INGENEIOUS

NEWS FROM COMBIGENE AB

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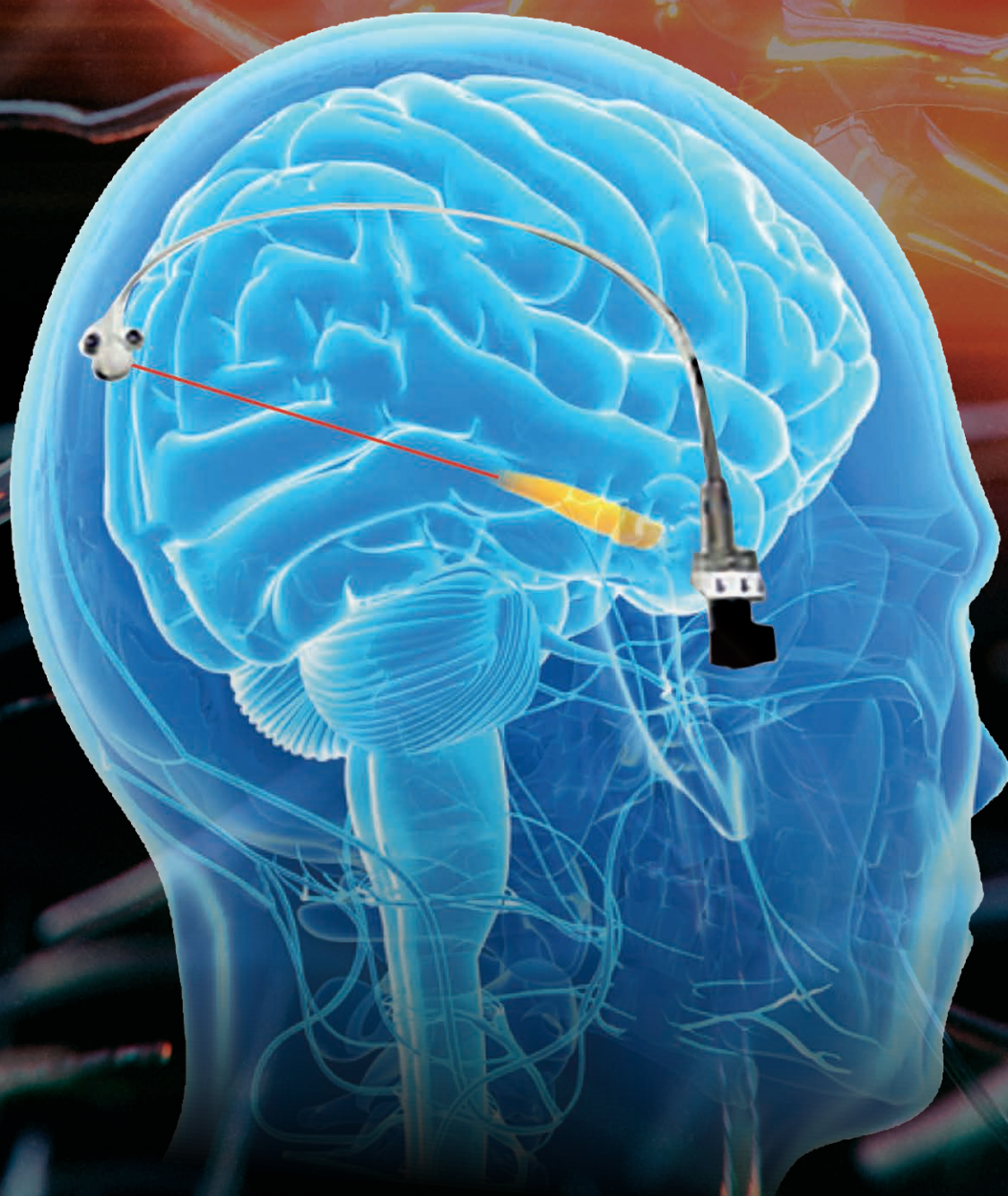
CombiGene and Spark Therapeutics enter exclusive global collaboration and licensing agreement for gene therapy candidate CG01

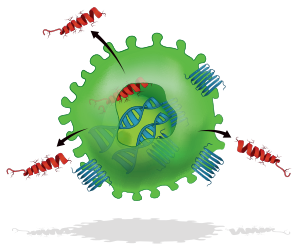


CombiGene

The gene therapy explorer

INTERVIEW WITH COMBIGENE'S CEO JAN NILSSON

As soon as Ingeneious heard the fantastic news that CombiGene has signed an agreement on clinical development and future global commercialization of the company's epilepsy project CG01, we contacted CEO Jan Nilsson to talk about what the agreement means for the company.



