

March 11, 2021

Investigator-Initiated Clinical Trial of Tamibarotene for Pancreatic Cancer Led by Nagoya University Approved as an Awarded Grant of the AMED Program; Promoting Clinical Trials for Development of New Drugs

We are pleased to announce that on March 8, 2021, the Japan Agency for Medical Research and Development (AMED) approved the “Development of stromal initialization therapy for pancreatic cancer using a domestically produced existing drug with a new indication and implementation of phase I/II investigator-initiated clinical trials” as a project of “2-(2) Investigator-initiated clinical trials (drugs with new indications or drugs with new dosage and administration)” in the AMED program of Promoting Clinical Trials for Development of New Drugs. Professor Mitsuhiro Fujishiro of the Department of Gastroenterology and Hepatology, Graduate School of Medicine, Nagoya University leads the project as the principal investigator.

Tamibarotene (AM80), a drug owned by our consolidated subsidiary TMRC Co., Ltd. (hereinafter, “TMRC”), will be used as an existing drug in Japan in this investigator-initiated clinical trial, and examined for its potential as an innovative treatment for pancreatic cancer. Our company and TMRC will provide the investigational product for a fee, and obtain and provide safety information on the investigational product.

The adoption by the AMED means that we will be granted research support (grant-in-aid) with smooth implementation of the investigator-initiated clinical trial over 4 years, the duration of this project (from 2021 to 2025).

Pancreatic cancer has the worst prognosis of all gastrointestinal malignancies, and its poor prognosis is attributable to resistance to anticancer drugs as well as the difficulty of early detection. The most distinctive feature of pancreatic cancer is that the stroma, of which cancer-associated fibroblasts (CAF) are a major component, accounts for about 90% of the tumor, and abundant stroma inhibits the penetration of anticancer drugs, resulting in anticancer drug resistance. Professor Atsushi Enomoto and his colleagues at the Department of Pathology, Nagoya University Graduate School of Medicine have found in previous studies

using model animals, etc. that cancer-promoting CAF can be initialized to cancer-restraining CAF (transformation) by the administration of tamibarotene, thereby softening stromal properties. This is expected to attenuate resistance to anticancer drugs, the biggest bottleneck for anticancer drug treatment in pancreatic cancer.

Our company and TMRC will offer as much cooperation as possible in the investigator-initiated clinical trial led by Professor Fujishiro at Nagoya University, and will think up and carry out various measures to maximize the value of tamibarotene, including this project, by utilizing the knowledge about this drug obtained to date.

End

For your info:

For the adoption results, please visit the AMED website.

Fiscal 2021 adopted proposals for the Project Promoting Clinical Trials for Development of New Drugs (1st Round of Public Offering) (disclosed on March 8, 2021)

https://www.amed.go.jp/koubo/11/03/1103C_00005.html

- Adoption category

Promotion of clinical research and clinical trials contributing to the development of drugs that meet patient needs

→ 2 "Promotion of clinical research and investigator-initiated clinical trials on drugs conducted based on protocols (or protocol synopses) already prepared [Implementation (Step 2)] Investigator-initiated clinical trials (drugs with new indications or drugs with new dosage and administration)"

→ (3) Investigator-initiated clinical trials (drugs with new indications or drugs with new dosage and administration)

- Research and development project

Development of stromal initialization therapy for pancreatic cancer using a domestically produced existing drug with a new indication and implementation of phase I/II investigator-initiated clinical trials

- Principal investigator and affiliation

Professor Mitsuhiro Fujishiro

Department of Gastroenterology and Hepatology, Nagoya University Graduate School of Medicine

- Persons in charge of research and development (Note: Those not directly related to our company are omitted.)

Shuzo Watanabe, Director and Executive Vice President, RaQualia Pharma Inc.

Hisao Yokumoto, Advisor, TMRC Co., Ltd.