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CombiGene

The gene therapy explorer

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EDITORIALS

CombiGene is very well positioned for continued success

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There is so much I want to say in this my first editorial in Ingeneious that it is almost difficult to know where to start, but let me first extend a big and warm thank you to Jan Nilsson who during his time as CEO developed CombiGene from a company with one project in early preclinical phase to the CombiGene we see today: an internationally recognized gene therapy company with one project, the epilepsy project CG01, licensed to Spark Therapeutics, one project aimed at treating the rare and severe disease partial lipodystrophy and the extremely exciting pain program COZY.

I would also like to thank Jan and the entire team for the great introduction to CombiGene that I have received during my time as the company's Chief Operating Officer. It is with great eagerness and enthusiasm that I now take on my new role as CEO of CombiGene. I am really looking forward to continuing the development of CombiGene with more successes in the gene therapy field together with the board and the rest of the CombiGene team.

License agreements are the goal

Crucial for our success is that we can produce conclusive and positive preclinical results with the potential to be translated into good results in humans. This is the way we can attract future partners to our projects. It is also important that we can take on more gene therapy projects that target patient populations with great needs and add value to them with our special expertise in drug development and gene therapy.

Having a project portfolio with several projects is important since it significantly increases the chances of reaching all the way to a license agreement. All drug development takes time and the costs of developing a new drug are high, at the same time the risk that a project does not go all the way to commercialization is significant. In other words, it is not enough with just one or two projects in the portfolio, several projects are needed to distribute risk and increase the chances of success.

Health economic aspects will be crucial

Another crucial aspect of our business is health economics. Gene therapy is, and will continue to be, an exclusive form of treatment. It is therefore crucial that we can demonstrate that our therapies can improve patients' quality of life to such an extent that it is possible for society to make a positive health economic calculation. It is my conviction that the projects in which we are engaged can succeed in this, namely both improving the quality of life for the individual patient and offering a treatment that is economically justifiable.

A great team

I am sometimes asked why I left a large group like Getinge, where I was previously CEO of the Swedish operations. The answer is very simple. I thrive in smaller companies where everyone helps each other to create success and where the paths to decisions are short. In recent years, I have been exclusively active in the ATMP area (Advanced Therapy Medicinal Products), which in itself is extremely interesting given the fantastic opportunities to develop completely new and effective therapies for otherwise incurable diseases and conditions.

The competent and hardworking team at CombiGene continues to develop our projects, not least the pain program COZY where we work together with our Danish partner Zyneyro. In addition to our existing product portfolio, we are also actively looking for more projects for in-licensing to establish a portfolio of commercially interesting gene therapy projects to increase our opportunities to reach more licensing agreements like the one we signed with Spark Therapeutics in 2021.

Peter Ekolind
CEO

Rapid advancements in the pain program COZY

Pain is a global problem. Between six and eight percent of the world's adult population suffers from severe chronic pain with enormous costs for society as a result. In the US alone, the cost to society is estimated at an unimaginable USD 636 billion annually, which is twice the cost of cardiovascular disease.[1]

There is a huge need for new options for pain relief

One thing that further complicates the picture is that there are no efficient treatment options. Today's treatments consist mainly of anti-inflammatory, antidepressant and anticonvulsant drugs and opioids, i.e., a group of substances with a morphine-like mechanism of action.

The problem is that these treatments often have a number of debilitating side effects such as substance abuse problems, depression, anxiety, fatigue and reduced physical and mental ability.

All in all, this means that there is an enormous need for new effective forms of treatment that do not have the side effects that current alternatives are associated with and that do not lead to tolerance development, i.e., that the patient over time needs increasingly higher doses to achieve effective pain relief.

The COZY program is based on a new biological mechanism of action

The pain program COZY, which CombiGene runs in collaboration with the Danish company Zyneyro, aims to develop alternatives for the treatment of chronic pain without addiction problems and without tolerance development. The pain program consists of two projects – a peptide treatment (COZY01) and a gene therapy treatment (COZY02), both of which are based on a new biological mechanism of action. Both the peptide and the gene therapy are being developed for treatment of severe chronic pain conditions, where the gene therapy is reserved for patients where the possibility of spontaneous reduction of chronic pain is judged to be limited (or unlikely).

