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KYORIN and Acadia Pharmaceuticals Enter into Distribution Agreement for DAYBUE® STIX (Trofinetide) for Rett Syndrome in Japan

KYORIN Pharmaceutical Co., Ltd. announced today that it has entered into an exclusive distribution agreement with Acadia Pharmaceuticals Inc. (San Diego U.S., CEO: Catherine Owen Adams), for DAYBUE® STIX (generic name: trofinetide), a treatment for Rett syndrome for which Acadia holds the rights.

Under this agreement, KYORIN has obtained exclusive rights to commercialize trofinetide for Rett syndrome in Japan. KYORIN will make an upfront payment of USD 30 million to Acadia, along with milestone payments of up to USD 45 million upon NHI price listing and the achievement of certain net sales targets, and other payments.

Trofinetide is a synthetic analogue of GPE (glycine-proline-glutamate), an endogenous tripeptide derived from the N-terminal domain of IGF-1 (insulin-like growth factor 1), which plays an important role in the normal development and function of the nervous system. In the United States, it has been marketed since 2023 as DAYBUE and DAYBUE STIX for the treatment of Rett syndrome in adults and pediatric patients two years of age and older. In Japan, trofinetide has been granted Orphan Drug Designation, and Acadia has completed a Phase 3 clinical trial demonstrating results consistent with the U.S. LAVENDER study.

Based on the results of this Phase 3 clinical trial, KYORIN will submit an application for manufacturing and marketing approval in Japan on behalf of Acadia. Following NHI drug price listing, KYORIN will receive product supplies from Acadia and exclusively commercialize trofinetide in Japan.

KYORIN aims to create high-value new drugs that meet medical needs and has prioritized the “Expansion of development pipeline through in-licensing” under its medium-term vision, “Vision 110

－Stage2－". Through this agreement, we are committed to actively advancing development to deliver new treatment options to patients as soon as possible, thereby contributing to people's health.

The impact on the consolidated financial forecasts for the fiscal year ending March 31, 2027 is expected to be negligible. The upfront payment to Acadia under this agreement has already been factored into the full-year consolidated forecasts and is expected to be recorded as SG&A expenses (R&D expenses) in the third quarter of the current fiscal year.
There are no capital, personnel, or business relationships between Acadia and KYORIN, and neither party is considered a related party to the other.

[Reference]

About DAYBUE®

Trofinetide is a synthetic analogue of glycine-proline-glutamate (GPE), an endogenous tripeptide derived from N-terminal domain of insulin-like growth factor 1 (IGF-1), a hormone critical for the normal development and function of the nervous system. In patients with Rett syndrome, impairments in IGF-1 signaling and synaptic function in the brain are thought to affect neural function. Following its initial launch in the United States in 2023 as DAYBUE, indicated for the treatment of Rett syndrome in adults and pediatric patients two years of age and older, it was also launched in Canada and approved under the brand name DAYBU in the European Union. In addition, DAYBUE STIX, an oral powder formulation of trofinetide, was launched in the U.S. in 2026.

About LAVENDER™ study

LAVENDER study is a pivotal Phase 3, 12-week, double-blind, randomized, placebo-controlled study evaluating the efficacy and safety of trofinetide versus placebo in 187 girls and women 5 to 20 years of age with Rett syndrome. The primary endpoints were the change from baseline to week 12 in the RSBQ total score and the CGI-I score, both of which demonstrated statistically significant improvement over placebo. The key secondary endpoint, measuring the change from baseline to week 12 in the CSBS-DP-IT Checklist–Social composite score, also showed statistically significant results compared to placebo.

Ref.) NCT04181723, J L. Neul, et al., *Nature Medicine*, 29(6), 1468-1475 (2023)

RSBQ (Rett Syndrome Behavior Questionnaire): A 45-item rating scale completed by caregivers that assesses a range of symptoms of Rett syndrome, including general mod, breathing problems, hand behavior, and repetitive behaviors.

CGI-I (Clinical Global Impression-Improvement): A 7-point scale used by clinicians to assess whether symptoms have improved or worsened.

CSBS-DP-IT (Communication and Symbolic Behavior Scales Developmental Profile™ Infant Toddler): Standardized screening scale for assessing communication and pre-linguistic skills in young children 12-24 months and can be used with older children with developmental delay.

About Rett syndrome

Rett syndrome is a neurodevelopmental disorder primarily affecting the nervous system, with symptoms typically appearing in infancy and early childhood. In Japan, its prevalence is reported to be approximately 0.9 per 10,000 females, occurring almost exclusively in girls. Children with Rett syndrome generally exhibit apparently normal development until approximately 6 to 18 months of age, followed by developmental delay or stagnation. This is typically followed by a "regression phase," in which children lose previously acquired communication skills and purposeful hand function. Subsequently, they may enter a "plateau phase," during which a slight recovery in cognitive interest can be observed, while motor function remains severely impaired. As individuals age, motor function further deteriorates, with reduced movement, muscle wasting in the limbs due to disuse, and the eventual need for a wheelchair. Muscle tone increases and involuntary movements known as dystonia may become prominent, which can persist throughout their lifetime.

Approximately 95% of Rett syndrome cases are caused by mutations in the methyl-CpG-binding protein 2 (MECP2) gene. Preclinical studies suggest that MeCP2 protein dysfunction leads to synaptic impairment, and these synaptic deficits may be associated with the symptoms of Rett syndrome. Symptoms also include the emergence of characteristic repetitive movements known as stereotypies, such as hand-wringing and hand-clapping, as well as gait abnormalities, with many individuals requiring 24-hour care. Rett syndrome carries a substantial physical, psychological, social, and economic burden, significantly affecting QOL of both patients and their caregivers.

About Acadia Pharmaceuticals

Acadia is committed to turning scientific promise into meaningful innovation that makes the difference for underserved neurological and rare disease communities around the world. Its commercial portfolio includes the first and only FDA-approved treatments for Parkinson's disease psychosis and Rett syndrome. It is developing the next wave of therapeutic advancements with a robust and diverse pipeline that includes mid- to late-stage programs in Alzheimer's disease psychosis and Lewy body dementia psychosis, along with earlier-stage programs that address other underserved patient needs. Acadia is here to be their difference.

For more information, visit https://acadia.com/en-us

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