

# THE GENE THERAPY EXPLORER

*"CombiGene's epilepsy project CGO1 continues to show strength. At the end of the second quarter of the year, as many as four value-creating milestones were achieved: the release of plasmids for GMP production, completed GMP production, initiated optimization of the administration of CGO1 in large animal studies, and the approval of patents in the U.S. and Russia."*

Jan Nilsson  
CEO

## Interim report

January – June 2021 for CombiGene AB (publ)



# Interim report January – June 2021 for CombiGene AB (publ)

## Second quarter April - June 2021

- Net sales: 0 (0) TSEK.
- Other operating income: 839 (2161) TSEK.
- Profit after financial items: -15 402 (-4 389) TSEK.
- Earnings per share: -0,06 (-0,04) SEK.

## Period January - June 2021

- Net sales: 0 (0) TSEK.
- Other operating income: 5 957 (6 219) TSEK.
- Profit after financial items: -26 258 (-12 055) TSEK.
- Earnings per share: SEK -0,11 (-0,11).
- Liquidity at the end of the period: 82 376 (18 026) TSEK.
- End-of-period equity/assets ratio: 97 (71) %.

## Events during the period

- CombiGene completes a fully guaranteed rights issue providing the company with approximately SEK 75 million before issue costs.
- On May 25, 2021, CombiGene AB held its Annual General Meeting (AGM) in Lund. The AGM resolved all matters in accordance with the proposal of the Board of Directors and the Nomination Committee. The AGM resolved to re-elect Peter Nilsson, Bert Junno, Jonas Ekblom and Per Lundin as Board members and to elect Gunilla Lundmark as new member of the Board. Bert Junno was also re-elected Chairman of the Board. Mazars AB was re-elected as auditor. The AGM resolved, in accordance with the Nomination Committee's proposal, on board fees and that auditor's fees shall be paid in accordance with approved invoices. The AGM further resolved to merge the company's shares, with twenty (20) existing shares being combined into one (1) new share (aggregation 1:20). The AGM also resolved to amend the Articles of Association in such a way that the Board of Directors shall have its registered office in Stockholm, instead of Lund, Skåne County.
- CombiGene and Neurochase initiated the work of optimizing the administration of CG01 in a preclinical study. The results of the study are expected to be completed in late summer 2021 and a positive outcome will mean that long-term studies in toxicology and biodistribution in large animals can start as planned.
- The plasmids to be used in the GMP production of CG01 have been manufactured and subjected to the usual quality assurance. The plasmids will be used as starting material for the GMP batch that will be used in the first clinical study scheduled to begin in 2022.

## Events after the end of the period

- GMP production of CG01 for the first human study.
- CG01 gets patents in the U.S. and Russia.



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



CombiGene's project CGT2 is supported by the Eurostars Programme. Project ID: 114714





## CEO comment

# Four value-creating milestones achieved in the epilepsy project CG01!

*CombiGene's epilepsy project CG01 continues to show strength. At the end of the second quarter of the year, as many as four value-creating milestones were achieved: the release of plasmids for GMP production, completed GMP production, initiated optimization of the administration of CG01 in large animal studies, and the approval of patents in the U.S. and Russia.*

### **Intense autumn for CG01**

CombiGene's epilepsy project is now approaching the final stage of the preclinical phase. The results of the now initiated study of optimized administration of CG01 are expected to be completed in late summer 2021. A positive outcome will mean that the long-term preclinical studies in toxicology and biodistribution in large animals can start after the summer as planned. In parallel with the studies in toxicology and biodistribution, we will during the autumn of 2021 conduct quality analyses of the GMP produced CG01 material, which will be used in the first human study. These analyses will continue for the most part of autumn 2021.

### **Additional patent protection for the gene therapy candidate CG01 in the U.S. and in Russia**

CG01 has received additional patent protection in the U.S. during the summer. The application for a patent was filed in 2016 and the patent now granted runs until 2037. The fact that CG01 has now obtained additional patent protection in the world's largest pharmaceutical market is extremely important from a future commercial perspective. In close proximity to the strengthened patent protection in the U.S., the patent for CG01 in Russia was also approved. The patents also verify the level of innovation in CG01, which has the potential to become the first approved gene therapy treatment for epilepsy.

