

Japan approval world-first for tumor-agnostic Rozlytrek in NTRK-positive solid tumors

By Jihyun Kim, Staff Writer

Japan has become the first country to give approval for Rozlytrek ([entrectinib](#)), a drug targeting patients with NTRK fusion gene-positive solid tumors, regardless of the site of disease origin. The Japanese Ministry of Health, Labour and Welfare (MHLW) had granted the drug both orphan drug designation and Sakigake status, which allows the accelerated approval of drugs designated as breakthrough therapies.

Developed by a Swiss pharmaceutical company [Roche Holding AG](#), Rozlytrek was cleared for use in locally advanced or metastatic solid tumors that reproduce NTRK (neurotrophic-tropomyosin receptor kinase) type 1/2/3 or ROS1 gene fusions. NTRK fusions are rare but occur in cancers arising in many parts of the body.

A CNS-active tyrosine kinase inhibitor, Rozlytrek is designed to target the kinase activity of TRK type A/B/C and ROS1 proteins. Their activating fusions drive proliferation in cancers such as breast, colorectal, gastric, head and neck, neuroendocrine, lung, ovarian, thyroid and pancreatic.

Approval of the new drug application, filed by Roche majority-owned subsidiary [Chugai Pharmaceutical Co. Ltd.](#), was based primarily on the results from the open-label, global phase II study. According to Tokyo-based Chugai, efficacy was evaluated in 51 adult patients with NTRK fusion gene-positive solid tumors, as well as in five pediatric patients, enrolled in overseas phase I and Ib studies.

“As Rozlytrek is the first and only MHLW-approved drug targeting the NTRK fusion gene in Japan, there are no approved drugs in this segment,” a spokeswoman at Chugai told *BioWorld*, though the company has declined to disclose its pricing strategy. “We don’t comment on the pricing strategy,” she said. “We’re waiting for the price to be listed on the national health insurance reimbursement list.”

Potential market size is also unclear. “Given the rarity of the condition, we assume the patient number is very limited,” the spokeswoman said. No specific numbers are known for Japan.

But, “in the U.S., the annual incidence of NTRK fusion-positive solid tumors is estimated to be around from 1,500 to 5,000 cases,” she said.

In the U.S., the drug, which has breakthrough therapy designation, is under FDA review, with a PDUFA date of Aug. 18. Upon approval, it would go up against rival Vitrakvi ([larotrectinib](#)), from Bayer AG, of Leverkusen, Germany, which won accelerated FDA approval in November as a treatment for adult and pediatric patients with NTRK fusion cancers. Vitrakvi was originally developed by U.S. company Loxo Oncology Inc. (later acquired by Eli Lilly and Co.) in partnership with Bayer.

Both Vitrakvi and Rozlytrek are under review in Europe.

“MHLW’s approval of Rozlytrek should enhance Chugai’s oncology franchise in Japan,” Sakai Fumiyoshi, an analyst at Credit Suisse Securities Ltd. in Tokyo, told *BioWorld*. “When it comes to its domestic marketing, we may know more details when the official reimbursement pricing takes place in August.”

The Japanese pharmaceutical firm agreed on a strategic alliance with Roche in 2002, which made Chugai a member of the Roche Group. Based on the agreement, the Swiss firm holds 59.9% of Chugai’s shares while allowing Chugai to maintain its managerial autonomy. Through the partnership, Chugai has the exclusive right to develop and market Roche’s products in Japan, and Roche can launch Chugai’s in-house products on the global market.

According to the Japanese company, its sales soared from ¥165.1 billion (US\$1.5 billion) in 2001 to ¥534.2 billion in 2017, while its operating profit increased from ¥25.7 billion in 2001 to ¥103.2 billion, thanks to the alliance.

On June 20, the stock price of Chugai (TYO:4519) went up slightly to ¥7,060 from ¥7,050. Roche’s (SWX:ROG) share price closed at CHF276.90 (US\$280.14) as of June 19, while Bayer AG’s (ETR:BAYN) stock closed at €54.98 (US\$62.07) on the same day. ♦