ACULYS

Press Release

October 18, 2023

Aculys Pharma, Inc.

Aculys Pharma delivers positive Phase 3 clinical study interim analysis result of a diazepam nasal spray: an antiepileptic drug for the treatment of epileptic seizures

- These results are from Japan's first domestic Phase 3 clinical trial of an intranasally administered antiepileptic drug for Japanese patients aged 6 to 17 for the treatment of status epilepticus or epileptic seizures that may lead to status epilepticus.
- The primary efficacy endpoint was met in a pre-specified interim analysis, and the drug was found to be safe and tolerable. No respiratory depression related adverse events causally related to the studied drug were observed.
- Based on the data obtained from the interim analysis of this study, Aculys plans to submit a New Drug Application for diazepam nasal spray.

Tokyo, Japan, January 24 2023 — Aculys Pharma, Inc., a clinical stage biopharmaceutical company focused on commercializing innovative treatments for neurological conditions, today announced that it has achieved its primary efficacy endpoint in a pre-specified interim analysis of its Phase 3 clinical study of a diazepam nasal spray (compound development code: NRL-1), an antiepileptic drug for the treatment of status epilepticus or epileptic seizures that may lead to status epilepticus targeting Japanese patients aged 6 to 17 years.

The study was designed to evaluate the clinical efficacy of diazepam nasal spray based on comprehensive evidence from efficacy, pharmacokinetic, safety, and tolerability data using multiple clinically relevant endpoints. Diazepam nasal spray is Japan's first nasally administered antiepileptic that has demonstrated efficacy and safety in Phase 3 clinical trials in Japan for the treatment of status epilepticus or epileptic seizures that may lead to status epilepticus.

The study demonstrated the drug’s effectiveness regarding its primary endpoint, which was the proportion of patients who achieved resolution of clinically relevant seizures within 10 minutes after administration of a single dose and who remained free from seizures or convulsions for 30 minutes after a single dose. Additionally, no adverse events leading to medication discontinuation or serious adverse events causally related to the study drug were observed, and no adverse events

related to respiratory depression were observed.

Based on the data obtained from the interim analysis of the Phase 3 clinical trial, Aculys Pharma intends to submit a New Drug Application for diazepam nasal spray as the first intranasally administered antiepileptic drug in Japan to meet the urgent treatment needs of patients with recurrent epileptic seizures. Aculys Pharma also plans to present the results of this interim analysis at an upcoming Japanese medical conference.

“Many epilepsy patients are able to lead normal social lives with appropriate treatment, but those who have difficulty controlling their seizures with medication are living with the anxiety of seizures that could occur anywhere and at any time.” said Kazunari Tsunaba, President and Representative Director of Aculys Pharma. “We believe that access to emergency treatment that is convenient and easy for non-medical personnel to use appropriately in the event of a seizure, in addition to being effective and safe, will help reduce the emotional burden on patients and their caregivers, as well as the risk of sequelae due to prolonged seizures. Intranasal anticonvulsants, which are easy for families and caregivers to administer to patients with epileptic seizures, have been approved in the U.S. since 2020 and are widely used there. In our efforts to eliminate the problems of drug lag and drug loss, we will continue to work with medical professionals and regulatory authorities to promote our business in order to bring innovative treatments and hope to patients with recurrent seizures and their caregivers as soon as possible.”

In addition to developing innovative drugs, Aculys Pharma is also working with external partners to identify issues and challenges for people with epilepsy in Japan. The data obtained through such surveys will help to improve the healthcare delivery system for epilepsy seizures in the future, as well as promoting the creation of an ecosystem to address epileptic seizures in the community as a whole. Aculys Pharma will continue to contribute to Japanese society by identifying medical care issues from a social perspective, utilizing the latest digital technologies to solve these issues, and proactively utilizing external partnerships to provide new means of medical care.

