INGENEIOUS

NEWS FROM COMBIGENE AB

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Welcome to special issue 1 of 3

Since the agreement with Spark Therapeutics, CombiGene has strengthened its positions in a number of areas, not least financially. The company is now actively looking for additional gene therapy assets for in-licensing and value-creating pre-clinical development.

In order to highlight our new position, we have decided to publish three issues of Ingeneious at a rapid pace to provide an in-depth picture of some of the areas that are important to us.

I hope you will find it a pleasant read.

Jan Nilsson,

CEO

CombiGene

The gene therapy explorer

THEME GENE THERAPY

Gene therapy has an amazing inherent potential!

Gene therapy is one of the areas that raises real hope in today's drug development. The potential to permanently cure diseases that currently lack effective treatment options has started intensive work both within pharmaceutical companies as well as within the global research community.

The medical community today knows about 2,800 diseases caused by single defective genes. The majority of these diseases still lack effective treatment methods. For some of them, there are symptom-relieving therapies, other diseases lack treatment options altogether.

CombiGene's partner Spark Therapeutics is one of the true pioneers

Gene therapy is a very young form of therapy. One of the very first companies to receive a gene therapy approval is CombiGene's partner Spark Therapeutics. In 2017, the US Food and Drug Administration (FDA) approved the company's gene therapy Luxturna, which was developed for the treatment of a rare genetic eye disease. Sparks' ambition is now to do the same with CombiGene's epilepsy project CG01, which was licensed to the company in the fall of 2021.

Great enthusiasm in the research community

The potential of gene therapy to cure a wide range of diseases has aroused great enthusiasm in the research community. A wide range of players in both academia and industry are making great efforts to move gene therapy forward. The level of activity is high not only in research and preclinical/clinical development, but also in areas such as production, development and the regulatory field. As in all dynamic research areas, the tempo is high and new knowledge is generated almost daily.

Thanks to its unique possibility for targeted therapy and the potential to meet major medical needs, gene therapy is one of the most exciting areas of development in today's pharmaceutical industry. Currently, there are 316 clinical studies in the gene therapy area divided into 75 phase 1 studies, 196 phase 2 studies and 45 phase 3 studies (Alliance for Regenerative Medicine, Final report 2021).

The number of approved therapies will increase

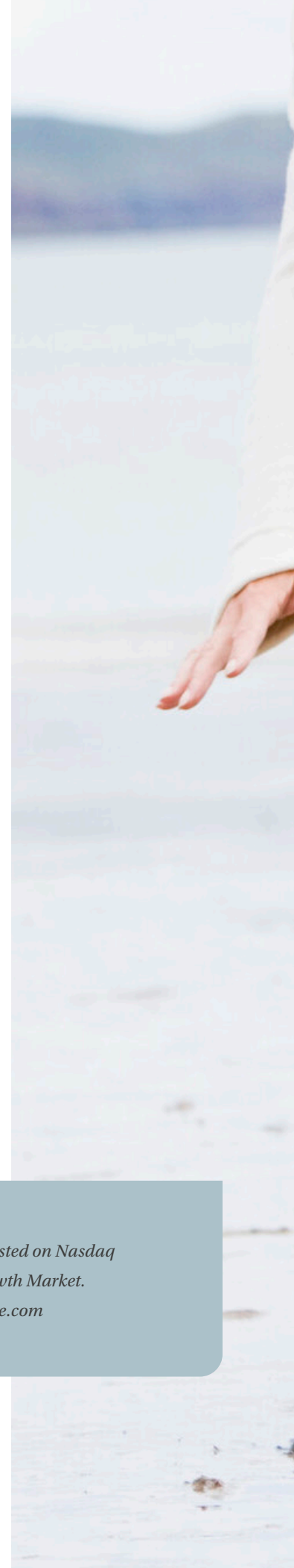
Unlike traditional medical treatment of chronic diseases, which, as a rule, require continuous medication, gene therapy has the great advantage of being able to achieve long-term effect through one or just a few treatments. In the last 5-10 years, there have been great advances in gene therapy and the interest from the major pharmaceutical companies is significant with a number of large acquisitions and licensing deals. Given the benefits that gene therapy offers and the many research and development projects underway worldwide, it is reasonable to assume that the number of approved gene therapy products will increase sharply in the coming years. A large number of patients who today cannot be treated for their illnesses may have significantly better lives thanks to the new therapies.

