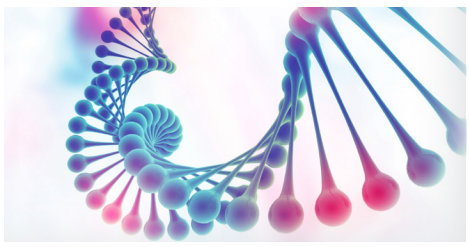


Future-proof production method in place for CG01

See page 2

Successful issues strengthen finances

See pages 4-5

INGENEIOUS

NEWS FROM COMBIGENE AB

ISSUE 3 • 2020

IN THIS ISSUEE:

CombiGene

The gene therapy explorer

This newsletter has been produced by CombiGene AB

LEADER

High pressure at CombiGene!

Let me begin this text by expressing my and CombiGene's very great appreciation to all who participated in the warrants of series TO3. The result was fantastic with a subscription rate of 97.25 percent, which means that CombiGene received more than 17 million SEK before issue costs. The confidence shown to us by our shareholders is greatly appreciated. Since the rights issue in April, we have worked hard with our procurement of capital to ensure that we have the necessary resources when our epilepsy project CG01 now enters an intensive phase of final design of production method and final preclinical studies. Through the rights issue and directed issue in April and a directed issue in July and the warrants in August, CombiGene has received SEK 63.45 million before issue costs. The July issue was made to the Dutch life science investor Nyenburgh Holding BV, which has made itself known as stable and knowledgeable owners.

The CG01 project is now advancing at high pace. Over the past few weeks, after intensive work, we have chosen a manufacturing method based on suspension to ensure that we can scale up our production in future commercial volumes. We have also chosen the Spanish company Viralgen as our production partner and have recently signed an agreement with them. Furthermore, we work together with CGT Catapult to develop analytical methods for quality assurance of production and together with Cobra Biologics we have produced so-called master cell banks, which means that we can now produce the plasmids that make up the starting material for the production of CG01 in a quality-safe way. Thanks to the fact that all parts of the production platform are now in place, we can start production of the CG01 material that we will use in the final preclinical studies during next year.

In our lipodystrophy project CGT2, we are currently testing various drug candidates with the aim of launching a proof-of-concept study next year and we have recently submitted a priority patent application to the UK Patent Office. Our goal right now is to work towards the final choice of drug candidate.

At the Annual General Meeting on June 29, 2020, a largely new Board of Directors was elected, which is presented in this issue of Ingeneious. Recently, BioStock conducted an interview with Bert Junno, CombiGene's new Chairman of the Board. With BioStock's kind permission, we publish the interview in its entirety in this issue of Ingeneious.

Finally, I would like to say that the entire team at CombiGene is looking forward to an intense autumn with many important activities and decisions. The summer weather is behind us, but when it comes to work at CombiGene there is high pressure!

Jan Nilsson
CEO

PROGRESS IN THE EPILEPSY PROJECT CG01

Future-proof production in place

CombiGene plans for the final preclinical steps and prepares for initial clinical studies

CombiGene's epilepsy project CG01 is in late preclinical phase. To take the final preclinical steps and the important step into clinical studies, CG01 must be produced according to the high standards of Good Manufacturing Practice, GMP. Since CG01 targets a significantly larger patient population (up to 10,000 patients a year) than the majority of today's gene therapies, production capacity is crucial for future commercial success. After intense work during the summer and the beginning of the autumn, Karin Agerman can report on several significant advances in this interview.

A lot has happened in the CG01 project lately. Can you give a quick overview of the most important things?

"Absolutely. Overall, it can be said that we have been working along two fronts in recent months. One front is about regulatory issues and quality control in production. The second front is about the choice of production method. There are two different principles for producing gene therapies, so-called adherent production and suspension production."

Let us start with the production. Which production method has CombiGene chosen and why?

"So far in the project we have used an adherent production method. This is a method that works great for the production of small and limited volumes. At the same time, the method is very difficult to scale up to large production volumes. For many gene therapies, this is not a problem since the patients to be treated are so few. For CG01, the situation is the reverse. The number of patients with epilepsy that we intend to treat can reach 10,000 a year. We therefore will use suspension production in order to produce the volumes we need in an efficient way."

So, the choice of method has been made. Have you also chosen a production partner?