What are your spontaneous comments to the agreement with Spark Therapeutics?

"Let me say first and foremost that I am incredibly proud and happy that CombiGene has reached this agreement with Spark. I have worked for a long time in the Swedish and international pharmaceutical industry and this agreement is one of the absolute highlights of my career"

"Many people have contributed to the fact that we can now hand over our epilepsy project CG01 in Spark's competent hands. First of all, I want to mention CombiGene's scientific founders Professor Merab Kokaia and Associate Professor David Woldbye. Their discoveries and hard work are the prerequisite for the entire CG01 project. Furthermore, I would like to thank all CombiGene's employees. CombiGene is a small company, something which places special demands on our employees in terms of flexibility, perseverance and – not least – deep and at the same time broad competences. I am very grateful for the tremendous commitment that has taken our epilepsy project forward day by day."

"Furthermore, I would of course like to thank our shareholders who have also shown great perseverance. All drug development takes a long time and is characterized by great uncertainty. The fact that we have shareholders who have continued to believe in what we are doing and have been prepared to inject new capital when needed has been absolutely crucial to getting to where we are today."

"I would also like to take this opportunity to thank the people at Spark. During the latter parts of the preclinical phase, we have had an ongoing and productive dialogue with Spark, and I am impressed by their resources, know-how and professional organization. I would also like to highlight the mutual trust that has characterised our negotiations and which has led to the agreement that we now have in place."

How do you want to describe the agreement?

"If I were to choose one word to describe the agreement, I would say it is natural. What I mean by that is that CombiGene gets more revenue from the agreement the more milestones that are achieved and that the really large compensations are tied to future sales."

"Specifically, this means that CombiGene, under the terms of agreement, is eligible to receive up to $328.5 million excluding royalties, with $8.5 million upon signing, up to $50 million at preclinical and clinical milestones. Upon commercialization, CombiGene is eligible for tiered royalties up to low double-digits based on net sales. CombiGene will also be reimbursed for certain authorized R&D expenses."

What are the main benefits of the agreement?

"The agreement with Spark means that we have now found a partner with the know-how and resources to continue the CG01 project during the cost-intensive clinical studies, i.e., human studies. The fact that Spark has this ability is demonstrated, among other things, by the fact that they were among the first companies to have a gene therapy approved for sale, namely Luxturna."

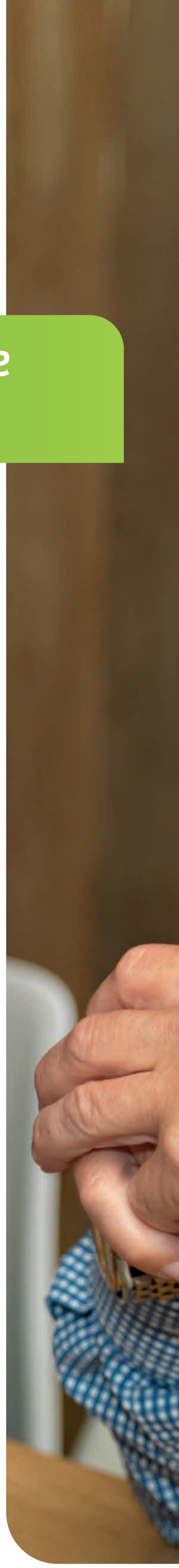
"For CombiGene, the agreement means that we verify our business model, which is to outlicense projects that target large patient populations in late preclinical/early clinical phase."

"However, the most important thing about the agreement is that CG01 is now taking another step closer to becoming an approved and effective treatment for all patients with drug-resistant focal epilepsy who today lack adequate treatment options. I have personally experienced the devastating effects of epilepsy among family members and close friends, and I have seen how deeply this disease can affect quality of life. After all, offering a better life for these patients has been the goal since CombiGene was founded!"

What happens to CombiGene now?