### **Clinical trial application 2022**

As previously communicated, our plan is for all parts of CG01's preclinical program to be completed in 2022. We will then submit a Clinical Trial Application (CTA), with the ambition to start the first human study in the second half of 2022.

### **CombiGene is open to collaboration with the strategically right Big Pharma partner**

There are several reasons why CombiGene sees a partnership with a Big Pharma partner as a possibly beneficial way to maximize the potential of CG01. The final clinical studies and the future commercialization of CG01 will require precisely the kind of resources in terms of finance, know-how and organizational strength that major pharmaceutical companies possess.

In recent years, CombiGene has gradually strengthened the value of the CG01 project and several major international players have shown so much interest that they requested, and have been given access to, CombiGene's so-called data room. CombiGene has ongoing dialogues with several of these companies.



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

## CombiGene is becoming an established name in gene therapy

CombiGene is a young gene therapy company. It is therefore particularly encouraging to note that our progress attracts attention among our colleagues in the pharmaceutical industry and that we are invited to central roles in various events. For example, in April Karin Agerman moderated a discussion on the manufacture of gene therapies for preclinical and clinical studies at the ATMP world tour and that in June, in collaboration with Dagens Medicin and together with Novartis and Pfizer, we arranged a webinar on gene therapy.

## Continued business development

The company's two projects, CGO1 and CGT2, are at the heart of CombiGene's operations. In addition to working on these projects, CombiGene also conducts continuous business development work to identify new and interesting gene therapies with high commercial potential.

## Merger of shares and move to Stockholm

At the Annual General Meeting (AGM) on May 25, 2021, it was decided to merge the company's shares, with twenty existing shares being added together into one new share. The decision was implemented on June 7, 2021. Gunilla Lundmark was also newly elected as a member of CombiGene's Board of Directors at the AGM and I would like to welcome Gunilla to CombiGene on behalf of the entire company. The AGM also decided that the articles of association be changed so that the Board of Directors shall have in its registered office in Stockholm instead of Lund.

*Jan Nilsson,*  
CEO



*Jan Nilsson*  
CEO



CombiGene's lead project CGO1 has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 823282

## CG01 on its way towards clinical studies

CombiGene's epilepsy project CG01 has come a long way in its preclinical development and has achieved a number of important milestones, and the clinical phase, i.e. human studies, is scheduled to begin in 2022. With each preclinical milestone achieved, the risk in the project decreases and the prospect of obtaining market approval for CG01 after completion of clinical studies increases step by step.

### Final preclinical development runs along three tracks toward the first human study

The final preclinical development of CG01 is conducted along three tracks:

*Final preclinical studies.* The toxicology study in small animals is currently underway, and is expected to be completed by the end of summer 2021. In parallel with this study, work is also ongoing to develop the injection strategy for CG01 (choice of injection aid and optimized injection method) for the toxicology study in large animals, which will start later in 2021.

*Production of CG01.* CombiGene's scalable production platform is essentially fully developed and GMP production of CG01 for the first human study was conducted in the summer of 2021.

*Study design.* CombiGene has started work on selecting CRO partners and the clinics where the first human study will be conducted. In collaboration with the CRO partner and the selected clinics, CombiGene will work out the study design and protocol for the upcoming phase 1/2 study (i.e. the first human study) scheduled to begin in 2022.

### Growing interest in CG01 from Big Pharma

The pharmaceutical industry is showing a growing interest in Advanced Therapy Medicinal Products (ATMP) drugs, i.e. drugs that offer groundbreaking opportunities for the treatment of diseases and injuries, e.g. gene therapies such as CG01.

CombiGene has for several years held ongoing discussions with representatives of several major pharmaceutical companies and a number of the major players have shown so great an interest that they requested, and have been given confidential access to, CombiGene's so-called data room in which information about the company and CG01 is archived.

As the CG01 project has successfully advanced through the preclinical phase with confirmed efficacy in animal studies and confirmed expression in human brain tissue as well as successful studies in memory/learning, pharmacokinetics and tropism, interest from the major pharmaceutical companies has grown continuously. Having a manufacturing structure that can be used for both preclinical/clinical development and commercial production is particularly important in the ATMP space and CombiGene's scalable production platform for CG01 developed in collaboration with Cobra and Viralgen, which was completed in 2020/2021, further strengthens the attractiveness of the project.

