

Initial Research

2024-06-20

CombiGene: Preclinical experts in gene therapy

- Focus on out-licensing CG01 again
- Promising development in the COZY programme
- We initiate coverage with a fair value of SEK 12.19 per share

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Stock ticker: COMBI
Industry: Biotech
Listed on: Nasdaq First North
Latest share price (SEK): 3.1
Market cap (MSEK): 60.6
Enterprise Value (MSEK): na
Total number of shares (M): 19.8
- of which free float (M): 13.7

VHCF fair value per share
DCF model SEK 12.19

CombiGene
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CEO: Peter Ekolind

Main owners (31 Mar 2024)

	Capital (%)
Orphazyme AS	10.0
Nordqvist, Ivar	9.5
Avanza Pension	6.0
Nordnet Pensionsförsäkring AB	2.7
M&L Industriförvaltning AB	2.6

Share price history (SEK)



	-1m	-3m	-12m
Change (%)	-10.1	-22.5	-55.9
52 w k range (Low /Hi) - SEK	2.3 / 7.3		

Source: Västra Hamnen Corporate Finance

The prospects of gene therapies have ignited hope and expectations from patients, healthcare professionals and investors in the life science industry. The first therapies have been approved, with many more to come.

Gene therapies are expected to break through during the 2020s as global pharmaceutical companies compete to position themselves in a field with great medical and commercial potential.

Swedish gene therapy specialist **CombiGene** focuses on discovering promising projects, developing them until the clinical phase and aiming to out-license them after achieving preclinical proof of concept.

In 2021 CombiGene outlicensed the drug candidate *CG01* for refractory focal epilepsy to **Spark Therapeutics**. The total deal value corresponded to MUSD 329. However, as a part of a strategic decision, Spark decided to return the project to CombiGene in 2023, and now the focus lies on finding a new partner.

In parallel, CombiGene develops treatments for chronic pain in collaboration with Danish biotech company **Zyneyro**. With a new approach, the companies aim to provide a peptide treatment, *COZY01*, and a gene therapy, *COZY02* for a large patient group.

We believe CombiGene's current market value does not reflect the potential of its pipeline. Our risk-adjusted DCF model suggests *CG01*, *COZY01* and *COZY02* to be valued at 12.19 SEK per share.

Investing in drug development is a risky venture, and CombiGene is no exception. The development risk is substantial, as the projects are pre-clinical. Financially, there is no imminent need to raise capital, but we see a financing round by the end of 2025.

Table 1: Valuation - SEK per share (left), MSEK market cap (right)

CG01	4.73	94
COZY01	3.57	71
COZY02	3.90	77
Sum	12.19	241

Source: Västra Hamnen Corporate Finance

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Developing gene therapies**What does CombiGene do?****CombiGene in short**

CombiGene develops gene therapies and recently a peptide track for severe life-altering diseases where adequate treatment is currently lacking. With a small, experienced and dedicated team, the company delivers value to its shareholders by in-licensing new projects, developing them up to the clinical phase, and out-licensing the drug candidates to a strategic partner for further development and commercialisation. The company is based in Stockholm and has been listed on Nasdaq First North Growth Market since 2018.

Currently, CombiGene has three preclinical projects in its pipeline:

- *CG01* - a gene therapy for refractory focal epilepsy
- *COZY01* - a peptide treatment, initially aimed at diabetic neuropathic pain
- *COZY02* - a gene therapy for chronic pain



Table 2: Key events timeline

IPO and selected drug candidate			Manufacturing and research			Patents and licensing			
2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
IPO on Spotlight Stock Market (MSEK 11.1)	- Drug candidate selected, CG01 - Jan Nilsson appointed CEO - Share issue (MSEK 2.5)	- Share issue (MSEK 11.4) - FDA approves the first gene therapies - Positive initial data on the CG01 long-term study	- Manufacturing agreement with Gene Therapy Catapult - UK subsidiary established - CombiGene featured in Nature, a leading scientific journal - List change to Nasdaq First North - Share issue (MSEK 27.1) - EU grants MEUR 3.4 from the Horizon 2020 programme for CG01	- Manufacturing agreement with Cobra Biologics of CG01 - License agreement with Lipigon Pharmaceuticals regarding the lipodystrophy project - Debt issued (MSEK 7)	- Share issue (MSEK 82.3) - Final candidates evaluation in the lipodystrophy project - CGT2 - Patent filed for vectors in the lipodystrophy project - Manufacturing agreement with Viralgen - CG01 administration agreement with Neurochase - Research published in Frontier, leading research publisher - Debt repaid (MSEK 7)	- Share issue (MSEK 65.9) - Reverse stock split 20:1 - CG01 patent approved in US and Russia - International patent application for CGT2 project - Exclusive global licensing agreement with Spark Therapeutics for CG01 (Upfront MSEK 84.5) - Horizon 2020 project successfully completed - EU grants MEUR 0.9 for CGT2 project through Eurostars programme	- GMP production of CG01 available for preclinical studies - Peter Ekolind appointed COO	- Collaboration with Zyneiro in chronic pain treatment (COZY01 and COZY02) - Manufacturing agreement with AmbioPharm within COZY01 - Peter Ekolind appointed CEO - Spark Therapeutics returns the CG01 project - EU grants MSEK 5 for COZY project through Eurostars programme - Charles River as preclinical toxicology partner for COZY01	- Discontinuance of CGT2 - Orphazyme acquires 10% of CombiGene - CG01 patent approved in Australia and India - CSO Karin Agerman decides to leave, Annika Ericsson to replace her

Source: Västra Hamnen Corporate Finance

In-licensing and out-licensing

Business model

CombiGene's business model starts with the in-licensing of gene therapy assets discovered by external researchers in the industry or academia. The assets are then developed to preclinical proof of concept before out-licensing them to a partner. A licensee will conduct the clinical development and commercialise the therapy.

Searching for new projects

The company is continuously searching for new projects to develop. CombiGene has an extensive evaluation process based on several key criteria. This includes reviewing and analysing intellectual property rights issues, preclinical data, intended contract structure, size of patient population, medical need, competitive situation, and commercial potential.

CG01 project returned from Spark

In 2021, CombiGene successfully out-licensed CG01 to **Spark Therapeutics**, a company within the **Roche Group**. The deal included an upfront payment of MUSD 8.5 and MUSD 50 for preclinical and clinical milestones. The total deal value amounted to MUSD 329 excluding royalties. In 2023, Spark decided to return the project due to a strategic overview. CombiGene's ambition is to find a new licensee for the project.

Developments in 2023 highlighted the importance of building an expanded product portfolio. During 2024, CombiGene will continue to drive business development with the ambition to in-license new early-stage projects.

Intellectual property rights

CombiGene operates within the framework of the Patent Cooperation Treaty (PCT), an international agreement that allows companies to seek patent protection for their innovations internationally in around 150 countries with a single application.

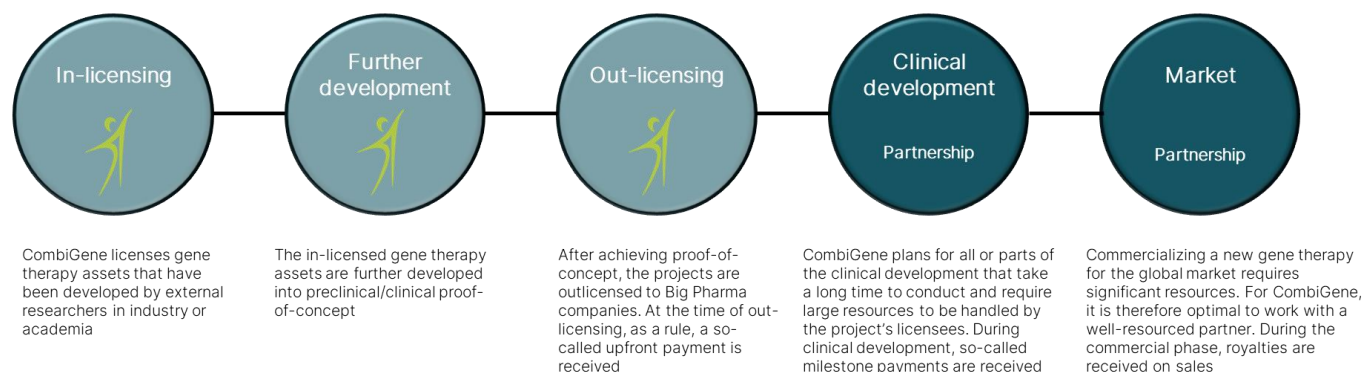
CG01 patent to expire in 2037

CombiGene currently holds patents in two families for the CG01 epilepsy project. The first family covers approximately ten countries, and within the second family, CombiGene has applied for patent protection in additionally ten countries and has so far been granted patent protection in four countries, the USA, Russia, Australia, and India. The patent expires in 2037.

COZY patents to expire 2040-2041

For the COZY projects, CombiGene has several pending patents submitted in 2020-2021 and if granted will be valid until 2040-2041.

Table 3: Business model



Source: CombiGene

To estimate a fair value of the company, we have theoretically assumed that CombiGene will develop its three projects through clinical phases and take them to market. We apply a risk-adjusted discounted cash flow model for each project. We also examine the latest deal flow for a sense of the industry's willingness to pay for assets in the field. For more details on the valuation approach and assumptions, see the section *What is the earnings outlook?* and *What is the fair value of the share?*

Potential for more effective and safer treatments

Gene therapy

Gene therapy aims to transfer a gene to relevant target cells to replace or improve the function of defective genes. Gene therapy may also reduce or eliminate disease-causing proteins, or proteins present in abnormally high amounts, such as in cancer. Hence, gene therapy could provide higher accuracy in targeting affected cells, longer-lasting effects and fewer side effects than conventional therapies.

Gene therapy still in its infancy

The area is still in its infancy with only 22 approved products, but it is expected to expand considerably as numerous clinical trials are in development.¹ Today, gene therapies are applied in a wide range of medical conditions such as neuromuscular disease, inherited blindness and cancer.