"Yes, we have. In August we completed a pilot production using the suspension method at the Spanish manufacturer Viralgen with very positive results, and in early September we signed an agreement with Viralgen. This agreement is very important because we now have a partner who can produce CG01 for both the final preclinical studies, clinical studies and commercial use. This is very significant and a major milestone in the CG01 project."

INGENEIOUS EDITORIAL STAFF

Contact:
redaktionen@combigene.com
Legally responsible publisher:
Jan Nilsson

Production:
Wiberg & Co Reklambyrå AB
Text: Columbi Communications AB

CombiGene AB (publ)
Medicon Village, SE-223 81 Lund
info@combigene.com

CombiGene is listed on Nasdaq First North Growth Market.
www.combigene.com

"The number of patients with epilepsy that we intend to treat can amount to 10,000 a year."

Is there anything else you would like to add about the production of CG01?

"Yes, there is. The starting material for the production of CG01 consists of something called plasmids, that is, small circular DNA molecules. Three plasmids constitute the starting material and key components in the production of CombiGene's gene therapy vector, CG01, and are tasked with 'transporting' CG01's active substances NPY and Y2 into the patient's brain tissue. In August, our partner Cobra Biologics completed the work of producing so-called master cell banks required for plasmid manufacturing and thanks to this we have now secured a quality-assured platform for future commercial access to plasmids for CG01."

If we look at the future. What happens in the fall?

"The most important thing is that we will soon start producing materials for the upcoming toxicology and biodistribution study, which is scheduled to begin early next year. We will also conduct some additional preclinical studies. The CG01 project has always been very exciting to work with, but the last few months have been quite exceptional. We now have all parts of our production in place and we have a clear plan to successfully complete the project's preclinical phase."

Karin Agerman, Chief Research and Development Officer

EUROPEISKA UNIONEN
Europeiska regionala utvecklingsfonden

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

CombiGene applies for patent protection for CGT2

■ In the lipodystrophy project CGT2, CombiGene is currently testing various drug candidates with the goal of launching a proof-of-concept study in 2021. The company has recently filed a priority patent application with the UK Patent Office. The filing of this patent application paves the way for global patent protection for CGT2, which is of great importance for protecting key functions of CGT2 during the continued development and commercialization.

"Since we licensed the project from Lipigon 2019, the pace has accelerated, and we are now beginning to see the first fruits of this work. The filing of the patent application is an early milestone in this very exciting project," says Annika Ericsson, Senior Project Manager at CombiGene. "We have also planned for the project's next stage of in vivo studies. Our main goal right now is to work towards the final choice of drug candidate."

ABOUT LIPODYSTROPHY

Lipodystrophy is a rare disorder that is characterized by abnormal distribution of fat in the body. Patients suffer from lipoatrophy, which means that body fat is lost. In the absence of normal body fat different organs begin to accumulate fat, which subsequently leads to serious metabolic complications, among them, extreme insulin resistance, hypertriglyceridemia (elevated levels of the blood fat triglyceride) and hepatic steatosis (fatty liver disease).

There are currently a few treatments that can alleviate the symptoms of lipodystrophy, but no form of therapy that is targeted directly at the fundamental cause of the disorder. For patients suffering from partial lipodystrophy there are currently no treatments whatsoever.

FUNDING

Focused efforts to create resources

CG01 enters a cost-intensive development phase

■ CombiGene has for a long time worked intensively with the company's fundraising to create resources for further development of the epilepsy project CG01, which is now entering a very cost-intensive phase, and for the lipodystrophy project CGT2.

So far in 2020, CombiGene has raised a total of SEK 63.5 million before issue costs. In April, a rights issue was carried out that brought the company SEK 26.3million and a directed issue of SEK 4.0 million. In July, a directed issue was carried out to the Dutch life science investor Nyenburgh Holding BV of SEK 15.5 million and in August the company received SEK 17.7 million after 97,3percent of the TO3 warrants were subscribed for. November is the time for the subscription period of the warrants in series TO4 and TO5, which can bring to the company a maximum of approximately SEK 36.2 million.

