



*CombiGene's ambition is to develop gene therapies for patients affected by severe life-altering diseases. In January 2023, we took another step on this journey when we signed a collaboration agreement with Zyneyro to jointly develop a unique program which aims to revolutionize pain treatment. We are now continuing our work to find interesting new projects for in-licensing.*

Interim Report  
January - June 2023

Q2

# Summary of the report

## Events during the period

- *Gene Therapy*, one of *Nature's* journals, publishes an article about CombiGene's epilepsy project authored by Esbjörn Melin, scientist at CombiGene.
- High activity level in the pain program COZY in preparation of the final preclinical toxicology program in the peptide project COZY01.
- CombiGene to play an integral part in the development of a national infrastructure for ATMPs. CombiGene's CEO Jan Nilsson elected Chairman of the Board of CCRM Nordic AB.
- CombiGene forms prominent Scientific Advisory Board within the pain program COZY.
- Jan Nilsson leaves his position as CEO of CombiGene – COO Peter Ekolind takes over as new CEO on September 1, 2023.

## Events after the end of the period

- There have been no significant events after the end of the period.

## Financial information

### April – June 2023

- Net sales: TSEK 1,788 (4,738).
- Other operating revenues: TSEK 1,413 (9,800).
- Profit from financial items: TSEK -6,286 (4,516).
- Earnings per share: SEK -0.32 (0.23).

### January – June 2023

- Net sales: TSEK 3,955 (16,141).
- Other operating revenues: TSEK 543 (12,602).
- Profit from financial items: TSEK -20,903 (1,832).
- Earnings per share: SEK -1.06 (0.09).
- Cash and cash equivalents: TSEK 115,442 (125,953).

## For further information:

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## Note to the reader

Amounts in brackets refer to the corresponding period of the previous year.

## CombiGene at a glance

### The company

CombiGene is the only listed gene therapy company in the Nordic Region. The company was listed on May 25, 2015 on SPOTLIGHT Stock Market (then AktieFörget). In December 2018, CombiGene was approved for listing on Nasdaq First North Stockholm.

### Our projects

CombiGene currently has four projects:

- The pain program COZY which consists of one peptide treatment and one gene therapy
- The lipodystrophy project CGT2
- The epilepsy project CG01, which was outlicensed to Spark Therapeutics 2021

### Our team

CombiGene has 10 employees. Our team is made up of very knowledgeable and experienced professionals with longstanding experience from the international pharma industry and the biotech arena with thorough knowledge of different aspects of drug development and gene therapy.

### Cash position

At the end of the first quarter 2023, CombiGene had cash and cash equivalents amounting to TSEK 115,442 (125,953).



# Thank you for seven amazing years!

*Let me begin this, my last CEO statement, by telling you how much fun and how exciting it has been to be part of CombiGene's fantastic journey. When I joined CombiGene in 2016, the company had one project (the epilepsy project CG01) in early preclinical phase and two employees. Since then, through the out-licensing of the epilepsy project to Spark Therapeutics, CombiGene has established itself as an internationally recognized gene therapy company. The number of projects has also expanded and CombiGene is now active in three very interesting areas: diseases of the central nervous system (the epilepsy project CG01), metabolic diseases (the lipodystrophy project CGT2) and pain (COZY program). At the same time, our organization has grown and today includes eleven dedicated employees.*

## A warm and heartfelt thank you to CombiGene's shareholders

Investing in early medical research is always associated with significant risk and I would like to thank all shareholders for the trust you have shown us. In total, you have contributed SEK 229 million to CombiGene. Without your investments, the rapid development of recent years would not have been possible. As a company, we have done everything we could to ensure that your investments have been translated into successful preclinical development. We have also been very active in applying for different types of research grants and in total we have been able to provide the company with SEK 37 million in various grants as well as the upfront payment from Spark Therapeutics of USD 8.5 million.

## A brief look back

In this last CEO statement, I would like to briefly summarize what for me have been the true highlights during my time at CombiGene. In May 2018, CombiGene received a grant of EUR 3.36 million from the EU's Horizon 2020 for the continued development of the epilepsy project CG01. The capital provided was very important for the continued development of CG01, and the recognition from Horizon 2020 put a seal of excellence on our business, which three years later led to the outlicensing of CG01 to Spark Therapeutics. The agreement with Spark has a potential value of USD 328.5

million excluding royalties and is by far the greatest success so far in CombiGene's history.

Other highlights include the in-licensing of the lipodystrophy project CGT2, which has given us valuable knowledge in the metabolic field. I would also like to highlight our pain program COZY, which we are developing together with our Danish partner Zyneyro. Chronic pain costs society huge amounts of money every year. If we succeed in our ambitions to develop effective therapies without the addiction problems that today's treatments are often associated with, the commercial potential is highly substantial.

## The first six months of 2023

During the first two quarters of the year, we have continued to develop the epilepsy project CG01 together with Spark Therapeutics (see below). Since January, we have also been collaborating with our partner Zyneyro to develop completely new ways to treat chronic pain. Within the pain program, we now have full focus on completing all preparations for the final toxicology studies. During the period, we also strengthened our competence on the CMC side through the recruitment of Sebastian Bauer. At the end of the period, CombiGene's cash position amounted to SEK 115 million, which means that we have the financial strength we need to implement our plans with full force in the coming year.



## A few words about the epilepsy project CG01

There are a number of important development activities within the epilepsy project CG01. Each of these activities helps to increase awareness of the project but can create delays, and each of the activities could stop the project if the outcome does not turn out as expected.

However, it is important to remember that the project is not ours. Spark has a global exclusive license and thus all control over the development activities. However, I would like to emphasize that we are not seeing any slowdown in interest or willingness to invest from Spark.

## Peter Ekolind takes over

On September 1, 2023, Peter Ekolind will take over as CombiGene's CEO. During his time as CombiGene's Chief Operating Officer, I have come to know him as a very competent and ambitious leader with extensive experience from the pharmaceutical and medtech industry. The company couldn't be in better hands.

With these words, I would like to express my gratitude. The time as CombiGene's CEO has been one of the absolute highlights of my career! So, a big thank you to all shareholders and everyone else who contributed to CombiGene's development!

