Neurocrine Biosciences, Inc.
SCN8A Phase 2 Kayak™ Clinical Study
Sentinel Cohort FAQ

SENTINEL COHORT:
The DEE2012 "KAYAK" study will enroll in two parts: a Sentinel Cohort of 8 participants and a Main Cohort of up to 52 participants. There will be a pause in participants screening and enrollment for data analysis by an independent data monitoring committee (DMC) and any needed protocol amendments following the full enrollment of the Sentinel Cohort.

- **What is the Sentinel Cohort and why do we need it?**

The first 8 participants enrolled in study DEE2012 will make up something called the Sentinel Cohort. Once these 8 participants are enrolled, there will be a pause on further screening and enrollment.

After all the Sentinel Cohort participants have reached their maximum dose of investigational study drug, an independent data monitoring committee (or DMC for short) will review their accumulated safety, tolerability (the degree to which the study drug is tolerated), and pharmacokinetic (PK) data (how the study drug is absorbed, distributed, and broken down in the body).

The DMC is comprised of experts in pediatric neurology and epilepsy. They will look at the safety and tolerability data and will check that the doses we are testing are being distributed in the body in the way we originally anticipated based on previous studies in animals and healthy adults.

- **Are Sentinel Cohorts a normal part of clinical trials?**

Sentinel Cohorts are common in pediatric studies, particularly those where the conditions being treated are so rare. (Less than 450 SCN8A-DEE participants have been diagnosed in the U.S., and less than 1,000 cases have been diagnosed worldwide[1]). Being able to have an independent DMC review the safety, tolerability and pharmacokinetic (PK) data from the Sentinel Cohort gives us the confidence that we are using the right doses and dosing schedule in the main part of the study.

- **What happens exactly when we pause the trial?**

During the pause between the Sentinel and Main Cohorts, the independent DMC will review the safety, tolerability, and pharmacokinetic (PK) data from the Sentinel Cohort and provide its recommendation, which may include continuing the study without modification; making changes to trial design; or ending the study. This type of review is a common practice in many clinical studies.

During the pause, clinical trial sites will not be able to screen or randomize any additional participants into the DEE2012 trial. However, Sentinel Cohort participants will be able to

[1] Data on file. Neurocrine Biosciences

continue in the DEE2012 study and upon completion, will have the option to enroll in the extension study.

Although screening and enrollment will be closed during the pause, trial sites may continue to identify potential participants for later screening in the Main Cohort that will enroll up to 52 participants. During this time, families can continue to register interest on kayakstudy.com for future enrollment evaluation.

- **How long is the pause expected to take?**

The duration of the pause will be determined by the time needed to analyze the data and to incorporate adjustments to study procedures if needed. Protocol amendments may be prompted by the DMC review or may be initiated by Neurocrine Biosciences, Inc., based on learnings from the Sentinel Cohort. Any protocol amendment must be submitted to regulatory agencies such as the FDA, and institutional review boards (IRB) for review.

- **What are possible types of changes to the trial that can result from the DMC review?**

Based on the recommendations of the DMC, it is possible that changes will be made to the trial including changes in the dosing of study drug or study assessments. Any changes would need to be reviewed by appropriate regulatory agencies (e.g., the FDA) and an institutional review board (IRB) prior to implementation.

- **What's the difference between the Sentinel Cohort and the Main Cohort?**

The Sentinel Cohort will be enrolled only in the U.S. and will include the first 8 participants. Data from the Sentinel Cohort participants will be reviewed for safety, tolerability, and pharmacokinetics (PK) prior to opening enrollment in the Main Cohort.

The Main Cohort is planned to enroll up to 52 participants in North America, Australia, and Europe.

TRAVEL SUPPORT:
If an individual qualifies to participate in this clinical trial, study-related medical exams and study-related laboratory tests will be performed at no cost to them. Compensation for travel or lodging support may also be available. For sites that have agreed to use it, a travel service is being provided to assist with booking flights, rail, car rentals, taxis, wheelchair vans, lodging, etc.

- **What travel support is available for my specific situation?**

Neurocrine supports participants and their families through participating study sites by offering financial, logistic, and travel options to ease the burden associated with attending study visits, including the screening visit. Please speak with your site about available options and don't hesitate to request the accommodations your family needs.

Neurocrine continues to monitor its travel support policy and offerings based on community needs expressed by patient advocacy leaders and feedback from participating study sites.