PRESS RELEASE
January 9, 2023

CombiGene enters into collaboration agreement with Zyneyro for the development of a unique concept for effective relief of chronic pain

STOCKHOLM — January 9, 2023. CombiGene AB ("CombiGene", the "Company") and the Danish company Zyneyro ApS today announce that they have entered into a collaboration agreement regarding the continued development of Zyneyro's peptide- and AAV-based treatment of chronic pain conditions. The agreement with Zyneyro is a cooperation agreement that means that Zyneyro and CombiGene share the project's costs and revenues equally. According to the agreement CombiGene will pay Zyneyro an upfront of DKK 5 million in connection with the signing of the agreement. CombiGene has furthermore committed to pay an additional maximum of DKK 11.4 million in continued development support towards clinical Phase 1. The peptide-based treatment is expected to be ready for the first human dosing in 2025, while the AAV-based treatment will need additional development time to reach the same point.

Pain is a major global problem. About 20 percent of the world's population suffers from some form of chronic pain. In the United States, it is estimated that between four and eight percent of the population is affected by High Impact Chronic Pain.[1] Conventional treatment of severe pain consists primarily of anti-inflammatory drugs, antidepressants, antispasmodic 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 often has a number of disabling side effects such as addiction problems, depression, anxiety, fatigue, impaired physical and mental ability, and harmful impact on the gastrointestinal and cardiovascular systems. In the United States, an estimated 700,000 people have died due to opioid abuse in the past 20 years.

A unique concept. The pain program is developed to offer effective pain relief without the side effects that today's treatments often give rise to. This is possible thanks to Zyneyro's researchers having identified a new biological mechanism of action, which forms the basis for the drug candidates. The program consists of two drug candidates: a peptide treatment (short-term treatment) and a gene therapy treatment with potentially lifelong effect. The patient's clinical picture and potentially other factors will guide the choice of drug candidate.

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

In chronic pain conditions due to illness or injury to the nervous system, including phantom pain and pain associated with various types of back injuries, which in conventional treatment require daily medication, pain relief can be achieved by treating the patient with an AAV vector that "instructs" the body to establish the pain-relieving mechanism on its own. In this way, one can achieve long-term pain relief without daily medication. Since the AAV vector encodes the peptide, the intention is that both the mechanism of action and the effect is the same as in the direct administration of the peptide.

The concept could potentially also offer an opportunity to check that a patient responds well to treatment with peptide before proceeding with the more costly AAV treatment. By screening potential

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

patients in this way before a costly gene therapy treatment could increase the accuracy of the gene therapy treatment.

Significant costs to society. The study "Pain in Europe" estimates the costs to society at 3-10 percent[1] of gross domestic product. In the US, the cost of pain relief is estimated at USD 560-635 billion.[2] The market for effective pain relief is thus large. The need for, and thus the market, for an effective pain relief treatment is great.

Preclinical phase. The pain program is still in the preclinical phase and there are still several preclinical studies to be performed before the project can proceed to the clinical phase with studies in humans. This means that it will be a number of years before the treatment can be put to clinical use.

CombiGene's CEO Jan Nilsson comments: "I am very impressed with Zyneyro's work in the field of pain management", says Jan Nilsson, CEO of CombiGene. "The concept of being able to give the pain-relieving peptide directly to patients with temporary pain conditions and to use AAV vectors that instruct the body to establish the pain-relieving mechanism on its own in chronic pain conditions is extremely attractive. All drug development is associated with risks. There are never any guarantees that a project will be successful. Zyneyro has shown impressive preclinical data from the studies they have conducted. It will now be extremely stimulating to take this project forward through the preclinical phase together with our colleagues at Zyneyro. My contacts with Zyneyro's CEO Peter Horn Møller have been characterized by openness and mutual respect. Although CombiGene is a gene therapy company, we have several employees with extensive experience of working with peptides in several different contexts."

Odd-Geir Berge comments: "Chronic pain is a major medical problem where good treatment is lacking for large patient groups. Existing drugs have limitations when it comes to pain relief and often have unacceptable side effects. The need for new forms of treatment is therefore great. The current project is based on a new concept with extensive scientific support, including data from animal models. In the CombiGene/Zyneyro concept, the pain can be attacked in two ways that complement each other: firstly, with a peptide with a shorter action, and secondly with a gene therapy that opens up the possibility of a lifelong effect. Patients with different needs would thus receive optimally adapted treatment. Being able to increase the likelihood of a successful gene therapy treatment by using the peptide as a screening method is extremely interesting. This is a promising project that gives hope for significant therapeutic progress," says Odd-Geir Berge, former Senior Principal Scientist, Analgesia, AstraZeneca R&D Södertälje, now active as an independent consultant at OGBConsulting AB. Odd-Geir Berge has been involved in CombiGene's evaluation of the project.

Zyneyro's CEO Peter Horn Møller comments: "In CombiGene we have found the optimal partner for this project. CombiGene and Zyneyro share the same basic approach to partnerships, and we are pleased that the collaboration with CombiGene is based on values such as trust, mutual respect, and focused work. In addition, CombiGene has a highly experienced drug development team that builds on and complements Zyneryo's very strong competencies in the early drug development phase. I therefore see a great advantage in the fact that Jan Nilsson and I have managed to transform the synergies into a unique team collaboration that gives us a fantastic opportunity to develop a peptide drug and a gene therapy in parallel. In collaboration with CombiGene, Zyneyro will have unique access to potential pharmaceutical partners with the resources and expertise to take the drugs to patients – in addition to the partners Zyneyro itself has been in contact with."

About Zyneyro ApS

Zyneyro was founded by a group of researchers from the Department of Neuroscience at the University of Copenhagen and a group of entrepreneurs who together have extensive experience in all aspects of early drug development and entrepreneurship. The company's researchers have worked for more than 15 years to understand the ability of the brain and nervous system to adapt to the influence of the

[1] EU ref Breivik et al. BMC Public Health 2013, 13:1229
[2] Gaskin DJ, Richard P: The economic costs of pain in the United States.

surrounding environment. Zyneyro's goal is to translate this knowledge of modulation of neuronal interaction into developing a number of drug candidates. The drug candidates included in the collaboration with CombiGene relate to the treatment of pain. Zyneyro also intends to develop other drug candidates for indications other than pain.

About CombiGene AB
CombiGene's vision is to offer patients affected by severe life-changing diseases opportunities for a better life through innovative gene therapies. CombiGene's business concept is to develop effective gene therapies for serious diseases that today lack adequate treatment methods. Research assets are taken in from a network of external researchers and developed further up to preclinical/clinical concept verification. Drug candidates for common diseases will be co-developed and commercialized through strategic partnerships, while CombiGene may drive the development and commercialization in-house for medicines aimed at limited patient populations.

The Company has signed an exclusive collaboration and licensing agreement for CombiGene's CG01 project with Spark Therapeutics.

The company is public and listed on the Nasdaq First North Growth Market and the company's Certified Advisor is FNCA Sweden AB, info@fnca.se.

This information is information that CombiGene is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact person set out below, at *2023-01-09 07:30 CET.*

For more information:
CombiGene AB (publ)
Jan Nilsson, CEO
Phone: +46 (0)704 66 31 63
jan.nilsson@combigene.com

Zyneyro ApS
Peter Horn Møller, CEO
Phone: +45 2066 0110
phm@zyneyro.com

Please read *Ingeneious*, a newsletter from CombiGene which contains general news and information that is judged not to have a significant effect on the share price. *Ingeneious* and press releases are available at www. combigene.com.