FUNDING

Directed issue gives SEK 15.5 million

■ *In August, CombiGene carried out a direct share issue corresponding to an initial investment of EUR 1.5 million or approximately SEK 15,5 million, before issue costs, to the Dutch specialized Life Science investor NYIP ("Nyenburgh Holding BV"). Warrants of series TO5 are delivered as part of the issue and have the same terms and conditions as CombiGene's series TO4 warrants. Upon full exercise of all warrants, the Company will be receiving a maximum of approximately SEK 15 million on top of the initial payment of SEK 15,5 million.*

INGENIOUS called NYIP's Director Investments Mr David .Q.J. Van Mastwijk to learn more about NYIP and their reasons to invest in CombiGene.

Thanks for taking your time to speak with INGENIOUS. It is much appreciated. Can you tell us a bit about your investment profile and how long you have been operating?

"We have been working together as a partnership since 2013, when we saw the opportunity to invest in the European Healthcare segment. We've been expanding our team and brought in two life science analysts to digest the science that is behind our investments."

Is CombiGene your first investment in gene therapy?

"No, we have had interactions with multiple gene therapy companies. Besides them using a viral vector to insert genes or modify gene expression, the scientific rationale for all of these companies is quite diverse, due to the underlying disease. Gene therapy is not really a therapy area, but more of a treatment modality, like antibodies and small molecules."

What attracted you to CombiGene?

"CombiGene is an undervalued company in gene therapy. And although epilepsy is a multifactorial disease (or symptom), there are some common denominators in the disease area, when looking at the origin of seizures and what the alteration of gene expression looks like following disease onset. CombiGene has found a way to increase the expression of neuropeptide Y (NPY), a peptide that is naturally released following epilepsy-like brain activity, which suppresses new episodes."

"The way that CombiGene's therapy works, using a natural, activity-dependent mechanism, should make for a safe profile, that mimics healthy mechanisms of activity control. Biologically, this makes sense."

Which are your expectations on CombiGene two years from now?

"First, there is the GMP manufacturing process, which is now being set up and optimized by Cobra Biologics when it comes to the production of plasmids and Viralgen when it comes to the production of the drug candidate CG01. This is a very important step, which can influence the properties of the drug candidate. Effective and consistent production is the first priority. With excellent partners such as Cobra and Viralgen, I expect this to be finalized in a timely manner."

"Second, I would expect a clear safety profile being demonstrated on the CG01 project. Although this might seem like a minor step when looking at more traditional biotech companies, this is a vital part when it comes to gene therapies. Also, this will trigger gene therapy companies to look for local gene therapy targets in the brain, where they are now more focused on single gene defects and eye diseases."

"Third, because this is gene therapy, even the initial safety study (Phase I) will be performed in patients. While it may be too early to really conclude on the efficacy of CG01 at that stage, efficacy signals may be observed, which are a basic proof of principle."

EUROPEISKA UNIONEN
Europeiska regionala utvecklingsfonden

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

FUNDING

Very high utilization rate of series TO3 warrants

■ On August 31, 2020 the period for exercising warrants of series TO 3 warrants ended. In total, 29 450 679 warrants had been exercised for subscription of shares and each warrant entitled to subscribe for one (1) new share in CombiGene at a subscription price of SEK 0.6 per share. The utilization rate thus amounted to approximately 97,25 per cent and through the warrants CombiGene was granted SEK 17 670 407,40 before issue costs.

"I am extremely pleased with the outcome of our warrants. The fact that more than 97 percent of the warrants were subscribed for indicates that our shareholders have confidence in the company. CombiGene has now entered a very intensive stage in the company's development and we will make major investments in production and final preclinical studies. The capital injection of more than 17 million SEK is therefore very welcome," says Jan Nilsson, CEO of CombiGene, in a comment to Genevägen.

SUMMARY

The subscription entails that the number of shares in CombiGene increases with 29,450,679 shares, from 147,210,132 shares to 176,660,811 shares and that the share capital increases by SEK 2,945,067.9 from SEK 14,721,013.2 to SEK 17,660,081.10.

The shares added as a result of the exercise of warrants of series TO 3 entails a dilution effect of approximately 16,67 per cent. Dilution effect refers to the number of newly issued shares as a result of exercised warrants of series TO 3 in relation to the total number of shares in CombiGene after the new shares have been registered.

Events

October 19 2020

Aktiedagen digitalt in Stockholm

Nov 9 – Nov 10 2020

Stora Aktiedagen digitalt in Göteborg

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. Everything is conveniently accessible at **combigene.com.**

Sign up here!
https://bit.ly/2wzacK4

Fantastically inspiring days at Gene Analytical Therapy Europe!

