Gene Therapy for CDD

Summary of the Elaaj Bio Webinar · Rare Disease Day 2026

Presented by Dr. Russ Addis · Chief of Pipeline Strategy and Head of Genetic Medicine, LouLou Foundation

Prepared for parents and families of the global CDKL5 community

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How to Read This Document

This document faithfully summarises the content of the webinar held on 28 February 2026 by Dr. Russ Addis, Chief of Pipeline Strategy and Head of Genetic Medicine at the LouLou Foundation. All topics covered in the webinar are included, from animal study results to the audience Q&A; session.

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1. Who Is Elaaj Bio

Elaaj Bio is a company founded in 2018, wholly owned by the **LouLou Foundation**, a non-profit organisation dedicated to CDD. It is not a traditional pharmaceutical company: it was created with the explicit purpose of developing therapies for CDD and has no other commercial objectives.

Elaaj Bio had worked in close collaboration with the **Gene Therapy Program at the University of Pennsylvania**, led by Dr. **Jim Wilson**, one of the world's foremost experts in gene therapy. Dr. Wilson is now the CEO of **Gemma Bio**, but the collaboration with Elaaj Bio continues.

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2. What Is CDD and Why Is It So Difficult to Treat

CDD (CDKL5 Deficiency Disorder) is a rare disease affecting approximately **1 in every 41,000 births**. It appears in the first three months of life with seizures that are resistant to medication and with severe delays in neurological development.

It is caused by changes (mutations or deletions) in the **CDKL5 gene** (Cyclin-Dependent Kinase-Like 5). This gene provides instructions for producing a protein that is essential to the functioning of brain cells. When the gene does not work, the brain does not receive that protein, with consequences across many functions: movement, communication, cognitive development, sleep, and seizures.

Currently there is **only one approved drug** for CDD: Ztalmy (formerly known as ganaxolone), approved in the US in 2022 and in Europe in 2023. This drug reduces some seizures, but **does not address the underlying causes** of the disease and does not improve other manifestations (development, communication, walking, sleep). Research conducted with families and caregivers showed that seizures are not even the top priority: parents most want improvements in **walking, communication, and developmental milestones**.

■ In brief: why a genetic approach?

The CDKL5 gene is both the problem and the potential solution: if a working copy of that gene can be delivered to brain cells, in theory it could address the root cause of the disease, not just the symptoms.

3. What Is "Gene Therapy"

Gene therapy is not a conventional drug: it is not a tablet or a chemical injection. It is a technique that delivers a correct copy of a faulty gene directly into the patient's cells.

To do this, a **vector** is needed — a carrier capable of transporting the gene to the target cells. Elaaj Bio uses a type of vector called an **AAV** (Adeno-Associated Virus): a virus modified in the laboratory so that it does not cause disease, but is very effective at entering cells and depositing genetic material. The specific version used by Elaaj Bio is called **AAVhu68**, developed at the University of Pennsylvania.

■ How it works, in plain terms

Think of the faulty gene as a torn page in an instruction manual. Gene therapy does not remove the torn page — it inserts a new, working one. The cells can then read the correct instructions and produce the CDKL5 protein that was missing.

4. Laying the Groundwork for a Clinical Trial

Before even testing a drug, researchers need to understand *how to measure* its effect. For CDD, this groundwork was done by two large international observational studies that involved families from around the world:

The CANDID Study (organised by the LouLou Foundation): more than 100 patients enrolled, still ongoing. It collected baseline data on many people with CDD over time, to establish a reference point against which future treatment results can be compared. It also prepared clinical centres around the world to be ready for trials.

The ICCRN / U01 Study: international, more than 100 patients, it contributed to developing tools for assessing the severity of CDD, such as the CCSA scale (Clinical Severity Assessment), which can be used in clinical trials.

■■ What this means for families who took part

Those who participated in these studies received no treatment. But their participation was essential: without that data, it would not have been possible to design a clinical trial that would hold up to regulatory scrutiny. The contribution of those families is what makes today's trial possible.

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5. The Drug ELJ-101: What the Mouse Studies Tell Us

How the mouse experiments were conducted

Researchers use **CDKL5 knockout mice** (referred to as KO mice): mice from which the Cdkl5 gene has been removed in the laboratory, so that the consequences of its absence can be studied. These mice display some behavioural differences compared to normal mice (called wild-type), though they are not equivalent to human patients with CDD.

In the efficacy tests, newborn mice were treated with a range of doses of ELJ-101 (from a low dose up to a high dose). After several weeks, they were assessed using behavioural tests and brain analysis, comparing treated KO mice with untreated KO mice and with normal mice.

Test 1 – Hyperactivity (open field)

Untreated KO mice move around an open arena much more than normal mice — they are hyperactive. After treatment with ELJ-101, KO mice moved progressively less as the dose increased: at the highest dose, their behaviour came close to that of normal mice. This **dose-dependent effect** (more drug = greater effect) is an important signal: it indicates that the behavioural change is genuinely caused by the drug and not by other factors.

