INGENEIOUS

NEWS FROM COMBIGENE AB

ISSUE 2 • 2023

CombiGene

The gene therapy explorer

EDITORIALS

CombiGene has a unique position with three projects aimed at large patient populations

It is just over four months since CombiGene began the collaboration on the pain program COZY with the Danish company Zyneyro. It has been four months of intensive work where we formed the team working on the program and where we initiated the extensive preparations for the preclinical toxicology program.

In parallel, we have also carried out a number of preparatory activities for the next step in the study of COZY01 conducted by the National Institutes of Health (NIH, a US government agency), in one of them funded program (Preclinical Screening Platform for Pain, PSPP). The background to the NIH's very early interest in COZY01 is not only the human suffering that chronic pain causes but also the enormous costs that pain gives rise to for American society in the form of direct and indirect costs and the galloping opioid crisis that the country suffers from. Estimates show that pain costs American society USD 635 billion each year.

The fact that COZY01 has already attracted the attention of the NIH is of course extremely encouraging and points to the great need for new forms of pain relief. COZY1 has passed the first of the three levels of the PSPP program and has moved on to the next where the substance will be tested in different pain models.

Through our collaboration with Zyneyro, CombiGene now has four projects where three of them, the epilepsy project CG01 and the pain projects COZY01 and COZY02, are aimed at large patient populations. This puts CombiGene in a unique position. Almost all of the gene therapy projects run by other companies are focused on rare diseases.

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

Jan Nilsson
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Production:
Form: **WibergComm from Scratch**
Text: **Columbi Communications AB**

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CombiGene is listed on Nasdaq First North Growth Market.
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INTERVIEW WITH ALVAR GRÖNBERG, SENIOR PROGRAM DIRECTOR AT COMBIGENE

High level of activity in the pain program COZY in preparation of the preclinical toxicology program

In early 2023, CombiGene and the Danish company Zyneyro initiated a collaboration to jointly develop the pain program COZY. The program consists of a peptide treatment and a gene therapy that are both based on the same unique mechanism of action. The goal of the project is to develop effective treatments for severe chronic pain, a common and often difficult-to-treat condition. Both the peptide and the gene therapy are being developed for the treatment of severe chronic pain conditions where the gene therapy is reserved for patients where the possibilities for spontaneous reduction of the pain are considered excluded or unlikely.

Ingeneious contacted Alvar Grönberg, Senior Program Director at CombiGene, to see how the work is progressing.

CombiGene and Zyneyro have now been working together since the beginning of the year. Can you briefly describe what you have focused on and how far the work has come?

"Let me first say that I find the COZY program extremely exciting. Chronic pain is one of the biggest challenges facing today's healthcare and to be involved in developing a new and effective treatment without the side effects that today's treatment options often give rise to is immensely stimulating."

"Together with our colleagues at Zyneyro, we have since we started the collaboration in January this year focused on the upcoming pivotal preclinical toxicology program within the peptide project COZY01. We are currently deeply involved in the extensive preparations for this very important part of the project. The work consists, among other things, of selecting the company that will produce material for the toxicological study program and also the company that will carry out the studies. Choosing the right partner is an extensive task that has long-term and important consequences, and we put a lot of effort into finding the very best partners."

"In addition to preparing the toxicology program, we have also worked on a number of preparatory activities for the next step in the program run by the National Institutes of Health (NIH) in the US. The program is called Preclinical Screening Platform for Pain (PSPP) and aims to find pain relief options that are not addictive or result in tolerance development. COZY01 has passed the first level of three and has been selected to move on to the next level where the substance will be tested in different pain models."

How would you describe the need for new treatments for chronic pain?

"The need is absolutely enormous. Between six and eight percent of the world's population is estimated to suffer from severe chronic pain. At the same time, current treatments are associated with a number of shortcomings. The conventional treatment options consist mainly of anti-inflammatory drugs, anti-depressants, anti-convulsants and opioids (a group of substances with a morphine-like mechanism of action). The problem is that these treatments are not specifically developed to treat chronic pain and that the pain relief that is achieved often has a number of debilitating side effects such as substance abuse problems, depression, anxiety, fatigue, reduced physical and mental ability. If we succeed with the COZY program, we could help a very large number of people to a better life."

The fact that so many people are affected by chronic pain must lead to great costs for society.

"That's absolutely right. Chronic pain is the single most costly disease for society. In the US alone, the cost to society is estimated at an unimaginable USD 635 billion a year –significantly more than the costs of cardiovascular disease, which amounts to USD 309 billion, and cancer, which costs American society USD 243 billion annually.[1]"

What is the near future for the COZY program?

"More of the same, you could say. We continue to work on the preparations for the pivotal preclinical toxicology program. In parallel, we will also continue to work on developing the final gene therapy vector and preparing for the next steps within PSPP."

