

# INGENEIOUS

NEWS FROM COMBIGENE AB

ISSUE 1 • 2021



 **combiGene**  
The gene therapy explorer

## EDITORIAL

# CombiGene celebrates International Epilepsy Day

■ February 8 was the annual International Epilepsy Day. For us at CombiGene, it was a natural opportunity to, for a moment, leave all the details that together make up our development projects and reflect on why we do what we do. The answer is simple and obvious. Everyone at CombiGene is inspired by the desire to make the world a little better by developing new gene therapies with the potential to improve the lives of people affected by severe diseases.

Our epilepsy project CG01 is the most advanced of our projects. In 2021, we will focus on the final parts of the preclinical program with the ambition to start the first study in humans in 2022.

In celebration of the International Epilepsy Day, we devote this whole issue of Ingeneious to various aspects of epilepsy.

I wish you a pleasant reading.

Best regards,

Jan Nilsson  
Vd



**” In celebration of the International Epilepsy Day, we devote this whole issue of Ingeneious to various aspects of epilepsy.**

# International Epilepsy Day!

■ *International Epilepsy Day is a special event which promotes awareness of epilepsy in more than 130 countries each year. Every year on the second Monday of February people join together to acknowledge and highlight the problems faced by people with epilepsy, their families and caretaker.*

The day is a joint initiative of the International Bureau for Epilepsy (IBE) and the International League Against Epilepsy (ILAE) and the two organizations urge anyone who in any way works in the field of epilepsy to pay attention to the day. Information about the day can be found here:  
<https://internationalepilepsyday.org>

### International Art Competition

To celebrate International Epilepsy Day 2021, an international art competition was held, for all ages, with the theme “Friendship and Inclusion”. There were three categories – under 8 years, between 8 and 15 years and 16 years and older. The competition was open to all and the winning entries can be seen here:  
<https://internationalepilepsyday.org/art-competition-2020-entries/>

### CombiGene presented on the Swedish Epilepsy Association's webinar

CombiGene is deeply involved in the problem of drug-resistant focal epilepsy through the epilepsy project CG01. In previous years, Professor Merab Kokaia, one of CombiGene's scientific founders, has had a tradition of lecturing on epilepsy at the City Library in Lund. Due to the ongoing pandemic, this was not possible this year, but CombiGene was still active during this important day when Karin Agerman, the company's Chief Research & Development Officer, spoke at the Swedish Epilepsy Association's webinarium under the heading *Is gene therapy a form of treatment for epilepsy?*  
Read an interview with Karin in this issue of Genevägen.



## International Epilepsy Day



“The CG01 project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 823282”

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*Every year, the International Epilepsy Day highlights the challenges people with epilepsy, their families and caretakers are facing.*

## What it's like to live with epilepsy

■ Epilepsy is a disease that through its erraticness often affects everyday life in a pervasive way. Many epileptics speak of a loss of independence and various forms of restrictions on daily life. Things that are taken for granted, such as driving a car or swimming in a lake, can be impossible for people with epilepsy.

The medicines available can also produce unwanted effects that make life more difficult to live.

In connection with International Epilepsy Day, several people talk about what it's like to live with epilepsy. You can take part of their stories here: <https://internationalepilepsyday.org/epilepsy-stories/>

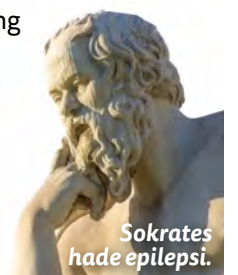
## Famous people with epilepsy

■ Although epilepsy can lead to significant limitations in everyday life, there are countless examples of people with epilepsy who have made big impression in both the present and history.

Socrates, Alexander the Great, Julius Cæsar and Joan of Arc all had epilepsy. There are also many people with an artistic focus who had epilepsy. Among them are the painters Michelangelo and Vincent Van Gogh as well as the authors Molière, Lord Byron,

Graham Greene, Agatha Christie and perhaps the most famous of all authors Fyodor Dostoyevsky.

Even in the field of politics and war there are several people who had epilepsy, among them the Russian Emperor Peter the Great, Napoleon Bonaparte and Lenin.



*Socrates hade epilepsi.*

Source: <https://epilepsi.ifokus.se/discussion/525219/kanda-personer-med-epilepsi>



Many people with epilepsy are helped by today's drugs, but there is still a need for new effective treatments.

## Different treatment options for epilepsy

■ There are a few different options for treating epilepsy. The most common form of therapy is medication, but also surgery, stimulation of the vagus nerve and so-called thermal ablation (laser treatment) are used to a relatively limited extent.

**Treatment with pharmaceuticals**  
Many patients with epilepsy can gain good control over their disease and live normal lives through daily medication. Today's drug does not cure the disease itself, but can prevent seizures.

To get the full effect of the medication, it is important that the medication is taken regularly every day so that the active substance of the drug is kept at a steady level over the day. As with any drug, you can get side effects from your epilepsy medicine.

### **Surgery may be an option**

The vast majority, about two-thirds, of those who medicate for epilepsy become seizure-free. Also in the remaining third, there is a clear decrease in the frequency and severity of seizures, but there is a group of patients who are not sufficiently helped by the medication. Among these is a small group of patients who can be helped by epilepsy surgery, which means that the part of the brain where seizures occur is surgically removed. In Sweden, about 50 people are operated each year, but the need is considered to be significantly greater.

