Epilepsy Portfolio

At Neurocrine Biosciences, our epilepsy portfolio consists of investigational therapies targeting rare and common epilepsies with high unmet need that may benefit from precision treatment.

Overview

Epilepsy

Epilepsy is one of the most common neurological disorders, affecting more than 65 million people worldwide.[1] Epilepsy can affect anyone at any age, but is more common in young children or older adults and is characterized by abnormal electrical activity in the brain that leads to seizures. Seizures can be unpredictable and can vary in frequency, from less than one per year to several per day.

Seizures can appear as:

- Brief lapses of attention
- Brief episodes of involuntary movements in part of the body
- Prolonged convulsions of the entire body

Epilepsy Fast Facts:

Seizures

At least **3.4 million people** in the U.S. live with seizures, including **470,000 children.**[2]

Pediatric Epilepsy

Children living with a rare pediatric epilepsy are at **higher risk** of **sudden unexpected death in epilepsy (SUDEP)** and have few or **limited treatment options.**[3–6]

Rare pediatric epilepsies affect fewer than **200,000 children** in the U.S.[7] They can differ in cause, seizure type, and severity.

Rare and Common Epilepsies

Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep (EE-CSWS)

EE-CSWS is a rare pediatric epilepsy syndrome characterized by onset of seizures with a unique electroencephalographic (EEG) pattern referred to as electrical status epilepticus in sleep (ESES). Cognitive stagnation and regression develop one to two years after onset. There is currently no approved treatment for EE-CSWS. Following puberty, seizure frequency tends to decline, however developmental delays often remain.

SCN8A Developmental and Epileptic Encephalopathy (SCN8A-DEE)

SCN8A-DEE is a rare pediatric epilepsy syndrome associated with a genetic mutation of the *SCN8A* gene. It is characterized by severe epilepsy, early onset developmental delay, cognitive impairment, and other medical challenges. Seizures begin at a median age of four months and are highly refractory to currently available antiseizure medication. Over 90% of children with SCN8A-DEE are non-verbal, and half are not ambulatory. There are currently no approved therapies for this form of pediatric epilepsy.

Focal Onset Seizures (FOS)

Focal onset seizures, previously referred to as partial-onset seizures, are the most common type of seizures in adults. They start in one area of the brain and can involve involuntary movements with alteration or loss of awareness that can last up to several minutes. These seizures can interfere with activities of daily living and negatively impact quality of life.

Less than **2%** **of children** living with epilepsy have **EE-CSWS** worldwide.[7]

SCN8A mutations are estimated to cause less than **1,000 cases** of epilepsy worldwide.[8]

Over **50%** of the **45 million people** living with active epilepsy worldwide have **focal onset seizures.**[9]

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NBI-827104

Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep

Status: Ongoing Phase 2 study

NBI-827104 is an investigational, selective, orally active, brain penetrating T-type calcium channel blocker (Ca_v 3.1, Ca_v 3.2, Ca_v 3.3) currently under development for the potential treatment of epileptic encephalopathy with continuous spike-and-wave during sleep (EE-CSWS).

We are conducting the STEAMBOAT™ Phase 2 double-blind study to assess the safety, tolerability, and pharmacokinetics of NBI-827104 in pediatric patients with EE-CSWS. Neurocrine Biosciences has received Orphan Drug Designation and Rare Pediatric Disease Designation from the U.S. Food and Drug Administration (FDA) for NBI-827104 in EE-CSWS.

For more information about the STEAMBOAT Phase 2 study, please visit **SteamboatStudy.com** and **ClinicalTrials.gov.**

Neurocrine Biosciences acquired the exclusive rights to NBI-827104 from Idorsia Pharmaceuticals Ltd

NBI-921352

NBI-921352 is an investigational, selective sodium channel inhibitor (Na_v1.6) currently under development for the potential treatment of SCN8A developmental and epileptic encephalopathy (SCN8A-DEE) in children and adults, and focal onset seizures in adults.

NBI-921352 for SCN8A Developmental and Epileptic Encephalopathy

Status: Ongoing Phase 2 study

We are currently conducting the KAYAK™ Phase 2 study of NBI-921352 as an adjunctive therapy in children and young adults living with SCN8A-DEE.

Neurocrine Biosciences has received Orphan Drug Designation and Rare Pediatric Disease Designation from the U.S. Food and Drug Administration (FDA) for NBI-921352 in SCN8A-DEE.

For more information about the KAYAK Phase 2 study, please visit **KayakStudy.com** and **ClinicalTrials.gov**.

NBI-921352 for Focal Onset Seizures in Adults

Status: Ongoing Phase 2 study

We are currently conducting a Phase 2 clinical study of NBI-921352 in adult patients with focal onset seizures.

For more information about the Phase 2 study of NBI-921352 for focal onset seizures, please visit **ClinicalTrials.gov**.

Neurocrine Biosciences licensed worldwide rights to NBI-921352 from Xenon Pharmaceuticals, Inc.

References

1. Epilepsy Foundation. Who gets epilepsy? Accessed Feb. 1, 2022. https://www.epilepsy.com/learn/about-epilepsy-basics/who-gets-epilepsy. **2.** Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy — United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2017;66:821–25. doi:10.15585/mmwr.mm6631a1. **3.** Johannesen KM, et al. Early mortality in SCN8A-related epilepsies. Epilepsy research. 2018;143:79-81. doi:10.1016/j.eplepsyres.2018.04.008. **4.** Gardella E, Møller RS. Phenotypic and genetic spectrum of SCN 8A-related disorders, treatment options, and outcomes. *Epilepsia.* 2019;60:S77-85. doi:10.1111/epi.16319. **5.** Meisler MH, et al. SCN8A encephalopathy: research progress and prospects. *Epilepsia.* 2016;57(7):1027-35. doi:10.1111/epi.13422. **6.** Kløvgaard M, et al. Epilepsy-related mortality in children and young adults in Denmark: a nationwide cohort study. *Neurology.* 2022;98(3):e213-24. doi: 10.1212/WNL.0000000000013068.]. **7.** NIH. FAQs about rare diseases. Accessed Feb. 1, 2022. https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases. **8.** Data on file. Neurocrine Biosciences. **9.** Fiest KM, et al. Prevalence and incidence of epilepsy, A systematic review and meta-analysis of international studies. *Neurology.* 2017 Jan 17; 88(3):296-303. doi:10.1212/WNL.0000000000003509.

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