Jan Nilsson,  
CEO



# The pain program COZY – a unique opportunity for a breakthrough in pain treatment

*The pain program COZY is being developed together with the Danish company Zyneyro with the goal of developing an effective treatment for severe chronic pain, a common and often difficult-to-treat condition. The program consists of two projects – a peptide treatment and a gene therapy treatment, both of which are based on a new biological mechanism of action that is expected to be without the side effects that current treatments often give rise to.*

## Pain is a major global problem

About 20-25 percent of the world’s adult population suffers from some form of chronic pain and between six and eight percent of the population suffers from severe chronic pain. Conventional treatment consists mainly of anti-inflammatory drugs, antidepressants, anticonvulsant drugs and opioids (a group of substances with a morphine-like mechanism of action).<sup>1</sup>

The problem with these treatments is that they are not specifically developed to treat chronic pain. The pain relief that is achieved therefore often has a number of debilitating side effects such as substance abuse problems, depression, anxiety, fatigue, reduced physical and mental ability. In the United States, an estimated 700,000 people have died due to opioid abuse in the past 20 years.

## One program – two projects

The program consists of two projects: a peptide treatment (COZY01) and a gene therapy treatment (COZY02), which expresses the active part of the peptide from COZY01, with potential lifelong effect.

*In severe chronic pain, the intention is to administer the peptide directly to the patient on one or more occasions to achieve effective pain relief.*

*In severe chronic pain where the possibilities for spontaneous reduction of the pain are considered excluded or unlikely and which with conventional treatment requires daily medication, the intention is to achieve pain relief by treating the patient with an AAV vector that makes the body produce the pain-relieving peptide itself. In this way, long-term pain relief can be achieved without daily medication. Since the AAV vector encodes the peptide, the mechanism of action and thus the expected effect are the same as in direct administration of the peptide.*

## Independent evaluation by the National Institutes of Health

An independent evaluation of the potential of COZY01 as a future pain treatment is underway at the National Institutes of Health (NIH) in the US, in a government-funded program (Preclinical Screening Platform for Pain, PSPP) aimed at finding pain management alternatives that are not opioid-based and that are not addictive or result in tolerance development. COZY01 has passed the first level of three and has been selected to move on to the next level where the substance will be tested in a behavioral model and in different pain models. During the first six months of the year, CombiGene and Zyneyro worked on preparatory activities for the next step.

## Annual medical and indirect costs of various diseases in the United States



**Pain: USD 635 billion**

**Cardiovascular diseases: USD 309 billion**

**Cancer: USD 243 billion**

**Diabetes: USD 188 billion**

Source: 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

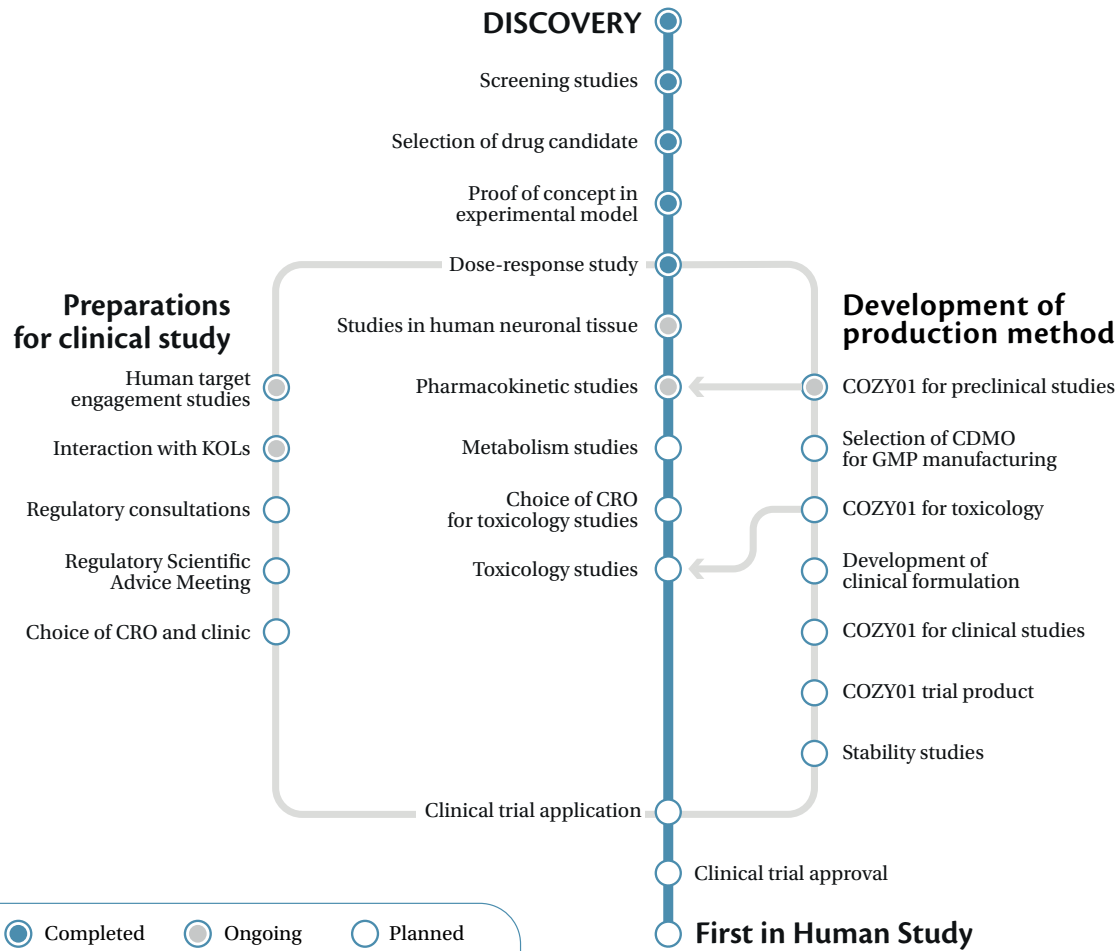
<sup>1</sup> Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults — United States, 2016; CDC; Morbidity and Mortality Weekly Report Weekly / Vol. 67 / No. 36 September 14, 2018

# COZY01

– Roadmap

## THE PAIN PROGRAM COZY

COZY01 – peptide treatment of severe chronic pain conditions



### COZY01 – peptide treatment of severe chronic pain

The peptide treatment has shown positive effects in various preclinical models. The continued development will focus 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 in humans with COZY01.

