

June 21, 2018  
Ohara Pharmaceutical Co., Ltd.

## **License Agreement on Novel Liver Cirrhosis Treatment**

Ohara Pharmaceutical Co., Ltd. (Head office: Shiga, Japan; CEO: Seiji Ohara; hereinafter, “Ohara”) has entered into a license agreement dated May 24, 2018 concerning the novel compound PRI-724 with PRISM Pharma Co., Ltd. (Head office: Kanagawa, Japan; President & CEO: Dai Takehara; hereinafter, “PRISM”).

Following the execution of this agreement, Ohara obtained the exclusive right to develop, manufacture and market injectable forms of PRI-724 for liver cirrhosis and other fibrotic diseases in Japan, as well as a first refusal right for the Asian region. Ohara will also pay PRISM an upfront payment, development milestone fees and sales-based royalty payments for PRI-724.

Below is a summary of the background to the consummation of this license agreement between Ohara and PRISM:

Approximately 60% of liver cirrhosis cases in Japan are caused by hepatitis C virus (HCV) infections. In recent years, we have observed an increase in the use of direct-acting antiviral agents, which is making it possible to eliminate HCV. However, the improvements of fibrosis following the elimination of HCV still takes significant time, during which time many patients’ QOL is significantly compromised due to complications such as carcinogenesis.

Amid the current absence of any approved drugs for the treatment of hepatic fibrosis or cirrhosis, PRI-724 was shown to have an inhibitory effect on the development of fibrosis and a fibrolytic effect on HCV liver cirrhosis based on an investigator-initiated study conducted at the Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital. The study was conducted with the support of the Infectious Disease Practical Research Project (Research Program on Hepatitis) under the Acceleration Transformative research for Medical innovation (ACT-M) Basic Scheme sponsored by the Japan Agency for Medical Research and Development (hereinafter, “AMED”).

These findings demonstrate a possibility to contribute to the prognosis of patients with liver cirrhosis, therefore Ohara decided to develop PRI-724 with the expectation that it will provide an innovative treatment option for patients with liver cirrhosis and other fibrotic diseases.

An investigator-initiated study is expected to commence during the current fiscal year and will primarily be conducted at the Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, with development support

provided by Kyushu University Center, as Seeds C in the AMED Translational Research Strategic Promotion Program. Ohara plans to continue the development efforts initiated by PRISM for PRI-724, and is supported by many Japanese medical institutions, and will make efforts to promptly obtain the marketing authorization for PRI-724 for the treatment of liver cirrhosis caused by hepatitis B and C viruses infection.

Ohara is actively growing its development pipeline to address unmet medical needs in Japan, and this strategic alliance with PRISM is part of these efforts. Ohara will accelerate the development of PRI-724 products such that treatment options can be provided to patients suffering from this intractable disease.

[About Ohara Pharmaceutical Co., Ltd.]

Ohara Pharmaceutical Co., Ltd. is one of the few Japanese pharmaceutical companies that engage in both orphan drug and in generic drug business. Its 3-year “Challenge 2020” business plan commenced in fiscal 2018, with one key objective of this plan being to challenge and address unmet medical needs. The company develops and markets orphan drugs mainly in the field of pediatric oncology and is also operates an innovative generic drug business which takes careful consideration to prevent of medical accidents. Ohara Pharmaceutical plans to further expand these businesses into emerging countries, primarily in the Asian region.

[About PRISM Pharma Co., Ltd.]

PRISM Pharma Co., Ltd. is a venture company that owns a drug discovery basis consisting of a library of low-molecular new drug candidate compounds that inhibit protein-protein interactions (PPIs), constructed by utilizing peptidomimetic compound synthesis technology that was developed independently by the company. PRISM Pharma aims to discover unprecedented therapeutic agents for intractable diseases by regulating intracellular signal transduction, which had been difficult before, using its own low-molecule compounds. The company’s future policy is to work on the creation of a new pipeline for a new target following PRI-724, to treat more diseases by making active use of its own drug discovery basis.

For details, please visit: <http://www.prismbiolab.com/>

[About PRI-724]

PRI-724 is a compound created by PRISM Pharma Co., Ltd. It is a CBP/beta-

catenin antagonist that inhibits the activation of the Wnt/beta-catenin signaling pathway. PRI-724 was originally developed as an anticancer drug, but a study at the Tokyo Metropolitan Institute of Medical Science using a liver cirrhosis mouse model independently developed by the institute confirmed that PRI-724 has antifibrotic effects showing improvement in liver histology. Based on these findings, an investigator-initiated phase I clinical trial has been completed in patients with liver cirrhosis in Japan, at the Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, with the support of the Japan Agency for Medical Research and Development (AMED).

## [About AMED]

Under the “Plan for the Promotion of Medical R&D” established by the national government, AMED promotes R&D mainly based on nine integrated projects covering drug discovery and development, regenerative medicine, cancer, etc. By consistently conducting R&D from basic research through practical application, AMED aims to deliver its products to patients as soon as possible.

For details, please visit: <https://www.amed.go.jp/>. Please direct your inquiries on AMED programs to:

- Acceleration Transformative research for Medical innovation (ACT-M) Basic Scheme  
Division of Industrial-Academic Collaboration, Department of Industrial-Academic Collaboration  
TEL: 03-6870-2214 E-mail: [sangaku-i@amed.go.jp](mailto:sangaku-i@amed.go.jp)
- Infectious Disease Practical Research Project (Research Program on Hepatitis)  
Contact for Research Program on Hepatitis, Division of Infectious Disease Research, Department of Research Promotion  
TEL: 03-6870-2225 E-mail: [hepatitis@amed.go.jp](mailto:hepatitis@amed.go.jp)
- Translational Research Strategic Promotion Program  
Division of Clinical Research and Trials, Department of Clinical Research and Trials  
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