■ Meeting colleagues, specialists and representatives of authorities in one's own industry is always very inspiring. The virtual conference Gene Therapy Analytical Europe at the beginning of September, which focused on analyses for quality control of the production of gene therapies, was no exception to this rule. During two packed days of digital meetings and sessions, there were very good discussions about new technologies to measure quality and reproducibility in the production of gene therapies.

A very fruitful session was held by the UK Medicines Agency (MHRA) where questions could be put directly to representatives of the Agency. There were also many companies that have progressed further in their development than CombiGene that gave presentations and were involved in panel discussions, where we received many good advices on how best to work with quality analysis in gene therapy. It is particularly satisfactory that I several times during the conference could conclude that CombiGene is on the right track.

It is also great to see that CombiGene works in a very dynamic field where we help each other, both between companies and between authorities and companies. All are driven by a genuine desire to take gene therapy's unique opportunities forward.

The main messages during the conference were to start early with analysis methods for quality assurance and, where possible, develop analytical platforms that can be used for several projects and to develop enough analytical methods to provide a comprehensive picture of how a product is affected during production and storage while waiting to be administered to the patient.

Karin Agerman
Chief Research
and Development Officer

"Several times during the conference, I could conclude that CombiGene is on the right track."

EUROPEISKA UNIONEN
Europeiska regionala utvecklingsfonden

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

Bert Junno takes the helm of the Board

At the Annual General Meeting on June 29, 2020, a largely new Board of Directors was elected in CombiGene. The new Chairman of the Board is Bert Junno and new board members are also Jan Nilsson, Jonas Ekblom and Per Lundin. Peter Nilsson, who has been on CombiGene's Board of Directors since 2014, was re-elected at the meeting. The new board has combined knowledge and experience from key areas important for CombiGene's continued development such as research, development, business development, intellectual property, marketing and sales, as well as finance and accounting.

Bert Junno has extensive experience in management and board work from the electronics, biotechnology and IT industries in both Europe and the U.S. and has been a member of several biotechnology companies. Bert holds a PhD in Physics and Engineering from Lund University. In addition to the chairmanship of CombiGene, Bert Junno is also Chairman of the Board of Cyxone AB (publ) and member of Accequa AB and Accequa GmbH.

Jan Nilsson is CombiGene's CEO since 2016 and was elected to the Board at the 2020 Annual General Meeting. Jan has extensive experience in life science and has worked in areas such as clinical research, business development, sales and marketing. Jan has built up and led successful organizations at Schering-Plough and Tripep AB and has held senior executive positions at a number of biotechnology companies such as Kringle Pharma, Lipopeptide and NeuroVive AB (now Abliva AB). Jan has an MSc in Biology and Chemistry at the University of Gothenburg and an MBA in International Business Management from Uppsala University.

Peter Nilsson has been on CombiGene's Board of Directors since 2014 and has extensive experience from the financial sector and is currently working as CFO with a focus on strategy and business development in the Rotorbulk Group (also known as Finja). Peter has been a partner and business area manager at Mazars SET Revisionsbyrå AB. Peter Nilsson has a master's degree in business administration at Lund University. In addition to his position on CombiGene's Board of Directors, Peter is also a board member of PN Finanskonsult AB and Chairman of the Board of Flisby AB.

Jonas Ekblom has over 25 years of experience in life science. He is currently CEO of Promore Pharma and has previously held senior and executive management positions in biotechnology companies in Sweden, the US and Switzerland, including Pharmacia and Biovitrum. Jonas is associate professor of pharmacology at Uppsala University, has a B.Sci in Chemistry at Stockholm University and a Ph.D.in experimental neurology from Uppsala University, and post-doctoral studies from the University of Southern California, School of Pharmacy in LA. He also has training in strategic planning and management. Jonas has published more than 60 articles in peer-reviewed journals. In addition to the assignment on the Board of Directors of CombiGene, Jonas is also a board member of World 5 Ventures and Pergamum AB and Chairman of the Board of EffRx Pharmaceuticals SA.