Continued in the next spread

[1] *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Appendix C. The Economic Cost of Pain in the US. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. Washington (DC): National Academies Press (US); 2011*

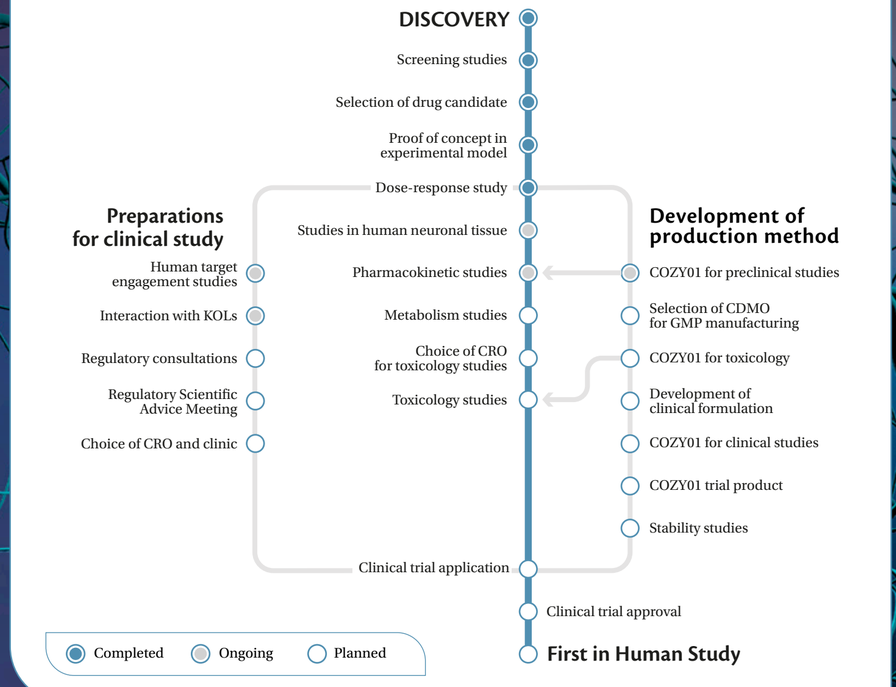
The peptide project COZY01

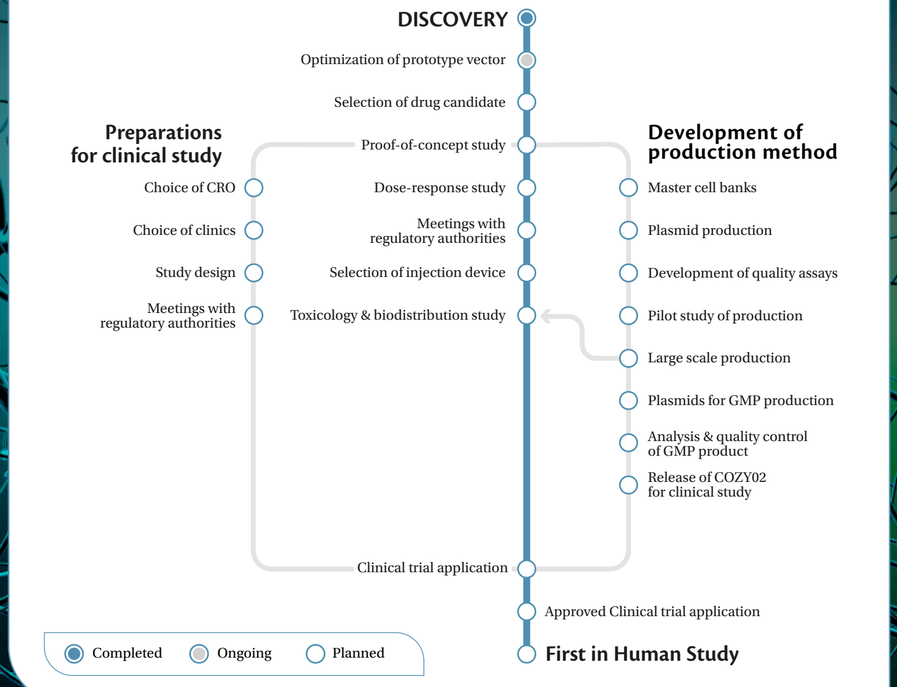
The peptide treatment, which is the one of the two projects that has advanced furthest in its development, has shown good effects in various preclinical models. CombiGene and Zyneyro are now focusing on conducting the necessary preclinical studies as quickly and efficiently as possible to evaluate safety and toxicology and to produce clinical trial material in order to obtain approval from regulatory authorities to conduct the first clinical trials on humans with COZY01 within a few years.