Of course, the large market size for drug resistant focal epilepsy drives the considerable commercial potential of CG01. Many other gene therapy projects are being developed to treat rare diseases with small patient populations. An analysis carried out by CombiGene in collaboration with MSC Nordics shows that CG01 has the potential to treat up to 10,000 patients annually..



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## CombiGene is open to collaboration with the right strategic Big Pharma partner

There are several reasons why CombiGene sees a partnership with a Big Pharma partner as a potentially beneficial way to maximize the potential of CG01. The final clinical studies and the future commercialization of CG01 will require precisely the kind of financial, knowledge and organizational resources that the major pharmaceutical companies possess.

The most likely form of potential collaboration between CombiGene and a Big Pharma company is some form of out-licensing of the CG01 project. It is, of course, too early to say anything more precise about what such a deal might look like, but

a common payment structure is that the company that licenses a project during the preclinical or clinical phase pays a sum up-front, provides for research and development costs, and pays fixed compensations as various milestones are achieved. Once the drug candidate has received market approval and been introduced to the market, a royalty payment is made on the sale.

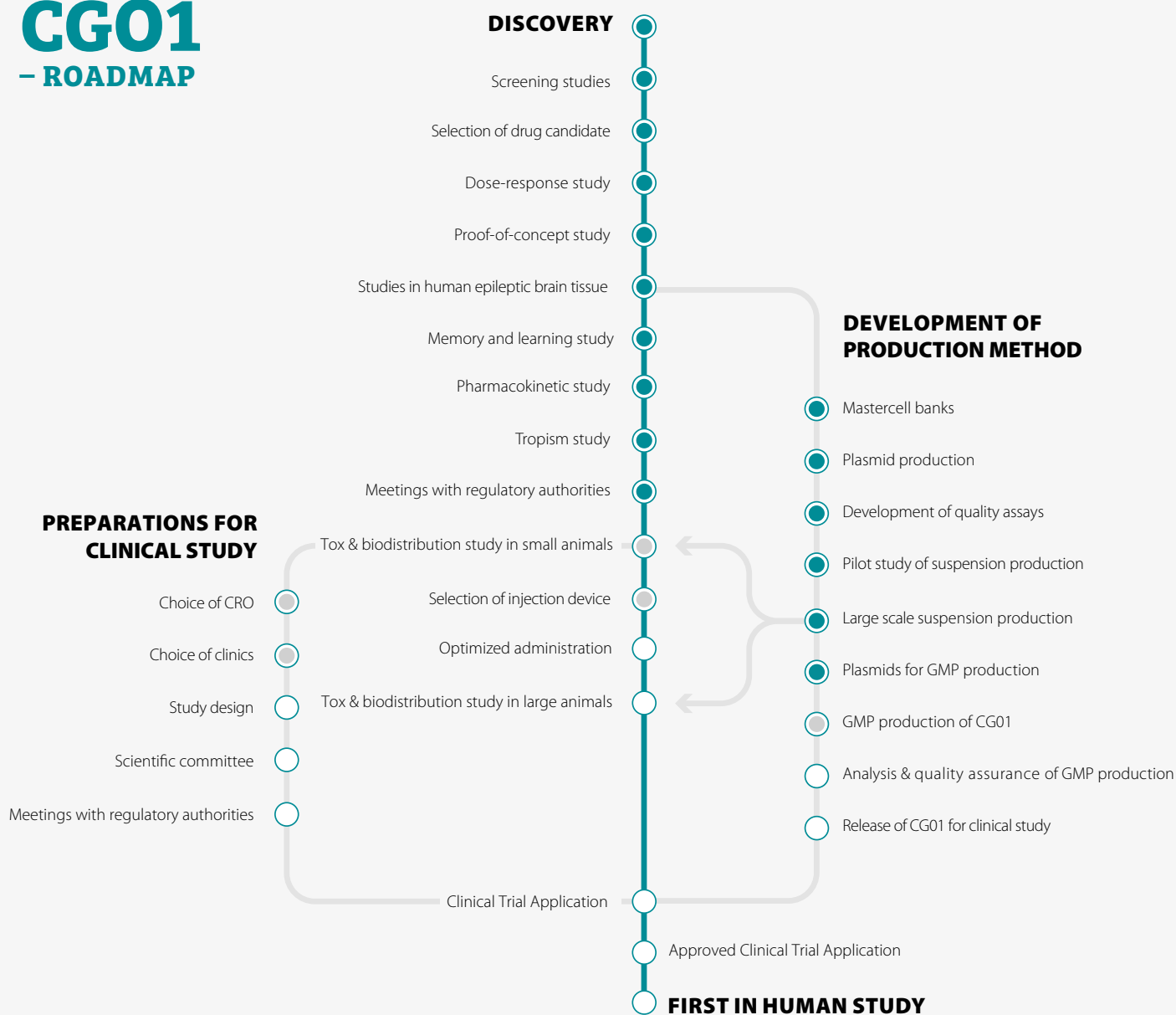
CombiGene believes that an out-licensing under this design would be a potentially beneficial solution for both patients and shareholders as a large company has completely different possibilities than CombiGene to ensure that CG01's unique gene therapy for the treatment of drug-resistant focal epilepsy can be offered within a short period of time to as many patients as possible.