#### Activities during the quarter

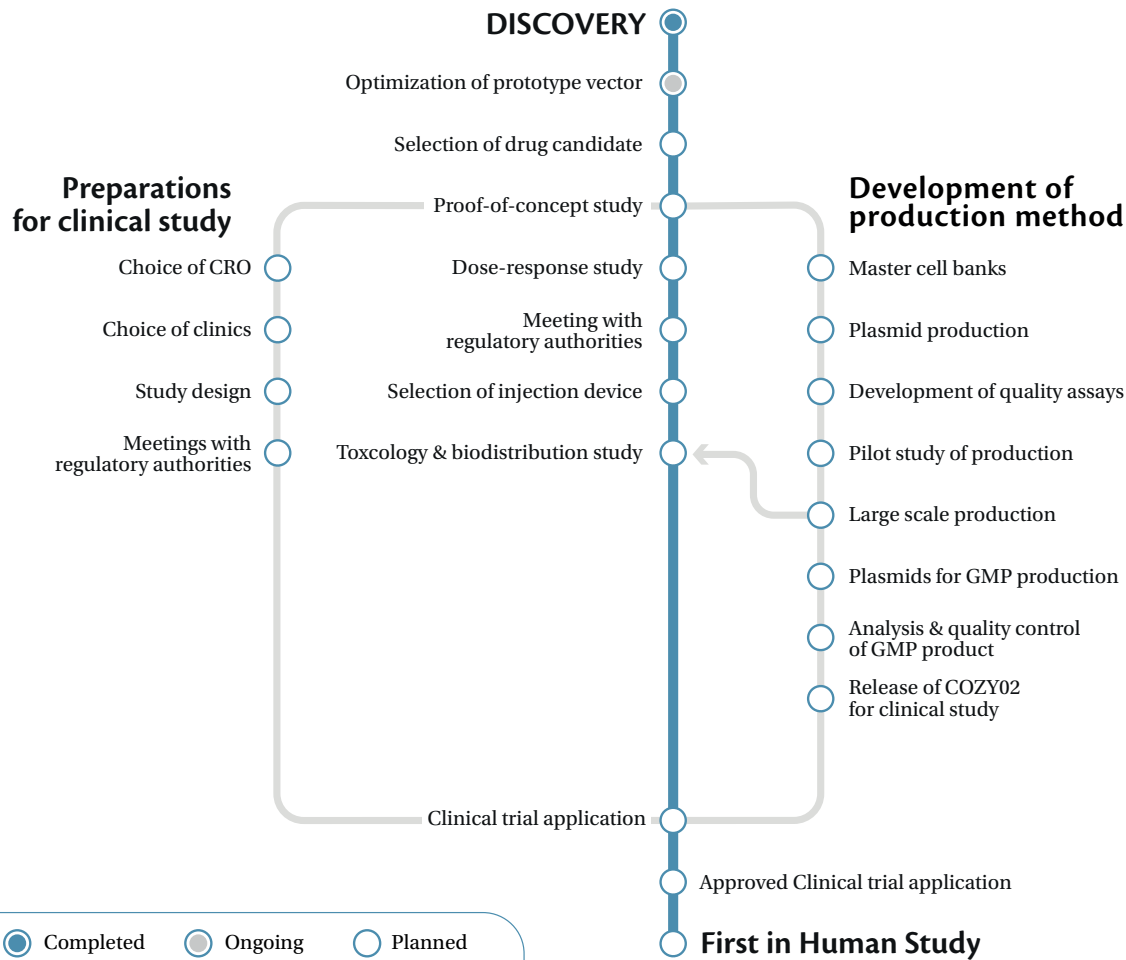
- Negotiation of manufacturing agreement (master service agreement) initiated
- Manufacturing of COZY01 for preclinical studies
- Preformulation for continued preclinical studies
- Procurement of
  - a pharmacokinetic study
  - human nerve tissue
  - metabolism studies
- Contacts with contract laboratories prior to selecting a service partner for the toxicological studies.

# COZY02

## - Roadmap

### THE PAIN PROGRAM COZY

COZY02 – gene therapy treatment for severe chronic pain conditions



### COZY02 – gene therapy treatment of severe chronic pain where the possibility of spontaneous reduction of pain is considered excluded

A prototype of the AAV vector that acts as a carrier of the genetic material in gene therapy 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 studies in humans. AAV is the vector type that CombiGene has extensive experience of from our other projects. When the vector is optimized, preclinical studies will follow to investigate and characterize distribution, protein expression, efficacy, dose-response and toxicology.

In parallel with the preclinical development, we will develop a process for manufacturing the selected vector for preclinical studies and for future clinical trials. Data from this work will form the basis for seeking permission to conduct a clinical trial on patients with severe chronic pain.

#### Activities during the quarter

- Improvement of the genetic components of the prototype vector
- Biochemical evaluation of novel humanized variants of COZY02 for adaptation to administration in humans

# CGT2 – further studies needed before a new timetable for the proof-of-concept study can be made

*CGT2, CombiGene's project to develop a gene therapy for partial lipodystrophy, is in early preclinical development. The first step in designing gene therapy vectors and testing them in vitro (tests on different liver cells) has been carried out with good results. Since then, several in vivo studies have been conducted to evaluate efficacy and gradually limit the number of potential gene therapy candidates.*

## Further studies needed

The ambition for 2022 was to bring the CGT2 project to the stage where a preclinical proof-of-concept study could be initiated. However, some of the studies conducted in 2022 produced results that are difficult to interpret and need to be repeated. CombiGene has therefore decided to conduct further studies before it is possible to proceed to the preclinical proof-of-concept study.

## Contribution from the EU's international funding program Eurostars

In February 2021, the lipodystrophy project was awarded EUR 882,500 in project grants by the EU's international funding program Eurostars. Through this grant, CombiGene collaborates with University Medical Center Hamburg-Eppendorf and its experts in lipid research.