The gene therapy COZY02

A prototype of the AAV vector that acts as a carrier of the genetic material has been developed by Zyneyro and tested in several preclinical models with very good and long-lasting effect. The upcoming work is focused on optimizing the genetic material that will be included in the vector so that we can administer this in future human studies. AAV is the vector type that CombiGene has extensive experience of from our other projects. When the vector is optimized, preclinical studies follow to investigate and characterize distribution, protein expression, efficacy, dose-response, and toxicology.

In parallel with the preclinical development, we will ensure that manufacturing of the selected vector takes place in an optimal way and that the necessary quality tests are in place for future clinical trials. This work will form the basis for seeking permission to conduct a clinical trial on patients with severe chronic pain.





Epilepsy Project CGO1 progressing through optimization activities in preparation for in-human studies

In June, CombiGene and Spark Therapeutics held a bi-annual Joint Research Committee meeting in Stockholm, Sweden, to make a detailed plan for the upcoming six months. Significant progress has been made in the gene therapy field since CG01 was first designed, both in terms of manufacturing and in the formulation of gene therapies. For the epilepsy project CG01, this means that now is the perfect time to take full advantage of this new and important knowledge and optimize some of the components of the project before moving it towards clinical studies.

Using the combined strength of CombiGene and Spark, the two companies are now engaged in optimization of the therapeutic AAV to achieve improved coverage of the brain regions affected by epilepsy.

"The Joint Research Committee meeting in Stockholm was highly productive, and again proved that we have an ideal partner in Spark", says Karin Agerman, Chief Scientific Officer at CombiGene. "I am really happy about the decision to optimize some of the components of the project. By doing this, we will be in a much more advantageous position once the project enters in-human studies," Karin concludes.

Interview with Member of the Board

Malin Almgren

Tell us a little about yourself and your background and when you were elected to CombiGene's board!

"I was entrusted to join CombiGene's board in May this year and hope and believe that my background is well suited to support the company. I have a master's degree in biochemistry from Stockholm University and a PhD in medicine from Karolinska Institutet. During my two decades in academia, I have had the privilege of doing research at prominent institutions such as Karolinska Institutet and UCSD (University of California San Diego). My focus has been in epigenetics, i.e., how the environment can affect gene expression and I have applied this in areas such as immunology, neuroscience, and oncology. One of my first projects as a PhD student involved viral vectors to adjust the level of brain-derived neurotrophic factor (BDNF) in a mouse model, a valuable experience of how potent virus vectors are as tools, but also one in a series of failed experiments."

"After many years in preclinical research, I switched to the world of finance, where I have, among other things, worked with strategic partnerships regarding sustainable investments at a fund manager. In addition, I have worked as a financial advisor, where I have collaborated with many development companies in the Life Science sector with capital raisings and M&A. This has given me a deep understanding of challenges and opportunities within these types of companies. Today I have the privilege of serving as CEO of a company that works with health data and have also in recent years been entrusted as a board member of three companies."

What are your impressions of CombiGene after almost four months as a board member?

"My overall impression of CombiGene is very positive. I am impressed by the company's clear and ambitious business concept that focuses on developing effective gene therapies for serious diseases that currently lack satisfactory treatment options. I think the company has a smart strategy where they collaborate with a network of external researchers to utilize expertise and ideas, which can then be developed further to preclinical or clinical proof of concept."

"Furthermore, I think about the company's strength when it comes to commercialization. CombiGenes focus on co-development and commercializing of drug candidates through strategic partnerships shows an understanding that collaboration and partnerships can be crucial to achieving success on a broader spectrum. I also had the pleasure of meeting CombiGene's competent team to get a crash-course of the exciting ongoing projects."

