438 For the Treatment of Acid-related Diseases in the Gastrointestinal Therapeutic Area

- Otsuka and Takeda signed an agreement for the future co-promotion of sales in Japan of TAK-438, whose New Drug Application was submitted in Japan by Takeda and is currently undergoing regulatory review.
- Otsuka, whose product MUCOSTA[®] has a top market share as a gastric mucosal protecting agent, and Takeda, whose product TAKEPRON[®] (generic name: Lansoprazole) has led the Japanese PPI market for over 20 years since its launch, will both leverage their strengths in the gastrointestinal therapeutic area to co-promote TAK-438, thus taking concrete actions to resolve issues encountered in the treatment of acid-related diseases and further contribute to healthcare needs.
- Under the terms of the agreement, Otsuka will pay Takeda an up-front payment of 20 billion yen and a milestone payment upon NDA approval, and Otsuka will receive a percentage of the sales (based on certain conditions specified in the contract) from Takeda.

Tokyo and Osaka, Japan, March 27, 2014 – Otsuka Pharmaceutical Co., Ltd. (Head office: Chiyoda-ku, Tokyo; President and Representative Director: Taro Iwamoto; “Otsuka”) and Takeda Pharmaceutical Company Limited (Head office: Chuo-ku, Osaka; President and CEO: Yasuchika Hasegawa; “Takeda”) announced today that the two firms have entered into a co-promotion agreement in Japan for TAK-438 (generic name: Vonoprazan Fumarate), a drug discovered by Takeda for the treatment of acid-related diseases.

Proton pump inhibitors (PPIs) are currently widely prescribed as first-line therapy for the treatment of acid-related diseases in Japan. However, PPIs do not always provide sufficient therapeutic efficacy, and the acid secretion inhibitory effects of PPIs may differ among individuals, because of the protein CYP2C19 which has gene polymorphisms that are involved in metabolism. TAK-438 inhibits proton pumps without the need for activation by acid, and the compound is distributed at high concentrations into the stomach, the target organ, thereby exerting a nearly maximum inhibitory effect from the first dose and remaining effective for 24 hours. Unlike PPIs, TAK-438 is not primarily metabolized by CYP2C19 (which has gene polymorphisms). Since TAK-438 is stable in acid and its immediate-release formulation is available without requiring an optimized formulation design (e.g., enteric-coating), the onset of efficacy does not significantly differ among treated patients. With these advantages, TAK-438 is expected to become a new therapeutic agent that resolves issues with current treatments for acid-related diseases.

Two of Otsuka's products have enabled Otsuka to establish a strong presence in the gastrointestinal therapeutic area: MUCOSTA, which has a top market share as a gastric mucosal protecting agent, and UBT which is a diagnostic drug for helicobacter pylori infections. Otsuka will co-promote TAK-438, if approved, in cooperation with Takeda, whose product TAKEPRON has led the Japanese PPI market for over 20 years since its launch. This co-promotion agreement will position the two companies to offer new treatment options to healthcare professionals working with acid-related diseases, and assist them in determining the presence of helicobacter pylori and evaluating the most suitable therapy for its eradication.

Otsuka's President and Representative Director, Taro Iwamoto, said, "We are very enthusiastic about entering this collaboration in Japan with Takeda, which has a leadership position in the gastrointestinal therapy area. Together we have the opportunity to bring to market an innovative new medicine that is hypothesized to significantly change the way in which acid-related disorders can be treated and thereby improve the QOL of many patients."

"TAK-438 offers a new therapy option for acid-related diseases that require strong acid secretion inhibitory effects," Takeda's President and CEO, Yasuchika Hasegawa said. "I am pleased that we have been able to sign a co-promotion agreement with the most suitable partner. Takeda will take every possible step in order to meet the diverse needs of patients and healthcare professionals. "

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About the co-promotion agreement

The details of this agreement are as below:

- Takeda will receive from Otsuka an up-front payment of 20 billion yen and a milestone payment upon regulatory approval.
- Otsuka will receive from Takeda a percentage of the sales (based on conditions specified in the contract).
- Japan will be the area of promotion.
- Further details will not be disclosed.

About TAK-438 (generic name: Vonoprazan Fumarate)

TAK-438, discovered by Takeda, belongs to a new class of acid secretion inhibitors called potassium-competitive acid blockers (P-CAB). It competitively inhibits the binding of potassium ion to H^+ , K^+ -ATPase (proton pump) in the final step of gastric acid secretion in gastric parietal cells. TAK-438 has strong and sustained acid secretion inhibitory effects and shows efficacy from the early stages of dosing. Phase III trials have been conducted in Japan on indications including gastric ulcer, duodenal ulcer, erosive esophagitis and *H.pylori* eradication. Based on results obtained from these trials, Takeda submitted a New Drug Application in Japan in February 2014.

About Otsuka Pharmaceutical Co., Ltd.

Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: "Otsuka – people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative and original products, with a focus on pharmaceutical products for the treatment of diseases and nutraceutical products for the maintenance of everyday health. Otsuka Pharmaceutical employs approximately 28,000 people globally and its products are available in 81 countries worldwide. Otsuka invites you to visit its global website at <https://www.otsuka.co.jp/en/>.

About Takeda Pharmaceutical Company Limited

Located in Osaka, Japan, Takeda is a research-based global company with its main focus on pharmaceuticals. As the largest pharmaceutical company in Japan and one of the global leaders of the industry, Takeda is committed to strive towards better health for people worldwide through leading innovation in medicine. Additional information about Takeda is available through its corporate website, www.takeda.com.

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