Massive financial investments

Confidence in gene therapy is also shown by the massive financial investments being made in the field. In 2021, investments in research and development in gene therapy amounted to USD 10.2 billion (Alliance for Regenerative Medicine, Final report 2021). The emphasis is in the field of oncology, but cardiovascular diseases and diseases related to the central nervous system are also common.

CombiGene is at the epicenter of the gene therapy development through the development of its two gene therapy projects and through its collaborations with several world-leading players.

Don't miss the next issue of Ingeneious where we will talk about how gene therapy works.



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THEME COMBIGENE

CombiGene – with gene therapy as a tool

CombiGene was born out of Professor Merab Kokaias and Associate Professor David Woldbye's shared vision of a gene therapy treatment for focal epilepsy. The ambition to make a real difference for patients affected by severe life-changing diseases has since the start of the company been one of the cornerstones of CombiGene and today the company formulates its vision as this: to offer patients affected by severe life-changing diseases opportunities for a better life through innovative gene therapies.

Development of external research assets

The start of CombiGene also established the company's fundamental modus operandi: to create value by developing in-licensed gene therapy assets in collaboration with internationally leading players in preclinical/clinical development as well as production development.

The advantage of in-licensing gene therapy assets is significant. CombiGene can get access to first-class research from both academia and industry without being burdened by large research costs. The external researchers, in turn, gain access to CombiGene's extensive expertise in pharmaceutical development and project management, as well as financial resources that enable continued development of the asset.

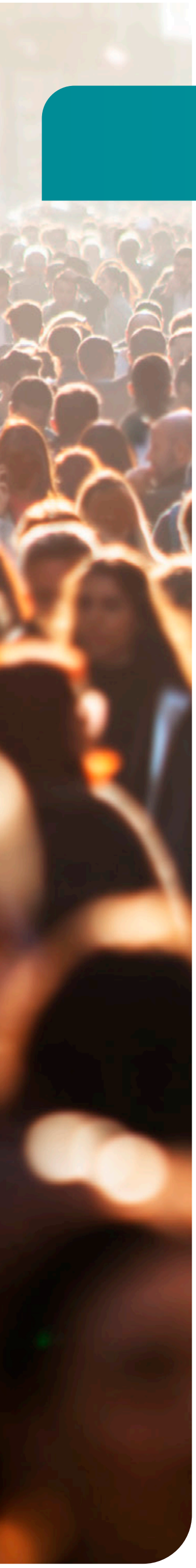
When it comes to gene therapies that target large patient populations, CombiGene is seeking strategic partnerships within the international pharmaceutical industry.

The collaboration and license agreement with Spark is a prime example of this. For gene therapies that target rare diseases, such as lipodystrophy, CombiGene may drive development and commercialization in-house.

Competence and experience

CombiGene has a team of highly knowledgeable and experienced professionals with a long and solid experience from the international pharmaceutical industry and the biotech arena as well as good knowledge in key aspects of gene therapy. The combination of experience and expertise means that CombiGene has the ability to, together with a network of selected external partners, who complement CombiGene's internal expertise, drive gene therapeutic development in an effective manner.

Our business model - the principles



About epilepsy

Epilepsy is a common disease that occurs in 0.5-1% of the population, corresponding to about 60,000 people in Sweden, of which 12,000 are children. Globally, the number of epilepsy patients is estimated at 50 million[1]. Epilepsy is often described as an invisible handicap. It is not possible to see if a person has epilepsy.

Epilepsy can be congenital or occur as a result of a brain injury, such as trauma, stroke, or tumor. Epilepsy produces recurrent seizures that may consist of a disturbance of consciousness, twitching of the arms and legs, or other neurological symptoms. The seizures are caused by transient electrical discharges in the nerve cells of the brain. Epilepsy is also associated with a higher incidence of sudden death. The vast majority of forms of epilepsy are not hereditary.

Treatment can prevent seizures

Epilepsy is treated primarily with drugs. The treatment, which lasts for a long time, does not cure the damage that causes the seizures, but limits the number of seizures. Full seizure freedom is achieved to 60-70 percent of patients.

What triggers an epileptic seizure?