"As far as the CG01 project is concerned, we will continue to run the final preclinical parts just as planned with the difference that we are now doing so in collaboration with Spark. This is something we are very much looking forward to. As CG01 enters the clinical phase, Spark will take over responsibility for the project."

"For CombiGene, this means that we will have the opportunity to intensify our business development and bring new promising projects into the company. Through the successful preclinical development of CG01 and the agreement with Spark, we have demonstrated that we are a competent company and an interesting partner for both academia and industry."



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What the agreement with Spark Therapeutics looks like

The agreement between CombiGene and Spark Therapeutics gives Spark the global and exclusive right to develop, manufacture and commercialize the drug candidate CG01. CombiGene will, in collaboration with Spark, carry out the remaining parts of the preclinical program, mainly the studies in toxicology and biodistribution. Once the preclinical program is completed, Spark will assume full responsibility for clinical development from the first human study onwards to global commercialization.

Under the terms of agreement, CombiGene is eligible to receive up to USD 328.5 million excluding royalties, with USD 8.5 million upon signing, up to USD 50 million at preclinical and clinical milestones. Upon commercialization, CombiGene is eligible for tiered royalties up to low double-digits based on net sales. CombiGene will also be reimbursed for certain authorized R&D expenses.

Spark THERAPEUTICS

This is how Spark present themselves

We Are Spark

At Spark Therapeutics, a fully integrated, commercial company committed to discovering, developing and delivering gene therapies, we challenge the inevitability of genetic diseases, including blindness, hemophilia, lysosomal storage disorders and neurodegenerative diseases.

Founded in March 2013 as a result of the technology and know-how accumulated over two decades at Children's Hospital of Philadelphia (CHOP), our investigational therapies have the potential to provide long-lasting effects, dramatically and positively changing the lives of patients with conditions where no, or only palliative, therapies exist. Greater understanding of the human genome and genetic abnormalities have allowed our scientists to tailor investigational therapies to patients suffering from very specific genetic diseases. This approach holds great promise in developing effective treatments to a host of inherited diseases. Our initial focus is on treating orphan diseases.

Headquartered in dynamic Philadelphia, we are a diverse, experienced team united in our goal to break down barriers for people and families affected by genetic diseases. As our name suggests, our investigational, one-time therapies are designed to spark healthy biology, and deliver potentially life-altering transformation for people and families affected by genetic disease. Spark is a member of the Roche Group.

Our mission

Challenge the inevitability of genetic disease by discovering, developing and delivering treatments in ways unimaginable – until now.

Our vision

A world where no life is limited by genetic disease.

You can find more information on the company's website: https://sparktx.com

Hard work and continuous progress have paved the way for the agreement with Spark Therapeutics

Since its IPO in 2015, CombiGene's epilepsy project CG01 has continuously reached one milestone after another. In the early years, great progress was made in the early preclinical studies leading up to the very important human expression and proof-of-concept studies.

After the successful proof-of-concept study, an intensive phase began when CombiGene conducted a thorough work to evaluate and subsequently select the right partners for continued and larger preclinical studies and for the production of CG01. In parallel with this work, CombiGene has conducted strategic work to build good relationships with potential partners to find the right partner for the continued development and global commercialization of CG01.

"It is the result of all these efforts – positive preclinical results that have been delivered according to plan; leading partners in pre-clinical development and production; and continuous business development on an international level – that led to the agreement with Spark Therapeutics," says Karin Agerman, CombiGene's Chief Research &Development Officer in a comment to Ingeneious.

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

CG01 – milestones

2016

- First screening study conducted.
- Selection of a candidate drug.