## PCT application

In August 2021, CombiGene submitted a PCT application to protect the vectors developed within the CGT2 project. The application builds on the UK patent application filed in 2020 and is a natural next step to ensure adequate patent protection for the lipodystrophy project CGT2. During the first half of 2023, CombiGene filed national patent applications in the US and EU.

## Important agreement with Professor Ormond MacDougald

In addition to collaboration agreements with Stockholm University and University Medical Center Hamburg-Eppendorf, CombiGene also has an agreement with Professor Ormond MacDougald at the University of Michigan Medical School in the US. This agreement includes a pilot study and a main study where CombiGene's most promising gene therapy candidate within the lipodystrophy project CGT2 will be tested and evaluated.

## Milestones

### 2019

- In-licensing of the project from Lipigon.

### 2020

- Design of expression plasmids, which are the starting material for gene-therapeutic vectors CombiGene intends to develop for treatment of partial lipodystrophy.
- In vitro studies (tests on liver cells) show intended protein expression.
- Priority-based patent application filed with the UK Patent Office.
- In vivo studies initiated for evaluation of the different gene therapy vectors.

### 2021

- The lipodystrophy project receives EUR 882,500 in development grants from the EU Eurostars program.
- PCT application submitted.

### 2022

- CombiGene signs agreement with University of Michigan to evaluate the leading gene therapy candidate within the lipodystrophy project CGT2. A number of in vivo studies are being conducted, but since some results are difficult to interpret, the company has chosen to repeat some studies in 2023.

### 2023

- National patent applications filed in the US and EU.



# CG01 – outlicensed to Spark Therapeutics since October 2021

*The epilepsy project CG01 was outlicensed to Spark Therapeutics in October 2021 and the remaining part of the preclinical phase is carried out by Spark in collaboration with CombiGene. When the project enters the clinical phase, Spark will take full responsibility for design and execution. Since October 2021, Spark also covers all agreed costs in connection with the preclinical development of CG01.*

## Scope of the agreement

The collaboration and license agreement between CombiGene and Spark is an exclusive global license agreement that gives Spark the right to develop the CG01 project during the program's preclinical and clinical phases, to manufacture CG01 and to commercialize CG01 to the global market. Spark also controls the external information regarding the development of the project.

## The economic terms of the agreement

The total potential value of the agreement amounts to USD 328.5 million, excluding royalties. The initial payment

amounted to USD 8.5 million. Milestone payments during the preclinical and clinical phase amount to a total of USD 50 million. Royalties on future sales of CG01 consist of tiered royalties up to low double digits based on net sales. All milestone payments will be communicated through CombiGene's press releases.

## The preclinical development program

The remainder of the preclinical program is carried out by Spark in collaboration with CombiGene. Spark soon decided to prioritize CG01's clinical development program to the US over Europe. This will allow the project to gain

a natural foothold in the world's largest pharmaceutical market, while allowing Spark to make optimal use of its impressive resources, know-how and network.

## The clinical development program

When the preclinical program is completed, Spark will take responsibility for the design and implementation of the clinical development. All results and know-how from the preparatory work for the clinic that CombiGene did before the agreement was signed have been transferred to Spark. As part of the current agreement, Spark will cover costs for all clinical development work.

## Communication about updates and timeline

Future updates regarding CG01 projects will be provided by Spark in accordance with their practices.



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

The CG01 team, from left to right: Peter Ekolind, David Dobry, Aparna Oza, Pernilla Fagergren, Jean Pedagna, Esbjörn Melin, Liz Ramsburg, Juha Savola, Karin Agerman, Lawrence Moon, Barbara Terzic, Jan Nilsson.

In June, CombiGene and Spark Therapeutics held a biannual joint steering committee meeting in Stockholm, Sweden, to make a detailed plan for the epilepsy project CG01 for the upcoming six months. The meeting was highly productive, and again proved that Spark is an ideal partner for the epilepsy project CG01.



# Strategy and business development

*CombiGene develops groundbreaking gene therapies with the ambition to offer patients affected by severe life-changing diseases opportunities for a better life. We source research assets from industry or academia and develop them through the preclinical phase up to preclinical/clinical proof-of-concept and then out-license them to a Big Pharma company for clinical development and commercialization. Gene therapies that we are developing for limited patient populations may be commercialized in-house.*

## Gene therapy has fantastic medical possibilities

There are a large number of diseases that today either require lifelong medical treatment or that completely lack effective therapies. It is precisely these diseases that are in focus for the development since gene therapy has the unique possibility of being able to replace defective/missing genes or change the expression of existing genes. This means that gene therapy in some cases can cure a disease instead of only alleviating the symptoms and that you can achieve long-term effects from one or a few treatments. There are currently about 300 gene therapy clinical studies conducted in the central nervous system, infectious and metabolic diseases among others.

## The commercial possibilities of gene therapy

Gene therapy is not just an interesting field of research. With two gene therapies approved in the second quarter of 2023, there are currently nine gene therapies approved in the EU and/or in the US and, according to the Alliance for Regenerative Medicines, and another three gene therapies may be approved in 2023. The US Food and Drug Administration (FDA) has previously announced that they expect to approve 10 to 20 new cell and gene therapies annually from 2025 onwards. According to Precedence Research, the gene therapy market is expected to grow globally to USD 15.7 billion in 2030.

## Extensive work to find new projects

CombiGene is currently working intensely to find interesting new projects to complement the current project portfolio. The evaluation of potential projects is a structured and rigorous process based on several key criteria. The work includes review and analysis of intellectual property issues, preclinical data, intended contract structure, size of patient population and medical need, competitive situation, and the project's commercial conditions.

All criteria are important and a weakness in one of them, such as an unclear intellectual property situation, means that CombiGene chooses not to proceed with the project.

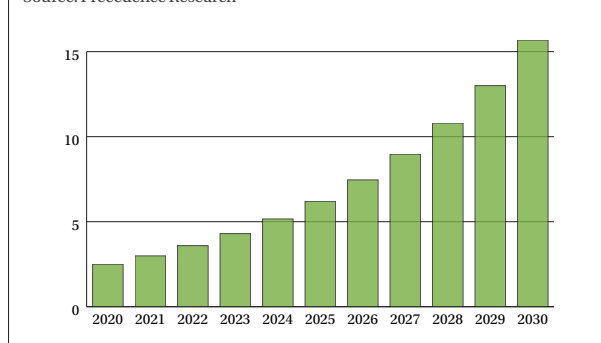
CombiGene has identified a number of projects that could be interesting to license. These include projects for diseases of the central nervous system, endocrine diseases, and genetic muscle diseases. CombiGene is currently conducting in-depth analyses of these projects.