[1] *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Appendix C. The Economic Cost of Pain in the US. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. Washington (DC): National Academies Press (US); 2011*

About the pain program COZY

Chronic pain can be devastating for those affected. The disease also leads to enormous costs for society. Between six and eight percent of the population is estimated to suffer from severe chronic pain, and the societal costs of chronic pain are estimated at USD 635 billion annually in the US alone.

Conventional treatment consists mainly of anti-inflammatory drugs, anti-depressants, anti-convulsant drugs and opioids (a group of substances with a morphine-like mechanism of action).

The problem with these treatments is that they are not specifically developed to treat chronic pain. The pain relief that is achieved therefore often has a number of debilitating side effects such as substance abuse problems, depression, anxiety, fatigue, reduced physical and mental ability.

The COZY program is being developed to address these enormous challenges by offering effective pain relief without the problems that today's drugs can bring.

THIS INTERVIEW WAS PREVIOUSLY PUBLISHED BY BIO STOCK

Zyneyro's CEO on the collaboration with CombiGene

At the beginning of the year, CombiGene and Zyneyro entered into a collaboration for the development of new treatments for severe chronic pain conditions. The pain programme COZY consists of a peptide treatment and a gene therapy treatment. The gene therapy is reserved for patients where the possibilities for spontaneous reduction of the pain are considered excluded or unlikely. Zyneyro's CEO Peter Horn Møller talks with BioStock about the collaboration and overall vision.

Pain is the most common reason people seek care and is the leading cause of disability in the world. Chronic pain, which affects 20-25 per cent of the world's population, is defined as pain that persists or recurs for longer than three months at a time.

In the United States alone, the annual cost in 2011 of chronic pain in adults was estimated to 635 billion USD. This represents a higher sum than the annual costs of cancer, heart disease and diabetes, respectively. This includes, among other things, health care costs, loss of productivity caused by substance abuse problems, depression, anxiety, fatigue, reduced physical and mental capacity.

Current treatment options are insufficient

Examples of common treatments for chronic pain are opioids and antidepressants. These, however, are likely to lead to addiction, overdoses, and serious side effects. Anti-inflammatory drugs (NSAIDs) are another option, but these do not provide long-term relief and are insufficient options for chronic pain conditions.

New collaboration in chronic pain

In early 2023, Swedish CombiGene and Danish Zyneyro entered into a collaboration to develop more effective treatments for severe temporary and chronic pain conditions. The companies' joint pipeline consists of the peptide treatment COZY01 and the gene therapy treatment COZY02. By using a new mechanism of action, both the peptide treatment and the gene therapy have the potential to offer effective pain relief.

According to the companies, the risk of side effects with both therapies is potentially lower compared to systemic and lifelong medication with, for example, painkillers. In addition, neither the peptide therapy nor the gene therapy has the addictive properties associated with opioids, for instance.

Zynero's CEO comments

To find out more about the collaboration with CombiGene, BioStock contacted Zyneyro's CEO Peter Horn Møller.

Peter, you want to redraw the map for future pain treatments. What have you seen so far in your studies that indicates that you are on the right track?

"Our data shows several things. Our peptide-based drug candidate can remove chronic pain at least as well as known painkillers, and we can restore the normal pain sensation and not just "numb" the feeling of pain."

"Pain is the most common reason people seek care and is the leading cause of disability in the world."

Fotograf: Jakob Boserup

Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Appendix C. The Economic Cost of Pain in the US. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. Washington (DC): National Academies Press (US); 2011

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“All our preclinical data indicate that COZY01 is a drug candidate that specifically addresses the pathological pain experience in chronic pain.”

“Having a normal sensation of pain is extremely important because it is our body’s warning system that tells us that something is wrong. With a limited or completely absent pain sensation, which is often a side effect of strong painkillers, we cannot take the necessary precautions to protect ourselves from dangers that can lead to serious injury. In addition, we do not see other known side effects, such as dependence, lethargy, impaired coordination and memory problems.”

“Our hypothesis is simply that we eliminate the biological cause of chronic pain – which is a different type of pain than, for example, acute pain – without affecting the normal experience of pain and sensation.”

“In addition, our data show that our gene therapy candidate provides complete pain relief in the same way as the peptide candidate, with the advantage that the effect is expected to be lifelong after one or a few treatments.”

Is the goal for COZY01 to become a complement or a direct challenger to today’s well-established NSAID drugs?

“The goal is clearly for COZY01 to become a competitor to the existing drugs. NSAIDs are anti-inflammatory. They also reduce pain, but mainly because inflammation decreases, i.e. NSAIDs are not specifically pain medications. All our preclinical data indicate that COZY01 is a drug candidate that specifically addresses the pathological pain experience in chronic pain.”

