# CombiGene

CombiGene's ambition is to develop transformative 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 - March 2023

## Summary of the report

#### Events during the period

- CombiGene entered into a collaboration agreement with the Danish company Zyneyro for the development of a unique concept for effective relief of chronic pain. The agreement with Zyneyro is a cooperation agreement that means that Zyneyro and CombiGene share the project's costs and revenues equally. According to the agreement CombiGene has paid Zyneyro an upfront of DKK 5 million in connection with the signing of the agreement. CombiGene has furthermore committed to pay an additional maximum of DKK 11.4 million in continued development support towards a clinical study in Phase 1.
- Doctoral dissertation at the University of Copenhagen confirms the pain-relieving effect of COZY01 and COZY02 in experimental models.

#### Events after the end of the period

• *Gene Therapy*, one of *Nature's* journals, publishes an article about CombiGene's epilepsy project authored by Esbjörn Melin, researcher at CombiGene.

#### **Financial information**

#### January – March 2023

- Net sales: TSEK 2,168 (11,403).
- Other operating revenues: TSEK 0 (2,801).
- Profit from financial items: TSEK -14,617 (2,684).
- Earnings per share: SEK -0.74 (0.14).
- Cash and cash equivalents: TSEK 120,506 (121,665).

#### 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	Our projects	Our team	Cash position
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 AktieTorget). In December 2018, CombiGene was approved for listing on Nasdaq First North Stockholm.	<ul> <li>CombiGene currently has four projects:</li> <li>The pain program COZY which consists of one peptide treatment and one gene therapy</li> <li>The lipodystrophy project CGT2</li> <li>The epilepsy project CG01, which was outlicensed to Spark Therapeutics 2021</li> </ul>	CombiGene has 11 employess. Our team is made up of very knowledgeable and experienced profes- sionals with longstanding experience from the in- ternational pharma industry and the biotech arena with thorough knowledge of different aspects of drug development and gene therapy.	At the end of the first quarter 2023, CombiGene had cash and cash equivalents amounting to TSEK 120,506 (121,665)



## Positive start to the COZY program

The first quarter of the year has largely been characterized by work on our new pain program COZY, which we run together with our partner Zyneyro, a Danish company with roots in the University of Copenhagen. During the quarter, we also continued the ongoing collaboration within the epilepsy project CG01 with our American partner Spark Therapeutics, one of the truly leading companies in the gene therapy field. Within the lipodystrophy project CG72, we have been busy planning the implementation of the complementary studies that this project requires. In addition to this, we have also continued to work on our business development to find further interesting projects for in-licensing to build an even stronger and more attractive project portfolio.

#### COZY activities in the first quarter

The pain program consists of two projects: one peptide treatment and one AAV-based gene therapy. The peptidebased treatment is expected to be ready for first dosing in humans within a few years, while gene therapy will need additional development time to reach the same point.

During the first quarter of the year, we had our first joint steering committee meeting with Zyneyro within the framework of the COZY program. The meeting was the start of intensive work on preparations for the preclinical pivotal toxicology program in the peptide project COZY01. In parallel, we have also carried out a number of preparatory activities for the next step in the study of COZY01 conducted by the National Institutes of Health (NIH, a US government agency), in a program funded by them (Preclinical Screening Platform for Pain, PSPP). The background to the NIH's very early interest in COZY01 is not only the human suffering that chronic pain causes, but also the enormous costs that pain gives rise to for the American society in the form of direct and indirect costs and the run-away opioid crisis that has hit the country. Estimates show that pain costs the American society USD 635 billion each year and that an estimated 700,000 Americans have died due to opioid abuse in the past 20 years.

The fact that COZY01 has already attracted the attention of the NIH is of course extremely encouraging and points to the great need for new forms of pain relief. COZY01 has passed the first of the three levels NIH has and has moved on to the next where the substance will be tested in different pain models.