Per Lundin hhas over 10 years of experience in leading companies in biotechnology with a focus on business strategy, scientific leadership, intellectual property and business development. Per is co-founder and chief operating officer of UK Evox Therapeutics. Prior to founding Evox, Per co-founded and was CEO of IsletOne Therapeutics, a cell therapy company that is a spin-off from Karolinska Institutet. Per was previously European Patent Attorney at one of the largest European intellectual property offices. He began his career as a drug delivery researcher at Apollo Life Sciences. Per received his Ph.D. from Karolinska Institutet and holds a Master of Science in Biotechnology from KTH and a Master of Science in Engineering from Stockholm University.

COMBIGENE BOARD

After the Annual General Meeting on June 29.

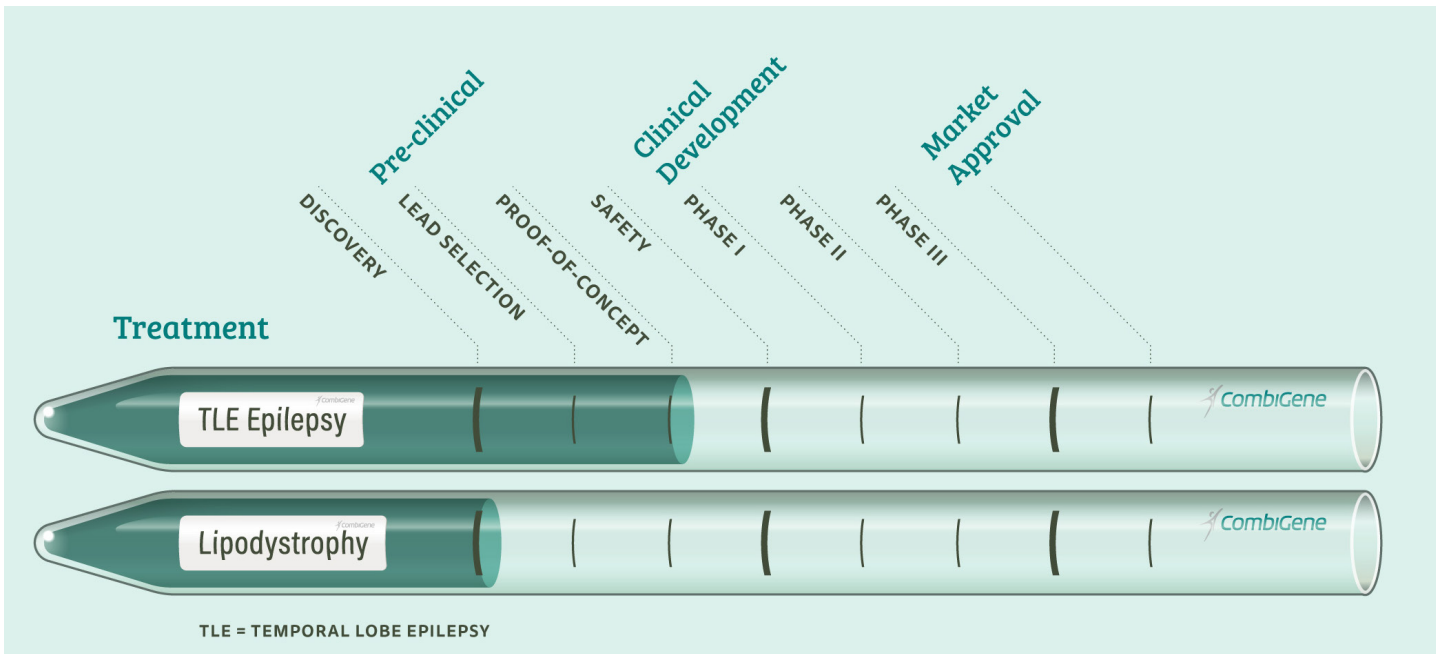
Bert Junno, Chairman of the Board

Jan Nilsson CEO/Board member

Peter Nilsson Board member

Jonas Ekblom Board member

Per Lundin Board member



PROJECT OVERVIEW

In the epilepsy project CG01, CombiGene has completed the work to establish a production platform for the production of material for final preclinical studies, upcoming clinical studies and future commercial use.

In the lipodystrophy project CGT2, intensive work is currently underway to identify the final drug candidate.