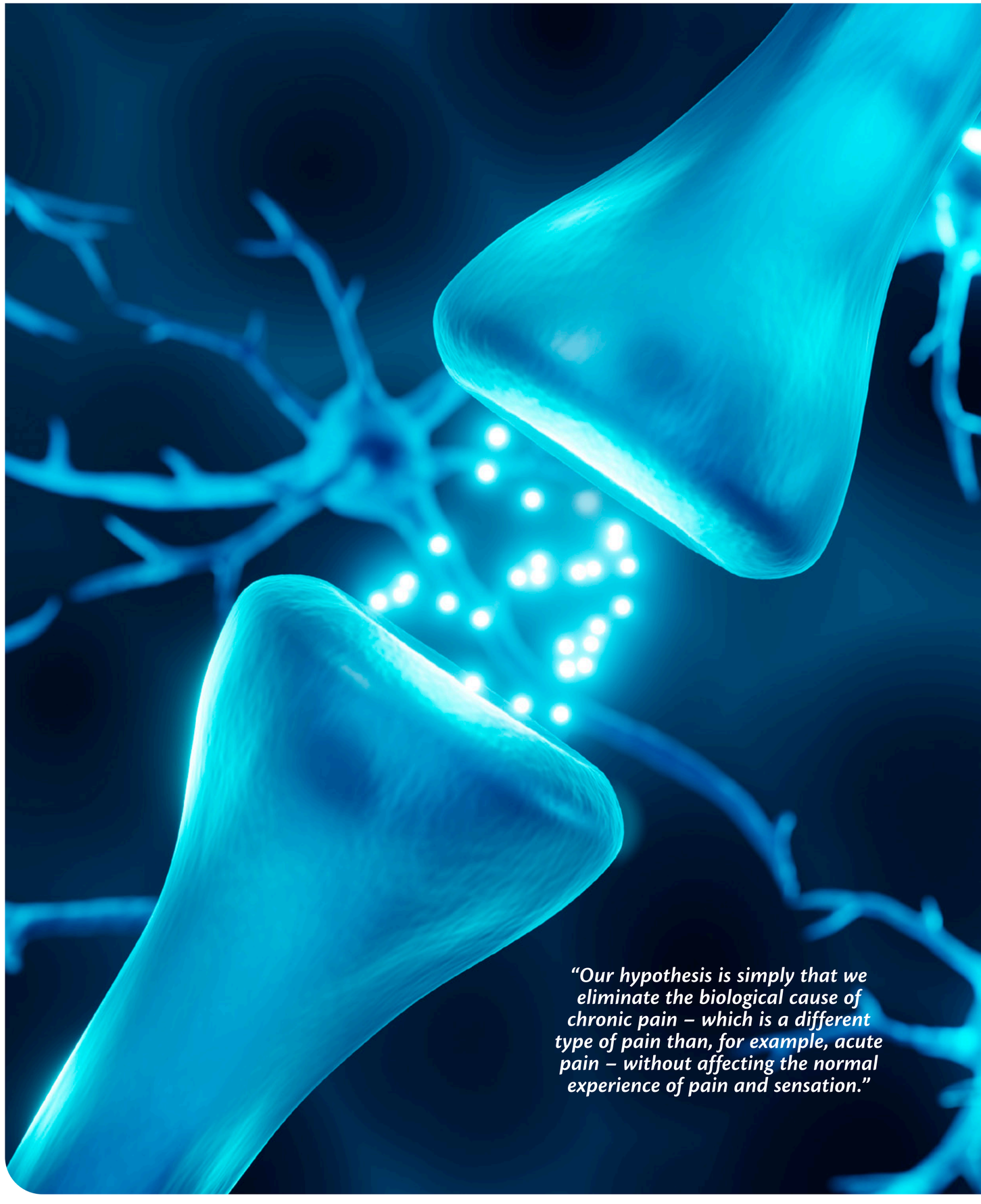
You expect both the mechanism of action and the effect of COZY02 to be the same as with direct administration of the peptide. Can you explain this?

“It’s quite simple. COZY02 – our gene therapy candidate – delivers the same active component as the peptide treatment COZY01. The only difference is that the gene therapy instructs the body to produce the peptide itself instead of having to inject it.”

Why did you choose to collaborate with CombiGene and what is the division of roles in the projects?

“One of the researchers behind our drug candidates and co-founder of Zyneyro had for a few years had an academic collaboration with CombiGene in some other projects that are not related to chronic pain. So, it was natural to contact the CombiGene management, as we felt ready to enter into a development collaboration. From the first online meetings, which took place at the end of the pandemic, it was clear that there was mutual respect, constructive dialogue and complementary competencies on both sides. We are Scandinavians, we understand each other (although there is a difference between Swedish and Danish business culture), and we can easily visit each other.”