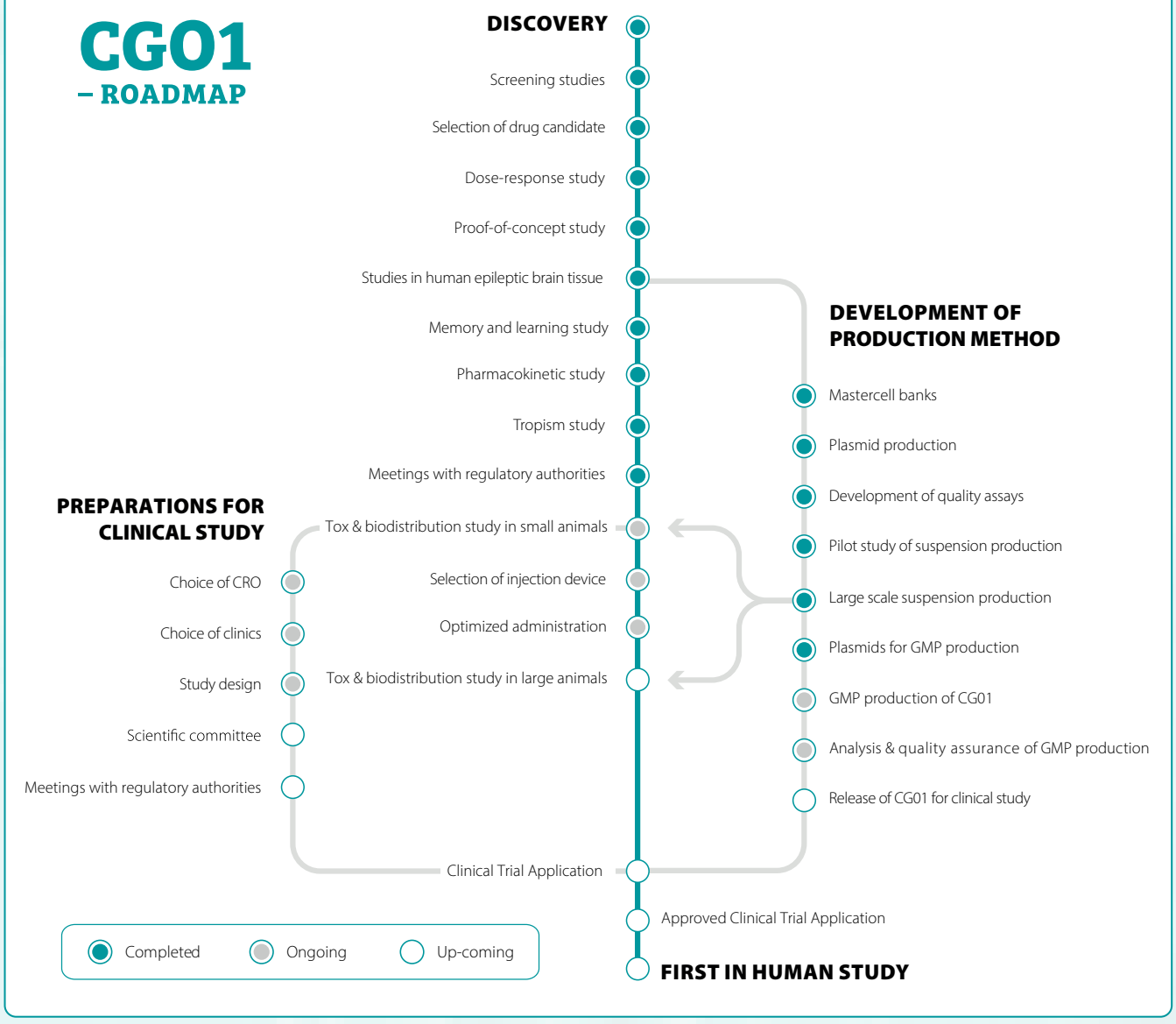
2017

- Data from the dose-response study indicate a dose-dependent anti-epileptic effect.
- The proof-of-concept study in a chronic epilepsy model is initiated.
- Studies in human epileptic brain tissue from patients with pharmacoresistant epilepsy confirm that CG01 is expressed in human cells.

2018

- Final data from the preclinical proof-of-concept study confirm positive treatment results in the form of significantly fewer and shorter seizures.
- CombiGene enters into collaboration with British Cell and Gene Therapy Catapult to develop a GMP manufacturing method for CG01.
- Horizon 2020, the EU framework program for research and development, allocates EUR 3.36 million for the development and commercialization of CG01.