## Further studies are required in our lipodystrophy project CGT2

Our ambition for 2022 was to take the CGT2 project to the stage where a preclinical proof-of-concept study can be initiated. However, some of the studies conducted last year produced incomplete results and need to be repeated. We therefore concluded that further studies are needed before proceeding to the preclinical proof-of-concept study. The current focus of the project is therefore on the preparation of these studies.

#### **Collaboration with Spark Therapeutics**

We have now been working together with Spark since mid-October 2021 and have established a very good cooperation. As I mentioned earlier, I am particularly pleased with the decision to prioritize the expansion of CG01's clinical development program to the US as this will allow the project to gain an early foothold in the world's largest pharmaceutical market, while allowing Spark to



make optimal use of its impressive resources, know-how and network.

#### Our business development continues unabated

Our new collaboration with Zyneyro on the pain program has strengthened CombiGene's position in a significant way. We now have two projects aimed at large patient populations, the epilepsy project CG01 and the pain program COZY – a rather unique position for a gene therapy company. In addition to these projects, we also have the lipodystrophy project CGT2, which, however, is aimed at a smaller number of patients. Going forward, it is our ambition to evaluate interesting opportunities to find additional projects to complement our current portfolio. Our focused work in this area continues with the same vigour as in 2022.

#### Prospects

In 2023, we will continue to develop all our projects as successfully as possible and continue to seek new and promising assets for in-licensing with the ambition to build an increasingly stronger gene therapy company.

Jan Nilsson, CEO

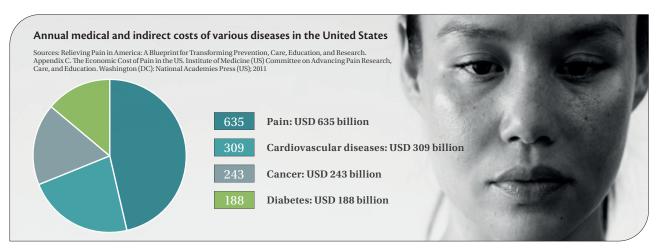
## The pain program COZY – a unique opportunity for a breakthrough in pain treatment

The pain program COZY is run together with the Danish company Zyneyro. The goal is to develop 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 principle for pain management with the same analgesic mechanism.

Both the peptide and the gene therapy are being developed for treatment of severe chronic pain conditions, the gene therapy is reserved for patients where the possibility of spontaneous reduction of chronic pain is judged to be limited (or unlikely). The peptide-based therapy is expected to be ready for human studies within a few years, while the gene therapy will need a few more years to reach the same point in its development. CombiGene's and Zyneyro's pain program is being developed to offer effective pain relief without the side effects that today's treatments often give rise to. This is possible as Zyneyro's researchers have identified a new biological mechanism of action, which forms the basis for both drug candidates.

#### Activities in the first quarter

During the first quarter of the year, the collaboration with Zyneyro began with the first joint steering group meeting



within the framework of the COZY program. The meeting kicked off intensive work on preparations for the pivotal preclinical toxicology program in the peptide project COZY01. The preparations include, among other things, the ongoing selection of the companies that will produce the material for the toxicological study and the company that will carry out the study. Choosing the right partners is an extensive task that has long-term and important consequences.

An independent evaluation of the potential of COZY01 as a future pain treatment is ongoing 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 relief options which are non-opioidbased and non-addictive and without development of tolerance. COZY01 has undergone the first level of three and has been selected to move on to the next level where the substance will be tested in different pain models. During the first quarter of the year, CombiGene and Zyneyro worked on preparatory activities for the next step.

#### 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 disabling side effects such as substance abuse problems, depression, anxiety, fatigue, reduced physical and mental ability. In the US, 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 (COZY01) and a gene therapy treatment (COZY02), which expresses the active part of the peptide from COZY01, with potentially 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 limited or unlikely and where conventional treatment requires daily medication, the intention is to achieve pain relief by treating the patient with an AAV vector that makes the body itself produce the pain-relieving peptide. In this way, long-term pain relief can be achieved without daily medication.

