PARTICIPANT INFORMATION SHEET
For carers of children/adults with CTNNB1 syndrome

The Dragonfly Study
An international, prospective, longitudinal, observational study of the natural course of disease in children and adults with CTNNB1 developmental neurological syndrome.

This study is being conducted across several countries, with ongoing participation in Slovenia, Spain, Brazil, the USA, and Australia. The global reach of the study enables us to gather diverse data and develop a comprehensive understanding of CTNNB1 syndrome across different populations and healthcare systems.

You and your child are invited to participate in a study that aims to define the **symptoms, signs and natural course of CTNNB1 neurodevelopmental syndrome**. Before consenting to take part in the study, we would like you to take time to read the following information about the study so that you can make an informed decision about whether or not you and your child/dependent choose to take part.

What is the purpose of the study?

The aim of this study is to gain a comprehensive understanding of the **mental, physical and social development of children and adults with CTNNB1 neurodevelopmental syndrome** and how their symptoms and abilities change over time. The study will also provide a baseline against which future studies can compare the development of children treated with disease-modifying drugs.

Does my child/dependent have to take part?

You and your child/dependent's participation is entirely **voluntary.** If you decide to participate in this study, you can withdraw your consent at any time. Withdrawing from the study will not impact your child/dependent's routine medical care.

What will happen if I consent on behalf of my child/dependent to join the study?

To accommodate families from many countries, we will offer you the opportunity to discuss the study **either in person or online** with a researcher from the study team.

If you choose to take part in the study, we will ask you to sign a Consent form confirming your understanding of the study, your consent to participate, and your consent for your child/dependent to participate. Participants aged 18 years or more will participate as adults. They will be asked to sign a consent form (if appropriate) or have a legally appointed representative provide consent on their behalf.

If you choose to consent online, this will involve a virtual meeting with a researcher from the study team and, if necessary, a translator. The Consent form will be sent to you in advance for review and consideration. During the online meeting, you would be invited to electronically sign the Consent form using a secure online platform. The form will be countersigned by the researcher, and a final copy would be provided to you.

If you choose to take part in the study, we will invite you and your child/dependent to **attend annual assessment visits** over a period of five years. At each visit we will assess your child/dependent's neurological function, developmental milestones, motor function, behaviour, speech and language.

We will ask you to complete questionnaires about your child/dependent's abilities, sleep, seizures, and the overall impact of CTNNB1 on you and your family's quality of life.

We will ask to take a blood sample from your child/dependent, to confirm their genetic variant, look for potential genetic markers that predict how the condition affects each child differently, and gain a better understanding of the *CTNNB1* gene.

To investigate the impact of CTNNB1 on eye sight, your child/dependent will be offered an assessment of their retina using a non-invasive technique called Optical Coherence Tomography.

We are also interested in how CTNNB1 syndrome affects brain development and brain activity. If your child has recently had an electroencephalogram (EEG) or brain magnetic resonance (MR) scan as part of their medical care, we will request that you provide us with digital copies where possible. If your child has not had a recent EEG, we will try to arrange one at your study visit.

At one visit, we may ask to photograph your child/dependent's face. This will be analysed using innovative software using artificial intelligence to identify facial features particular to CTNNB1 neurodevelopmental syndrome. This could help to diagnose other children with the syndrome.

A subset of participants who are able to walk will also be offered the opportunity to have a smalll wearable device (Syde®) fitted to their ankle for 30 days. This is state of the art technology which was developed to accurately record a participant's gait and movements in their natural environment. Data from the device is automatically uploaded when you charge it.

Future research into CTNNB1 neurodevelopmental syndrome

In order to improve the lives of children and adults with CTNNB1 syndrome, we are committed to collaborating with reputable researchers around the world. If you agree, we would like to share your child/dependent's anonymised information and blood (or DNA) sample with other researchers investigating CTNNB1 syndrome.

What are the potential benefits and risks of taking part in this study?

This study may help you learn more about your child's development. The questionnaires we use are standardised and may give you a more accurate picture of your child's development. We can also interpret and explain the EEG and MRI results to you.

There are no major physical risks involved in participating in this study. All physical assessments and tests will be perfomed by trained professionals. Blood taking can cause temporary pain, discomfort and minor bruising. However, appropriate measures to minimise this will be taken. EEG is a safe and non-invasive procedure to record brain activity, which will be performed by trained neurophysiologists.

You will not have to pay anything to take part in this study. You will not be charged for any of the research activities. You will also not be paid for your participation in this study.

How will my child/dependent's data be stored?

You and your child/dependent's data will be pseudo-anonymised with an identification code and stored in the study database. Only delegated staff will be able to link your study data to personal data. The joint controllers of personal data collected as part of the study are:
- CTNNB1 Foundation, The Gene Therapy Research Institute, Dalmatinova ulica 5, Ljubljana.
- University of Ljubljana (UL), Kongresni trg 12, Ljubljana, Data Protection Officer: dpo@uni-lj.si
- Faculty of Medicine, University of Ljubljana (UL MF), Vrazov trg 2, Ljubljana, Data Protection Officer: dekanat@mf.uni-lj.si

Data will be processed by investigators at the University of Ljubljana and the University of Oxford. Your data will be stored on secure servers and storage facilities managed by the University Clinical Centre Ljubljana and the University of Oxford, as the contracted data processors. The data will be retained for a minimum of 10 years, in accordance with European legislation and ICH-GCP standards. The data will be processed on the basis of a task in the public interest in medical research (Article 6(1)(a) of the General Data Protection Regulation (GDPR) and Article 9(1)(a) of the GDPR), in accordance with Article 26(3) of the PDPA and Article 69(2) of the GDPR.

What will happen if I no longer wish to participate in the study?

Participation in this study is entirely voluntary, and you may withdraw your child/dependent from the study at any time. If you choose to withdraw, you will be offered the following options:

- To withdraw but permit the continued use of anonymised data and storage of anonymised samples collected before the date of withdrawal.
- To withdraw and request that all data and samples collected before withdrawal be discarded.

Additionally, the following withdrawal procedures will apply:

- **Missed contact attempts:** We will contact you annually to confirm attendance at the next study visit. If we cannot reach you after **three contact attempts**, your child/dependent will be withdrawn from the study. Data and samples collected up to that point will continue to be used unless you contact us to specifically withdraw consent for their use.
- **Missed visits:** If your child/dependent cannot attend study visits for **two consecutive years**, they will be withdrawn from the study. Data and samples collected before this point will still be used unless you specifically withdraw consent for their use.

This ensures clarity and transparency in the withdrawal process while maintaining the integrity of the research.

Who is organising and funding the research?

The principal investigator is Dr Damjan Osredkar, Associate Professor of Paediatrics at the University of Ljubljana, Slovenia (damjan.osredkar@kclj.si). The research is being carried out under the auspices of the University of Ljubljana Faculty of Medicine. The study is funded by the CTNNB1 Foundation (CTNNB1 Foundation, The Gene Therapy Research Institute, Dalmatinova ulica 5, Ljubljana).

Who has reviewed the study?

The study has been reviewed and approved by the Ethics committe of Slovenia. The research will be conducted in accordance with the principles of the Declaration of Helsinki on Biomedical Research and the principles of the Slovenian Code of Medical Ethics.

What if there is a problem?

If you have any questions or problems regarding the study, please contact the principal investigator, Assoc. Prof. Dr. Damjan Osredkar, MD (damjan.osredkar@kclj.si).

Thank you for taking the time to consider participating in the Dragonfly Study.