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

# CG01

## - ROADMAP



*The illustration shows how CombiGene's epilepsy project CG01 is approaching the first in human study, scheduled to begin in 2022.*

Completed
  Ongoing
  Up-coming



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



# A few words from our Research & Development Officer

## CG01 Update

CombiGene's drug candidate CG01 is a potentially groundbreaking AAV-based gene therapy with the potential to dramatically improve the quality of life of a group of epilepsy patients for whom there is currently no effective treatment. CombiGene uses a gene therapy vector, an adeno-associated virus (AAV), to administer a combination of neuropeptide Y (NPY) and its receptor Y2 directly to the part of the brain where the epileptic attack starts. CG01 continues to advance towards the first clinical trial scheduled to begin in 2022.

### Optimized administration of CG01.

In collaboration with the British company Neurochase, we have now started work on developing an optimized method for injecting small volumes of CG01 with high precision into the human brain in a preclinical study in large animals. Neurochase and its founder neurosurgeon Professor Steven Gill specialize in administering drugs to various parts of the central nervous system and have extensive experience in administering the very type of gene therapy vectors used in CG01.

In the study, the administration will be followed by so-called real-time imaging, which means continuously monitoring how the injected substance spreads locally at the injection site in the brain. In this way, it can be seen in real time that the gene therapy vectors reach the intended part of the brain. The study also includes analyses of the protein expression itself in the brain to ensure that the expression of the proteins follows the same pattern as the administered substance. The study will be carried out in two steps. In the first step, the injection technique itself is evaluated with a gene therapy vector that expresses a fluorescent protein together with a contrast fluid that makes it possible to follow the course of injection all the way to the target area and see where the proteins are expressed. In the second step, the process is repeated with



*Karin Agerman  
Chief Research and Development Officer*

CG01 to confirm that the administration also results in local natural production of the active substances NPY and Y2.

The results of the study are expected to be completed in late summer 2021 and a positive outcome means that long-term studies in toxicology and biodistribution in large animals can be initiated.

### GMP plasmids approved.

At the end of June, a batch of the plasmids to be used in the production of our experimental drug was completed and approved after a customary quality assurance carried out with a variety of analyses. The plasmids were produced by contract manufacturer Cobra in the first quarter of the year in accordance with GMP (Good Manufacturing Practice). These plasmids are ready to be used as a starting material for the GMP batch of experimental drugs that will be used in the first clinical trial scheduled to begin in 2022.



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 analyzed plasmids are now part of a stability study, which is required for the company's upcoming application for a Clinical Trial Application (CTA). The plasmid production itself was carried out according to plan and generated so much material that, according to today's calculations, they are likely to be sufficient for more productions of CG01 than originally assumed.

### **GMP production of CG01 for the first study in humans.**

In July, in collaboration with one of our manufacturing partners, the leading AAV gene therapy manufacturer Viralgen, we started the GMP production of CG01. The CG01 material is produced on a large scale for use in the first clinical study. The produced material will be analyzed from all relevant aspects and data from the analyses will form a central part of the upcoming CTA. The material will then be used in CG01's first clinical study, which is scheduled for the second half of 2022.

