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Chugai Files a New Drug Application for a ROS1/TRK Inhibitor Entrectinib for the Treatment of *NTRK* Fusion-Positive Solid Tumors

TOKYO, December 19, 2018 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it filed a new drug application to the Ministry of Health, Labour and Welfare (MHLW) for a ROS1/TRK inhibitor entrectinib for the treatment of *NTRK* fusion-positive solid tumors. Entrectinib received *Sakigake* designation and orphan drug designation from MHLW.

"Entrectinib obtained the first *Sakigake* designation for Chugai. Entrectinib demonstrated efficacy across tumor types in extremely rare *NTRK* fusion-positive solid tumors in the global studies," said Dr. Yasushi Ito, Chugai's Executive Vice President, Co-Head of Project & Lifecycle Management Unit. "Chugai is committed to seek approval of entrectinib so that we may contribute to advancing personalized healthcare which may enable the most optimal treatment decision for patients based on genetic profiles of individual tumors."

This application for approval is based on an integrated analysis of an open-label, multicenter, global phase II study (the STARTRK-2 study) and three overseas phase I studies (the STARTRK-NG study, the STARTRK-1 study and the ALKA-372-001 study). Efficacy was evaluated in 54 patients with untreated *NTRK* fusion-positive solid tumors while safety assessment was conducted with 355 patients registered in the four trials.

[Reference information]
About the integrated analysis results
Media release issued by Roche on October 21, 2018
Title: Roche's investigational personalised medicine entrectinib shrank tumours in people with *NTRK* fusion-positive solid tumours
https://www.roche.com/media/releases/med-cor-2018-10-21.htm

Entrectinib has been granted Breakthrough Therapy Designation (BTD) by the U.S. Food and Drug Administration (FDA) in May 2017, Priority Medicines (PRIME) designation by the European Medicines Agency (EMA) in October 2017 for the treatment of *NTRK* fusion-positive, locally advanced or metastatic solid tumors in adult and pediatric patients who have either progressed following prior therapies or have no acceptable standard therapies.

As the top pharmaceutical company in the field of oncology in Japan, Chugai will work for the early approval to provide entrectinib as a new treatment option for patients and medical professionals.

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL: +81-(0)3-3273-0881 E-mail: pr@chugai-pharm.co.jp
Investor Relations Group TEL: +81-(0)3-3273-0554 E-mail: ir@chugai-pharm.co.jp

About entrectinib

Entrectinib is an investigational, oral medicine in development for the treatment of locally advanced or metastatic solid tumors that harbor *NTRK1/2/3* or *ROS1* gene fusions. It is a selective, CNS-active tyrosine kinase inhibitor designed to inhibit the kinase activity of the TRK A/B/C and ROS1 proteins, whose activating fusions drive proliferation in certain types of cancer. Entrectinib can block ROS1 and NTRK kinase activity and inhibit proliferation of cancer cells with *ROS1* or *NTRK* gene fusions. Entrectinib is being investigated across a range of solid tumor types, including breast, cholangiocarcinoma, colorectal, gynaecological, neuroendocrine, non-small cell lung, salivary gland, pancreatic, sarcoma and thyroid cancers.

About *NTRK* fusion gene positive cancer

NTRK fusion gene is an abnormal gene that can be formed by fusing the *NTRK* genes (*NTRK1*, *NTRK2*, *NTRK3* encode TRKA, TRKB, TRKC protein, respectively) and other genes (*ETV6*, *LMNA*, *TPM3*, etc.) as a result of chromosomal translocation. The TRK fusion kinase made from *NTRK* fusion gene is thought to promote cancer cell proliferation. There is very rare expression of *NTRK* fusion but in various adult and pediatric solid tumors, including appendiceal cancer, breast cancer, cholangiocarcinoma, colorectal cancer, gastrointestinal stromal tumor (GIST), infantile fibrosarcoma, lung cancer, mammary analogue secretory carcinoma of the salivary gland, melanoma, pancreatic cancer, thyroid cancer, and various sarcomas.