EUROPEISKA UNIONEN
Europeiska regionala utvecklingsfonden

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

THIS INTERVIEW WAS DONE BY BIOSTOCK AND PREVIOUSLY PUBLISHED ON THEIR WEBSITE WWW.BIOSTOCK.SE

CombiGene's new Chairman of the Board talks about the future visions for the company

■ *At the gene therapy company CombiGene's Annual General Meeting in June, Bert Junno was elected as the new Chairman of the Board. With extensive experience in the biotechnology industry and having founded five companies in the sector, Junno will be a valuable addition to the company's continued development. BioStock contacted Junno to learn more about his past experience and how he will make his mark on the company, which in its pipeline has a drug candidate for epilepsy and a project to develop a drug candidate against partial lipodystrophy.*

With a background as Ph.D. in physics and technology for semiconductors and M.Sc. in physics from Lund University, Bert Junno has a long experience of management and board work for a number of companies active in biotechnology in both Europe and the U.S.

Bert Junno has, in cooperation with others, founded several biotechnology companies, such as WntResearch, Galecto Biotech, Gabather, Aptahem and Cyxone. In addition to being CombiGene's Chairman of the Board, Junno holds the same assignment in Cyxone. He is also a board member of Accequa and Accequa GmbH.

In addition, Junno has held board assignments in Taurus Energy, Cardiovax llc., Galecto Biotech, Aptahem, and has been CEO and board member WntResearch and Gabather and board member of Patent & Registreringsverket (PRV) transparency council between the years 2010-2019.

New Chairman of the Board comments

BioStock contacted Bert Junno for a comment regarding his new role as new Chairman of the Board in CombiGene.

Bert Junno, you have founded several biotechnology companies and have a long experience of board work. How do you intend to make your mark on CombiGene's business?
I am very impressed with CombiGene's development of its unique projects so far. The epilepsy project CG01 has continuously delivered according to plan.

In addition to deliver our projects according to plan, it is my ambition that we will create additional shareholder value by developing the company's intangible assets such as patents and know-how and through good communication with the market and the many shareholders who have invested in CombiGene. The market's confidence in CombiGene is strong, as was shown in the recently closed subscription period for TO3 where the subscription rate was an impressive 97.25 percent and contributed just over SEK 17 million to the company.

What attracted you to accept the position as Chairman of the Board and do you see, based on past experience, any special challenges in the position where CombiGene is today??
One thing that is attractive about CombiGene is the enormous opportunities in gene therapy for the treatment of diseases where no effective therapy currently exists. It will be very exciting to follow the development of gene therapy in general and CombiGene's development in particular in the coming years. CombiGene's projects are unique and offer new opportunities that can help a large number of patients with severe medical conditions. This also means that additional values can be built using new intangible assets.

A clear shift in a company like CombiGene is usually the transition from development to commercialization phase. What is the company's strategy regarding business development, for example in terms of partnerships, industrial partnerships, out-licensing, etc.?
For projects that are developed for broad indications, such as the epilepsy project CG01, the ambition is to take the project into clinical phase and then form some kind of partnership with a large pharmaceutical company that can take the project throughout the clinical program and on to commercialization. I know that CombiGene has an ongoing dialogue with several major pharmaceutical companies that follow the development of CG01 with great interest.

"It will be very exciting to follow the development of gene therapy in general and CombiGene's development in particular in the coming years."

For projects that are developed for rare diseases, the ambition is to take them all the way to the market with internal recourses. Pharmaceuticals developed for small patient populations have a good prospect of receiving orphan drug designation, which brings significant benefits in terms of lower development costs and attractive pricing. This also means that smaller companies such as CombiGene may have sufficient internal resources to handle this type of project on their own.

Finally, what are you looking forward to in terms of future milestones for CombiGene?
In the semi-long term, I look forward to the first studies in humans for CG01. Going into clinical studies is always a significant milestone. In the shorter term, I look forward to the milestones that are closer in time, such as getting all the parts of the production process in place. This is a comprehensive work where it is important to meet all regulatory requirements. In addition, we will make sure to establish a production process that can deliver in sufficient volumes, at the right cost and quality throughout the product's life cycle. When all parts of our production are in place, we will produce materials for the final preclinical studies, including the very important toxicology and biodistribution studies. In short, CombiGene has a lot of exciting things to look forward to both in the short and long term!

EUROPEISKA UNIONEN
Europeiska regionala utvecklingsfonden

"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 CG01 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 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