### **Additional patent protection for the gene therapy candidate CG01 in the USA and patent granted in Russia.**

In July, CG01 obtained additional patent protection in the United States, the world's largest pharmaceutical market and patent in Russia. The patent application was filed in 2016 and the patents now granted extend until 2037 with in some cases the possibility of further extension through so-called SPC for medicines.

*Karin Agerman  
Chief Research & Development Officer*



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

## CG01 – milestones

### 2016

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

### 2017

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

### 2018

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

### 2019

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

### 2020

- Preclinical pharmacokinetic study completed with positive results. The study confirms that CG01 creates long-term expression of the active substances NPY and Y2.
- The preclinical learning and memory study shows that NPY and Y2 have no significant negative effect on cognitive functions.
- Delivery of all three plasmids needed to produce CG01.
- Delivery of master cell banks for the three plasmids.
- Successful pilot study performed with suspension production method.

- Positive results in tropism study.
- Agreement on GMP production with Cobra for plasmids for CG01.
- Analytical methods for quality control of the production of CG01 developed in collaboration with CGT Catapult.
- Manufacturing agreement with Viralgen for the production of CG01.
- Agreement with the British company Neurochase regarding the development of optimized administration of CG01.
- First large-scale production of CG01 at the Spanish gene therapy manufacturer Viralgen.

### 2021

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



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# A few words from our Preclinical Project Manager

## CGT2 Update

CGT2, CombiGene's project to develop a gene therapy treatment for partial lipodystrophy, is in preclinical development. Since we licensed the project from Lipigon in 2019, the pace of the project has accelerated, and we are now starting to see the first fruits of this work. The first step in designing gene therapy vectors and testing these in vitro (tests on different liver cells) has been carried out with good results. Since then, in vivo studies have begun.

## Key events in the second quarter of 2021

In February 2021, the Lipodystrophy project was awarded EUR 882,500 in project grants by the EU's Eurostars international funding program. Thanks to this funding, CombiGene has been able to start a collaboration with University Medical Center Hamburg-Eppendorf, which has a research group of experts in lipid research that is now linked to the CGT2 project. During the second quarter of the year, the researchers at Hamburg-Eppendorf started a small dose-response study that will form the basis for a larger study starting in autumn 2021. The evaluation of possible drug candidates is ongoing and will form the basis for an upcoming patent application.

*Annika Ericsson*  
Preclinical Project Manager



*Annika Ericsson*  
Preclinical Project Manager

## Lipodystrophy project – milestones

### 2019

- In-licensing of the project from Lipigon.

### 2020

- Design of expression plasmids, which are a starting material for gene-therapeutic vectors CombiGene intends to develop for treatment of partial lipodystrophy.
- In vitro studies (tests on liver cells) show proper 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 projects receive EUR 882 500 in development grants from the EU Eurostars program.



CombiGene's project CGT2 is supported by the Eurostars Programme. Project ID: 114714

## Financial information

### Income and earnings

The Group has a total net sale of SEK 0 (0) thousand during the period January-June. Other operating revenues amounts to SEK 5,957 (6,219) thousand, of which SEK 4,586 (5,241) thousand refers to the revenue-earned portion of the grant received from Horizon 2020 and SEK 1,016 (0) thousand refers to the revenue-earned portion of the grant received from Eurostars. Operating profit for the period amounted to SEK -26,258 (-12,055) thousand. The main costs during the period have been related to research & development, fees for consultants and personnel costs.

### Cash flow and financial position

Cash flow for the period January-June amounts to SEK 33 481 thousand. Liquidity at the end of the period amounts to SEK 82 376 thousand. The equity ratio is 96,6%.

### Liquidity and financing

The total Horizon 2020 grant amounts to EUR 3,36 million of which EUR 2,9 million so far has been paid to the Company. 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 0.5 million has so far been paid out.

In March / April 2021, a guaranteed rights issue of shares was carried out. The rights issue provided the company with approximately SEK 75 million before issue costs. The company's share capital increased by SEK 16,674,692.6, from SEK 22,927,702.4 to SEK 39,602,395. The number of shares increased by 166,746,926 shares, from 229,277,024 shares to 396,023,950 shares.