## The importance of a broad portfolio

Thanks to the outlicensing of the epilepsy project CG01 to Spark Therapeutics in the autumn of 2021, CombiGene's financial position was strengthened, which enabled us to focus on the in-licensing of additional projects. The

**Expected gene therapy sales 2020–2030, MUSD**

Source: Precedence Research



first concrete result of this is the cooperation agreement with Zynevro that was signed in early 2023. We are now continuing to seek new projects to in-license with the ambition to build a broad portfolio that includes projects in several phases of drug development, ranging from projects in early preclinical evaluation to projects in clinical development. By having a broad portfolio of projects, we increase the chances of achieving commercial success.

# The CombiGene share

*CombiGene is a public company and is listed on Nasdaq First North Growth market. The share capital of the Company shall amount to no less than SEK 990,000 and no more than SEK 3,960,000 divided into no less than 19,800,000 shares and no more than 79,200,000 shares. CombiGene has one class of share. Each share carries equal rights to CombiGene's assets and profits and is entitled to one vote at the Annual General Meeting (AGM). The quota value is SEK 0.05. The CombiGene share register is maintained electronically by Euroclear. The share trades under the name CombiGene, the ticker is COMBI, and the ISIN-Code is SE0016101935.*

## The share

The average number of shares for the period is 19,801,197. All shares are of the same type and have the same voting rights.

## Authorization to issue new shares, warrants or convertibles

The AGM 2023 resolved, in accordance with the Board of Directors' proposal, to authorize the Board of Directors to, at one or several occasions and for the period up until the next AGM, resolve to increase the Company's share capital by issuing new shares, warrants and/or convertibles. Such issue resolution may be carried out with or without deviation from the shareholders' pre-emption rights and with or without provisions for contribution in kind,

set-off or other conditions. The total number of shares that may be issued, or in the event of an issue of warrants or convertibles, any additional shares after conversion or exercise of any warrant, by virtue of the authorization, for issue resolutions made without deviation from the shareholders' pre-emption rights, shall not be limited in any other way than by the limits for the share capital and number of shares, as set forth from time to time in the registered Articles of Association.

For issue resolutions made by virtue of the authorization, with deviation from the shareholders' pre-emption rights, the total number of shares that may be issued, or in the event of an issue of warrants or convertibles, any additional shares after conversion or exercise of any

warrant, shall be limited to 50 percent of the outstanding shares in the Company at any given time. Should the Board of Directors resolve on a share issue with deviation from the shareholders' pre-emption rights, the reason for this shall be to broaden the ownership structure, procure working capital, increase the liquidity of the share, or acquire businesses, or enable the acquiring of capital for acquisitions.

## LTI 2022

The AGM 2022 resolved, in accordance with the board of directors' proposal, on the implementation of a performance-based incentive program, named LTI 2022, directed issue of 900,000 warrants, transfer of the warrants to participants in LTI 2022 and transfer of warrants to cover costs for LTI 2022 and authorization to enter into swap agreement. A more detailed description of LTI 2022 can be found in the notice convening the Annual General Meeting 2022.

Ten largest shareholders as of June 30, 2023	Total holdings	Holding %
Pareto Securities AS	1,562,754	7.89%
Nordqvist, Jan Ivar	1,440,852	7.28%
Avanza Pension	1,099,125	5.55%
Thoren Tillväxt AB	494,894	2.50%
Nordnet Pensionsförsäkring AB	474,296	2.40%
Försäkringsaktiebolaget Skandia	273,175	1.38%
Olsson, Per Magnus	246,794	1.25%
Ferstad, Arne	214,072	1.08%
Thomassen Skaar, Christian	189,744	0.96%
Darlista, Flamur	187,172	0.95%

# Financial information

## Income and earnings

Net sales consist of milestone payments and compensation from license and cooperation agreements. For January-June, the net sales consist of compensation from Spark regarding costs during the preclinical development of CG01, and compensation from Zyneyro for 50 percent of the costs for the COZY program incurred in the quarter. Due to the nature of the business, there may be large fluctuations between revenues for different periods when revenue from milestone payments is recognized at the time when the performance obligations are met. The Group has a total net sale of TSEK 3,955 (16,141) during the period January-June. The decrease is explained by CombiGene, as planned, is putting less resources into CG01 as Spark takes increasingly greater responsibility for the project. Other operating revenues amounts to TSEK 543 (12,602) and consist of TSEK 345 (1,440) which refers to the revenue-earned portion of the grant received from Eurostars. Operating profit for the period amounted to TSEK -20,903 (1,832). The main costs during the period have been related to research & development, fees for consultants and personnel costs, and initial payment of DKK 5 million to Zyneyro.

## Cash flow and financial position

Cash flow for the period January-June amounts to TSEK -16,470 (-10,791). Cash and cash equivalents at the end of the period amounts to TSEK 115,442 (125,953). The equity ratio is 95.3% (96.7).

## Liquidity and financing

The EU's Eurostars program, which is aimed at small and medium-sized enterprises wishing to collaborate on research and development projects, has allocated development grants to the CGT2 project. The total grant for CombiGene amounts to SEK 5 million, of which SEK 3.8 million has so far been paid out. The board and company

management continuously evaluate alternatives to ensure the company's financing in the short and medium term.

## Incentive programs and warrants

The 2022 Annual General Meeting resolved on a performance-based incentive program (LTI 2022). The duration of the program is approximately three years and will be offered to certain employees and consultants, or newly hired persons, in the company. A maximum of 617,220 Performance Share Rights may be allocated to the participants, corresponding to approximately 3 percent of the out-standing shares and votes in the Company, as well as 282,780 warrants that can be issued to hedge the Company's cost under the Program, which corresponds to approximately 1.4 percent of the outstanding shares and votes in the Company. In accordance with the Board's proposal, the AGM resolved on a directed issue of 900,000 warrants with the right to subscribe for new shares in the company for the implementation of LTI 2022.

