News Release

New Drug Application Approval of TAKECAB® for the treatment of Acid-related Diseases in Japan

- Takeda received approval of its New Drug Application for TAKECAB® for the treatment of acid-related diseases in Japan.
- Takeda and Otsuka executed an agreement at the end of March 2014 to co-promote TAKECAB® in Japan. Under the agreement, the two companies will conduct informational activities for healthcare professionals with the aim of addressing unmet clinical needs in the treatment of acid-related diseases.
- At this time, Takeda will receive a milestone payment for the NDA approval. Otsuka will receive co-promotion fee based on sales amounts (in accordance with certain conditions specified in the agreement) from Takeda.

Osaka and Tokyo, Japan, December 26, 2014 – Takeda Pharmaceutical Company Limited (Head office: Chuo-ku, Osaka; President and COO: Christophe Weber; "Takeda") and Otsuka Pharmaceutical Company, Limited (Head office: Chiyoda-ku, Tokyo; President and Representative Director: Taro Iwamoto; "Otsuka") announce today that the Japanese Ministry of Health, Labour and Welfare has approved the New Drug Application submitted by Takeda ("NDA") of TAKECAB® (generic name: Vonoprazan fumarate, hereafter "TAKECAB"), a drug for treating acid-related diseases.

TAKECAB, discovered by Takeda, is a new medicine for treating acid-related diseases with a novel mechanism of action called potassium-competitive acid blockers (P-CABs) which competitively inhibits the binding of potassium ions to H^+,K^+-ATPase (also known as the proton pump) in the final step of gastric acid secretion in gastric parietal cells. TAKECAB provides a strong and sustained acid secretion inhibitory effect.

The approval granted is based on the results of multiple Phase III clinical trials for TAKECAB in Japan. Takeda has conducted trials for indications including gastric ulcer, duodenal ulcer, erosive esophagitis and *H. pylori* eradication. In these trials, TAKECAB demonstrated efficacy and has a favorable profile for safety and tolerability.

Takeda and Otsuka executed an agreement at the end of March 2014 to co-promote TAKECAB in Japan. Under the agreement, Takeda will manufacture and market TAKECAB, and Takeda and Otsuka will jointly conduct informational activities for healthcare professionals. Through this partnership, the two companies aim to address issues related to the treatment of acid-related diseases and address unmet clinical needs in the gastrointestinal field.

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＜**References**＞

Product name	TAKECAB®
Generic name	Vonoprazan Fumarate
Indications	○ Gastric ulcer, duodenal ulcer, erosive esophagitis, prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration, prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration ○ Adjunct to *Helicobacter pylori* eradication in the following settings: Gastric ulcer, duodenal ulcer, gastric mucosa-associated lymphatic tissue (MALT) lymphoma, idiopathic thrombocytopenic purpura, the stomach after endoscopic resection of early stage gastric cancer, or *Helicobacter pylori* gastritis
Dosage and administration	○ Gastric ulcer, duodenal ulcer The usual adult dosage for oral use is 20 mg of Vonoprazan administered orally once daily an 8 week treatment for gastric ulcer and a 6 week treatment for duodenal ulcer. ○ Erosive esophagitis The usual adult dose for oral use is 20 mg of Vonoprazan administered once daily for a total of 4 weeks of treatment. If that dosing proves insufficient, the administration should be extended, but for no longer than 8 weeks of treatment. For the maintenance therapy of reflux esophagitis showing recurrence and recrudescence, the dose for oral use is 10 mg once daily. However, when the efficacy is inadequate, the dosage may be increase up to 20 mg once daily. ○ Prevention of recurrence of gastric or duodenal ulcer during low-dose aspirin administration The usual adult dosage is one tablet of 10 mg of Vonoprazan administered orally once daily. ○ Prevention of recurrence of gastric or duodenal ulcer during non-steroidal anti-inflammatory drug (NSAID) administration The usual adult dosage is one tablet of 10 mg of Vonoprazan administered orally once daily ○ Adjunct to *Helicobacter pylori* eradication: For adults, the following three-drug regimen should be administered orally at the same time twice daily for seven days: 20 mg dose of Vonoprazan, 750 mg (potency) dose of amoxicillin hydrate, and 200 mg (potency) dose of clarithromycin. The dose of clarithromycin may be increased as clinically warranted. However, dosage should not exceed 400 mg (potency)/dose twice daily. If *Helicobacter pylori* eradication with a three-drug regimen comprising a proton pump inhibitor, amoxicillin hydrate and clarithromycin has been unsuccessful, as an alternative treatment, adults should be administered the following three drugs orally twice daily for seven days: 20 mg dose of Vonoprazan, 750 mg (potency) dose of amoxicillin hydrate, and 250 mg dose of metronidazole.

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 co-promotion fee based on the sales amount (based on conditions specified in the contract).
- Territory: Japan

Further details are not disclosed.

About Otsuka Pharmaceutical Company, Limited
Otsuka 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 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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