Kyowa Hakko Kirin Submits the Partial Change Approval Application of KHK7580 (evocalcet) in Japan

Tokyo, Japan, April 24, 2019---Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, President and CEO: Masashi Miyamoto, "Kyowa Hakko Kirin") announces today that it has submitted a supplemental application of KHK7580 (evocalcet)[*1] for the treatment of hypercalcemia in patients with parathyroid carcinoma or primary hyperparathyroidism who are unable to undergo parathyroidectomy or relapse after parathyroidectomy[*2] to the Ministry of Health, Labor and Welfare (MHLW) in Japan.

This application is based on the interim result (24 weeks) of the phase 3 study that evaluates the efficacy of KHK7580 for hypercalcemia in patients with parathyroid carcinoma or primary hyperparathyroidism who are unable to undergo parathyroidectomy or relapse after parathyroidectomy. The primary endpoint is the percentage of subjects whose corrected serum calcium level is maintain ≤ 10.3 mg/dL for 2 weeks in the evaluation period in a time frame up to 24 weeks. The primary endpoint was met with a 77.8% result, which exceeds the threshold set in the protocol.

KHK7580 was also granted Orphan Drug Designation for the treatment of hypercalcemia in patients with parathyroid carcinoma or primary hyperparathyroidism who are unable to undergo parathyroidectomy or relapse after parathyroidectomy by the MHLW on March 4, 2019.

“We are delighted to submit the supplemental application for evocalcet,” said Mitsuo Satoh, Ph.D., Head of Research and Development Division of Kyowa Hakko Kirin. “As it was granted Orphan Drug Designation by the MHLW, we believe that evocalcet has the potentials to provide more efficient treatment for hypercalcemia patients with parathyroid carcinoma and primary hyperparathyroidism.”

The Kyowa Hakko Kirin Group companies strive to contribute to the health and well-being of people around the world by creating new value through the pursuit of advances in life sciences and technologies.

***1. About KHK7580 (evocalcet)**

KHK7580 is a small molecular compound and a novel type of calcimimetics discovered by Mitsubishi Tanabe Pharma Corporation (President & Representative Director, CEO: Masayuki Mitsuka, "Mitsubishi Tanabe Pharma"). Kyowa Hakko Kirin signed a license agreement of KHK7580 with Mitsubishi Tanabe Pharma for the rights to cooperative research, develop, market and manufacture the product in Japan and some parts of Asia in March 2008. On March 2018, Kyowa Hakko Kirin received approval of KHK7580 for secondary hyperparathyroidism in maintenance dialysis patients and later on May 2018, the product was launched in Japan market, named Orkedia® Tablets.

***2. About Hypercalcemia in patients with parathyroid carcinoma or primary hyperparathyroidism under inability parathyroidectomy or relapse after parathyroidectomy**

Parathyroid carcinoma and primary hyperparathyroidism (PHPT) are diseases in which serum calcium levels elevates due to over autonomous secretion of parathyroid hormone (PTH) from tumors of the parathyroid gland. Parathyroidectomy (PTx) is the only reliable method to treat parathyroid carcinoma and PHPT. Control of hypercalcemia can prove challenging in cases of PHPT where PTx cannot be considered because of

concomitant diseases or where PHPT recur after PTx and parathyroid carcinoma, although patients with such hypercalcemia are very rare. Hypercalcemia causes symptoms of fatigue, polyuria, thirst, and renal impairment and severe hypercalcemia can result in death due to a hypercalcemic crisis.