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

### The share

At the Annual General Meeting of CombiGene on 25 May 2021 a reverse share split was resolved upon, whereby twenty (20) existing shares were consolidated into one (1) new share. Through the reverse share split, the number of shares in CombiGene decreased from 396,023,950 to 19,801,197, with a quota value

of approximately SEK 2 per share until the reduction of the share capital is executed, after which each share has a quota value of SEK 0.05. The authorization to reduce the share capital was registered on 6 August 2021. The average number of shares for the period is 244,886,389. All shares are of the same type and have the same voting rights.

### Employees

The number of employees in the Group at the end of the period was 7 (3), of whom 4 (2) are women. In addition, there was an administrative resource who was hired as 1 (2) consultants, of whom 1 (2) were women.

### Risks and uncertainties

A drug development company of CombiGenes type is characterized by a high operational and financial risk. There are many factors that can negatively affect the likelihood of commercial success. The risks, which at the company's current stage are considered most important to consider, is the risk that CombiGene's method is not safe or not effective, and the risk that the business may not receive the necessary financing. During the current period, significant changes in these risk or uncertainty factors have occurred.

### 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.

### Review by auditors

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

### Future reporting date

Interim report January – September 2021, 12 November 2021.

### For further information, please contact:

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### Stockholm, Sweden, August 20, 2021, CombiGene AB (publ)

Bert Junno  
Chairman

Jonas Ekblom  
Board member

Per Lundin  
Board member

Gunilla Lundmark  
Board member

Peter Nilsson  
Board member

Jan Nilsson  
CEO



## Group income statement in summary

Figures in TSEK	2021 Apr-Jun	2020 Apr-Jun	2021 Jan-Jun	2020 Jan-Jun	2020 Jan-Dec
Net sales	0	0	0	0	0
Other operating revenues	839	2 161	5 957	6 219	12 029
<b>Operating expenses</b>					
Other external expenses	-12 689	-3 451	-25 320	-12 012	-29 640
Personnel expenses	-2 328	-1 571	-4 791	-3 033	-7 185
Other operating expenses	-576	-119	-807	-731	-869
<b>Profit/loss before depreciation</b>	<b>-14 754</b>	<b>-2 980</b>	<b>-24 961</b>	<b>-9 557</b>	<b>-25 665</b>
Depreciation	-649	-611	-1 297	-1 222	-2 495
<b>Profit/loss after depreciation</b>	<b>-15 402</b>	<b>-3 591</b>	<b>-26 258</b>	<b>-10 779</b>	<b>-28 159</b>
Net financial income/expense	0	-798	0	-1 276	-1 392
<b>Income after net financial items</b>	<b>-15 402</b>	<b>-4 389</b>	<b>-26 258</b>	<b>-12 055</b>	<b>-29 551</b>
Tax	0	0	0	0	0
<b>Net profit/loss for the period</b>	<b>-15 402</b>	<b>-4 389</b>	<b>-26 258</b>	<b>-12 055</b>	<b>-29 551</b>
Attributable to					
Parent company shareholders	-15 402	-4 303	-26 258	-11 886	-29 383
Non-controlling interests	0	-86	0	-169	-169
Earnings per share before dilution	-0,06	-0,04	-0,11	-0,11	-0,17
Earnings per share after dilution	-0,06	-0,04	-0,11	-0,11	-0,17
Average number of shares before dilution	260 495 754	100 748 665	244 886 389	109 696 581	178 780 152
Average number of shares after dilution	260 495 754	100 748 665	244 886 389	109 696 581	178 780 152
Total outstanding shares	19 801 197	125 622 007	19 801 197	125 622 007	229 277 024

