

INGENEIOUS

NEWS FROM COMBIGENE AB

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CombiGene – World-leading Swedish gene-therapy company

EDITORIAL:

- The design of the first clinical study* page 2
- Johan Hyllnér coaches CombiGene* page 2
- A small company with many strengths* page 3
- CG01 – update autumn 2018*..... page 3
- Calendarium* page 4

 **combiGene**
The gene therapy explorer

CombiGene is well-positioned for the future

2018 is drawing to a close and, although it is too soon to sum up the year in its entirety, I would like to take the opportunity in this editorial to look back over the past and to look into the future. Overall, 2018 has been a good year for CombiGene. The obvious highlights have been the positive final results from our proof-of-concept study early in the year, the agreement with CGT Catapult, funding from Horizon 2020 and the very successful new issue that was carried out in September. Another of this year's highlights has been the recruitment of our Chief Research and Development Officer, Karin Agerman. Thanks to her very considerable knowledge, energy and willpower, Karin has already had a great impact on the development of our company.

And, thanks to this year's successes, we have established a very strong position for CombiGene. Our preclinical research has now been concluded and we have taken important steps towards process development, the final stage of development before we can conduct toxicology/biodistribution studies and, subsequently, begin the first clinical studies. We have recently had several interesting meetings with representatives from both academia and industry, with the twofold ambition of broadening our business with an additional gene therapy project and, eventually, finding appropriate partners to help us to take our CG01epilepsy project all the way to market launch.

Jan Nilsson, VD,
CombiGene

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CombiGene's Scientific Advisory Board discusses the design of the first clinical study

On November 9th CombiGene's Scientific Advisory Board met for an important meeting. In attendance were the board's three permanent members (see below), CombiGene's scientific founders, Professor Merab Kokaia and Associate Professor David Woldbye, CombiGene's Chief Research and Development Officer, Karin Agerman and CEO Jan Nilsson, as well as Robert Doblhofer from Granzer, CombiGene's long-time regulatory consultant.

The purpose of the meeting was to review CombiGene's plan for the design of the first clinical study for the CG01epilepsy project. A synopsis of the study was presented for Läke-medelsverket (the Swedish Medical Products Agency) and for the FDA in meetings held with these authorities. The study, which is intended to be conducted with epilepsy patients, is primarily a safety study, but the scientific advisory board has also discussed which efficacy data may be potentially deduced from the findings.

This was the first occasion for the scientific advisory board to review the intended design of the phase-I study for CG01. All clinical studies demand the utmost care in preparation and much remains to be done before CombiGene has a complete and fully-defined study design, but the Copenhagen meeting was a decisive step closer to a definitive result.



CombiGene's Scientific Advisory Board

Annamaria Vezzani

Head of the Laboratory of Experimental Neurology at the Mario Negri Institute for Pharmacological Research in Milan



Deniz Kirik

Professor, Brain Repair and Imaging in Neural Systems (BRAIN), Faculty of Medicine, Lund University



Margitta Seeck

Margitta Seeck, Professor of Neurology, University of Geneva

Johan Hyllnér coaches CombiGene



Horizon 2020's support for CombiGene not only includes 3.36 million euros in funding for the development of the CG01 epilepsy project, but also the services of a business coach. In CombiGene's case, Professor Johan Hyllnér, former chief scientific officer at CGT Catapult, has taken the role of the latter.

"It is a great advantage for CombiGene to have Johan Hyllnér as a coach," says Jan Nilsson, CEO,

CombiGene AB. "After leaving CGT Catapult, Johan is now back in Sweden and we have already had very productive discussions surrounding issues of central importance, such as business strategy, process development and manufacturing. Johan's advice and opinions will be invaluable for CombiGene's onward journey."

Read all of our news in one place

We would like to keep you well informed about what is happening in the company. Therefore, we are now launching CombiGene's digital newsletter to allow you to read all of our news first-hand.

Subscribe via our website, where you can register the e-mail address to which you wish the newsletter to be sent. Use the link "Subscribe to our newsletter" at the top-right corner of the page. The subscription is free of charge and you can cancel it whenever you please.

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Karin Agerman: "CombiGene is a small company with many strengths"



Your employment began on March 5th. Has your time thus far at CombiGene corresponded to the expectations you had when you started with the company?

"Yes, I would have to say so. I expected it to be very intensive and it certainly has been. I had been searching for a company like CombiGene for several years and, when I finally found the company, I followed it quite closely before contacting Jan Nilsson, CombiGene's CEO, to express my interest, so to speak. In other words, I was already well acquainted with CombiGene from day one."

How would you describe CombiGene?

"The easiest way to describe CombiGene is to say that it is a small company with great strengths. A common mistake

among many small biotech firms is that the researchers/academics believe they can run a company that is based on their research while they continue to pursue a full-time academic research career. The outcome is seldom good. There are big, fundamental differences between research and business. Another common pitfall among small companies is that they think they can do everything on their own. CombiGene has avoided both of these potential mistakes."

What has CombiGene done to avoid these mistakes?

