Notice regarding Approval of a Partial Change to the Marketing Authorization for Sodium Phenylbutyrate for Progressive Familial Intrahepatic Cholestasis (PFIC) Types 1 and 2

Tokyo, Japan — August 24, 2026 — OrphanPacific, Inc. (Head Office: Minato-ku, Tokyo; President and Representative Director: Megumi Hara; hereinafter "OrphanPacific") has been jointly developing sodium phenylbutyrate (brand name: Buphenyl®; hereinafter "Buphenyl") as a treatment for Progressive Familial Intrahepatic Cholestasis (PFIC) Types 1 and 2, together with the University of Tokyo, Osaka University, Kindai University, Juntendo University Hospital, and Miyagi Children's Hospital.

Buphenyl is commercialized in Japan by OrphanPacific under an exclusive license from Immedica.

OrphanPacific is pleased to announce that, based on the results of a series of clinical studies and an investigator-initiated clinical trial (*see Note 1), it has received approval from the Ministry of Health, Labour and Welfare to expand the indications for Buphenyl to include PFIC 1 and PFIC 2. Buphenyl has also received orphan drug designation for the anticipated indication of PFIC.

Buphenyl is currently used for the treatment of urea cycle disorders. Research led by Associate Professor Hisamitsu Hayashi of the Graduate School of Pharmaceutical Sciences, the University of Tokyo, identified a novel pharmacological action of Buphenyl in promoting bile secretion, suggesting its potential efficacy in PFIC 1 and PFIC 2. Subsequently, a series of clinical studies and an investigator-initiated clinical trial were conducted, confirming the efficacy and safety of Buphenyl in patients with PFIC 1 and PFIC 2.

With this approval, Buphenyl will provide a new pharmacological treatment option based on the underlying disease mechanism for patients with PFIC 1 and PFIC 2, for whom treatment options have previously been limited to symptomatic treatment and liver transplantation. OrphanPacific will continue to work closely with relevant stakeholders toward launch so that Buphenyl can be made available to patients with PFIC 1 and PFIC 2 and their families as soon as possible.

Note 1: Investigator-Initiated Clinical Trial

An investigator-initiated clinical trial is a clinical trial that is planned and conducted primarily by physicians or medical institutions rather than pharmaceutical companies. Such trials may help address unmet needs encountered in clinical practice, including the development of treatments for rare diseases for which commercial development by pharmaceutical companies can be challenging.

■ About Progressive Familial Intrahepatic Cholestasis (PFIC)

Progressive Familial Intrahepatic Cholestasis (PFIC) is a rare, inherited and intractable liver disease that typically develops in infancy or early childhood. The disease is characterized by impaired bile flow from the liver to the intestines, resulting in progressive symptoms such as jaundice, pruritus (itching), and liver dysfunction. Multiple causative genes have been identified, and abnormalities in these genes can lead to the development of PFIC. There are multiple types of PFIC, and the present approval of Buphenyl covers PFIC 1 and PFIC 2.

In Japan, PFIC is designated as an intractable disease (Disease Notification No. 338) under the Act on the Medical Care for Patients with Intractable Diseases. Current medical treatment is limited to symptomatic treatment, and liver transplantation may be required as the disease progresses. Given the significant burden that liver transplantation places on patients and their families, together with the substantial unmet medical need that remains in PFIC, new treatment options are highly anticipated.

■ About OrphanPacific, Inc.

OrphanPacific is a Japanese pharmaceutical company dedicated to the development, manufacturing, and marketing of drugs for rare diseases, thereby delivering new treatment options to patients with rare diseases. Our mission is “Bringing smiles and happiness to patients with rare diseases and their families.” With a commitment to “Leave No One Behind,” we are proactively engaged in the development and provision of therapies for rare diseases with extremely small patient populations.

OrphanPacific is a wholly owned subsidiary of CMIC Holdings (https://en.cmicgroup.com/?cl=navi), a pioneer and leading CRO (Contract Research Organization) in Japan. By leveraging the full breadth of CMIC Group’s expertise and experience in pharmaceutical development, manufacturing, and marketing, we strive to ensure that as many patients with rare diseases as possible have access to therapies. https://www.orphanpacific.com/en/

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