# STK-001 for Dravet Syndrome - Frequently Asked Questions
## *April 2021*

**What is STK-001?**

STK-001 has been developed to treat genetic disorders where someone has one healthy copy of a gene and one mutated copy, as is the case in *SCN1A*-related Dravet Syndrome. If there's only one functional copy of *SCN1A* then it may produce too little protein for the brain to work as it should, causing seizures, intellectual disabilities and a range of other conditions. STK-001 works by helping the functional gene to increase protein production, with the aim of restoring protein levels to near normal levels, and hopefully in doing so addressing the underlying causes of Dravet Syndrome.

**How is STK-001 given to patients?**

STK-001 is not like traditional daily anti-seizure medications. It is not given orally and dispersed throughout the bloodstream and brain. Instead, it targets the specific cells that need it, namely neurons that produce a certain type of sodium channel made from the gene *SCN1A*. STK-001 is administered directly to the fluid surrounding the brain via a lumbar puncture (spinal tap) at an anticipated frequency of 2-3 times per year.

**What does STK-001 mean for the future treatment of Dravet Syndrome?**

STK-001 targets the underlying problem caused by the mutation and has the potential to be the first disease-modifying therapy for Dravet Syndrome, with the aim of treating both seizures and the other comorbidities associated with the condition. However, it is not anticipated to be a one-time treatment or a cure. Whilst this is an encouraging development, recruitment to the trials is some months away and this is very much a first step in finding out how safe and effective STK-001 will be for the future treatment of Dravet Syndrome.

**What data is available so far about STK-001?**

STK-001 significantly decreased seizure frequency and increased survival in a mouse model of Dravet Syndrome. STK-001 has also been tested in healthy non-human primates and shown to increase the Nav1.1 sodium channel without any adverse effects on the animals

The highlights most relevant to our community include:

***Mouse Data***

- When given to mice with Dravet Syndrome on the 2nd day after birth, 97% of the animals survived to Day 90, compared to only 23% survival in non-treated mice.
    - 80% reduction in spontaneous seizures between Day 22 and 46

    - 76% of treated mice were seizure free, compared to 48% of the non-treated mice.
    - No adverse effects of increasing sodium channels above "normal" levels
- When given to mice with Dravet 14 days after birth, closer to when seizures begin, 65% of the animals survived.
- No data suggest that STK-001 makes the condition *worse,* considering nearly 2/3 of the animals die without any treatment.

***Non-human Primates (NHPs)***

- Non-human primate data are on healthy primates, not animals with Dravet Syndrome, but show up to a 3-fold increase in sodium channel levels in all parts of the brain that express *SCN1A.*
- No observed adverse events at highest dose tested
- No change in platelet counts or renal/hepatic function
- No adverse histopathology in brain, liver or kidney

These preclinical data are encouraging, but mice are not tiny humans, and healthy non-human primates are not Dravet patients. Safety will be the primary focus as Stoke moves from animals to humans.

**What do we know about the planned UK study (called 'ADMIRAL'?)**

The ADMIRAL study is a Phase 1/2a open-label study of children and young people aged 2 to up to 18 who have a diagnosis of Dravet Syndrome and evidence of a genetic mutation in the SCN1A gene.

The primary objectives for the study are to assess the safety and tolerability of multiple doses of STK-001, as well as to characterise human pharmacokinetics.

A secondary objective is to assess the effect of multiple doses of STK-001 as an adjunctive anti-seizure treatment with respect to the percentage change from baseline in convulsive seizure frequency over a 24-week treatment period. Stoke also intends to measure non-seizure aspects of the disease, such as overall clinical status and quality of life, as secondary endpoints.

Stoke plans to enrol approximately 22 patients in the study across multiple sites in the UK. More information can be found here.

**How will study participants be selected for ADMIRAL? Can we apply?**

Clinical trials will be open to a small number of children and young people with *SCN1A*-related Dravet Syndrome, aged 2-17 years. Professor Helen Cross, Chair of DSUK's Medical Advisory Board, is confirmed as the study's lead investigator. Recruitment to ADMIRAL is some months away and we will share more information as it becomes available.

**What do we know about the ongoing US study (called 'MONARCH')?**

Enrolment and dosing are currently ongoing in the US MONARCH study. Overall, Stoke plans to enrol approximately 48 patients in the study across 20 sites in the US. The study design

for MONARCH is similar to the ADMIRAL study (see above). MONARCH is expected to conclude in late 2022.

**When will STK-001 be available outside clinical trials?**

Because clinical trials (phase 1/2a) are currently ongoing for STK-001, it is too early to speculate about future availability, timelines for further phase 2 or 3 clinical trials, inclusion of adult patients, availability, or cost. If the treatment proves safe (first) and effective (second) in the ongoing clinical trials in children and young people with Dravet Syndrome, Stoke is committed to expanding access to those who need it as quickly as possible.