What are the key milestones in the company's development as you see it?

"Continued identification and evaluation of new promising projects, positive results from preclinical studies, identifying gene therapy candidate within the lipodystrophy project CGT2 and success in the independent evaluation of the potential of COZY01 that is ongoing at NIH where the substance will be tested in a behavioral model and in different pain models are all important potential milestones. Overall, I think that these milestones could be critical to maintaining a strong pipeline of gene therapies and securing the future of the company."

How do you see the potential of the COZY pain program?

"The COZY program is really exciting and focuses on developing effective treatment options for severe chronic pain. This is of great importance because the conventional treatments used today often have side effects and may be insufficient to effectively manage the pain. The great potential is that COZY is based on new biological mechanisms of action that are expected to reduce or eliminate the side effects that are common with today's treatments. Perhaps the greatest potential of the COZY program is the ability to offer pain relief without being addictive and may be a promising alternative to opioid-based treatments that have been shown to be associated with substance abuse problems and serious side effects."

How do you think CombiGene will develop over the next three to five years?

"Over the next three to five years, we can expect that CombiGene has started to interact more with regulatory authorities such as the FDA and EMA to discuss plans for clinical trials and the approval process. In particular, COZY01 could be in or near the phase of clinical trials. This is a strong value-up that would further increase interest from potential partners, investors, or larger pharmaceutical companies. In summary, I am convinced that CombiGene has a strong foundation and strategy to make a real difference in gene therapy."

Interview with CombiGene's Director CMC

Sebastian Bauer

Earlier this year, Sebastian Bauer took up the position as Director CMC at CombiGene. The English Wikipedia lists 93 different meanings of the abbreviation CMC, in this case the three letters should be read as Chemisty, Manufacturing, and Control. More concretely, this means that Sebastian Bauer will work with the development of the processes and assays necessary for the manufacturing of CombiGene's drug candidates. Ingeneious contacted Sebastian for an interview.

Can you tell us a little about your background?

"Absolutely. I am originally from Germany, specifically Karlsruhe in Baden-Württemberg. I did my PhD in analytical biochemistry at the University of Konstanz and my post-doc at Karolinska Institutet in Stockholm. During the last twenty years or so, I have held several senior positions in the pharmaceutical industry, often focusing on CMC issues. I most recently came from a large CDMO company, that is, a company that helps other companies in the pharmaceutical industry with various services in development and manufacturing."

What attracted you to CombiGene?

"One of the most important things was the size of the company. I have previously worked at smaller companies, and I really enjoy that format. Smaller companies can be very agile, which means that some project elements can be carried out much faster than at larger companies, which suits my personality, I like to get things done."

What is required for successful CMC work?

"Many things! But if I had to pick one thing, it would be that early in the project you have to have a fairly precise understanding of what is needed to get a product approved by the pharmaceutical authorities. If you do not have that understanding, there is a very great risk that you will choose the wrong path and that later in the project you will have to redo different elements, which means losses in both time and money. If, on the other hand, you have a clear picture of the goal right from the start, you can do things intelligently, which means that the work can be carried out very efficiently. If I were to add something to this, it would be that I would like to underline the great importance of the various assays that are produced to ensure that factors such as security and stability are handled in the absolute best way. The design of these analyses can be crucial."

What are you mainly focusing on right now?

"To be honest, I'm still learning. CombiGene is a small company, but the scientific matter we deal with is at a high level. So far, I have had very good help from CombiGene's Senior Program Director Alvar Grönberg who has introduced me to the COZY program, which has the greatest need of a CMC director right now. I have also spent a lot of time with CombiGene's Chief Scientific Officer Karin Agerman, which has allowed me to quickly gain an understanding of critical CMC aspects in gene therapy projects. I have also had several contacts with CombiGene's broad CDMO network. My first focus will now be the peptide project within the pain program COZY, which suits me very well as I have ten years of experience working with peptides."

"My first focus will now be the peptide project within the pain program COZY."

CombiGene

The gene therapy explorer

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

www.combigene.com