Test 2 – Hind limb clasping

When a KO mouse is lifted by its tail, it tends to draw its hind legs together (a behaviour called hind limb clasping). Normal mice do not do this. Mice treated with ELJ-101 showed a reduction in this behaviour, again in a dose-dependent manner: higher doses produced the greatest reduction.

Brain analysis

Beyond the behavioural tests, researchers analysed the brains of the treated mice to verify two things:

a) Production of CDKL5 protein: untreated KO mice produce no CDKL5 protein. KO mice treated with ELJ-101 showed increasing levels of CDKL5 protein as the dose increased. This demonstrates that the gene delivered by the vector is being read by brain cells and translated into the protein.

b) Activity of the CDKL5 protein (EB2 phosphorylation): producing the protein is not enough — it also needs to do its job. One of CDKL5's functions is to activate another protein called EB2 (through a process called phosphorylation). In untreated KO mice, this activity is almost absent. In mice treated with ELJ-101, EB2 activity increased with dose. Results were not a perfect 100%, but they represent a significant improvement over the untreated baseline.

■ What researchers conclude from the mouse studies

ELJ-101 works in KO mice: it reduces abnormal behaviours, stimulates CDKL5 protein production in the brain, and demonstrates its biological activity. Results are dose-dependent, which strengthens the scientific credibility of the data. These results also help estimate the doses to use in humans.

■■ Important: mice are not patients

The researchers were explicit: these mice do not have CDD — they only display some measurable behavioural differences. Results in mice are encouraging and necessary to move forward, but they do not guarantee the same will happen in people. This leap — from mice to humans — is always the most uncertain step in medical research.

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6. Safety Studies in Non-Human Primates

Before testing a drug in humans, it is mandatory to demonstrate its safety in animals whose brains are more similar to ours. Elaaj Bio conducted a toxicity study in **non-human primates (monkeys)**, whose brains are far more similar in size and complexity to the human brain than a mouse brain.

The results of this study were positive: **no clinical adverse events**, CDKL5 protein expression was detected throughout the primate brain, and **no significant abnormalities in brain tissue** were found (histopathological examination). This allowed Elaaj Bio to proceed with clinical development.

■ An open question

One question raised during the webinar asked what percentage of neurons had been reached by the vector in the primate study. Dr. Addis answered honestly that this percentage was not measured: the presence of the gene throughout the brain was confirmed, but the exact number of cells reached was not quantified. This is an acknowledged gap.

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7. Manufacturing the Drug for Clinical Use

Producing a gene therapy drug for human use requires far more rigorous standards than laboratory work. Manufacturing of ELJ-101 in sufficient quantities and to the quality required for clinical trials is currently underway at **ViralGen**, a specialist AAV vector manufacturer based in **Spain**. Dr. Addis reported that things are going well.

This is a critical step: historically, many gene therapies have faced significant delays precisely due to manufacturing problems. Elaaj Bio is aware of this risk and is actively monitoring it.

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8. The First-in-Human Clinical Trial (ELJ-101)

What this trial will study

The primary objective of the first clinical trial is to **assess the safety and tolerability** of the drug. In plain terms: the priority is to establish whether the drug is safe for patients, not yet to measure

its effectiveness. Exploratory efficacy data will also be collected (effects on seizures, cognition, communication, sleep, etc.).

Who may be eligible to participate

The trial aims to enrol approximately **12 patients** with CDD. Inclusion and exclusion criteria have not yet been finalised: they will be shared later in 2026, through a follow-up webinar and on the Elaaj Bio website. The stated long-term goal is to include patients of **any age, sex, and mutation type**, including deletions.

How the drug is administered

The drug is given as a **single one-time dose** injected into the cisterna magna — a fluid-filled space at the base of the brain (intracisterna magna, or ICM injection). This approach has already been used successfully by other gene therapy programmes to deliver AAV to the brain.

Duration and follow-up

The main trial period will last **one year**, with assessments every three months. This will be followed by a **four-year extension study** to monitor long-term effects on both safety and efficacy.

Where and when

Enrolment is expected to open in the **first quarter of 2027**. Clinical sites have not yet been selected. Elaaj Bio intends to make the trial internationally accessible, but the details will depend on the chosen centres. Families not living near a trial site may need to travel.

> **■■ What this trial is not**
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> This is not an efficacy trial: it is not designed to prove that the drug works. It is a safety trial. The 12 patients enrolled is a very small number: no conclusions about effectiveness can be drawn from such a limited group. The results of this trial will be used to design the next one — the full efficacy trial (the pivotal trial) — which, if all goes well, would begin within 2 to 4 years from now.

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9. Where We Are on the Roadmap

The path to an approved drug is a long one. Here is where Elaaj Bio stands as of February 2026:

Phase	Status
Mouse efficacy studies (CDKL5 KO)	■ Complete
Primate toxicity studies (NHP)	■ Complete
Positive interactions with FDA, MHRA and other regulators	■ Complete
Clinical-grade drug manufacturing (ViralGen, Spain)	■ Ongoing
Regulatory approval for the first-in-human trial	■ Expected early 2027
Opening of the first-in-human clinical trial	■ Expected early 2027

Pivotal trial (efficacy)	■ ~2-4 years after the first trial
First commercial approval	■ Years thereafter

10. What We Know About Treating Adults and Older Children

One of the most pressing questions concerns whether this therapy could ever benefit people with CDD who are already older, with neurological impairments that appear to be long established.