The **US Food and Drug Administration** (FDA) has noted a large upswing in the number of investigational new drug (IND) applications for new gene therapies. By 2025, the FDA predicts that they will be approving 10 to 20 cell and gene therapy products a year based on an assessment of the current pipeline and the clinical success rates of these products.²

586 clinical trials within gene therapy

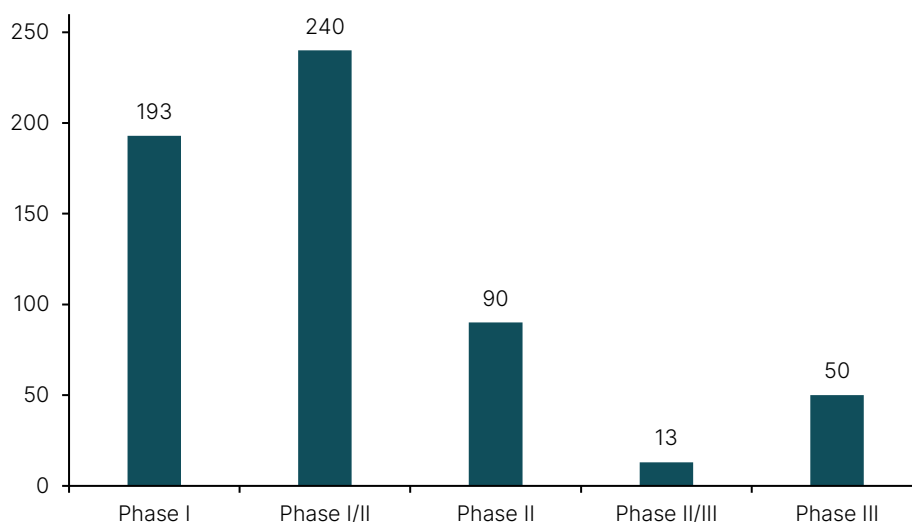
According to data from the **Alliance for Regenerative Medicine**, there are currently 586 clinical trials globally in gene therapy. Including preclinical studies, the total number would likely be significantly higher. The clinical and preclinical activity in the field indicates that a considerable amount of capital and research efforts are being put into adding new gene therapies to the market in the coming years.³

¹ Shchaslyvyi, Antonenko, Tesliuk and Telegeev, (2023), *Current State of Human Gene Therapy: Approved Products and Vectors*, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10609992/>

² FDA, (2019), <https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-peter-marks-md-phd-director-center-biologics>

³ Alliance for Regenerative Medicine (2024) <https://alliancerm.org/data/>

Graph 1: Current global clinical trials within gene therapy (586)



Source: Alliance for Regenerative Medicine

CombiGene's gene therapy projects use an adeno-associated virus (AAV) vector to deliver the gene therapy into the cells. AAV is the most frequently used delivery mechanism in gene therapy. The method has several properties that make it suitable for gene therapy. AAV is not known to cause human disease and does not replicate in the body as normal viruses. Further, the AAV provides stable integration into the target genome which makes it possible to control the amount of AAV very precisely.⁴

Spark Therapeutic's *Luxturna* for retinal dystrophy was the first AAV-based gene therapy approved by the FDA in 2017. Since then, four such therapies have been approved, including **Novartis Zolgensma** for spinal muscular atrophy and **BioMarin Pharmaceutical's Roctavian** in haemophilia A.⁵

Financing

When CombiGene out-licensed CG01 to Spark Therapeutics, the company received an upfront payment of MUSD 8.5. As Spark decided to return the project to CombiGene, the agreement will not generate any future income. CombiGene has also been successful in applying for soft money and has received funds from the EU.

Since CombiGene is developing projects and out-licensing them before commercialisation, the current main sources of income are grants and upfront payments from license agreements.

To its fund operations, the company has raised capital through new share issues amounting to MSEK 207 between 2011 and 2021. The near future financing strategy depends on the CG01 process. For more details about the financials, see the section *What is the cash situation?*

Owners

With 10 per cent of the shares, **Orphazyme** is CombiGene's largest shareholder. Orphazyme is a Danish life science investment firm listed on **Nasdaq Copenhagen**. The company previously focused on research and development of novel therapeutics for neurodegenerative diseases but changed its strategy in 2022 to focus on life science investments. **Ivar Nordqvist** is the largest individual owner with 9.54 per cent of the

⁴ Issa et al., (2023), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10000783/>

⁵ The Scientist (2023), <https://www.the-scientist.com/introduction-to-aav-gene-therapies-71193>

**CG01 upfront
payment of MUSD
8.5**

shares, followed by **Nordnet Pensionsförsäkring** and **Avanza Pension** with 5.95 and 2.66 per cent respectively.

Management

An experienced, knowledgeable and well-connected team is key to success. CombiGene is led by CEO **Peter Ekolind** who has extensive experience in the life science industry. Together with Chief Scientific Officer **Karin Agerman** and CFO **Louise Aspenberg**, they form the executive management team.



Peter Ekolind joined CombiGene in September 2023 as COO and was appointed CEO in 2023. Ekolind has over 20 years of experience in the life science industry, with previous positions at **Xintela**, **Bristol-Myers Squibb**, **Getinge** and **Airsonett**. In recent years, the focus has been on working in smaller start-ups. Ekolind holds an Executive MBA from the **School of Economics, Lund University**. Stock ownership: 43,811 shares.



Karin Agerman is the Chief Scientific Officer and joined in 2018. Agerman holds a PhD in molecular neurobiology from the **Karolinska Institutet** and an Executive MBA from the **School of Economics, Stockholm University**. Agerman has over 15 years of research experience ranging from infectious diseases to central nervous system indications. Before CombiGene, Agerman worked at **AstraZeneca**, **Merck** and **Uppsala BIO**. In 2024, CombiGene announced that Agerman will leave the company and appointed Annika Ericsson as the new CSO. Stock ownership: 0 shares.



Louise Aspenberg was appointed Chief Financial Officer in 2020. Louise holds a Bachelor's degree in Economics from **Örebro University**. Aspenberg is an experienced financial professional with broad experience in group accounting and financial reporting in public companies. Stock ownership: 0 shares.

The team

Below, we list everyone in the current organisation as the business model heavily relies on a well-functioning team. By the end of the first quarter of 2024, the company had ten full-time employees with the former CEO Jan Nilsson acting as a consultant on a part-time assignment.



Sebastian Bauer joined CombiGene in July 2023 as CMC Director. Bauer holds a PhD in analytical biochemistry from the **University of Konstanz**, Germany. Bauer has worked in the pharmaceutical industry for the past 22 years. Initially as a project manager in drug development (protein drugs) for **Biovitrum/Sobi**. Later, also in several senior positions at a **Recipharma/SHL** joint venture. Most recently he held a position as PMO director in the CDMO industry for Recipharma. Stock ownership: 28,997 shares.



Annika Ericsson was appointed Director Preclinical Development in 2018 and has been appointed new CSO in 2024. Ericsson has over 17 years of experience in the biotechnology industry, especially at **Zymenex** and **Chiesi**. There she worked in the laboratory developing and scaling up production processes for protein drugs and was project manager for preclinical studies in various lysosomal diseases. Ericsson holds a PhD from the Karolinska Institute in medical biochemistry with a thesis in enzyme and gene therapy for acute intermittent porphyria. Ericsson also has a post-doctoral experience from the **Mount Sinai School of Medicine** in New York. Stock ownership: 0 shares.



Pernilla Fagergren joined in 2021 as the Director Clinical Translation. Fagergren holds a PhD from the Karolinska Institute and has conducted research at Mount Sinai School of Medicine in New York, USA. She has broad experience from academia and industry, most recently from **Merck** where she worked as a medical advisor and manager in neurology. Before that, she worked as a scientist with early drug projects at **Karo Bio**. Her expertise covers key areas such as drug development, project management and neuropharmacology. In her professional career, Fagergren has consistently collaborated

with physicians and leading medical opinion leaders both nationally and internationally. Stock ownership: 0 shares.



Alvar Grönberg joined in 2022 and was appointed Senior Program Director. Grönberg has extensive experience in academia and the international pharmaceutical industry. Grönberg has previously held senior positions at **Lipopeptide/Pergamum** and **Neuro-Vive Pharmaceutical /Abliva**, among others. Grönberg holds a PhD from the Karolinska Institute. Stock ownership: 0 shares.



Esbjörn Melin joined in 2021 as Scientist. Melin holds a PhD in the field of gene therapy treatment of epilepsy from **Lund University** and an MSc in Engineering Nanoscience from **Lund Institute of Technology**. As a PhD student, Esbjörn worked in close collaboration with Professor **Merab Kokaia**, one of CombiGene's scientific founders, and has also co-authored several scientific articles in the field of gene therapy treatment of epilepsy. Stock ownership: 3,600 shares.



Daniela Morath was appointed Administrator in 2018 with previous experience in various industries and also a couple of years in finance and payroll. Morath is a graduate of a specialised natural science program and holds a vocational college degree as a 3D printing specialist. Stock ownership: 0 shares.



Birgitta Ståhl joined in 2022 as the Senior Director In-licensing. Ståhl holds an MSc in Pharmacy from **Uppsala University** and an MBA from the **University of Westminster** in the UK. She has long and broad experience in the life science industry, from a corporate perspective and project management in all stages of drug development. Recently as Global Project Director at **Oncopeptides**. Before that, she worked for several years in smaller biotech companies within **Karolinska Development's** portfolio and also at **No-vartis** and **Pfizer**. Stock ownership: 0 shares.



The former CEO is a Senior Advisor

Jan Nilsson was appointed CEO in October 2016 and stepped down in 2023. Nilsson has been active in several different areas of the pharmaceutical industry such as drug development, product launch, sales and marketing of established international brands. Nilsson holds a Master's degree from the **University of Gothenburg** and an MBA from Uppsala University. Nilsson is currently a Board member of **Aptahem**, **CarryGenes Therapeutics**, and Chairman of **CCRM Nordic**. Since 2023, Nilsson has been the Senior Executive Advisor for CombiGene. Stock ownership: 55,000 shares through **Urbicum Ledningskonsult**.

Pipeline

Epilepsy

Epilepsy is a brain disorder that causes different types of seizures. A seizure can involve having cramps or losing part of your consciousness for a short or long time. Between seizures, you may feel completely normal.⁶

Epilepsy treatments made progress in the 1990s and early 2000s when several new drugs with broad efficacy profiles were introduced, such as **Union Chimique Belge's (UCB) Keppra** (levetiracetam) and **GlaxoSmithKline's Lamictal** (lamotrigine).

Since then, other treatments have shown limited improvement in comparative studies, placing UCB and GlaxoSmithKline as the leading players in the area. To maintain this position, both companies have introduced extended-release (ER) formulations of their

Need for better epilepsy treatment

⁶ 1177, (2022), <https://www.1177.se/sjukdomar--besvar/hjarna-och-nerver/yrsel-svimning-och-kramper/epilepsi/>

previously well-selling products, while strengthening their relationships with epilepsy physicians in key regions. Learn more in the *How is the competitive situation?* section.

Overall, according to CombiGene, with the introduction of ER products and generics, the market has not seen any major medical breakthroughs in the last 15 years, underlining the medical need for improved treatments.

Refractory focal epilepsy

There are different kinds of epilepsy with focal epilepsy being the most common. Focal epilepsy affects around 60 per cent of all epilepsy patients and is characterised by seizures that begin on one side of the brain.⁷

CG01 targets refractory focal epilepsy

CG01 aimed at refractory focal epilepsy

Some patients with epilepsy do not respond to medication, this is known as refractory epilepsy and patients require alternative treatments. CombiGene's candidate CG01 is a gene therapy specifically designed for refractory focal epilepsy.

CG01 consists of an AAV carrying two therapeutic genes transferred into the patient's brain via injection. CG01 will then inhibit the excess release of glutamate which causes epileptic seizures.⁸

The CG01 project is in preclinical development. CombiGene is currently looking to out-license the project to advance it into the clinical phase.

COZY projects to treat chronic pain

Chronic pain

In the two COZY projects, CombiGene focuses on chronic pain, specifically neuropathic pain. This type of pain is associated with damage to the body's neurological system. Excessive pain signals caused by inflammation and injury are sent to the brain.

Large socio-economic effects

Neuropathic pain is a major health concern

Neuropathic pain is a major health concern worldwide. It has highly detrimental effects on the quality of life for people affected. The condition also has substantial socio-economic effects. The direct cost to the medical system has been estimated to be BUSD 560 annually.⁹

In Europe, estimates suggest the direct annual healthcare cost for neuropathic pain amounts to EUR 2,000 to 3,000 per patient. Indirect costs, such as costs associated with sick leave are also substantial. The total annual costs of neuropathic pain per patient range from EUR 9,300 to 14,400.¹⁰

Diabetic neuropathic pain

Diabetic neuropathy is common, affecting as many as 50 per cent of patients diagnosed with diabetes.¹¹ According to the WHO, around 422 million people have diabetes worldwide.¹²

There are different kinds of neuropathic pain, CombiGene's COZY01 addresses neuropathic pain where diabetes is one of the underlying causes.

⁷ Healthline, (2021), <https://www.healthline.com/health/epilepsy/types-of-epilepsy>

⁸ CombiGene, (2020), prospect

⁹ Dahlhamer (2018), <https://www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm>

¹⁰ Liedgens et al., (2016), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4853004/>

¹¹ Ibid.