"First of all, the company made sure to recruit a very experienced and driven CEO. The company also has a highly qualified board that is well aware of where the company is heading. The company has also taken great care in building

■ One bleak Monday afternoon in November Ingenieious phoned Karin Agerman, CombiGene's Chief Research and Development Officer, for an interview. Karin's calendar is full, but on this particular afternoon she promised us a few minutes of her time. It soon became apparent that, even during this brief interlude, numerous obligations had to be met. During the interview Karin managed to pick the kids up at school, check their seatbelts, ask how their day was, see to it that all the gear needed for a planned outdoor activity was in place, and even send an email. Even so, the interview proceeded without a hitch.

a network of external specialists. This gives CombiGene access to leading-edge expertise in all of the key areas, despite having a very small organization. Today, CombiGene only consists of Jan and me, with one more person on the way in."

Do you see any other advantages with CombiGene?

"Yes. There is one factor that is very important. CombiGene's scientific founders, Professor Merab Kokaia and Associate Professor David Woldbye, are still involved in the company. We have excellent collaboration with both Merab and David. The way in which they introduce new ideas into CombiGene is invaluable."

One of your tasks in CombiGene is to work with business development. Can you comment on that?

"Absolutely. An important ambition for CombiGene is to broaden the business with additional gene therapy projects. This is pursued in various ways. During the autumn a PhD student from KI has helped us to survey all ongoing Swedish

research projects within gene therapy in order to gain a good overview of what is happening in the academic landscape. For a small company like CombiGene, business development also entails participation in various national and international contexts. There are many examples to illustrate this; two of which are Swelife ATMP and CAMP, two Vinnova-funded projects of which the aim is to strengthen Sweden's competitiveness in advanced medical therapies. Among other things, these two projects give us the opportunity to establish valuable contacts with researchers and other companies. So far, this has been very valuable and inspiring."

It sounds as though you are very satisfied with your time thus far at CombiGene.

"I am, indeed. The days are intensive and (almost) always fun. I have gotten to know many fantastic people who are driven by a deep passion and an uncompromising ambition to actually make the world a better place. It couldn't be more stimulating."

CG01 – update autumn 2018

■ August 1st was the official starting date for CombiGene's collaboration with Horizon 2020, the EU framework programme for research and development.

All specifications from GeneDetect, who manufactured CG01 for preclinical studies, have been transferred to CGT Catapult.

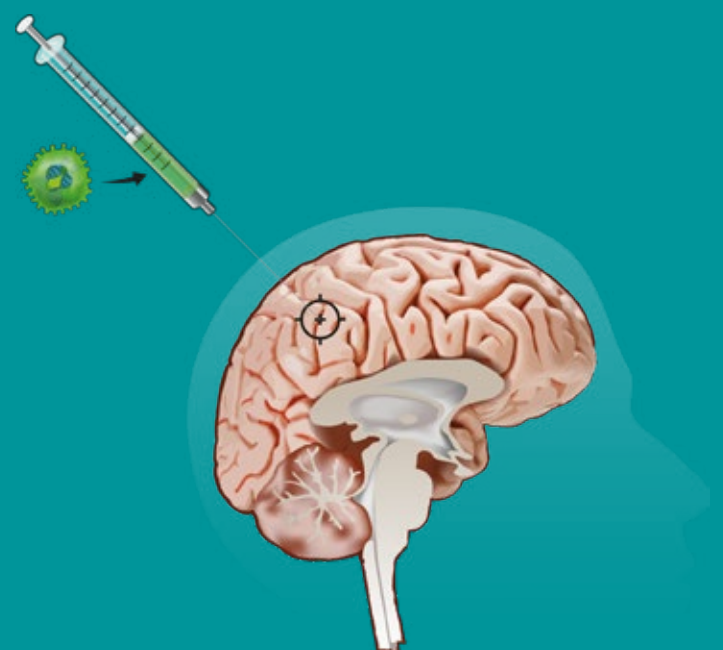
CGT Catapult has now implemented the same analysis methods employed by GeneDetect and the next step is to refine the analysis methods so that they can be adapted for future GMP manufacturing.

At the European Medicines Agency (EMA) meeting in June, in which CombiGene participated together with Panion, it was recommended that CombiGene make several minor changes in the company's plasmids (ring-shaped DNA molecules).

This has now been accomplished and CombiGene has been notified that it will not affect production of CG01.

During the autumn CombiGene has also presented the CG01 project for several interesting potential collaborative partners at, among other events, Nordic Life Science Days in Stockholm and Bio-Europe in Copenhagen.

In November a meeting was held with CombiGene's Scientific Advisory Board for initial discussions on the design of the phase-I study for CG01 (see separate article).



For many sufferers, there is no help – yet.

We hope to change this. We are in the process of developing a world-leading method for treating epilepsy. The potential is enormous, the outlook is good.

For very many people.

Events

January 29, 2019
Aktiedagen, Lund

April 4, 2019
National ATMP Conference 2019, Göteborg
<https://bit.ly/2QTRUeP>

June 3-6, 2019
BIO International Convention, Philadelphia USA
<https://convention.bio.org/2019/>

September 10-12, 2019
NLSDays, Malmö
<https://www.nlsdays.com/>

September 10, 2019
Aktiedagen, Stockholm

October 22-25, 2019
European Society of Gene and Cell Therapy 27th
annual congress, Barcelona
<https://www.esgct.eu/congress/barcelona-2019.aspx>

November 4, 2019
Stora Aktiedagen, Göteborg



The gene therapy explorer

CombiGene's objective is to develop treatment methods that can improve the quality of life for millions of people throughout the world.

www.combigene.com