### **Vagus nerve stimulation (VNS)**

VNS treatment involves an implanted electrode sending electrical impulses to the left vagus nerve in the throat, slowing down the nerve cell activity that can give rise to epileptic seizures.

The goal of this treatment is to reduce the number of seizures and reduce their duration and severity. VNS therapy is not an alternative to drug therapy or surgery but should be seen as a complement to these therapies.

### **Thermal ablation**

Thermal ablation (laser treatment) is similar to epilepsy surgery. As with surgery, the goal is to remove the part of the brain where the epileptic seizures occur, but instead of traditional surgery, a much less invasive laser-based technique is used that, through heat, destroys the brain cells that give rise to the seizures.

### **No approved gene therapy yet**

CombiGene's ambition is to contribute to the range of possible therapies. The epilepsy project CG01 is in a late preclinical phase. The ambition is to start the first study in humans in 2022. The clinical program will be extensive and carefully regulated as in all drug development, which means that a possibly approved gene therapy from CombiGene is still several years into the future.

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**CombiGene's ambition is to contribute to the range of possible therapies.**



"The CG01 project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 823282"

Sources: <https://epilepsi.se/om-epilepsi/behandling/>  
<https://www.epilepsy.com/learn/treating-seizures-and-epilepsy/surgery/types-epilepsy-surgery/litt-thermal-ablation>

# Karin Agerman spoke about gene therapy at the Swedish Epilepsy Association's webinar

■ The Swedish Epilepsy Association celebrated this year's International Epilepsy Day with, among other things, a webinar where a number of aspects of epilepsy were discussed. One of the invited speakers was Karin Agerman, CombiGene's Chief Research & Development Officer. Ingeneious managed to have a short chat with Karin shortly after her presentation.

**A little while ago you presented on the Swedish Epilepsy Association's webinar under the heading *Is gene therapy a future form of treatment for epilepsy? Why were you invited to talk about this?***

"The Stockholm Epilepsy Association has, as I understand it, been following the development of CombiGene's epilepsy project CG01 for some time and they simply thought that now was an appropriate time to hear more about the role gene therapy might play in future treatment of patients with epilepsy."



**Karin Agerman,**  
Chief Research and Development Officer

**What was the most important thing you wanted to convey?**

"A central part of my presentation was that all drug development is difficult, that development processes are strictly regulated to keep a focus on both safety and efficacy at all times, that it takes a long time to develop new therapies and that there is no guarantee that a development project will be successful no matter how hard and accurately you work."

**Why was this so important to highlight?**

"CombiGene's epilepsy project has developed very positively so far and our ambition is to start the first study in humans in 2022. Although the project has progressed according to plan so far, it is important to keep a few things in mind. As I said earlier, there is no guarantee that this project will succeed and, even if everything goes exactly as we hope, it will be a number of years before we have an approved therapy on the market. I simply do not want to raise hopes that we cannot then live up to."

**What other areas were you talking about?**

"I was invited to talk about gene therapy, so it was that topic that took



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**Our effort is characterized by energy and determination.**

up most of my presentation. On the one hand, I presented gene therapy in more general terms, what the theoretical model looks like, you might say, and secondly, I went more specifically into how a therapy with CG01 is supposed to work. Then I also tried to convey the energy and determination that exists in CombiGene. We are a small company where everyone is focused on moving our projects forward step by step."

## Read all of our news in one place

We would like to keep you well informed about what is happening in the company. CombiGene's digital newsletter allows you to read all of our news from one source. Subscribe via our website, where you can register the e-mail address to which you wish the newsletter to be sent. The subscription is free of charge and you can cancel it whenever you please. On our website you'll also find financial reports, press releases and all previous issues of Ingeneious.

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<https://bit.ly/2UiguHm>

## What happened in the CG01 project in 2020?

■ CombiGene epilepsy project CG01 advanced at a fast pace in 2020. During the year, we established a future-proof production platform, completed three preclinical studies with positive results and signed agreements on the development of an optimized drug administration for this unique gene therapy.

The project is thus well positioned for the final preclinical studies. We have already initiated preparations for the clinical programme with the ambition to start the first study in humans in 2022.

**Karin Agerman**  
Chief Research and Development Officer



"The CG01 project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 823282"

# CombiGene – The gene therapy explorer

With one project nearing the clinical-study phase and one project in an early preclinical phase, CombiGene is the leading Nordic gene therapy company. Gene therapy has seen rapid development in recent years, with a number of approved therapies and several major corporate deals. During this period we've built up a unique position with respect to knowledge within this field in the Nordic region. The company's expertise covers all central areas of the gene therapy field: viral vectors, preclinical studies including biodistribution and toxicity studies, development of GMP-classed manufacturing methods, upscaling of production volumes and regulatory strategy.

Few areas of pharmaceutical development are exciting and promising as gene therapy and, in many respects, CombiGene is at the very forefront of development. During our work with the CGO1 epilepsy project, on a nearly daily basis, we have won new ground, gained new insights and expanded our knowledge. You might say that we are on an expedition, exploring the fantastic possibilities of gene therapy. We are now continuing our voyage of discovery with another exciting project – the CGT2 lipodystrophy project.

Even here, we expect to create new and valuable knowledge as we carry this project forward.

And that's why we've chosen to call ourselves the gene therapy explorer.

 **combiGene**

**The gene therapy explorer**

CombiGene's vision is to provide patients affected by severe life-altering diseases with the prospect of a better life through novel gene therapies.

[www.combigene.com](http://www.combigene.com)