CG01 – ROADMAP



2019

- **Acquisition of Panion Animal Health gives CombiGene full control over the company's intangible assets in the CG01 project.**
- **Agreement with CRO Northern Biomedical Research (NBR), which specializes in preclinical studies in the central nervous system (CNS). The agreement covers assessment of the candidate drug, CG01, in a smaller pilot study, a biodistribution study and a safety study, a so-called toxicity study.**
- **CombiGene signs an agreement with the CDMO, Cobra Biologics, regarding production of plasmids for GMP manufacturing of CG01.**

2020

- **Preclinical pharmacokinetic study completed with positive results. The study confirms that CG01 creates long-term expression of the active substances NPY and Y2.**
- **The preclinical learning and memory study shows that NPY and Y2 have no significant negative effect on cognitive functions.**
- **Delivery of all three plasmids needed to produce CG01.**
- **Delivery of master cell banks for the three plasmids.**
- **Successful pilot study performed with suspension production method.**
- **Positive results in tropism study.**
- **Agreement on GMP production with Cobra for plasmids for CG01.**
- **Analytical methods for quality control of the production of CG01 developed in collaboration with CGT Catapult.**
- **Manufacturing agreement with Viralgen for the production of CG01.**
- **Agreement with the British company Neurochase regarding the development of optimized administration of CG01.**
- **First large-scale production of CG01 at the Spanish gene therapy manufacturer Viralgen**

2021

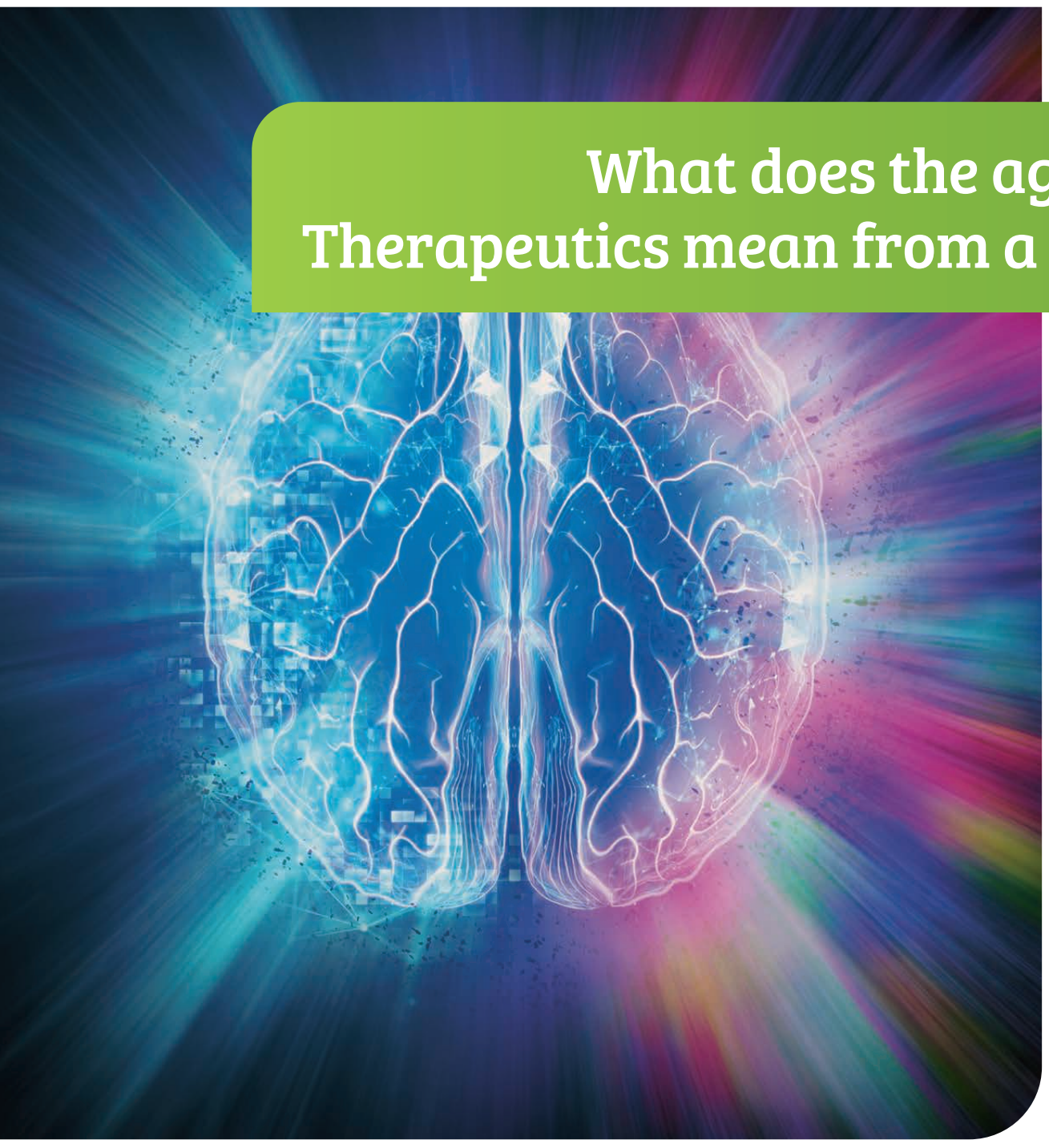
- **The material from the first large-scale production of CG01 released for use in the final parts of the preclinical program.**
- **The CG01 project initiates preclinical biodistribution and toxicology studies in small animals.**
- **GMP-produced plasmids (starting material for the production of CG01) released for GMP production of CG01.**
- **GMP production of CG01 for the first human study.**
- **CG01 gets patents in the U.S. and Russia.**
- **Global and exclusive cooperation and licensing agreement with Spark Therapeutics.**