¹² WHO <https://www.who.int/news-room/fact-sheets/detail/diabetes>

Nerve damage caused by diabetes

Diabetic neuropathy is a nerve damage caused by diabetes. High levels of glucose and fats in the blood, such as triglycerides, could damage your nerves over time. The condition often harms the nerves in the feet and legs, but internal organs such as the heart, the digestive system, and the urinary tract could also be affected.¹³ The symptoms vary, but the condition is often associated with a tingling or burning feeling, sharp pains or cramps, muscle weakness, extreme sensitivity to touch, and serious foot problems such as ulcers, infections and bone and joint damage. The condition can substantially affect the patient's quality of life.¹⁴

Current treatments are not designed for neuropathic pain

Diabetic neuropathic pain (DNP) is often managed by excluding other causes of painful peripheral neuropathy. First-line drug treatments include anticonvulsants, pregabalin, and gabapentin. Antidepressants are also used, especially treatments addressing the reuptake of serotonin and noradrenaline (SNRI). Clinical and experimental evidence is in favour of also using opioids in combination with first-line treatments.¹⁵

The problem is that these treatments are not specifically designed for chronic pain. They are often associated with serious side effects such as depression, anxiety, fatigue, and impaired physical and mental performance.

The opioid crisis in the US is well-documented. According to a study published in the **Lancet** in 2022, without urgent intervention, 1.2 million people in the US and Canada will die from opioid overdoses by the end of the decade. To date, more than 600,000 people have died since 1999.¹⁶

Partnering with Zyneyro

CombiGene and Zyneyro - COZY

CombiGene aims to provide treatments for chronic pain together with the Danish biotechnology company **Zyneyro**. Zyneyro was founded by researchers at the **University of Copenhagen** in 2021. The collaboration involves two projects, COZY01, a peptide treatment, and COZY02, a gene therapy. CombiGene paid an upfront fee of MDKK 5 to Zyneyro with an additional payment of up to MDKK 11.4. Apart from this, the companies will evenly share costs and revenues from the programme.

A peptide and a gene therapy

In severe chronic pain, the intention is to administer the peptide (COZY01) directly to the patient to achieve effective pain relief. In severe chronic pain where the chances of spontaneous reduction of pain are deemed unlikely and require medication for life, the intention is to provide the gene therapy treatment (COZY02) for the body to self-produce the peptide locally.

Targeting the PICK1 protein

Many neurologic diseases and conditions are seen to have their origin in the dysfunction of glutamate receptors, such as Parkinson's, Alzheimer's, and schizophrenia. Glutamate receptors are cell-surface proteins that bind to the neurotransmitter and amino acid glutamate, the most common mediator of fast excitatory synaptic transmission in the CNS.

The excess of glutamate receptors in the dorsal horn synapse has been the focus of several research groups and drug developers. Inhibiting the receptors directly has been shown to cause serious side effects.

¹³ Mayo Clinic, (2022), <https://www.mayoclinic.org/diseases-conditions/diabetic-neuropathy/symptoms-causes/svc-20371580>

¹⁴ Ibid.

¹⁵ Schreiber et al., (2015) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4398900/>

¹⁶ The Lancet, (2022), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02252-2/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02252-2/abstract)

A new approach in chronic pain

The approach is to modulate the synaptic transmission in the spinal cord by targeting PICK1 – a scaffold protein that binds to and organises a variety of receptor subtypes that regulate the cell's function. PICK1 is involved in receptor activation and trafficking from the cell membrane to the intracellular compartment.

By inhibiting PICK1, this activation process is modulated and the pain signal transmission is decreased. The COZY programme has developed a synthetic bivalent protein that inhibits PICK1 with high specificity and selectivity.

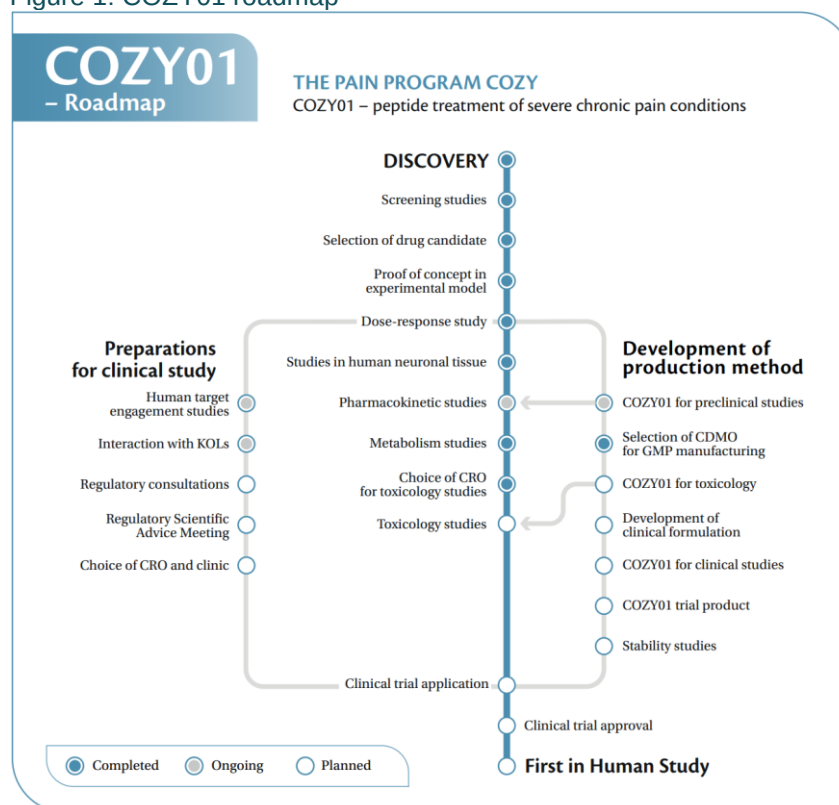
Promising preclinical results

The principle has been shown in animal models to relieve severe chronic pain and restore nerve sensitivity without the usual side effects, such as addiction.

Subcutaneous administration of the synthetic inhibitor provides pain relief in a mouse model of inflammatory, neuropathic and diabetic pain. In a 12-month preclinical study, the gene therapy provided full pain relief for the whole period.

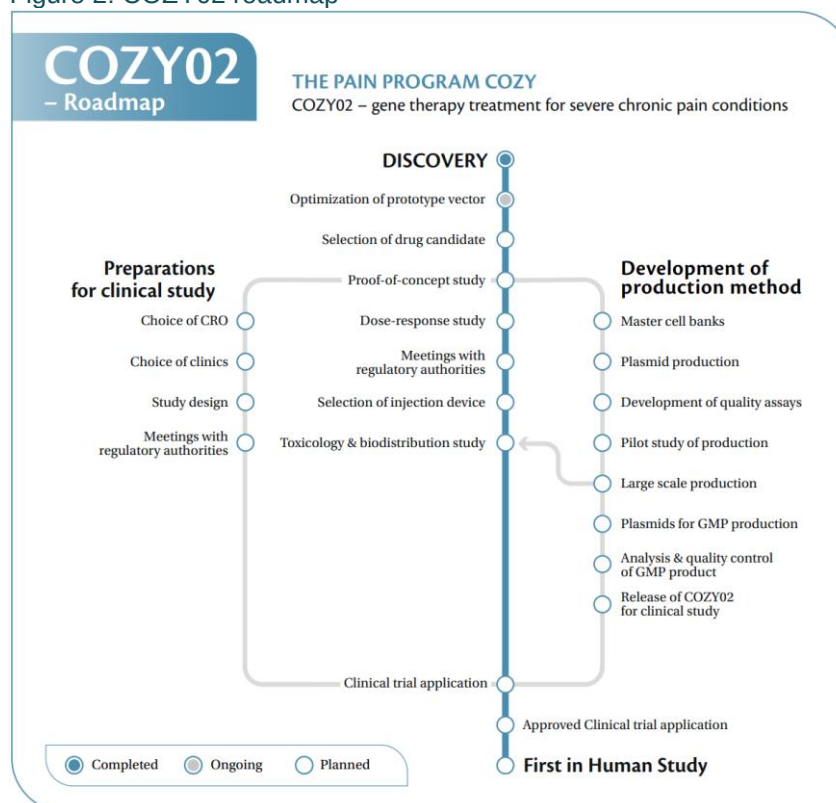
Figure 1 and 2 shows a roadmap of the COZY programmes. CombiGene and Zyneyro will run a series of activities with the ambition of reaching positive results in the pre-clinical toxicology study – the last step before human studies.

Figure 1: COZY01 roadmap



Source: CombiGene

Figure 2: COZY02 roadmap



Source: CombiGene

Production

CombiGene has historically worked with several contract development and manufacturing organisations (CDMO), contract research organisations (CRO) and other external parties for optimising the development of its drug candidates. These collaborations are vital for the company as they include the different levels of manufacturing, quality assurance, and the planning and execution of preclinical trials, among other things.

Ambio Pharm and Charles River

For the COZY01 programme, CombiGene entered an agreement with the CDMO **Ambio Pharm** for the manufacturing process in 2023. The same year CombiGene chose **Charles River** as its preclinical toxicology partner and the CRO will perform the preclinical toxicology studies required to start the first human studies.

What is the market potential?

We have segmented the following patient groups in the US, EU¹⁷, the UK and Japan regarding CombiGene's different projects and calculated the total market value. In accordance with industry standards, we have assumed a 50 per cent price discount in Europe and Japan compared to the US. We also assume a gross to net price of 80 per cent, representing a 20 per cent discount to distributors.

Note that below, we estimate the total markets, which is not equivalent to the market share CombiGene will capture with its products. Estimates for the addressable patients are provided in detail in the *What is the earnings outlook?*

CG01

We estimate around 1 million people suffer from refractory focal epilepsy and that 10 per cent of these are offered treatment, based on Ryvlin and Rheims (2022). Hence,

100,000 addressable patients

¹⁷ France, Germany, Italy and Spain

these one hundred thousand individuals are addressable patients for CG01. A treatment with CG01 will be expected to have a life-long effect, which means that it only needs to be taken once. We moderately estimate a price of MSEK 5 in the US and MSEK 2.5 in EU4, the UK and Japan, based on existing gene therapy treatments with a price range of MSEK 0.7-40.¹⁸

As mentioned above, *Luxturna* is a gene therapy for retinal dystrophy. The treatment is applied locally in the eye through a surgical procedure, comparable to CombiGenes CG01 which is thought to be applied locally in the brain. The current cost of this treatment for both eyes is MUSD 0.85 or MSEK 9.¹⁹

We expect manufacturing costs for gene therapies to decrease in the future as the technology will develop. The benefit of the therapy, medical, societal and for the patient, motivate a high price level for gene therapies also in the future. The addressable market for CG01 amounts to BSEK 426.

COZY01

Around 3.5 million people are treated for diabetic neuropathic pain yearly with slight variations between the regions.²⁰ We estimate a yearly treatment cost of TSEK 49 based on existing alternatives such as pregabalin.²¹ This represents an addressable market of BSEK 106.

COZY02

COZY02 is in early development and a specific indication or patient group is not yet defined. Therefore, we have used a broad population with severe chronic pain, which represents around 8 per cent of the total population.²² This group could include several indications, such as patients suffering from phantom limb pain, postoperative pain, and chemotherapy induced pain.

Since there is no current available gene therapy for chronic pain, we have assumed that around 0.5 per cent of these patients will be offered COZY02, representing 1 out of 200 patients.

The patients receiving COZY01 have been excluded from this group, which explains why the starting population is slightly lower. Based on existing treatments, we have estimated a price of MSEK 4 in the US and 2 in EU4, the UK and Japan.