Since the AAV vector encodes the active part of COZY01, the objective is that both the mechanism of action and the effect are the same as with direct administration of the peptide.

The concept could potentially also offer an opportunity to check that a patient responds well to treatment with the peptide before proceeding with the more expensive gene therapy. By using the peptide treatment on potential gene therapy patients, it could potentially be possible to confirm effectiveness in each patient before a costly AAV treatment is initiated.

#### COZY01 - peptide treatment of severe chronic pain

The peptide treatment has shown good effects in various preclinical models. The continued development will focus on conducting, as quickly and efficiently as possible, the necessary preclinical studies to evaluate safety and toxicology and to produce clinical trial material in order to obtain approval from regulatory authorities to conduct the first trials in humans with COZY01.

#### 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 to be included in the vector. AAV is a vector type that CombiGene has extensive experience of from our other projects. When the vector is optimized, preclinical studies follow to investigate and characterize distribution, protein expression, efficacy, 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.

1 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

## 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.

#### CombiGene's project CGT2 is supported by the EUFOSTATS<sup>2</sup> Eurostars Programme.Project ID: 114714

#### **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.

## Important agreement with Professor Ormond MacDougald

In addition to collaboration agreements with Stockholm University, University Medical Center Hamburg-Eppendorf and Accelero, 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.

## 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 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.

#### 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. Since the agreement was signed, the preclinical program has been expanded. The decision to prioritize the expansion of CG01's clinical development program to the US 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.

The agreement with Spark has a potential value of USD 328.5 million – excluding royalties

CombiGene's lead project CG01 has received funding from the European Union's lorizon 2020 research and innovation programme under grant agreement No 23282

## 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. There are currently seven gene therapies approved in the EU and/or in the US and, according to the Alliance for Regenerative Medicines, and another five 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

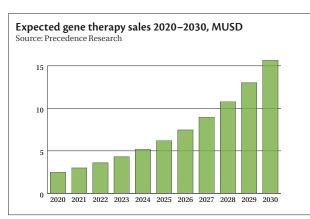
project portfolio. The evaluation of potential projects is a structured and rigorous process based on several key criteria. The work includes review and analysis of intellectual property issues, preclinical data, intended contract structure, size of patient population and medical need, competitive situation, 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.

#### Outcome so far

The most obvious outcome of the work to identify interesting new projects so far is of course the collaboration agreement signed with Zyneyro in early 2023, but the actual results are significantly greater than that. CombiGene has evaluated many projects that, for one reason or another, did not meet the company's selection criteria and were therefore not prioritized.

CombiGene has also 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 first concrete result of this is the cooperation agreement with Zyneyro 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 2022 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 annual general meeting, resolve to increase the company's share capital by issuing new shares, warrants or convertibles. Such issue resolution may be carried out with or without deviation from the shareholders'

preferential 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 as regards issue of convertibles or warrants, issued by conversion or exercise, under the authorization 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.

#### 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

Ten largest shareholders as of March 31, 2023	Total holdings	Holding %
Pareto Securities AS	1,474,032	7.44%
Nordqvist, Jan Ivar	1,363,322	6.89%
Avanza Pension	1,081,947	5.46%
Thoren Tillväxt Ab	494,894	2.50%
Nordnet Pensionsförsäkring AB	478,971	2.42%
Försäkringsaktiebolaget Skandia	273,639	1.38%
Olsson, Per Magnus	240,764	1.22%
Ferstad, Arne	214,072	1.08%
Darlista, Flamur	180,444	0.91%
Thomassen Skaar, Christian	153,494	0.78%

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.