## Employees

The number of employees in the Group at the end of the period was 10 (10), of whom 6 (5) are women.

## Risks and uncertainties

A drug development company of CombiGene's type is characterized by a high operational and financial risk. The Company is dependent on current and future licensing, collaboration, and other agreements with experienced partners for the development and successful commercialization of existing and future drug candidates. The most significant example of this is CombiGene's exclusive global collaboration and licensing agreement with Spark Therapeutics, which has a potential total value of USD 328.5 million excluding royalties. The agreement with Spark is thus of great importance for CombiGene's future operations, earnings, and financial position.

Other factors that may negatively affect the likelihood of commercial success include, among other things, the risk that CombiGene's gene therapies are not deemed safe or not effective, and the risk that the business may not receive the necessary funding.

## Principles for preparation of the interim report

CombiGene prepares its financial reports in accordance with the Swedish Annual Accounts Act and BFAR 2012:1 (K3) Annual Accounts and Consolidated Accounts. The same accounting principles have been applied in this interim report as were applied in the most recent annual report.

## Deviation from Interim report January-June 2022

The comparative figures for the periods April-June and January-June last year differ from the interim report for January-June 2022. In the Group's and the Parent Company's reports on profit for the period, exchange rate differences in Other operating income and Other operating expenses have been reported net for both 2023 and 2022.

## Review by auditors

This report has not been subject to review by the Company's auditors.

## Future reporting dates

- Interim report January – September 2023, 10 November 2023.
- Year-end report 2023, 16 February 2024.

## For further information, please contact:

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## Group income statement in summary

Figures in TSEK	2023	2022	2023	2022	2022
	Apr-Jun	Apr-Jun	Jan-Jun	Jan-Jun	Jan-Dec
<b>Operating income</b>					
Net sales	1,788	4,738	3,955	16,141	26,699
Other operating revenues	1,413	9,800	543	12,602	15,044
<b>Operating expenses</b>					
Other external expenses	-4,778	-6,212	-16,543	-19,787	-32,567
Personnel expenses	-4,060	-3,161	-7,561	-5,827	-13,032
Other operating expenses	0	0	0	0	-496
<b>Profit/loss before depreciation</b>	<b>-5,637</b>	<b>5,164</b>	<b>-19,605</b>	<b>3,130</b>	<b>-4,352</b>
Depreciation	-649	-649	-1,297	-1,297	-2,595
<b>Profit/loss after depreciation</b>	<b>-6,286</b>	<b>4,516</b>	<b>-20,903</b>	<b>1,832</b>	<b>-6,947</b>
Net financial income/expense	0	0	0	0	790
<b>Income after net financial items</b>	<b>-6,286</b>	<b>4,516</b>	<b>-20,903</b>	<b>1,832</b>	<b>-6,157</b>
Tax	0	0	0	0	0
<b>Net profit/loss for the period</b>	<b>-6,286</b>	<b>4,516</b>	<b>-20,903</b>	<b>1,832</b>	<b>-6,157</b>
Attributable to					
Parent company shareholders	-6,286	4,516	-20,903	1,832	-6,157
Earnings per share before dilution	-0.32	0.23	-1.06	0.09	-0.31
Earnings per share after dilution	-0.32	0.23	-1.06	0.09	-0.31
Average number of shares before dilution	19,801,197	19,801,197	19,801,197	19,801,197	19,801,197
Average number of shares after dilution	19,801,197	19,801,197	19,801,197	19,801,197	19,801,197
<i>Total outstanding shares</i>	<i>19,801,197</i>	<i>19,801,197</i>	<i>19,801,197</i>	<i>19,801,197</i>	<i>19,801,197</i>

## Group balance sheet in summary

Figures in TSEK	2023	2022	2022
	30 Jun	30 Jun	31 Dec
<b>ASSETS</b>			
<b>Fixed assets</b>			
Intangible fixed assets	17,815	20,301	19,004
Financial fixed assets	5	0	0
<b>Total fixed assets</b>	<b>17,820</b>	<b>20,301</b>	<b>19,004</b>
<b>Current assets</b>			
Accounts receivable	1,032	11,989	4,216
Other receivables	3,344	7,256	3,223
Cash and cash equivalents	115,442	125,953	131,777
<b>Total current assets</b>	<b>119,818</b>	<b>145,197</b>	<b>139,217</b>
<b>TOTAL ASSETS</b>	<b>137,638</b>	<b>165,499</b>	<b>158,221</b>
<b>SHAREHOLDERS' EQUITY AND LIABILITIES</b>			
Share capital	990	990	990
Other capital contribution	224,124	224,124	224,124
Other shareholders' equity	-72,992	-66,835	-66,835
Profit/loss for the period	-20,903	1,832	-6,157
<b>Equity attributable to parent company shareholders</b>	<b>131,220</b>	<b>160,111</b>	<b>152,122</b>
<b>Total equity</b>	<b>131,220</b>	<b>160,111</b>	<b>152,122</b>
<b>LIABILITIES</b>			
Current liabilities	6,419	5,387	6,099
<b>Total liabilities</b>	<b>6,419</b>	<b>5,387</b>	<b>6,099</b>
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>	<b>137,638</b>	<b>165,499</b>	<b>158,221</b>

## Summary report of changes in the Group's shareholders' equity

Figures in TSEK				
	Share capital	Other capital contribution	Accumulated profit/loss	Total shareholders' equity
Balance brought forward	990	224,124	-72,992	152,122
Net profit/loss for the period			-20,903	-20,903
Amount as per the end of the reporting period	990	224,124	-93,894	131,220



## Group cash flow statement in summary

Figures in TSEK	2023	2022	2022
	Jan-Jun	Jan-Jun	Jan-Dec
Cash flow from operating activities	-16,356	-10,791	-16,666
Cash flow from investing activities	-114	0	0
Cash flow from financing activities	0	0	0
<b>Cash flow for the period</b>	<b>-16,470</b>	<b>-10,791</b>	<b>-16,666</b>
Liquid assets at the beginning of the reporting period	131,777	136,744	136,744
Exchange rate difference cash and cash equivalents	135	0	11,699
<b>Liquid assets at the end of the reporting period</b>	<b>115,442</b>	<b>125,953</b>	<b>131,777</b>