A big thank you to CombiGene's shareholders! You've made CombiGene's amazing journey possible!

It is no secret that drug development takes a long time, requires considerable financial resources, and contains a great deal of uncertainty. Since the IPO of CombiGene in 2015, the company has carried out a number of new share issues, most of which have been rights issues. The fact that the new share issues have been relatively frequent is quite natural. The company as well as its shareholders have an interest in seeing that the projects are developing positively and at the pace one can expect before moving forward and investing additional resources. CombiGene's epilepsy project CG01 has from this perspective performed fantastically well. Defined milestones have been achieved according to plan, which step by step has made the project increasingly attractive. The final proof of this is the agreement with Spark Therapeutics.

CombiGene's management and board would therefore like to extend a big and warm thank you to the company's shareholders. You're the ones who made the development of CG01 possible. The agreement with Spark Therapeutics is a fantastic milestone in CombiGene's history – after briefly celebrating this amazing success, we now roll up our sleeves and return to work. CombiGene's journey has only just begun and we will do everything to ensure that it continues to be successful.

What does the agreement with Spark Therapeutics mean from a patient perspective?



The agreement with Spark is very positive for the continued development of CombiGene's epilepsy project CG01. CombiGene now has a strong and competent partner who has the resources, know-how, organization, and experience to take CG01 all the way through clinical development and on to the global market.

For patients with focal, drug-resistant epilepsy, this is of course good news. At the same time, one must be aware that a lot of work remains to be done. CG01 has undergone a number of preclinical studies with different purposes and the important preclinical studies in toxicology and biodistribution have just begun. Thereafter, the clinical program, i.e. human studies, will be initiated with the aim to ensure that CG01 is both safe to use and that the treatment has the intended effect. There is no guarantee that CG01 will get through the entire and very comprehensive clinical program, but the agreement with Spark is a big and very significant step forward.

CombiGene's Chairman Bert Junno comments on the agreement with Spark

What are your first spontaneous comments on the deal with Spark?

"First of all, the deal is extremely gratifying – and very important for CombiGene's continued development as a company. In Spark, we have found a partner who understands the opportunities within our epilepsy project CG01 and who realizes the value of the technology track chosen by CombiGene. The fact that we are now licensing CG01 to Spark means that this important project will have the best conditions to reach patients in the shortest possible time."

What have been the key factors in the successful deal with Spark?

"Here I would like to highlight a few different things. Firstly, CombiGene has a very high quality of its research and development. The scientific quality of the work carried out by the company's scientific founders Professor Merab Kokaia and Associate Professor David Woldbye is at a very high level. Their discoveries are the very prerequisite for the preclinical development of CG01 that the company has so successfully implemented in recent years."

"The second thing I want to highlight is CombiGene's management, which has developed CG01 completely according to plan, and subsequently conveyed the knowledge of the CG01 project's scientific base, preclinical successes and commercial opportunities in a very stringent way to Spark."

"If we look at the pharmaceutical industry a little more broadly, it quickly becomes apparent that gene therapy is a very hot area right now and there are several large companies looking for interesting projects. The fact that CG01 is aimed at a patient population that is very substantial in the context of gene therapy obviously makes the project particularly interesting."