## **Financial information**

#### Income and earnings

Net sales consist of milestone payments and compensation from license and cooperation agreements. In quarter 1 2023, 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 2,168 (11,403) during the period January-March. The decrease is explained by CombiGene putting less resources into CG01 as Spark takes increasingly greater responsibility for the project. Other operating revenues amounts to TSEK 0 (2,801) and consist of TSEK 0 (1,969) which refers to the revenue-earned portion of the grant received from Eurostars. Operating profit for the period amounted to TSEK -14,617 (-2,684). 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-March amounts to TSEK -10,403 (-15,079). Cash and cash equivalents at the end of the period amounts to TSEK 120,506 (121,665). The equity ratio is 95.94% (95.72).

#### 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 3.4 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 11 (9), 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 BFNAR 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-March 2022

The comparative figures for the period January-March last year differ from the interim report for January-March 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.

#### AGM and Annual Report

The Annual General Meeting for 2023 will be held on 25 May, in Stockholm. The Annual Report is available to the public at the Company's office in Lidingö and has been published on the Company's website.

#### **Review by auditors**

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

#### Future reporting dates

- Interim report January June 2023, 25 August 2023.
- 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

	2023	2022	2022
Figures in TSEK	Jan-Mar	Jan-Mar	Jan-Dec
Operating income			
Net sales	2,168	11,403	26,699
Other operating revenues	0	2,801	15,044
Operating expenses			
Other external expenses	-11,764	-13,574	-32,567
Personnel expenses	-3,501	-2,665	-13,032
Other operating expenses	-871	0	-496
Profit/loss before depreciation	-13,968	-2,035	-4,352
Depreciation	-649	-649	-2,595
Profit/loss after depreciation	-14,617	-2,684	-6,947
Net financial income/expense	0	0	790
Income after net financial items	-14,617	-2,684	-6,157
Tax	0	0	0
Net profit/loss for the period	-14,617	-2,684	-6,157
Attributable to			
Parent company shareholders	-14,617	-2,684	-6,157
Earnings per share before dilution	-0.74	-0.14	-0.31
Earnings per share after dilution	-0.74	-0.14	-0.31
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

## Group balance sheet in summary

	2023	2022	2022
Figures in TSEK	31 Mar	31 Mar	31 Dec
ASSETS			
Intangible assets	18,464	20,950	19,004
Total fixed assets	18,464	20,950	19,004
	10,104	20,000	15,004
Current assets			
Accounts receivable	0	6,826	4,216
Other receivables	4,359	13,114	3,223
Cash and cash equivalents	120,506	121,665	131,777
Total current assets	124,866	141,604	139,217
TOTAL ASSETS	143,330	162,554	158,221
SHAREHOLDERS' EQUITY AND LIABILITIES			
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	-14,617	-2,684	-6,157
Equity attributable to parent company shareholders	137,505	155,595	152,122
Total equity	137,505	155,595	152,122
LIABILITIES			
Current liabilities	5,824	6,959	6,099
Total liabilities	5,824	6,959	6,099
TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES	143,330	162,554	158,221

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

Figures in TSEK	Other capital	Accumulated	Total shareholders'	
	Share capital	contribution	profit/loss	equity
Balance brought forward	990	224,124	-72,992	152,122
Net profit/loss for the period			-14,617	-14,617
Amount as per the end of the reporting period	990	224,124	-87,609	137,505

## Group cash flow statement in summary

Figures in TSEK	2023	2022	2022
	Jan-Mar	Jan-Mar	Jan-Dec
Cash flow from operating activities	-10,295	-15,079	-16,666
Cash flow from investing activites	-109	0	0
Cash flow from financing activities	0	0	0
Cash flow for the period	-10,403	-15,079	-16,666
Liquid assets at the beginning of the reporting period	131,777	136,744	136,744
Exchange rate difference cash and cash equivalents	-868	0	11,699
Liquid assets at the end of the reporting period	120,506	121,665	131,777

## Group financial key ratios

	2023	2022	2022
	Jan-Mar	Jan-Mar	Jan-Dec
Earnings per share before dilution, SEK	-0.74	-0.14	-0.31
Earnings per share after dilution, SEK	-0.74	-0.14	-0.31
Shareholders' equity per share, SEK	6.94	7.86	7.68
Equity ratio, %	95.94	95.72	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