## Group financial key ratios

	2023	2022	2022
	Jan-Jun	Jan-Jun	Jan-Dec
Earnings per share before dilution, SEK	-1.06	0.09	-0.31
Earnings per share after dilution, SEK	-1.06	0.09	-0.31
Shareholders' equity per share, SEK	6.63	8.09	7.68
Equity ratio, %	95.34	96.74	96.15
Average number of shares before dilution	19,801,197	19,801,197	19,801,197
Average number of shares after dilution	19,801,197	19,801,197	19,801,197
Total outstanding shares	19,801,197	19,801,197	19,801,197

## Parent Company income statement in summary

Figures in TSEK	2023	2022	2023	2022	2022
	Apr-Jun	Apr-Jun	Jan-Jun	Jan-Jun	Jan-Dec
<b>Operating income</b>					
Net sales	1,788	4,738	3,955	16,141	26,699
Other operating revenues	1,424	9,788	556	12,575	15,044
<b>Operating expenses</b>					
Other external expenses	-4,778	-6,179	-16,525	-19,736	-32,494
Personnel expenses	-4,060	-3,161	-7,561	-5,827	-13,032
Other operating expenses	0	0	0	0	-492
<b>Profit/loss before depreciation</b>	<b>-5,626</b>	<b>5,186</b>	<b>-19,574</b>	<b>3,153</b>	<b>-4,275</b>
Depreciation	-75	-75	-150	-150	-300
<b>Profit/loss after depreciation</b>	<b>-5,701</b>	<b>5,111</b>	<b>-19,724</b>	<b>3,003</b>	<b>-4,575</b>
Net financial income/expense	-574	-574	-1,147	-1,148	-1,505
<b>Income after net financial items</b>	<b>-6,275</b>	<b>4,537</b>	<b>-20,871</b>	<b>1,856</b>	<b>-6,080</b>
Tax	0	0	0	0	0
<b>Net profit/loss for the period</b>	<b>-6,275</b>	<b>4,537</b>	<b>-20,871</b>	<b>1,856</b>	<b>-6,080</b>

## Parent Company balance sheet in summary

Figures in TSEK	2023	2022	2022
	30 Jun	30 Jun	31 Dec
<b>ASSETS</b>			
Intangible fixed assets	4,046	4,237	4,087
Financial fixed assets	18,056	19,733	18,585
<b>Total fixed assets</b>	<b>22,102</b>	<b>23,970</b>	<b>22,673</b>
<b>Current assets</b>			
Accounts receivable	1,032	11,989	4,216
Other receivables	3,512	7,964	3,980
Cash and cash equivalents	115,251	125,758	131,583
<b>Total current assets</b>	<b>119,795</b>	<b>145,712</b>	<b>139,779</b>
<b>TOTAL ASSETS</b>	<b>141,897</b>	<b>169,682</b>	<b>162,452</b>
<b>SHAREHOLDERS' EQUITY AND LIABILITIES</b>			
<b>Restricted equity</b>			
Share capital	990	990	990
Statutory reserve	4	4	4
Reserve for development expenses	868	760	760
<b>Non-restricted equity</b>			
Share premium reserve	165,826	165,826	165,826
Accumulated loss including profit/loss for the period	-32,161	-3,245	-11,181
<b>Total shareholders' equity</b>	<b>135,527</b>	<b>164,334</b>	<b>156,398</b>
<b>LIABILITIES</b>			
Current liabilities	6,370	5,348	6,054
<b>Total liabilities</b>	<b>6,370</b>	<b>5,348</b>	<b>6,054</b>
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>	<b>141,897</b>	<b>169,682</b>	<b>162,452</b>



## Summary report of changes in the Parent Company's shareholders' equity

Figures in TSEK	Share capital	Statutory reserve	Reserve for development expenses	Share premium reserve	Accumulated profit/loss	Total shareholders' equity
<b>Balance brought forward</b>	<b>990</b>	<b>4</b>	<b>760</b>	<b>165,826</b>	<b>-11,181</b>	<b>156,398</b>
Provisions for reserve for development expenses			109		-109	0
Net profit/loss for the period					-20,871	-20,871
<b>Amount as per the end of the reporting period</b>	<b>990</b>	<b>4</b>	<b>868</b>	<b>165,826</b>	<b>-32,161</b>	<b>135,527</b>

## Parent Company cash flow statement in summary

Figures in TSEK	2023	2022	2022
	Jan-Jun	Jan-Jun	Jan-Dec
Cash flow from operating activities	-16,354	-10,787	-16,661
Cash flow from investing activities	-114	0	0
Cash flow from financing activities	0	0	0
<b>Cash flow for the period</b>	<b>-16,467</b>	<b>-10,787</b>	<b>-16,661</b>
Liquid assets at the beginning of the reporting period	131,583	136,545	136,545
Exchange rate difference cash and cash equivalents	135	0	11,699
<b>Liquid assets at the end of the reporting period</b>	<b>115,251</b>	<b>125,758</b>	<b>131,583</b>

