

## **Kyowa Hakko Kirin Announces Top-Line Results of Japanese Phase 3 Clinical Study of ARQ197 (tivantinib) in Hepatocellular Carcinoma**

Tokyo, Japan, March 27, 2017 --- Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, President and CEO: Nobuo Hanai, "Kyowa Hakko Kirin") announced today that the top-line results of a Japanese Phase 3 study of ARQ 197 (generic name: tivantinib) did not meet its primary endpoint.

JET-HCC is a randomized, double-blind placebo-controlled study in Japan, to evaluate the efficacy and safety of tivantinib in the patients with c-Met diagnostic-high inoperable hepatocellular carcinoma with a history of prior sorafenib therapy.

The primary endpoint is progression-free survival (PFS), and the top-line results did not show a significant difference in PFS, between the tivantinib group and the placebo group. In terms of safety, the results showed that the safety profiles were similar as previously observed, and a novel safety issue was not found.

The details of the study results will be presented at upcoming scientific congresses and/or in scientific journals.

"I sincerely thank all of the patients, their families, and all of the personnel who contributed to completing this Japanese study of tivantinib." said Mitsuo Satoh, Executive Officer, Vice President, Head of R&D Division of Kyowa Hakko Kirin. "The result was disappointing, but Kyowa Hakko Kirin has gained great experiences in oncology fields through this study."

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.

### < Outline of the study design >

Target disease	Patients with c-Met diagnostic-high inoperable hepatocellular carcinoma with a history of prior sorafenib therapy,
Design	Multi-center, randomized, double-blind, placebo-controlled study
Dose	One tablet of the study drug (tivantinib 120 mg, or placebo) is daily administered to the subjects of each group twice in a day
Subject Number	approximately 190
Primary endpoint	Progression-free survival
Study Location	Japan

### **About ARQ197 (tivantinib)**

Tivantinib, an oral agent whose molecular target is c-MET, was discovered by ArQule, Inc. (NASDAQ: ARQL). Kyowa Hakko Kirin signed a license agreement with ArQule for the exclusive rights to the development and sales of tivantinib in Japan and some parts of Asia (China, Korea, and Taiwan) on April 27th, 2007.

**About c-Met**

c-Met is receptor tyrosine kinase. When abnormally activated, the c-Met receptor tyrosine kinase plays multiple roles in aspects of human cancer, including cancer cell growth, survival, angiogenesis, invasion and metastasis.

**About Kyowa Hakko Kirin**

Kyowa Hakko Kirin Co., Ltd. is a research-based life sciences company, with special strengths in biotechnologies. In the core therapeutic areas of oncology, nephrology and immunology/allergy, Kyowa Hakko Kirin leverages leading-edge biotechnologies centred on antibody technologies, to continually discover innovative new drugs and to develop and market those drugs world-wide. In this way, the company is working to realise its vision of becoming a Japan-based global specialty pharmaceutical company that contributes to the health and wellbeing of people around the world.

You can learn more about the business at: [www.kyowa-kirin.com](http://www.kyowa-kirin.com).

**About ArQule**

ArQule is a biopharmaceutical company engaged in the research and development of targeted therapeutics to treat cancers and rare diseases. ArQule's mission is to discover, develop and commercialize novel small molecule drugs in areas of high unmet need that will dramatically extend and improve the lives of our patients. Our clinical-stage pipeline consists of five drug candidates, all of which are in targeted, biomarker-defined patient populations, making ArQule a leader among companies our size in precision medicine. ArQule's proprietary pipeline includes: ARQ 087, a multi-kinase inhibitor designed to preferentially inhibit the fibroblast growth factor receptor (FGFR) family, in phase 2 for iCCA and in phase 1b for multiple oncology indications; ARQ 092, a selective inhibitor of the AKT serine/threonine kinase, in phase 1 for multiple oncology indications as well as ultra-rare Proteus syndrome, in partnership with the National Institutes of Health (NIH); ARQ 751, a next generation AKT inhibitor, in phase 1 for patients with AKT1 and PI3K mutations; and ARQ 761, a  $\beta$ -lapachone analog being evaluated as a promoter of NQO1-mediated programmed cancer cell necrosis, in phase 1/2 in multiple oncology indications in partnership with the University of Texas Southwestern Medical Center. In addition, we have advanced ARQ 531, an investigational, orally bioavailable, potent and reversible inhibitor of both wild type and C481S-mutant BTK, through toxicology testing and plan to initiate a phase 1 trial by the third quarter of 2017. ArQule's most advanced product tivantinib (ARQ 197), an oral, selective inhibitor of the c-MET receptor tyrosine kinase, that recently completed two phase 3 trials in second-line treatment of MET-overexpressing hepatocellular carcinoma in partnership with Daiichi Sankyo in the West and Kyowa Hakko Kirin in Asia. ArQule's current discovery efforts are focused on the identification and development of novel kinase inhibitors, leveraging the Company's proprietary library of compounds. You can follow us on [Twitter](#) and [LinkedIn](#).