“Most importantly, we agreed very quickly on a collaboration model where we share the tasks equally, from the development work with the drug candidates to raising the necessary capital. A natural consequence of this is that we also share the future economic return. In other words, we work as a unit. Zyneyro has thus gained a top-professional drug development department in a very short time. And since the time to approval is, of course, very important, this form of cooperation represents the fastest way to move the project forward.”



The National Institutes of Health in the US evaluates CombiGene's and Zyneyro's peptide-based pain project COZY01

The National Institutes of Health (NIH) is a U.S. government agency with a proud history with several important discoveries that improve health and save lives. Over the years, 169 Nobel Prize winners have either conducted their research at the NIH or received support from the NIH. Major discoveries include the development of MRI (magnetic resonance imaging), understanding of how viruses can cause cancer and knowledge of how the brain processes visual information. The NIH's roots go back to 1887.

The NIH consists of 27 different units. Each unit has its own specific research agenda, often focusing on specific diseases or bodily functions. 24 of the 27 entities receive their grants directly from the US Congress. NIH is headquartered in Bethesda, Maryland, USA. Some research is conducted at the Bethesda campus, but more than 80 percent of the research activities are conducted by researchers around the US and the world.

PSPP Program

One of the programs that NIH runs is called PSPP – Preclinical Screening Platform for Pain. The program stems from the urgent need to reduce the use of opioid-based drugs through the development of new, non-opioid-based pharmacological and non-pharmacological treatments for pain. According to the NIH, there are currently 25 million Americans living with daily chronic pain who rely on opioid-based drugs for pain relief. The goal of the PSPP program is to identify and characterize non-addictive therapies for pain.

The program offers testing including an assessment of in vitro and pharmacokinetic profiles, adverse event profiles, addiction liability, and efficacy in models relevant to human pain conditions.

COZY01 and PSPP

An independent evaluation of the potential of COZY01 as a future pain treatment is currently underway under the PSPP program. COZY01 has passed the first level of three and has been selected to move on to the next level where the substance will be tested in a behavioral model to investigate possible effects on the central nervous system and subsequently in different pain models. During the first quarter of the year, CombiGene and Zyneyro worked on preparatory activities for this next step.

Source: https://www.nih.gov

Bloomberg predicts strong growth for the gene and cell therapy market

In an article from May 3, 2023, Bloomberg forecasts an annualized growth of 22.8 percent for the cell and gene therapy markets. This means that the market for cell and gene therapies will reach USD 62.5 billion by 2032. The article is based on a study by Prophecy Market Insights.

According to the article, there are several things that will drive growth in the coming years. The number of clinical studies has increased continuously in recent years. As more and more clinical data becomes available, acceptance of new therapies will increase. The large private and public investments in cell and gene therapy have created good conditions for research and development, which in itself will accelerate the pace of innovation. CombiGene is an excellent example of private and public capital working together. In total, CombiGene has received SEK 229 million from the company's shareholders and SEK 37 million in various forms of public funds.

One challenge mentioned in the article is the high cost of cell and gene therapy, both in terms of the development of new therapies and the high manufacturing costs. Uncertainty in the regulatory area is also mentioned.

Among the ten leading companies in the field of cell and gene therapy, the article mentions Spark Therapeutics, CombiGene's partner in the epilepsy project CG01. Other companies include Gilead Sciences and Novartis.

Ingeneious contacted Peter Ekolind, CombiGene's Chief Operating Officer, for a comment.

Peter, what is your spontaneous reaction to the Bloomberg article?

"The article shows that CombiGene is part of a very dynamic part of the pharmaceutical market with fantastic growth opportunities. We are, of course, deeply involved in all aspects of the development of our own projects and we have acquired important knowledge regarding the treatment of the diseases in which we are involved. Through the epilepsy project CG01, we have also learned a lot about the challenges and solutions that exist in manufacturing. We are also involved in the GeneNova project, which is led by KTH and which, among other things, aims to find solutions that make gene therapies available to a larger number of patients. Gene therapy is a complex field that requires us to work in a variety of disciplines. The fact that the article specifically mentions Spark Therapeutics as one of the world's leading players is not news to us at CombiGene, but it is still very encouraging since Spark is our partner in the CG01 project."

Source: https://www.bloomberg.com/press-releases/2023-05-03/cell-and-gene-therapy-market-projected-to-grow-at-a-cagr-of-22-8-and-reach-us-62-5-billion-by-2032

"The article shows that CombiGene is part of a very dynamic part of the pharmaceutical market with fantastic growth opportunities."

CombiGene

The gene therapy explorer

CombiGene's vision is to provide patients affected bysevere life-altering diseases with the prospect of a better life through novel gene therapies.

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