## Share capital development

Year	Event	Total share capital (SEK)	Change (SEK)	Total shares	Change shares	Quotient (SEK)
1990	Company registration	50,000	50,000	500	500	100.00
1997	Bonus issue	100,000	50,000	1,000	500	100.00
2010	New share issue	102,600	2,600	1,026	26	100.00
2013	New share issue	143,600	41,000	1,436	410	100.00
2014	Bonus issue	574,400	430,800	5,744	4,308	100.00
2014	New share issue	604,400	30,000	6,044	300	100.00
2014	Split 1 000:1	604,400	0	6,044,000	6,037,956	0.10
2014	New share issue	884,400	280,000	8,844,000	2,800,000	0.10
2015	New share issue	1,134,400	250,000	11,344,000	2,500,000	0.10
2015	New share issue	1,138,197	3,797	11,381,970	37,970	0.10
2016	New share issue	1,180,159	41,962	11,801,590	419,620	0.10
2017	New share issue	1,652,223	472,064	16,522,230	4,720,637	0.10
2018	New share issue	1,719,783	67,560	17,197,836	675,596	0.10
2018	New share issue	5,159,348	3,439,565	51,593,476	34,395,650	0.10
2019	New share issue	6,372,384	1,213,036	63,723,836	12,130,360	0.10
2019	New share issue	6,373,090	706	63,730,896	7,060	0.10
2019	New share issue	6,505,365	132,275	65,053,647	1,322,751	0.10
2020	New share issue	11,762,201	5,256,836	117,622,007	52,568,360	0.10
2020	New share issue	12,562,201	800,000	125,622,007	8,000,000	0.10
2020	New share issue	14,721,013	2,158,813	147,210,132	21,588,125	0.10
2020	New share issue	17,666,081	2,945,068	176,660,811	29,450,679	0.10
2020	New share issue	17,822,218	156,137	178,222,176	1,561,365	0.10
2020	New share issue	20,768,890	2,946,672	207,688,899	29,466,723	0.10
2020	New share issue	22,927,702	2,158,813	229,277,024	21,588,125	0.10
2021	New share issue	39,602,395	16,674,693	396,023,950	166,746,926	0.10
2021	Reverse share split (1:20)	39,602,395	0	19,801,197	-376,222,753	2.00
2021	Reduction of share capital	990,060	-38,612,335	19,801,197	0	0.05
<b>At the end of the period</b>		<b>990,060</b>		<b>19,801,197</b>		<b>0.05</b>

# Declaration by the Board of Directors and the CEO



Jonas Ekblom



Malin Almgren



Gunilla Lundmark



Per Lundin



Peter Nilsson



Jan Nilsson

The Board of Directors and the Chief Executive Officer certify that the interim report provides a true and fair view of the company's business, financial position, performance and describes material risks and uncertainties, to which the company is exposed.

The interim report has not been reviewed by the company's auditors.

Stockholm, August 25, 2023

**Jonas Ekblom**  
Chairman

**Malin Almgren**  
Board member

**Gunilla Lundmark**  
Board member

**Per Lundin**  
Board member

**Peter Nilsson**  
Board member

**Jan Nilsson**  
CEO

# Glossary

**AAV** Adeno-associated virus.

**AMPA receptor** A transmembrane receptor subtype for glutamate that acts as an ion channel and mediates fast synaptic signal transmission in the central nervous system (CNS). AMPA receptors are also present in peripheral nerves and may play a role in pain signaling.

**C-kinase** A family of protein kinase enzymes that are involved in controlling the function of other proteins through the phosphorylation of hydroxyl groups of serine and threonine amino acid residues on these proteins, or a member of this family.

**CDMO** Contract development and manufacturing organization is a company that serves other companies in the pharmaceutical industry on a contract basis to provide comprehensive services from drug development through drug manufacturing.

**Chronic pain** Pain that has lasted longer than three to six months. In some cases, the chronic pain may disappear at a later stage. Thus, chronic pain is not necessarily permanent.

**Clinical development** Comprises three phases, see clinical phase I, II, III below.

**Clinical phase I** Phase I refers to the first instance of testing of a candidate drug on humans. Phase I trials are often conducted with a small group of healthy volunteer trial subjects to determine the safety and dosage of an as yet non-approved treatment method.

**Clinical phase II** Phase II trials refer to a pharmaceutical product under development that is administered to a small group of patients to study the safety, dosage and efficacy.

**Clinical phase III** Phase III studies include a sufficient number of patients to meet regulatory prerequisites for approval. The aim is to determine the statistical significance with respect to the effect of a new candidate drug, without major side effects and under carefully controlled real-world conditions. The new drug is

sometimes compared with an established treatment, such as an approved drug.

**Clinical study** Research studies that explore whether a new, as yet non-approved, drug, medical strategy, treatment, or device is safe and effective for humans.

**CRO** Contract Research Organization is a company that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis.

**Eurostars** A funding instrument that supports innovative SMEs (Small and Medium-sized Enterprises), and project partners (large companies, universities, research organizations and other types of organizations) by funding international collaborative R&D and innovation projects.

**Gene therapy** A medical field which focuses on the genetic modification of cells to produce a therapeutic effect or the treatment of disease by repairing or reconstructing defective genetic material.

**GMP** Good Manufacturing Practice is a system for ensuring that pharmaceutical products are consistently produced and controlled according to quality standards. Permits for GMP are granted by the Food and Drug Administration in the country in question and the process is characterized by extremely rigid and high demands on quality in all respects.

**In vitro** A term used in biomedical science to describe a biological process made to occur in a laboratory vessel or other controlled experimental environment, for example cultivated cells, rather than within a living organism.

**In vivo** A term used in biomedical science to describe an experimental biological process, and observations thereof, made to occur within a living organism.

**Lipodystrophy** A rare disease characterized by altered fat distribution on the body. In the absence of normal body fat,

various organs, primarily the liver, begin to accumulate fat, leading on to serious metabolic complications, including extreme insulin resistance, hypertriglyceridemia (elevated values of blood fat triglyceride) and liver steatosis (fatty liver).

**Neuropathic pain** Nerve pain can occur after diseases and injuries of the somatosensory nervous system and spread within a neuroanatomical innervation area. The term neuropathic pain is usually associated with pain that persists after healing of the initial insult.

**PCT** Patent Cooperation Treaty, an international patent law treaty, concluded in 1970. It provides a unified procedure for filing patent applications to protect inventions in each of its contracting states.

**Peptide** Short chains of amino acids linked by peptide bonds.

**PICK1** A protein that interacts with C-kinase 1.

**Plasmid** Small, extrachromosomal DNA molecule within a cell that is physically separated from chromosomal DNA.

**Preclinical study** In vitro and in vivo studies carried out before the clinical development (see above) with the objective to make sure that the new therapy is safe and has the intended effect.

**Proof-of-concept** Documented evidence that a potential product or method has the intended effect.

**Viral vector** Viral vectors are tools that are used to deliver genetic material to cells. Examples of viral vectors are lentivirus, adeno-associated virus (AAV), retrovirus and adenovirus. AAV vectors are non-hazardous viruses that can infect human cells without causing disease and can be used to deliver genetic material into human cells.





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.

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