This represents an addressable market of BSEK 722.

In summary, these projects operate in markets with a total value of BSEK 1,256.

3.5 million addressable patients

Specific indication or patient group not yet defined

¹⁸ AJMC, (2023), <https://www.ajmc.com/view/high-cost-gene-therapies-present-reimbursement-access-challenges>

¹⁹ CNBC, (2018), <https://www.cnbc.com/2018/01/03/spark-therapeutics-luxturna-gene-therapy-will-cost-about-850000.html>

²⁰ Global data, (2024)

²¹ Drugs.com, (2024), https://www.drugs.com/dosage/pregabalin.html#Usual_Adult_Dose_for_Diabetic_Neuropathy, <https://www.drugs.com/price-guide/pregabalin>

²² Dalhamer et al., (2016), https://www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm?s_cid=mm6736a2_w

Table 4: Market estimation

CG01 population in thousands	U.S	EU5	Japan	Sum	Source
Population over 18 years old	267 993	270 842	100 178	639 013	PopulationPyramid
Active diagnosed prevalent cases (1.3%, 0.8%, 0.3%)	3 486	2 183	301	5 970	GlobalData
Focal epilepsy (60%)	2 092	1 310	180	3 582	CombiGene
Refractory epilepsy (30%)	627	393	54	1 075	CombiGene
Offered treatment (10%)	63	39	5	107	Västra Hamnen estimate based on Ryvlin & Rheims (2022)
Price SEK	5 000 000	2 500 000	2 500 000		Västra Hamnen estimate
Market value (TSEK)	313 749 270	98 234 730	13 531 815	425 515 815	
COZY01 population in thousands	U.S	EU5	Japan	Sum	Source
Population over 18 years old	267 993	270 842	100 178	639 013	PopulationPyramid
Diagnosed prevalent cases of type 1 and type 2 diabetes (9.5%, 9.9%, 3.8%)	25 332	26 815	3 766	55 913	GlobalData
Total diabetic neuropathic pain treated cases (3.3%, 8.2%, 12%)	837	2 194	439	3 470	GlobalData
Price yearly SEK	49 056	24 528	24 528		Comparable alternatives from Drugs.com
Market value (TSEK)	41 053 370	53 813 825	10 768 662	105 635 857	
COZY02 population in thousands	U.S	EU5	Japan	Sum	Source
Population over 18 years old	267 993	270 842	100 178	639 013	PopulationPyramid
Severe chronic pain (8%)	21 439	21 667	8 014	51 121	Dahlhamer et al. (2016)
Offered treatment (0.5%)	107	108	40	256	Västra Hamnen estimate
Price SEK	4 000 000	2 000 000	2 000 000		Västra Hamnen estimate
Market value (TSEK)	428 789 101	216 673 562	80 142 218	725 604 881	
Total addressable market value of all projects (TSEK)	783 591 741	368 722 117	104 442 695	1 256 756 553	

Source: Västra Hamnen Corporate Finance

How is the competitive landscape?

The global pharmaceutical industry is highly competitive. Companies, universities and research institutions are conducting extensive research and developing new treatments and blockbuster drugs. There is a risk that competitors may reach commercialisation before CombiGene, making its market entry more challenging. However, increased competition could also attract investor interest by demonstrating proof of concept for a new mechanism of action.

CG01 - epilepsy

Treatment for epilepsy consists primarily of preventive medicines, which reduce the risk of seizures but do not cure the disease.²³ The most common anti-epileptic drugs are Lamotrigine (Lamictal), Gabapentin (Neurontin), Levetiracetam (Keppra, Spritam), and Phenytoin (Dilantin).²⁴

UCB and GSK are industry leaders

According to CombiGene, the pharmaceutical market for epilepsy is mainly dominated by UCB and GlaxoSmithKline.

Belgian-based UCB focuses on developing drug candidates for diseases of the nervous system and the immune system. UCB generated sales of BEUR 5.3 in 2023 and has 9,000 employees. UCB has several approved drugs within the treatment of epilepsy such as Keppra (Levetiracetam) and its successor Keppra XR, Briviact (Brivaracetam), and Vimpat (Lacosamide), generating sales of MEUR 636, 576, and 394 in 2023 respectively.²⁵

British GlaxoSmithKline focuses on the immune system and has four core therapeutic areas, infectious diseases, HIV, respiratory/immunology, and oncology. In 2023 the firm generated sales of BGBP 30 and has over 70,000 employees. The firm's competing epilepsy drug is Lamictal, which generated sales of MGBP 435 in 2023.²⁶

Although new pharmaceuticals have emerged, the efficacy has been limited for 20-40 per cent of drug-resistant epilepsy patients. Refractory epilepsy patients are referred

²³ 1177, (2024), <https://www.1177.se/stockholm/sjukdomar--besvar/hjarna-och-nerver/yrsel-svimning-och-kramper/epilepsi/>

²⁴ GoodRx, (2022), <https://www.goodrx.com/classes/anti-epileptics/best-antiepileptic-seizure-medication>

²⁵ UCB, (2024), <https://www.ucb.com/investors/download-center>

²⁶ GlaxoSmithKline, (2024), <https://www.gsk.com/en-gb/investors/financial-reports/annual-report-2023/>

to surgery, a ketogen-based diet, vagus nerve stimulation or deep brain stimulation. This is the patient group addressed by CG01.

New therapies are under development. The Netherlands-based **uniQure** will initiate a phase I/II trial in 2024 with its drug candidate *AMT-260* in mesial temporal lobe epilepsy.²⁷

COZY01 – diabetic neuropathy

There is no current cure for diabetic neuropathy, only treatments to slow progression, relieve symptoms, and manage complications.²⁸ Treatment methods involve medication and alternative methods such as acupuncture.²⁹ The drugs used are not specifically designed for neuropathic pain but are originally anti-depressants, anti-seizures, or general pain relief.

Pregabalin (*Lyrica*), gabapentin (*Gralise*, *Neurontin*) are recommended by the **American Diabetes Association** (ADA). SNRIs are a class of antidepressants that could help against nerve pain. The ADA recommends duloxetine (*Cymbalta*, *Drizalta Sprinkle*) as a first treatment. Also, venlafaxine (*Effexor XR*) is used.³⁰ Tricyclic antidepressants could also ease mild to moderate nerve pain. These include nortriptyline (*Pamelor*) and desipramine (*Norpramin*).

COZY01 to compete on a broad market

COZY01 will compete on a broad market of pain medications and other advanced therapies with large pharmaceutical firms. COZY01's unique selling point revolves around giving lifelong treatment of pain relief without daily medication and its potential side effects. Some patients are also non-responding to opioids and need other treatment alternatives.

Gene therapy for long lasting effect

COZY02 – chronic pain

Similar to COZY01, the gene therapy COZY02 is aimed at severe chronic pain. Due to the complexity of developing a gene therapy, COZY02 is further away from reaching patients than COZY01. Competitors are other pain-relieving medicines and other therapies in development.

What is the earnings outlook?

For most smaller biotech companies, such as CombiGene, potential revenues are forecasted for the distant future, while development costs are incurred in the present. Many biotech companies plan their strategic development to achieve proof-of-concept in phase II, to be able to out-license the innovation to a larger partner for further development, approval and marketing.

Valuing the projects individually

CombiGene differs in that sense as the strategy is to find early-stage projects, develop them until the clinical phase, and out-license them to a strategic partner for further development and commercialisation. To estimate the value of the projects, we have projected the earnings outlook as if the company will take it to market on its own. We have used a sum of the parts valuation, adding the value of the projects.

Combigene's projects are in the preclinical stage with a long period of development before approval and commercialisation. We have estimated the following timelines until

²⁷ uniQure, (2024), <https://www.uniqure.com/programs-pipeline/temporal-lobe-epilepsy-tle>

²⁸ Mayo Clinic, (2022), <https://www.mayoclinic.org/diseases-conditions/diabetic-neuropathy/diagnosis-treatment/drc-20371587>

²⁹ Healthline, (2024), <https://www.healthline.com/health/type-2-diabetes/diabetic-neuropathy>

³⁰ Bril et al., (2011), *Evidence-based guideline: Treatment of painful diabetic neuropathy*, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3100130/>

approval for CombiGene's projects. We have assumed a launch cost of MSEK 1,500 for each of the projects, based on the findings of Chang et al. (2020).³¹

Table 5: Project timeline

Activity	Phase I	Phase II	Phase III	Approval
CG01	2028-2029	2030-2031	2032-2034	2035
COZY01	2026-2027	2027-2029	2029-2033	2033
COZY02	2028-2029	2030-2031	2032-2034	2035

Source: Västra Hamnen Corporate Finance

In our model, the relevant markets for the three projects are the US, EU4, the UK and Japan.

CG01

The estimated prevalence of active diagnosed cases is 1.3 per cent of the population in the US, 0.8 per cent in EU4, the UK and 0.3 per cent in Japan. Continuing, 60 per cent has focal epilepsy of that group and 30 per cent is left with refractory epilepsy. We believe 10 per cent is offered treatment which indicates around 115,000 patients in 2036.

CG01 to reach market in 2035

In our model, we project that CG01 will enter the market in Q4 2035 and grow steadily with the launch curve to a 3 per cent market share at peak 2041. Thereafter, we lower the market share due to sales erosion after the expiry of key patents in 2037.

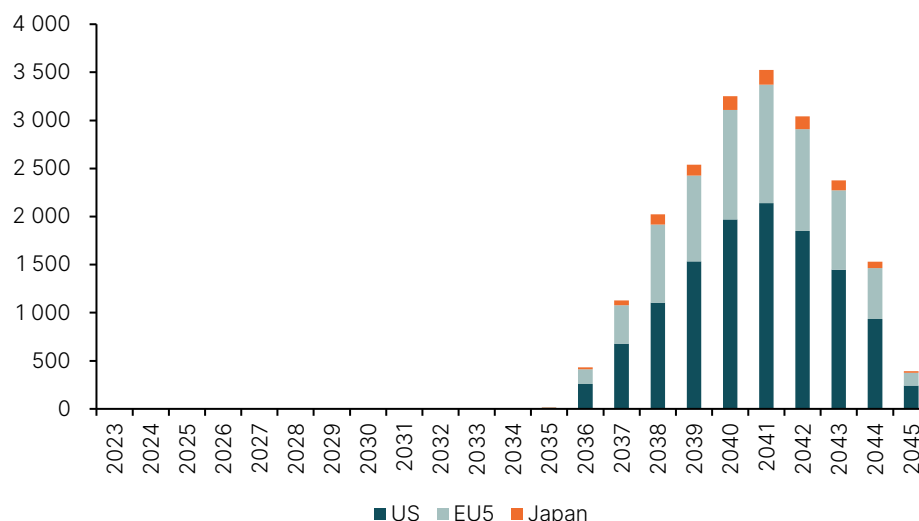
Graph 2 shows that the company will generate sales of MSEK 14,164 and an EBIT of MSEK 9,133 at peak sales in 2041. We estimate a net price of MSEK 5 in the US, and MSEK 2,5 in EU4, the UK and Japan. We expect that most patients that are offered the treatment will go through with it.

We estimate a gross-to-net price of 80 per cent, which reflects a 20 per cent discount to distributors relative to end customers, in line with industry benchmarks.³² The assumption on gross-to-net price are common practice in the valuation of biotech assets. Treated patients at the peak are estimated to be 3,526.