## Group balance sheet in summary

Figures in TSEK	2021 30 Jun	2020 30 Jun	2020 31 Dec
<b>ASSETS</b>			
Intangible assets	22 748	23 714	24 046
<b>Total fixed assets</b>	<b>22 748</b>	<b>23 714</b>	<b>24 046</b>
<b>Current assets</b>			
Inventories	824	0	824
Other receivables	9 115	4 822	6 473
Cash and bank balances	82 376	18 026	48 895
<b>Total current assets</b>	<b>92 315</b>	<b>22 847</b>	<b>56 192</b>
<b>Total assets</b>	<b>115 063</b>	<b>46 561</b>	<b>80 237</b>
<b>SHAREHOLDERS' EQUITY AND LIABILITIES</b>			
Share capital	39 602	12 562	22 928
Other capital contribution	185 512	88 094	136 305
Other shareholders' equity	-87 800	-57 393	-58 248
Profit/loss for the period	-26 258	-11 886	-29 551
<b>Equity attributable to parent company shareholders</b>	<b>111 056</b>	<b>31 377</b>	<b>71 433</b>
<b>Minority interest</b>	<b>0</b>	<b>1 672</b>	<b>0</b>
<b>Total shareholders' equity</b>	<b>111 056</b>	<b>33 049</b>	<b>71 433</b>
<b>Liabilities</b>			
Current liabilities	4 007	13 513	7 981
<b>Total liabilities</b>	<b>4 007</b>	<b>13 513</b>	<b>7 981</b>
<b>Total shareholders' equity and liabilities</b>	<b>115 063</b>	<b>46 561</b>	<b>79 414</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
<b>Balance brought forward</b>	<b>22 928</b>	<b>136 305</b>	<b>-87 800</b>	<b>71 433</b>
Issue	16 675	58 361		75 036
Issue costs		-9 155		-9 155
Net profit/loss for the period			-26 258	-26 258
<b>Amount as per the end of the reporting period</b>	<b>39 602</b>	<b>185 512</b>	<b>-114 058</b>	<b>111 056</b>

## Group cash flow statement in summary

Figures in TSEK	2021	2020	2020
	Jan-Jun	Jan-Jun	Jan-Dec
Cash flow from operating activities	-32 401	-17 938	-38 346
Cash flow from investing activities	0	-4	-104
Cash flow from financing activities	65 881	20 803	72 179
<b>Cash flow for the period</b>	<b>33 481</b>	<b>2 861</b>	<b>33 729</b>
Liquid assets at the beginning of the reporting period	48 895	15 165	15 166
<b>Liquid assets at the end of the reporting period</b>	<b>82 376</b>	<b>18 026</b>	<b>48 895</b>

## Parent Company income statement in summary

Figures in TSEK	2021	2020	2021	2020	2020
	Apr-Jun	Apr-Jun	Jan-Jun	Jan-Jun	Jan-Dec
Net sales	0	0	0	0	0
Other operating revenues	839	2 161	5 957	6 219	12 029
<b>Operating expenses</b>					
Other external expenses	-12 664	-3 462	-25 289	-11 595	-29 136
Personnel expenses	-2 328	-1 571	-4 791	-3 033	-7 185
Other operating expenses	-576	-119	-807	-731	-869
<b>Profit/loss before depreciation</b>	<b>-14 729</b>	<b>-2 991</b>	<b>-24 930</b>	<b>-9 140</b>	<b>-25 160</b>
Depreciation	-75	-38	-150	-75	-200
<b>Profit/loss after depreciation</b>	<b>-14 804</b>	<b>-3 028</b>	<b>-25 080</b>	<b>-9 215</b>	<b>-25 360</b>
Net financial income/expense	-574	-316	-1 147	-794	-4 352
<b>Income after net financial items</b>	<b>-15 378</b>	<b>-3 344</b>	<b>-26 227</b>	<b>-10 009</b>	<b>-29 712</b>
Tax	0	0	0	0	0
<b>Net profit/loss for the period</b>	<b>-15 378</b>	<b>-3 344</b>	<b>-26 227</b>	<b>-10 009</b>	<b>-29 712</b>