*****

About diazepam and diazepam nasal spray

Diazepam has been used in Japanese medical practice for about 60 years as a treatment for epileptic seizures in the form of injections and other forms. It is also administered as a suppository by non-medical personnel, such as patients and caregivers, outside medical institutions.
Diazepam nasal spray was developed by the U.S. pharmaceutical company Neurelis, Inc. Aculys Pharma holds an exclusive license to develop and commercialize this treatment in Japan and the Asia-Pacific region*(excluding Greater China and Singapore). In 2020, the FDA approved Neurelis’ VALTOCO® (diazepam nasal spray) as acute treatment of intermittent, stereotypic episodes of

frequent seizure activity (ie, seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older. In June 2023, China's National Medical Products Administration (NMPA) approved diazepam nasal spray as effective for the same indication.
(*Asia-Pacific region: Australia, Brunei, Cambodia, Indonesia, South Korea, Laos, Malaysia, Myanmar, New Zealand, Philippines, Thailand, Vietnam)

About epilepsy

Epilepsy is a chronic brain disorder that causes loss of consciousness and/or convulsions (epileptic seizures) as the result of excessive electrical excitation of nerve cells (neurons) in the brain. An estimated 600,000 to 1,000,000, or 5 to 8 in 1,000 people in Japan have epilepsy.[1,2] As treatment has advanced, many people with epilepsy are able to control their seizures with proper diagnoses and antiepileptic medications and are able to lead normal social lives; however, about 30% of patients, as well as their families and caregivers, still need to deal with frequent, repeated seizures.[1,2]

The causes, symptoms, and severity of epilepsy vary greatly from one individual patient to another, and similarly, epileptic seizures are diverse in nature from patient to patient. Among the diverse seizure types, some people experience seizures that recur many times a day or that do not terminate after a certain period of time (status epilepticus). These patients are at increased risk of brain damage and reduced life expectancy.[1] When repetitive seizures occur, people with epilepsy must seek emergency treatment by healthcare professionals. On average, in Japan it takes 20~40 minutes from the time an emergency call is placed until a person is transferred to a hospital for treatment.[3] An extensive overseas survey of patients, their families, and physicians has reported that recurrent epileptic seizures cause significant emotional, social, and financial burdens on patients and their families.[4]

About Neurelis, Inc.

Neurelis, Inc., is a neuroscience company focused on the development and commercialization of therapeutics for the treatment of epilepsy and orphan neurologic disorders characterized by high unmet medical needs. For more information about Neurelis, please visit www.neurelis.com.

About Aculys Pharma

Aculys Pharma is a clinical stage biopharmaceutical company that is pioneering ways to eliminate drug lag/drug loss in Japan, and is working to resolve social issues related to neurological and psychiatry diseases. Its corporate name was created from the philosophy of serving as a "Catalyst to Access." Aiming to act as a bridge for innovative medical care in the field of neuropsychiatry, Aculys Pharma develops and commercializes novel pharmaceuticals and provides innovations for

better medical care to patients, their families, healthcare professionals, and society.

Company name: Aculys Pharma, Inc.
Address: 6F, the ARGYLE aoyama, 2-14-4 Kita-Aoyama, Minato-ku,Tokyo, Japan
Representative: Kazunari Tsunaba
Established: Jan 2021
URL: https://aculys.com/en/

Information concerning pharmaceutical product (compound under development) contained herein is not intended as advertising or as medical advice, but intended for disclosure of management information.

Sources:

1. Epidemiological survey on the prevalence, diagnosis, and treatment of epilepsy and issues to be solved to establish a healthcare system for the disease, 2013 https://mhlw-grants.niph.go.jp/project/22749 (Japanese only) (Accessed on Oct 5, 2023)
2. Kwan P., Brodie, M.J. Early identification of refractory epilepsy. N. Engl. J. Med., 2000 Feb 3; 342(5): 314–9.
3. Treatment guidelines for pediatric status epilepticus & pediatric convulsive status epilepticus 2023 (Japanese Society of Child Neurology) (Japanese only)
4. Penovich, P.E., Buelow, J., Steinberg, et al. Burden of seizure clusters on patients with epilepsy and caregivers survey of patient, caregiver, and clinician perspectives. *The Neurologist*. 2017; 22: 207–214.

[Media Contact]

Aculys Pharma Communications Office (within Cosmo Publication Relations Corporation)

aculys_pr@cosmopr.co.jp

Yuka Kayashima, Aculys Pharma ykayashima@aculys.com

Mika Shirai, Aculys Pharma mshirai@aculys.com