	2023	2022	2022
Figures in TSEK	Jan-Mar	Jan-Mar	Jan-Dec
Operating income			
Net sales	2,168	11,403	26,699
Other operating revenues	0	2,787	15,044
Operating expenses			
Other external expenses	-11,747	-13,557	-32,494
Personnel expenses	-3,501	-2,665	-13,032
Other operating expenses	-868	0	-492
Profit/loss before depreciation	-13,948	-2,032	-4,275
Depreciation	-75	-75	-300
Profit/loss after depreciation	-14,023	-2,107	-4,575
Net financial income/expense	-574	-574	-1,505
Income after net financial items	-14,597	-2,681	-6,080
Tax	0	0	0
Net profit/loss for the period	-14,597	-2,681	-6,080

## Parent Company balance sheet in summary

	2023	2022	2022
Figures in TSEK	31 Mar	31 Mar	31 Dec
ASSETS			
Intangible assets	4,121	4,312	4,087
Financial assets	18,012	20,306	18,585
Total fixed assets	22,133	24,619	22,673
Current assets			
Accounts receivable	0	6,826	4,216
Other receivables	5,126	13,788	3,980
Cash and cash equivalents	120,315	121,487	131,583
Total current assets	125,441	142,101	139,779
TOTAL ASSETS	147,573	166,719	162,452
SHAREHOLDERS' EQUITY AND LIABILITIES			
Restricted equity			
Share capital	990	990	990
Statutory reserve	4	4	4
Reserve for development expenses	868	760	760
Non-restricted equity			
Share premium reserve	165,826	165,826	165,826
Accumulated loss including profit/loss for the period	-25,886	-7,781	-11,181
Total shareholders' equity	141,802	159,797	156,398
LIABILITIES			
Current liabilities	5,772	6,922	6,054
Total liabilities	5,772	6,922	6,054
TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES	147,573	166,719	162,452

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

			Reserve for			Total
		Statutory	development	Share premium	Accumulated	shareholders'
Figures in TSEK	Share capital	reserve	expenses	reserve	profit/loss	equity
Balance brought forward	990	4	760	165,826	-11,181	156,398
Provisions for reserve for development expenses			109		-109	0
Net profit/loss for the period					-14,597	-14,597
Amount as per the end of the reporting period	990	4	868	165,826	-25,886	141,802

### Parent Company cash flow statement in summary

Figures in TSEK	2023	2022	2022
	Jan-Mar	Jan-Mar	Jan-Dec
Cash flow from operating activities	-10,291	-15,058	-16,661
Cash flow from investing activites	-109	0	0
Cash flow from financing activities	0	0	0
Cash flow for the period	-10,400	-15,058	-16,661
Liquid assets at the beginning of the reporting period	131,583	136,545	136,545
Exchange rate difference cash and cash equivalents	-868	0	11,699
Liquid assets at the end of the reporting period	120,315	121,487	131,583

## Share capital development

		Total share capital	Change		Change	Quotient
Year	Event	(SEK)	(SEK)	Total shares	shares	(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
At the e	nd of the period	990,060		19,801,197		0.05

## Declaration by the Board of Directors and the CEO







bord member





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, May 12, 2023

**Bert Junno** Chairman Gunilla Lundmark Board member

Peter Nilsson Board member Jonas Ekblom Board member

**Per Lundin** 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

We are now looking forward to a really busy 2023 with continued development of all our projects. Our next quarterly report will be published on August 25, 2023, but there will ample opportunities to follow the development of CombiGene before that date. You are always welcome to visit our web site and to follow us on LinkedIn, Facebook, and Twitter. We will also be presenting at a number of shareholder events during the coming months and publish at least one new issue of our magazine *Ingeneious*. You can find detailed information on our web. We wish you all the best until next time.

The CombiGene Team

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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