What does this deal mean for CombiGene's future?

"It means a lot. This success validates CombiGene's technology, development team, commercial capabilities, and business model in an absolutely fantastic way. The company has now shown that it has the capacity and ability to take a project from discovery phase to successful outlicensing and is now well positioned to develop new value-creating therapies."

CombiGene's scientific founders talk about the quantum leap that the epilepsy project CG01 is about to take

The original scientific work on the neurotransmitter NPY and its receptor Y2 was done by CombiGene's scientific founders Professor Merab Kokaia and Associate Professor David Woldbye in 2010. In 2016, the preclinical development of the epilepsy project resulted in the selection of CG01 as the gene therapy candidate. The deal with Spark Therapeutics has the potential of being a quantum leap for the CG01 project, and we contacted Merab and David to get their reactions to the news.

Can you describe your feelings now that your NPY/Y2 discovery which forms the basis of CG01 is moving towards clinical studies with Spark Therapeutics, a large and experienced gene therapy company?

Merab:
"This is like a dream come true. After so many years of research and development, we finally see an opportunity to bring our preclinical studies to clinical application for patients with difficult-to-treat epilepsy. I get e-mails and calls from such patients and it is so frustrating that there is not much one can offer these people, who have exhausted all today's available drugs in their fight against epilepsy. It feels good that now we have hope that a novel treatment strategy with gene therapy will be tested in clinical application, and there could be a better future for these patients. It has been really fulfilling to experience the whole journey of translating our research in the lab into potential clinical treatment that may help many patients. I have been interacting with the team in Spark Therapeutics during our discussions, and I have full confidence that this is a right set of people to bring this treatment all the way from clinical trials to a finished product on the market."

David:
"I am thrilled to see that pioneering scientific work with the neurotransmitter NPY – the key component in CombiGene's gene therapy – may now result in new treatment for epilepsy patients. As a scientist, it is not often that your findings are translated into novel treatment for patients. I am very confident that CombiGene in Spark Therapeutics has found a perfect partner to ensure success of the project of developing the first gene therapy treatment for drug-resistant temporal lobe epilepsy patients."

What would it mean for patients if the clinical program is successful?

Merab:
"If the program is successful, it will mean a lot for the patients suffering from drug-resistant epilepsy. These patients have very limited if any alternative treatments, but gene therapy may bring such alternative to them and change their life completely. Experiencing uncontrolled seizures, as they do, have a really negative impact on the quality of life, and if successful, this novel treatment strategy will change this dramatically."

David:
"If CombiGene's gene therapy, which targets the seizure focus selectively, proves successful in drug-resistant temporal lobe epilepsy patients, this will also open up the possibility that gene therapy can be used for the large group of epilepsy patients who currently do respond to antiseizure drugs but experience life-long side effects. Thus, it is my hope that gene therapy may reduce the use of traditional drugs for treatment of seizures among these patients and also let them experience significant improvement in quality of life."

Any other comments you want to make

Merab:
"I would like to thank all the people that believed in our research as something valuable for a potential treatment of patients with epilepsy. This road has not been easy, but their dedication and hard work really made this possible. I really hope that the outcome of the clinical trials will be of value for epilepsy treatment, but also be an emotional reward for all of those people who contributed up to this point and all of those who will work on the project in coming years down the road."

David:
"It has been a life-time experience to develop the gene therapy project in collaboration with my long-term scientific partner Prof. Merab Kokaia as well as the dedicated and very competent team of CombiGene."

David Woldbye

Merab Kokaia

About CombiGene AB

CombiGene's vision is to provide patients affected by severe life-altering diseases with the prospect of a better life through novel gene therapies. CombiGene's business concept is to develop effective gene therapies for severe life-altering diseases where adequate treatment is currently lacking. Development assets are sourced from an external research network and developed to achieve clinical proof of concept. Drug candidates for common diseases will be co-developed and commercialized through strategic partnerships, while the company may manage this process on its own for drugs targeting niched patient populations.

The Company has an exclusive collaboration and licensing agreement for the CG01 project with Spark Therapeutics.

The company is public and listed on the Swedish marketplace Nasdaq First North Growth Market and the company's Certified Advisor is FNCA Sweden AB, +46 (0)852 80 03 99 info@fnca.se.

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