³¹ Chang et al., (2020), https://healthadvances.com/application/files/5216/9341/5243/health_advances_launch_costs_spend_wisely.pdf

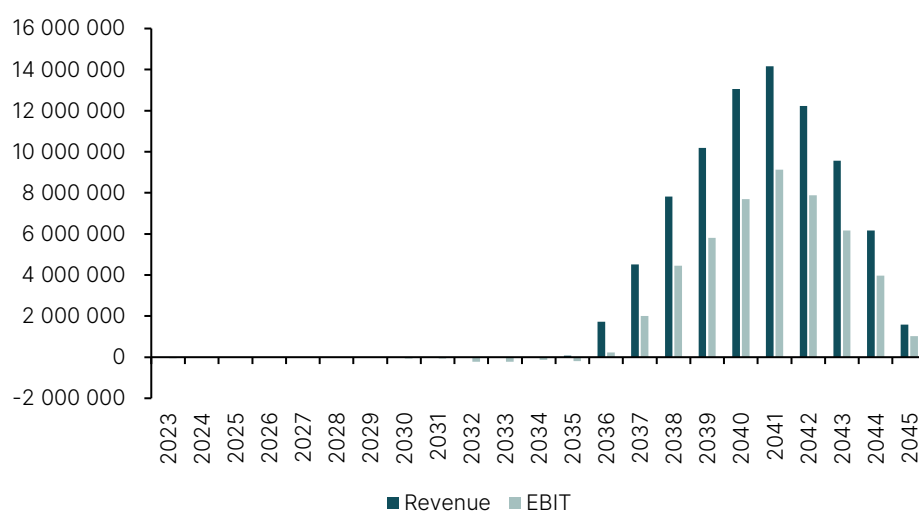
³² Thornblad and Carlsson (2021), *Biotech Valuation, A playbook for dealmakers*, MSC Nordics

Graph 2: CG01 patients



Source: Västra Hamnen Corporate Finance

Graph 3: CG01 earnings overview



Source: Västra Hamnen Corporate Finance

On the cost side, we estimate the total costs associated with the clinical development to amount to MSEK 822 and MSEK 1,500 in launch costs.

After launch, we have modelled a set of projections for the company's future costs in all markets. We estimate the costs as a percentage of sales, according to industry benchmarks.³³ The cost of goods sold (COGS) is 18 per cent of sales. Selling, general and administrative expenses (SG&A) are estimated to be 25 per cent of total revenue until peak market share, thereafter we estimate 17.5 per cent. To conclude, we expect CG01 to achieve an EBIT margin of 64 per cent at its peak.

COZY01

For COZY01, we have chosen to include some of the same projections as for CG01. In the US, we have estimated diagnosed prevalent cases of type 1 and 2 diabetes, ages > 20 years to 9.5 per cent of the population. Thereafter, we assume 3.3 per cent of that group are the total diabetic neuropathic pain-treated cases. For EU4 and the UK, we have estimated 9.9 per cent of diagnosed prevalent cases and 8.2 per cent are

³³ Thornblad and Carlsson (2021), *Biotech Valuation, A playbook for dealmakers*, MSC Nordics

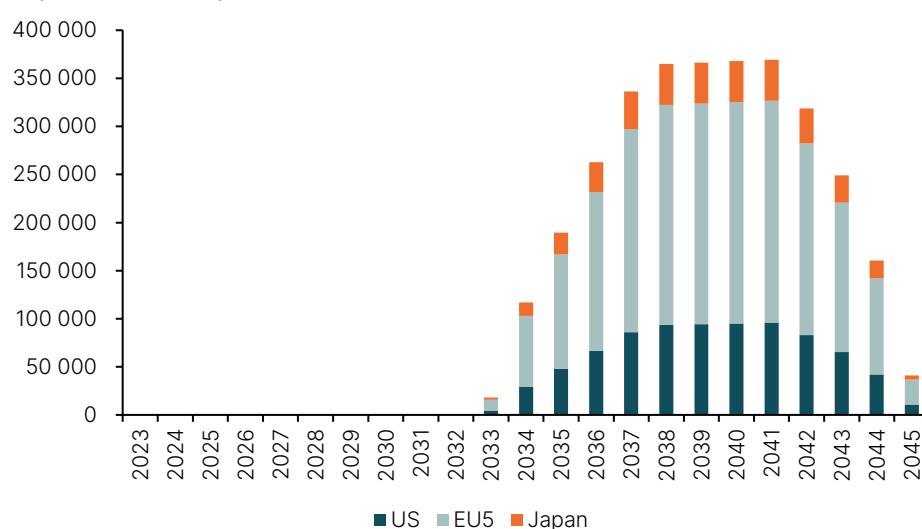
treated. In Japan, we have modelled for 3.8 per cent as diagnosed prevalent cases and 12 per cent are treated.³⁴

COZY01 to reach market in 2033

From the expected market launch in Q3 2033, we have modelled an increasing launch curve until reaching peak market share at 10 per cent in 2037. Thereafter we lower the market share due to sales erosion after the expiry of key patents in 2040-2041. Due to the collaboration with Zyneyro, we have modelled that all revenues and costs are evenly split between the partners.

Graph 4 shows that the company will generate sales of MSEK 4,277 and EBIT of MSEK 3,312 at peak sales in 2041. This is calculated based on an estimated net price of TSEK 49.1 in the US, and TSEK 24.5 in EU4, the UK and Japan. We have applied a compliance rate of 75 per cent and a gross-to-net price of 80 per cent, in line with industry benchmarks. Altogether, treated patients at the peak are estimated to be 369,174.

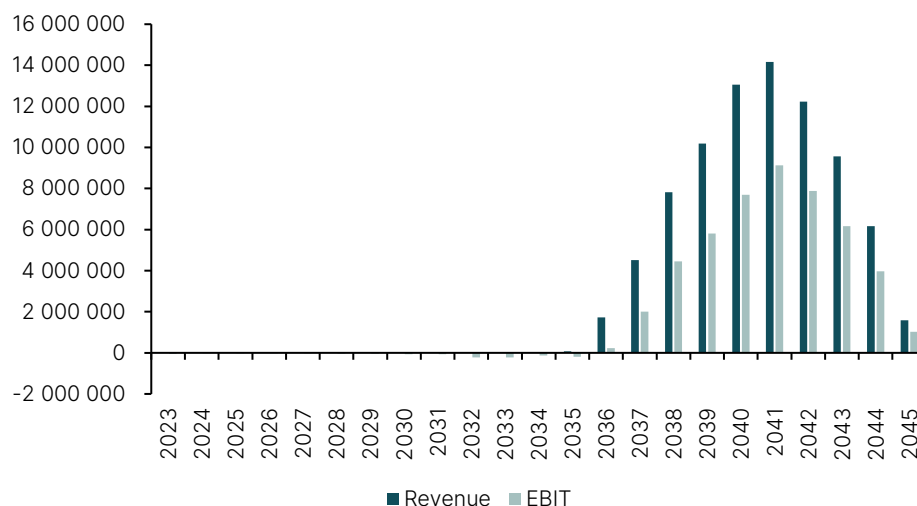
Graph 4: COZY01 patients



Source: Västra Hamnen Corporate Finance

³⁴ GlobalData, (2017), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9480957/table/brb32589-tbl-0001/?report=objectonly>

Graph 5: COZY01 earnings overview



Source: Västra Hamnen Corporate Finance

On the cost side, we estimate the total costs associated with the clinical development to amount to MSEK 629 and 1,500 in launch costs.

We estimate 10 per cent COGS, 25 per cent in SG&A until peak as a percentage of total revenue, thereafter 12.5 per cent. EBIT margin is expected to reach 77 per cent at peak 2041. Note that the COGS are lower for this project due to our estimate of it being less expensive to produce the peptide than the gene therapy.

COZY02 to reach market in 2035

COZY02

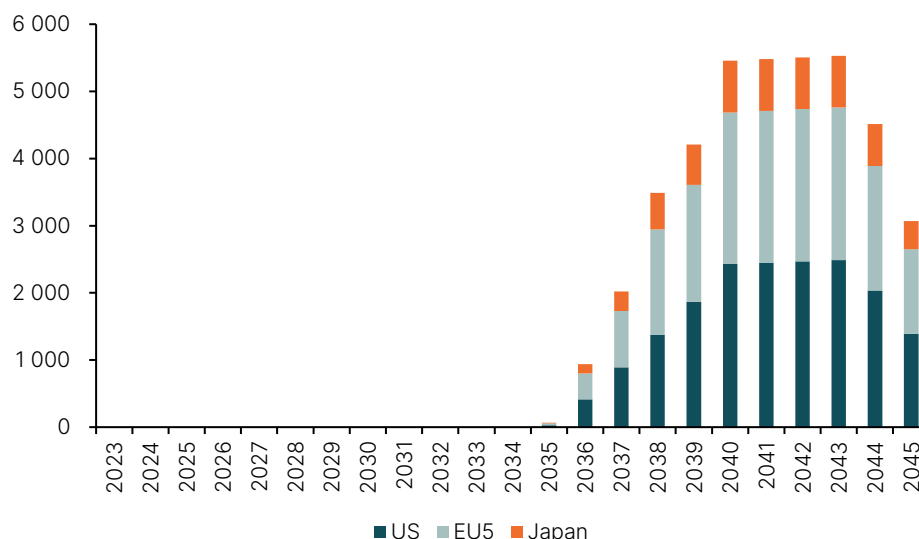
For COZY02, CombiGene does not yet have an explicit strategy for which indication and patient group it will target. However, we have estimated a prevalence of adults with high-impact chronic pain of 8 per cent in all regions. In our model, we estimate that COZY02 will enter the market in Q4 2035 and grow steadily according to the launch curve to a 0.5 per cent market share at the peak in 2040. Thereafter we lower the market share due to sales erosion after the expiry of key patents in 2040-2041. Due to the collaboration with Zyneyro, we have modelled that all revenues and costs are split 50 per cent for our projections.

The estimated net price amounts to MSEK 4 in the US, and MSEK 2 in EU4, the UK and Japan. We assume that most patients will go through with the gene therapy. Further, we estimate a gross-to-net price of 80 per cent. Treated patients at the peak are estimated to be 5,561.

On the cost side, we estimate the total costs associated with the clinical development to amount to MSEK 683 and 1,500 in launch costs.

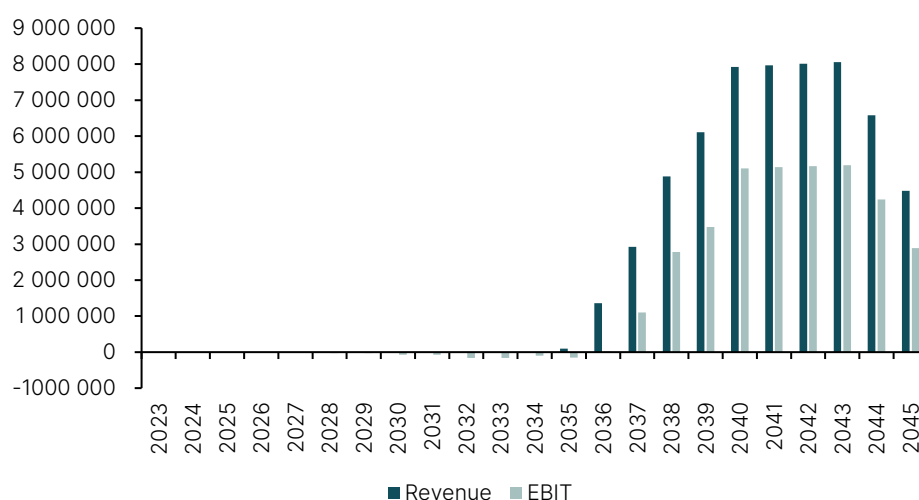
We expect COZY02 to have the same projections for future costs as in COZY01. We estimate 18 per cent COGS, 25 per cent in SG&A until peak as a percentage of total revenue, thereafter 17.5 per cent. EBIT margin is expected to reach 64 per cent at peak 2043. Graph 6 shows that the company will generate sales of MSEK 8,056 and EBIT of MSEK 5,194 at peak sales in 2043.