Epileptic seizures can be triggered by external factors such as fever (especially common in children), lack of sleep, mental or physical stress, or the intake of alcohol. The number of seizures can also be affected by concerns about the social and/or professional consequences of the seizures. Many seizures also occur without any clear explanation.

What should I do if someone has an epileptic seizure?

If a person around you has an epileptic seizure, you can initially wait. Most seizures go away by themselves. If the seizure does not stop or if there have been bodily injuries during the attack, you should call for an ambulance. The same applies if you do not know if it is an epileptic seizure or some other medical condition.

If the person has a severe seizure (previously called Grand mal), one should try to protect the person from physical injuries by putting something soft under the head. However, you should not put anything in the mouth, the risk is it causes more damage than help. Of course, you should stay at the scene until the attack is over and you see that the person can care of himself or herself.

In the next issue of Genevägen we will talk about what it is like to live with epilepsy.

[1] https://www.who.int/news-room/fact-sheets/detail/epilepsy

THEME LIPODYSTROPHY PROJECT CGT2

What is partial lipodystrophy?

Partial lipodystrophy is a collective term for a spectrum of rare diseases characterized by altered fat distribution on the body. In the absence of normal body fat, various organs, mainly the liver, begin to accumulate fat, which leads to serious metabolic complications such as extreme insulin resistance, hypertriglyceridemia (elevated values of the blood fat triglyceride) and liver steatosis (fatty liver). In other words, partial lipodystrophy is a very serious disease that today has few treatment options.

How much different areas of the body are affected by altered fat distribution can vary greatly between different patients. For some patients, the disease is limited to cosmetic problems, while other patients develop life-threatening complications.

Common symptoms include progressive loss of subcutaneous fat in the arms, legs, and chest and torso, abnormal accumulation of subcutaneous fat in other areas, and a variety of metabolic complications. In general, women are more affected than men by the metabolic complications. Additional symptoms, including those affecting the liver or heart, may also occur.

Lost adipose tissue cannot be re-formed. Consequently, cosmetic surgery can be beneficial in improving appearance. Interventions such as liposuction can be performed to remove unwanted excess fat in areas where it accumulates, such as the chin.

In the next issue of Ingeneious we will talk about the possibilities for the CGT2 project to be classified as orphan drug.

Source: https://rarediseases.org/rare-diseases/familial-partial-lipodystrophy/

Interview with Gunilla Lundmark on CombiGene's Board of Directors

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

In short, I would say that I have a strong background from the life science industry. After studying at Uppsala University, there was only one way for me to go and that was into this amazing industry. I have worked with the development of new diagnostic methods, pharmaceuticals, and medical devices, which has given me a base and understanding of both the potential and complexity of developing products and services with the aim of improving the quality of life for patients and, if possible, curing serious diseases. On a day-to-day basis, I work as CEO of Uppsala University Invest, a company that supports researchers to take their research further by setting up companies and being involved in developing ideas that can benefit society. When I was invited in 2021 to join the CombiGene Board of Directors, I was both pleased and honored, as I believe that CombiGene's team has the cutting-edge expertise and ability needed to develop effective gene therapies for diseases that currently lack adequate treatment methods.

For more info see LinkedIn.

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

The main milestones are:

- continued development of CG01 in collaboration with Spark and a major milestone is when the first patient can be treated in a clinical study.
- continued development of CGT2, our gene therapy treatment for partial lipodystrophy to proof-of-concept with positive outcome.
- initiation of at least a couple of additional gene therapy projects

What does the agreement with Spark mean for CombiGene as a company?

The agreement between CombiGene and Spark means a lot from different aspects. This agreement is a confirmation that CombiGene has the expertise and technology to develop advanced gene therapies. The agreement is of course also beneficial financially, which enables CombiGene to broaden its gene therapy portfolio and develop new therapies for diseases where there is currently no relevant treatment. CombiGene's vision is to offer patients affected by severe life-altering diseases opportunities for a better life through innovative gene therapies and through the agreement with a strong partner like Spark, the conditions are created to conduct the costly clinical studies required and if the outcome is positive, Spark has the capacity to commercialize the product CG01.

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

I think the company will develop very favorably. There are all the prerequisites for that with the strong team that is in place in CombiGene, the fruitful collaboration with Spark and with the work that is underway to broaden the company's gene therapy portfolio.

About CombiGene

● *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.

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