Dr. Addis answered honestly: **we do not yet know**. Gene therapy has never been tested in adults or older children with CDD. There are, however, two considerations that keep the door open — without guaranteeing anything:

1. CDD is not a degenerative disease. Neurons do not die over the years. They are still there — they simply are not functioning as they would with a healthy CDKL5 gene. This theoretically leaves room for an intervention even in adulthood.

2. Adult mouse studies. Experiments in which the CDKL5 gene was switched back on in adult mice that had been deprived of its function showed some improvements. This is an interesting finding, but it must be treated with great caution: the technique used can only be applied in mice (it is not applicable to humans), and results in animals do not automatically transfer to people.

> **■■ A word of caution on expectations**
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> Dr. Addis explicitly said: we should not use the term 'irreversible damage' because we do not yet know whether certain impairments are truly irreversible. But this is not the same as saying they will be reversible. It simply means we do not have an answer yet. The clinical trial will help address this question.

11. Risks the Researchers Are Monitoring

Dr. Addis was transparent about the risks facing the programme:

Clinical safety risks: in other gene therapy trials (not for CDD), serious adverse events have occurred, in some cases including patient deaths. This is precisely why the first trial is focused primarily on safety. Nothing guarantees that ELJ-101 will be risk-free, even though the primate data have so far been reassuring.

Manufacturing risks: producing AAV vectors is technically complex and costly. Many gene therapy programmes have faced years of delay due to manufacturing problems. Elaaj Bio is aware of this and is working to get ahead of these challenges.

Regulatory risks: approval from agencies such as the FDA and EMA is not guaranteed and may require time or additional studies.

12. Other Avenues Elaaj Bio Is Exploring

ELJ-101 is the priority project, but Elaaj Bio is already working on next-generation options, recognising that no single therapy is the final answer:

• **New AAV vectors** (different capsids, potentially more efficient or more targeted).

• **Targeted X-reactivation**: a technique to wake up the silent copy of the gene present on the second X chromosome (which in females is normally inactive). This could potentially work for female patients, who theoretically have a backup copy of the gene.

• **Non-viral delivery methods**: carriers other than AAV to deliver the gene.

• **Gene editing**: techniques to directly correct the faulty gene in the patient's DNA (technologies such as CRISPR, still at a very early stage for brain applications).

Questions and Answers: What a Worried Parent Will Probably Ask

Q: When will my child be able to access this therapy?

A: The honest answer is: not for many years. The first trial will open (if everything goes to plan) in 2027, and it will be open to only 12 patients. If the results are positive, a larger trial will follow (the pivotal trial), within 2 to 4 years. Only after that trial will it be possible to apply for commercial approval. Realistically, the timeline for a drug available to the general public is at least 5 to 10 years — and that is assuming things go well.

Q: My child is already 12 years old. Will they be excluded from the therapy?

A: No age limits have been set as yet. Elaaj Bio's stated goal is to include patients of all ages, but the definitive criteria will be announced later in 2026. The first trial may carry some restrictions for safety reasons, but the long-term programme aims to cover all age groups.

Q: Will gene therapy cure my child?

A: Nobody can say. It has never been given to a person with CDD. The mouse data are encouraging, but mice are not people. The goal of the first trial is not even to assess whether it works: it is to establish whether it is safe. Only subsequent trials will be able to address the question of effectiveness. Using the word 'cure' at this stage would be premature.

Q: Will the therapy help someone who already has established neurological impairments?

A: We do not know. Researchers hope so, based on the fact that neurons in people with CDD are still alive (the disease is not degenerative). But hope is not the same as certainty. This will be one of the key questions the trial aims to answer.

Q: My daughter has a CDKL5 gene deletion. Can she participate?

A: There are currently no exclusions based on mutation type. The intention is to include all patients, including those with deletions. However, the definitive criteria have not yet been established.

Q: Can we participate from Italy / Europe?

A: Clinical sites have not yet been chosen. Dr. Addis said that the goal is to make the trial globally accessible, but this will depend on where the centres are opened. Travel may be required. More details will be available later in 2026.

Q: Are there risks? Is gene therapy dangerous?

A: Yes, there are potential risks, and the researchers say so openly. In other gene therapy trials (for other diseases), serious adverse events have occurred. This is precisely why the first trial has safety as its primary objective. The primate data showed no problems, but primates are not humans with CDD.

Q: Is Elaaj Bio a trustworthy organisation, or is it selling false hope?

A: Elaaj Bio is a subsidiary of the LouLou Foundation — not a conventional pharmaceutical company with commercial goals. During the webinar, Dr. Addis was explicitly cautious, acknowledged uncertainties, and made no promises. This does not guarantee the programme will succeed, but it is a sign of scientific good faith.

Q: When will we know the criteria for taking part in the trial?

A: By the end of 2026 (estimated), through a follow-up webinar and the Elaaj Bio website. There are no other official channels at this time.