Graph 6: COZY02 patients



Source: Västra Hamnen Corporate Finance

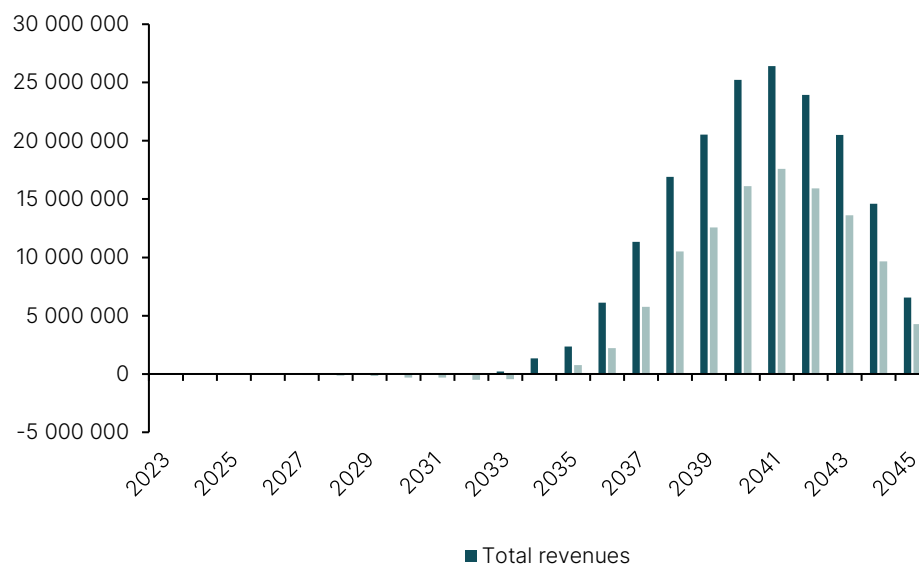
Graph 7: COZY02 earnings overview



Source: Västra Hamnen Corporate Finance

In summary, we estimate a peak of sales of BSEK 26.4 and EBIT of BSEK 17.6 for all projects. Note that the revenue from these projects is not risk-adjusted, but will be in the DCF model, with a likelihood of approval (LOA) 4.8 per cent for all projects. As the projects develop, the LOA will change. See the section *What is the fair value of the share?*

Graph 8: Total projects earnings overview

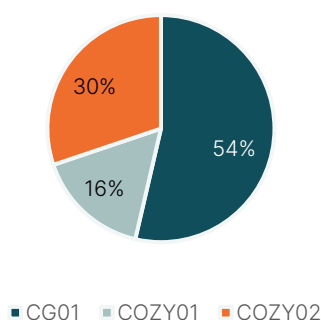


Source: Västra Hamnen Corporate Finance

CG01 to generate highest sales

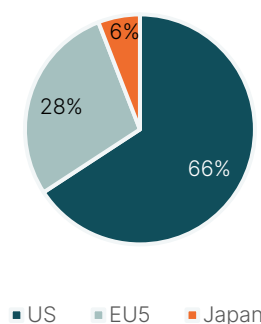
We estimate that CG01 will be the largest sales-generating project due to its high price point of MSEK 5 in the US and MSEK 2.5 in other regions. In addition, the US will be a key region due to its higher prices on medical treatments and contribute to most of the sales.

Graph 9: Sales split by product at the peak year of 2041



Source: Västra Hamnen Corporate Finance

Graph 10: Sales split by region at peak year of 2041



Source: Västra Hamnen Corporate Finance

MSEK 90 in cash**What is the cash situation?**

By Q1 2024, CombiGene's cash position amounted to MSEK 90.3. Given the company's pre-clinical activities, we expect CombiGene to fund its operations by the end of Q4 2025. Moreover, we see additional financing of MSEK 2,400 to cover future clinical development, the filing and approval process, and the market launch of CG01, COZY01, and COZY02.

Note that these development costs will in practice be carried by a future partner. In our model, these costs appears in the financial statements of our model, see *appendix*. We have modelled for additional funding in CombiGene's cash flow statement under financing activities on page 29.

Also, the EU programme *Eurostars*, aimed at small and medium-sized enterprises, has awarded grants to the COZY01 project of MSEK 5. Thus far, the company has received MSEK 0.6.

We repeat that the financing in our model is theoretical since we expect CombiGene to out-license the projects. A licensing deal would typically include upfront payments, milestone payments and royalties affecting the cash position. Any such deal will be included in the model once it materialises.

What is behind the numbers?**Deferred tax asset**

In our research, we try to look beyond the reported numbers to see if the company uses accounting methods or reports items off the income statement or balance sheet, that could impact our interpretation of its official figures. The underlying financials of the company could be stronger or weaker than they look at first glance and this could be important for our valuation.

Due to previously reported losses, we estimate that CombiGene has accumulated losses of MSEK 155.9 which implies a tax asset of MSEK 32.1. Due to the uncertainty of when the firm would reach profitability, the deferred tax asset is not recognised on the balance sheet. Incurred losses can be used to offset future tax payments and we estimate that CombiGene will start paying taxes in 2037.

What could go wrong?**Financial risk**

Drug development is costly, lengthy, and uncertain. CombiGene has a strong cash position as of today but if they fail to out-license its projects, a shortage of capital may limit the ability to expand and maintain its pipeline. The company will likely need to seek additional external financing and we have considered this in our model. The timing, magnitude and type of financing are however highly uncertain at this stage.

Development risk

This is the largest risk for any drug-developing company. CombiGene's projects are in preclinical stages and are several years out from potential commercialisation. The company or its partner must find a reliable manufacturing process, pass the drug candidates through clinical trials, and have them approved by regulatory authorities. Any milestone reached in this process will de-risk the investment case, but any failure could inflict serious damage to it.

Commercialisation risks

The market for pain treatment is crowded. Even if CombiGene is targeting a large patient group currently lacking adequate treatment options, several new approaches are

under development. The firm needs to convince a future partner of its project's potential, strategically, clinically and commercially. Competition from biosimilars and new treatments could also change market prices drastically and affect profitability.

People

CombiGene is a small organisation and is highly dependent on keeping the staff. The proper experience and competence in science, drug development, business development and financing are keys to being successful. Development plans and timelines could also be severely affected if the company is not able to keep its personnel.

What is the fair value of the share?

As explained above, we realise that CombiGene will not take all its projects through the clinical phases and to market on its own. This exercise is to calculate the present value of its pipeline.

DCF valuation

To calculate a fair net present value of CombiGene, we use a risk-adjusted discounted cash flow (DCF) approach. Our DCF calculation comprises two steps, see the appendix for details of the method. In the first step, we estimate the fair enterprise value based on our estimated projections. We then adjust for the development risk, applying probabilities for success based on benchmark statistics. This method is recommended for developing companies before reaching sustainable profits. See the *What is the earnings outlook?* segment for estimates, assumptions and calculations.

We apply a WACC of 21.6 per cent

We derive the discount factor, the weighted average cost of capital (WACC), from the *capital asset pricing model* (CAPM). We use benchmarks for the equity risk premium and additional risk premia associated with smallcap companies as accounted for in PwC's report *Equity Risk Premium on the Swedish market* from 2024.³⁵ The WACC in our model amounts to 21.6 per cent.

Risk adjustment

After discounting the cash flows, we adjust for development risk, using probabilities for the likelihood of approval - LOA. The LOAs reflect the chances for each drug candidate to successfully pass the clinical phases and be approved by regulatory authorities. In all drug development, development risk is a substantial part of the total project risk.

We apply an LOA of 4.8 per cent

LOAs in our model are based on data from statistical surveys published by Hay (2014) and BIO (2021). In neurology, the LOA for a project from phase I is 5.9 per cent.³⁶ Data regarding preclinical projects are scarce. However, available data suggests average success rates from the preclinical stage of around 80 per cent. Thus, we arrive at an LOA of 4.8 per cent for preclinical projects in neurology.³⁷ As the projects reach and pass clinical stages, the LOA for each drug candidate will increase.

Moreover, we have used a terminal growth rate of 2 per cent.

For more detailed estimates of all the projects, see the section *What is the earnings outlook?*

CG01

CG01 SEK 4.73 per share

Our risk-adjusted DCF model of CG01 suggests a fair value of MSEK 94, representing SEK 4.73 per share. The LOA will change as the project advances. If achieving preclinical proof-of-concept, the benchmark probability increases to 5.9 per cent phase I. We

³⁵ PwC, (2024), *Riskpremiestudien*, <https://www.pwc.se/sv/corporate-finance/riskpremiestudien.html>

³⁶ BIO (2021) <https://www.bio.org/clinical-development-success-rates-and-contributing-factors-2011-2020>

³⁷ Thornblad och Carlsson (2021)

expect that CG01 will enter phase I in 2028. See the sensitivity table for the project value in SEK per share, depending on the discount rate WACC and LOA.

The LOAs in the tables below are benchmarks for drug candidates in neurology, e.g. the probability for the approval of a phase I asset is 5.9 per cent.³⁸

Table 6: Sensitivity table CG01, SEK per share

		LOA				
		Preclinical	Phase I	Phase II	Phase III	NDA/BLA to approval
		4.8%	5.9%	12.3%	46.0%	86.7%
WACC	19.6%	5.90	6.90	12.73	43.46	80.57
	20.6%	5.27	6.13	11.12	37.42	69.19
	21.6%	4.73	5.47	9.75	32.28	59.49
	22.6%	4.27	4.90	8.57	27.89	51.22
	23.6%	3.88	4.42	7.57	24.14	44.15

Source: Västra Hamnen Corporate Finance

COZY01

**COZY01 SEK 3.57
per share**

In COZY01, we have used a similar model, with the same WACC and LOA of 4.8 per cent. If successful in the preclinical stage, we expect COZY01 to enter phase I in Q4 2026. Hence, our model suggests a risk-adjusted market capitalisation of MSEK 71, representing a value of SEK 3.57 per share.

Table 7: Sensitivity table COZY01, SEK per share

		Preclinical	Phase I	Phase II	Phase III	NDA/BLA to approval
		4.8%	5.9%	12.3%	46.0%	86.7%
WACC	19.6%	4.26	4.89	8.55	27.81	51.07
	20.6%	3.89	4.43	7.59	24.22	44.29
	21.6%	3.57	4.03	6.76	21.12	38.46
	22.6%	3.29	3.69	6.05	18.45	33.43
	23.6%	3.05	3.40	5.43	16.14	29.08

Source: Västra Hamnen Corporate Finance

COZY02

**COZY02 SEK 3.90
per share**

For COZY02, we apply the same WACC and LOA of 4.8 per cent as in COZY01. However, the timeline is different and if successful in the preclinical stage, we expect COZY02 to enter phase I in Q1 2028. Hence, our model suggests a risk-adjusted market capitalisation of MSEK 77, representing a value of SEK 3.90 per share.