## Parent Company balance sheet in summary

Figures in TSEK	2021 30 Jun	2020 30 Jun	2020 31 Dec
<b>ASSETS</b>			
Intangible assets	4 390	3 060	4 540
Financial assets	22 027	23 467	23 175
<b>Total fixed assets</b>	<b>26 417</b>	<b>26 527</b>	<b>27 714</b>
<b>Current assets</b>			
Inventories	824	0	824
Other receivables	9 732	5 376	6 233
Cash and bank balances	82 192	17 838	48 703
<b>Total current assets</b>	<b>92 749</b>	<b>23 214</b>	<b>55 759</b>
<b>Total assets</b>	<b>119 166</b>	<b>49 741</b>	<b>83 474</b>
<b>SHAREHOLDERS' EQUITY AND LIABILITIES</b>			
<b>Restricted equity</b>			
Share capital	39 602	12 562	22 928
Statutory reserve	4	4	4
Reserve for development expenses	612	508	612
<b>Non-restricted equity</b>			
Share premium reserve	165 826	68 001	116 619
Accumulated loss including profit/loss for the period	-90 831	-44 796	-64 604
<b>Total shareholders' equity</b>	<b>115 212</b>	<b>36 278</b>	<b>75 558</b>
<b>Liabilities</b>			
Current liabilities	3 954	13 463	7 916
<b>Total liabilities</b>	<b>3 954</b>	<b>13 463</b>	<b>7 916</b>
<b>Total shareholders' equity and liabilities</b>	<b>119 166</b>	<b>49 741</b>	<b>83 474</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>22 928</b>	<b>4</b>	<b>612</b>	<b>116 619</b>	<b>-64 604</b>	<b>75 558</b>
Issue	16 675	58 361				75 036
Issue costs		-9 155				-9 155
Net profit/loss for the period					-26 227	-26 227
<b>Amount as per the end of the reporting period</b>	<b>39 602</b>	<b>49 210</b>	<b>612</b>	<b>116 619</b>	<b>-90 831</b>	<b>115 212</b>

## Parent Company cash flow statement in summary

Figures in TSEK	2021 Jan-Jun	2020 Jan-Jun	2020 Jan-Dec
Cash flow from operating activities	-32 392	-17 920	-38 284
Cash flow from investing activities	0	-4	-3 259
Cash flow from financing activities	65 881	20 803	75 286
<b>Cash flow for the period</b>	<b>33 489</b>	<b>2 879</b>	<b>33 743</b>
Liquid assets at the beginning of the reporting period	48 703	14 959	14 959
<b>Liquid assets at the end of the reporting period</b>	<b>82 192</b>	<b>17 838</b>	<b>48 703</b>

## Group financial key ratios

Figures in TSEK	2021	2020	2020
	Jan-Jun	Jan-Jun	Jan-Dec
Earnings per share before dilution, SEK	-0,11	-0,11	-0,17
Earnings per share after dilution, SEK	-0,11	-0,11	-0,17
Shareholders' equity per share, SEK	5,61	0,26	0,31
Equity ratio, %	96,52	70,98	89,95
Average number of shares before dilution	244 886 389	109 696 581	178 780 152
Average number of shares after dilution	244 886 389	109 696 581	178 780 152
Total outstanding shares	19 801 197	125 622 007	229 277 024

## 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
<b>At the end of the period</b>		<b>39 602 395</b>		<b>19 801 197</b>		<b>2,00</b>

# Glossary

## AED

Anti-Epileptic Drug.

## 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 studies

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

## GMP

A Good Manufacturing Practice (GMP) 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 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.

## Neuropeptide

Neuropeptides are small, protein-like molecules (peptides) that are used by neurons to communicate with each other.

## NPY

Neuropeptide Y, a neurotransmitter that is widely distributed in the central nervous systems of animals and humans.

## 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.



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# CombiGene – The gene therapy explorer

*With one project nearing the clinical-study phase and one project in an early preclinical phase, CombiGene is the leading Nordic gene-therapy company. Gene therapy has seen rapid development in recent years, with a number of approved therapies and several major corporate deals. During this period we've built up a unique position with respect to knowledge within this field in the Nordic region. The company's expertise covers all central areas of the gene therapy field: viral vectors, preclinical studies including biodistribution and toxicity studies, development of GMP-classed manufacturing methods, upscaling of production volumes and regulatory strategy.*

*Few areas of pharmaceutical development are as exciting and promising as gene therapy and, in many respects, CombiGene is at the very forefront of development. During our work with the CGO1 epilepsy project, on a nearly daily basis, we have won new ground, gained new insights and expanded our knowledge. You might say that we are on an expedition, exploring the fantastic possibilities of gene therapy. We are now continuing our voyage of discovery with another exciting project – the lipodystrophy project. Even here, we expect to create new and valuable knowledge as we carry this project forward.*

*And that's why we've chosen to call ourselves the gene therapy explorer.*



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