Notice regarding Designation as an Orphan Drug and Supplemental New Drug Application for Sodium Phenylbutyrate for Designated Intractable Disease "Progressive Familial Intrahepatic Cholestasis (PFIC)"

Tokyo, Japan — October 16, 2025 — OrphanPacific, Inc. (Head Office: Minato-ku, Tokyo; President and Representative Director: Megumi Hara; hereinafter "OrphanPacific") announced that sodium phenylbutyrate is being advanced as a potential new treatment for Progressive Familial Intrahepatic Cholestasis (PFIC), a rare and life-threatening liver disease that primarily affects children. Sodium phenylbutyrate was jointly developed with the University of Tokyo, Osaka University, Kinki University, Juntendo University Hospital, and Miyagi Children's Hospital. Based on the results of a series of clinical researches and investigator-initiated clinical trials (*see Note 1), sodium phenylbutyrate (Buphenyl®) has received orphan drug designation for the anticipated indication of PFIC, and OrphanPacific has submitted a supplemental new drug application to the Ministry of Health, Labour and Welfare to add PFIC as a new indication for Buphenyl®.

Buphenyl®, currently approved for the treatment of urea cycle disorders, has demonstrated a novel therapeutic effect: it promotes bile secretion. This discovery, led by researchers at the University of Tokyo, suggested that Buphenyl® could help address the underlying disease process in PFIC rather than only managing its symptoms.

Clinical researches and independent investigator-led trials confirmed both the efficacy and safety of Buphenyl® in PFIC patients. Based on these results, OrphanPacific is working toward regulatory approval to expand the drug's indications.

If approved, Buphenyl® would become the first treatment option to directly target the mechanisms of PFIC in Japan, offering a meaningful alternative to the current standards of care, which are limited to symptom management or liver transplantation.

■ About Progressive Familial Intrahepatic Cholestasis (PFIC)

PFIC is a rare and inherited liver disorder that typically appears in infancy or early childhood. The disease is caused by genetic mutations that disrupt the normal flow of bile from the liver to the intestines. This leads to a buildup of bile in the liver, resulting in symptoms such as persistent jaundice, severe itching, and progressive liver damage.

In Japan, PFIC is officially recognized as an intractable disease (Disease Notification No. 338) under the Act on the Medical Care for Patients with Intractable Diseases. Currently, treatment options are limited to managing symptoms, and in severe cases, liver transplantation may be necessary.

Note 1: Investigator-Initiated Clinical Trials

These are clinical trials that are planned and conducted primarily by physicians or medical institutions, rather than pharmaceutical companies. Such trials aim to address unmet medical needs in real-world clinical settings, including the development of treatments for rare diseases that are often difficult to commercialize through traditional industry-led approaches.

■ 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://www.cmicgroup.com/), 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/

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