Table 8: Sensitivity table COZY02, SEK per share

		LOA				
		Preclinical	Phase I	Phase II	Phase III	NDA/BLA to approval
		4.8%	5.9%	12.3%	46.0%	86.7%
WACC	19.6%	4.89	5.67	10.16	33.84	62.44
	20.6%	4.35	5.00	8.77	28.63	52.62
	21.6%	3.90	4.44	7.61	24.29	44.44
	22.6%	3.52	3.98	6.64	20.67	37.60
	23.6%	3.20	3.59	5.83	17.63	31.88

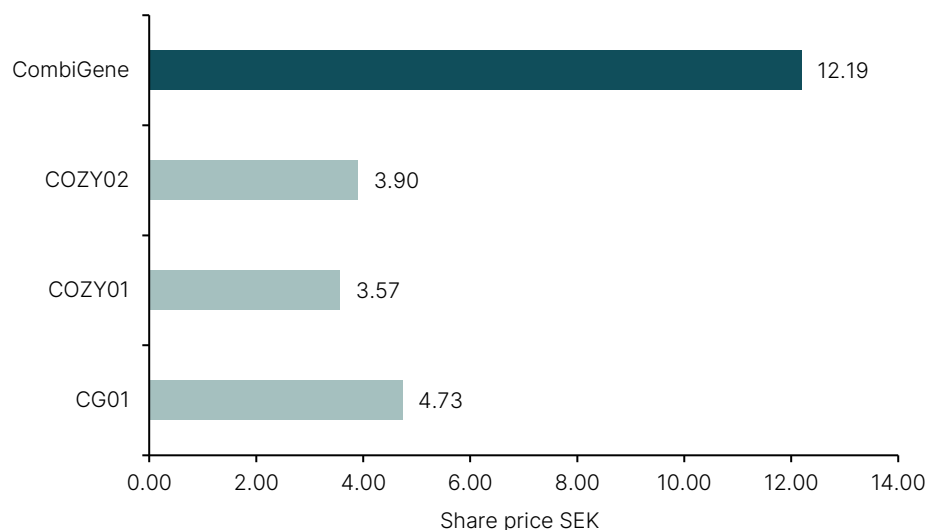
Source: Västra Hamnen Corporate Finance

**CombiGene SEK
12.19 per share**

The sum of these projects amount to MSEK 241 representing a share price of SEK 12.19.

³⁸ Biotechnology Innovation Organization (2021) – Clinical Development Success rates 2011-2020

Graph 11: Valuation summary



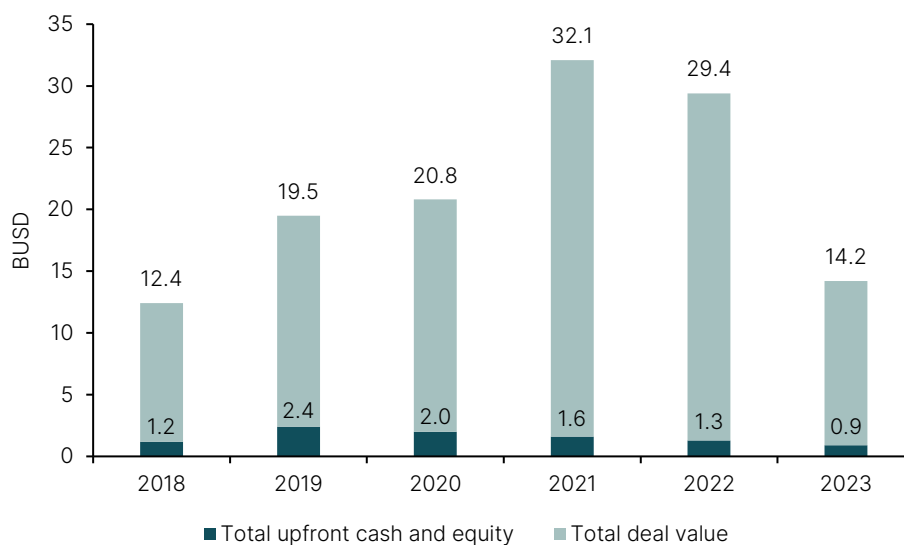
Source: Västra Hamnen Corporate Finance

Average licensing deals of MUSD 212 in 2023

Licensing deals

In the *2023 Annual Biopharma Licensing Report*, issued by the investment bank **J.P. Morgan**, statistics showed that the market for cell and gene therapy declined compared to 2022, as illustrated in graph 12. The total deal value amounted to BUSD 14.2 with 0.9 in upfront cash and equity payments. The number of deals amounted to 67, representing an average total deal value of MUSD 212, as seen in graph 13 below.³⁹

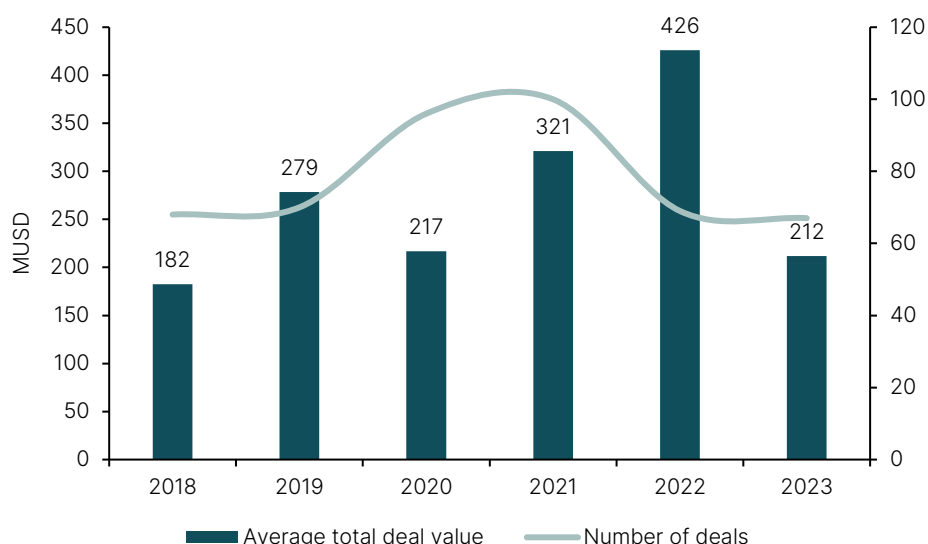
Graph 12: Cell and gene therapy total deal values



Source: J.P. Morgan

³⁹ J.P. Morgan, (2023), <https://www.jpmorgan.com/insights/outlook/market-outlook/biopharma-report-for-2023>

Graph 13: Cell and gene therapy average deal value and number of deals



Source: J.P. Morgan

CombiGene out-licensed the CG01 project in 2021 for MUSD 329. Since then, the risk appetite and the willingness to pay has changed significantly, affecting average deal value and the number of deals, as shown in graph 13.

Table 6 show some recent licensing deals in the sector with Eli Lilly being a frequent licensee. The total deal value ranges from MUSD 380 to 1,640.

Table 9: Licensing deals (MUSD)

Year	Licensee	Licensor	Area/drug/candidate	At phase	Upfront	Total value	Type
2023	Eli Lilly	Confo	Neuropathic pain	Phase I	40	1 220	Licence
2021	Eli Lilly	Asahi Kasei	Chronic pain	Phase I	20	410	Licence
2021	Eli Lilly	Lycia	Pain	Preclinical	35	1 640	Licence
2020	Biohaven	Sosei Heptares	Migraine	Preclinical	10	380	Licence
2019	Eli Lilly	Centrexion	Pain	Phase I	47	997	Licence

Source: Västra Hamnen Corporate Finance

CombiGene focuses on finding a new partner for the CG01 project and if successful, this would positively impact the valuation and cash position. The previous agreement for CG01 and the average deal value in 2023 for cell and gene therapies indicate that a deal would be valued in the hundreds of millions of USD.

In summary, our risk-adjusted DCF model suggests a fair value of SEK 10.58 per share.

Potential triggers

Study results

CombiGene is currently in the preclinical stage of its projects. New data is likely to affect the share price as investors are trying to price the value of the projects.

Licensing deals

Licensing deals are significant triggers due to the potential deal sizes and proof of concept of the project. As illustrated in graph 13, deals can range within several hundred million dollars.

Additional indications

During development, the drug candidate could be found useful in other indications than the one it will be clinically tested for. Chronic neuropathic pain affects many people, and CombiGene could find support to broaden the focus for the COZY programme.

New projects

CombiGene is continuously evaluating new projects that could add significant value.

Financing

Since CombiGene is not generating a stable cash flow, it is liable for capital raises which can dilute existing shareholders. Depending on the reason for raising capital, this can affect the share price both positively and negatively.

Upcoming events

Financial calendar

23 Aug 2024	Q2 report 2024
8 Nov 2024	Q3 report 2024
14 Feb 2025	Year-end report 2024

Appendix: Valuation method

Early-stage companies usually report negative net profits and may have many years left until they turn a profit. Sometimes they even have years until their first significant sales revenues. The difficulty in valuing growth companies with limited historical records is that the valuation rests on uncertain estimates of future earnings, more uncertain than for companies with years of stable profits on record. There is little in terms of historical figures on which to base estimates of future revenues, future profit margins and other items.

To handle these challenges, we choose to follow a generally accepted method for valuing growth companies described by finance professor Aswath Damodaran among others. Instead of scaling the discount rate (WACC) to account for all the risks and uncertainties associated with a young company, we use a two-stage valuation approach:⁴⁰

- Firstly, we estimate fair enterprise value under the explicit assumption that the company survives until its first year of sustainable profits. We use a WACC commensurate with the circumstances of the company once it reaches profitability.
- Secondly, we adjust the estimated enterprise value by multiplying it with a probability factor reflecting the likelihood that the company survives.

With each passing period after the initial valuation, the probability factor may be adjusted based on the company's development and our updated assessment of its chances of survival.

Discount rate WACC

To estimate the fair value of the company, we use a well-established model to calculate the present value of future cash flows. In this model, there are several assumptions and parameters that we discuss here.

An important factor in the model is the discount rate for the future cash flows. We use the company's weighted average cost of capital (WACC) and other recognised risk

⁴⁰ Damodaran, Aswath, (2009), Valuing Young, Start-up and Growth Companies: Estimation Issues and Valuation Challenges", Stern School of Business, New York University.

premiums. The WACC is derived from the weighted cost of equity and debt. To calculate the cost of equity, we use the Capital Asset Pricing Model (CAPM), with an added small-cap premium:

$$Re = Rf + Rp + \beta(Rm - Rf)$$

The risk-free rate (Rf), the market premium ($Rm - Rf$) and the small cap premium (Rp) are all taken from PwC's 2024 risk premium study.⁴¹ The beta value for CombiGene's share is based on beta values for peers. The process can be described in three steps:

1. First, we calculate each company's beta where, according to Koller et.al (2020), we used monthly returns over five years. As the identified peer companies are active globally, we have used the broad index S&P 500 as the market index.
2. We then calculate the unlevered beta for each company according to the formula: $\frac{B_L}{(1 + \frac{D}{E} * (1 - t))} = B_u$
We can now calculate a median value of the beta values of the peer group without debt.
3. In the last step, we take into account the indebtedness of the CombiGene according to the formula: $B_u * \left(1 + \frac{D}{E} * (1 - t)\right) = B_L$

By taking the capital structure into account in the beta calculation, we create a more dynamic beta value. This approach captures a leverage effect on equity which increases as leverage increases.

⁴¹ PWC, (2024), *Riskpremiestudien*, <https://www.pwc.se/sv/corporate-finance/riskpremiestudien.html>

Income Statement - Annual Data

TSEK	2021	2022	2023	2024e	2025e	2026e	2027e	2028e
Net revenues	84 042	26 700	5 544	326	0	0	0	0
Other revenues	0	14 552	1 464	0	0	0	0	0
Total revenues	84 042	41 252	7 008	326	0	0	0	0
Cost of goods sold	0	0	0	0	0	0	0	0
Personnel costs	-11 692	-13 032	-14 868	-15 091	-16 287	-17 613	-19 050	-20 605
Other external costs	-54 591	-32 494	-26 834	-26 132	-26 194	-42 173	-71 783	-128 009
Other operating expenses	-1 677	0	-1 281	0	0	0	0	0
EBITDA	16 082	-4 275	-35 975	-40 896	-42 480	-59 786	-90 833	-148 614
Amortisation & depreciation	-2 596	-300	-2 624	-3 344	-3 672	-3 836	-4 008	-4 188
EBIT	13 486	-4 575	-38 599	-44 240	-46 152	-63 622	-94 841	-152 802
Financials, net	0	-1 505	2 935	0	0	0	0	0
EBT	13 486	-6 079	-35 665	-44 240	-46 152	-63 622	-94 841	-152 802
Taxes	0	0	0	0	0	0	0	0
Net profit	13 486	-6 079	-35 665	-44 240	-46 152	-63 622	-94 841	-152 802
Earnings per share (SEK)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Growth (%)								
Net revenues	na	-68.2%	-79.2%	na	na	na	na	na
EBITDA	na	na	na	na	na	na	na	na
EBIT	na	na	na	na	na	na	na	na
Net profit	na	na	na	na	na	na	na	na
% of revenues (%)								
EBITDA margin	19.1%	na	na	na	na	na	na	na
EBIT margin	16.0%	na	na	na	na	na	na	na
EBT margin	16.0%	na	na	na	na	na	na	na
Profit margin	16.0%	na	na	na	na	na	na	na
Personnel costs	13.9%	48.8%	268.2%	4629.0%	na	na	na	na
Total OPEX	80.9%	170.5%	775.3%	12644.8%	na	na	na	na
Profitability (%)								
ROE	8.5%	na	na	na	na	na	na	na
ROIC	49.7%	na	na	na	na	na	0.0%	0.0%

Source: Västra Hamnen Corporate Finance

Balance Sheet - Annual Data

TSEK	2021	2022	2023	2024e	2025e	2026e	2027e	2028e
Inventories	0	0	0	0	0	0	0	0
Receivables	0	4 216	0	0	0	0	0	0
Other short-term receivables	686	1 395	1 799	2 065	2 179	2 207	2 213	2 215
Prepaid costs & accrued incc	7 193	1 829	0	0	0	0	0	0
Cash and cash equivalents	136 744	131 777	101 440	60 202	13 205	148 792	53 146	499 508
Total current assets	144 623	139 217	103 239	62 266	15 384	150 999	55 360	501 724
Tangible assets	0	0	851	856	927	1 003	1 086	1 176
Intangible assets	21 599	19 004	16 518	16 350	17 014	17 705	18 423	19 171
Financial assets	0	0	5	5	5	5	5	5
Total fixed assets	21 599	19 004	17 374	17 211	17 946	18 713	19 515	20 352
Total assets	166 222	158 221	120 613	79 478	33 329	169 711	74 874	522 076
Accounts payable	3 377	1 788	0	0	0	0	0	0
Accrued cost & prepaid incor	3 844	3 720	0	0	0	0	0	0
Other short term liabilities	700	513	4 156	6 219	6 223	6 227	6 231	6 235
Short term tax liabilities	21	77	0	0	0	0	0	0
Total current liabilities	7 942	6 099	4 156	6 219	6 223	6 227	6 231	6 235
Long term liabilities	0	0	0	0	0	0	0	0
Total equity	158 279	152 122	116 457	73 259	27 106	163 484	68 643	515 840
Total equity and liabilities	166 221	158 221	120 613	79 478	33 329	169 711	74 874	522 076

Source: Västra Hamnen Corporate Finance

Cash flow statement

TSEK	2021	2022	2023	2024e	2025e	2026e	2027e	2028e
Operating activities	23 560	-15 261	-34 255	-39 854	-42 480	-59 786	-90 833	-148 614
Changes in working capital	-1 445	-1 404	3 697	2 984	-110	-24	-2	2
Investing activities	-148	0	-989	-3 181	-4 407	-4 603	-4 810	-5 026
Financing activities	65 881	0	0	0	0	200 000	0	600 000
Cash flow for the period	87 848	-16 666	-31 546	-40 051	-46 997	135 587	-95 645	446 362
Other adjustments		11 704	1 213					
Beginning cash balance	48 891	136 739	131 777	84 791	44 740	-2 257	133 330	37 685
Ending cash balance	136 739	131 777	101 444	44 740	-2 257	133 330	37 685	484 047

Source: Västra Hamnen Corporate Finance

Income Statement - Quarterly Data

TSEK	Q3 2022	Q4 2022	Q1 2023	Q2 2023	Q3 2023	Q4 2023	Q1 2024	Q2 2024e
Net revenues	5 213	5 346	2 168	1 788	992	596	326	0
Other revenues	8 313	674	0	1 413	173	875	1 042	0
Total revenues	13 526	6 020	2 168	3 201	1 165	1 471	1 368	0
Cost of goods sold	0	0	0	0	0	0	0	0
Personnel costs	-2 985	-4 221	-3 501	-4 060	-2 804	-4 504	-3 707	-3 769
Other external costs	-5 912	-6 869	-11 764	-4 778	-5 985	-4 307	-11 162	-4 748
Other operating expenses	-28	-7 013	-871	0	-127	-1 281	0	0
EBITDA	4 601	-12 083	-13 968	-5 637	-7 751	-8 621	-13 501	-8 517
Amortisation & depreciation	-649	-649	-649	-649	-649	-678	-693	-874
EBIT	3 952	-12 732	-14 617	-6 286	-8 400	-9 299	-14 194	-9 391
Financials, net	0	-2	0	0	-4	0	0	0
EBT	3 952	-12 734	-14 617	-6 286	-8 404	-9 299	-14 194	-9 391
Taxes	0	0	0	0	0	0	0	0
Net profit	3 952	-12 734	-14 617	-6 286	-8 404	-9 299	-14 194	-9 391
Earnings per share (SEK)	0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	na
Y-o-Y Growth (%)								
Net revenues	na	-93.6%	-81.0%	-62.3%	-81.0%	-88.9%	na	na
EBITDA	na	na	na	na	na	na	na	na
EBIT	na	na	na	na	na	na	na	na
Net profit	na	na	na	na	na	na	na	na
% of revenues (%)								
EBITDA margin	34.0%	na	na	na	na	na	na	na
EBIT margin	29.2%	na	na	na	na	na	na	na
EBT margin	29.2%	na	na	na	na	na	na	na
Profit margin	29.2%	na	na	na	na	na	na	na
Personnel costs	22.1%	70.1%	161.5%	126.8%	240.7%	306.2%	271.0%	na
Total OPEX	66.0%	300.7%	744.3%	276.1%	765.3%	686.1%	1086.9%	na
Profitability (%)								
ROE	2.4%	na	na	na	na	na	na	-10.1%
ROIC	16.4%	na	na	na	na	na	na	na

Source: Västra Hamnen Corporate Finance

Balance Sheet - Quarterly Data

TSEK	Q3 2022	Q4 2022	Q1 2023	Q2 2023	Q3 2023	Q4 2023	Q1 2024	Q2 2024e
Inventories	0	0	0	0	0	0	0	0
Receivables	0	4 216	0	1 032	183	0	0	0
Other short-term receivables	5 608	1 395	4 359	3 344	3 706	1 799	1 480	2 583
Accrued cost & prepaid incor	0	1 829	0	0	0	0	0	0
Cash and cash equivalents	144 940	131 777	120 506	115 442	107 187	101 440	90 318	79 650
Total current assets	150 548	139 217	124 865	119 818	111 076	103 239	91 798	82 233
Tangible assets	0	0	0	0	0	851	807	823
Finacial assets	0	0	0	5	5	5	5	5
Intangible assets	19 652	19 004	18 464	17 815	17 167	16 518	15 869	16 028
Total fixed assets	19 652	19 004	18 464	17 820	17 172	17 374	16 681	16 856
Total assets	170 200	158 221	143 329	137 638	128 248	120 613	108 479	99 089
Accounts payable	0	1 788	0	0	0	0	0	0
Other short-term liabilities	6 136	513	5 824	6 419	5 431	4 156	6 216	6 217
Short term tax liabilities	0	77	0	0	0	0	0	0
Accrued cost & prepaid incor	0	3 720	0	0	0	0	0	0
Total current liabilities	6 136	6 099	5 824	6 419	5 431	4 156	6 216	6 217
Long term liabilities	0	0	0	0	0	0	0	0
Total equity	164 064	152 122	137 505	131 220	122 817	116 457	102 263	92 872
Total equity and liabilities	170 200	158 221	143 329	137 639	128 248	120 613	108 479	99 089

Source: Västra Hamnen Corporate Finance

Cash flow statement

TSEK	Q3 2022	Q4 2022	Q1 2023	Q2 2023	Q3 2023	Q4 2023	Q1 2024	Q2 2024e
Operating activities	-14 008	-5 176	-13 100	-6 640	-6 703	-10 751	-13 501	-8 517
Changes in working capital	14 386	-1 869	2 806	578	-501	815	3 566	-1 102
Investing activities	0	0	-109	-5	0	-880	0	-1 049
Financing activities	0	0	0	0	0	0	0	0
Cash flow for the period	378	-7 045	-10 403	-6 067	-7 204	-10 816	-9 935	-10 668
Other adjustments								
Beginning cash balance	125 953	144 940	131 777	120 506	115 442	107 187	101 440	90 318
Ending cash balance	144 940	131 777	120 506	115 442	107 187	101 440	90 318	79 650

Source: Västra Hamnen Corporate Finance

Abbreviation	Description
AAV	Adeno-associated virus
CDMO	Abbreviation for Contract development and manufacturing organisation. Provide comprehensive services from drug development through drug manufacturing on a contractual basis to companies in the pharmaceutical industry.
Chronic pain	Defined as pain lasting longer than three to six months, chronic pain may eventually disappear and is not necessarily permanent.
CRO	A Contract Research organisation is a company provides support to pharmaceutical, biotechnology, and medical service industries through offering outsourced research services on a contractual basis.
Eurostars	Funding international collaborative R&D and innovation projects through a funding instrument that aims to support SMEs and their partners. These include, large companies, universities, research, and other types of organisations.
Gene therapy	Defined as a medical field that focuses on modifying genes within cells to produce a therapeutic effect or to treat diseases by repairing or reconstructing defective genetic material.
LOA	Likelihood of approval. The probability of getting a drug development from phase I to regulatory approval
Neuropathic pain	Neuropathic pain is nerve pain that occurs after diseases or injuries to the somatosensory nervous system and can spread within a specific neuroanatomical innervation area. It often associated with a type of pain persists even after the initial insult has healed.
PCT	PCT is an abbreviation for Patent Cooperation Treaty, an international law treaty, that was established in 1970. It serves to provide a unified procedure for filing patent applications in order to protect inventions in each of its contracting states.
Peptide	Short chains of amino acids linked by peptide bonds.
Pharmacokinetics	Pharmacokinetics (how the body interacts with the administered substance), oral bioavailability and half-life of the drug are observed. Low doses of the drug candidate are used.
Pick 1	A scaffold protein that binds to and organises a variety of receptor subtypes that regulate the cell's function.
Proof-of-concept	Proof of concept is documented evidence demonstrating that a proposed product or method works as intended.

Clinical phases

Preclinical	Objective of the phase is to make sure that the new therapy is safe and has the intended effect. Preclinical study in vitro and vivo are carried out before the clinical development.
Phase I	The first stage of clinical studies. The main goal is to evaluate the safety of the drug candidate.
Phase II	In the second stage of clinical development, the study evaluates the efficacy of the treatment and further examines the safety. Positive results here obtain proof-of-concept, motivating further development.
Phase III	A study that aims to further examine the effectiveness and safety of the treatment. A phase III study involves a larger group of patients than the studies in the previous phases.

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