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Year-end report January–December 2024

AlzeCure® is a Swedish pharmaceutical company that develops new innovative small-molecule drug therapies for the treatment of severe diseases and conditions that affect the central nervous system, such as Alzheimer's disease and pain – indications for which currently available treatment is very limited. The company is listed on Nasdaq First North Premier Growth Market in Sweden and is developing several parallel drug candidates based on three research platforms: NeuroRestore®, Alzstatin® and Painless.

NeuroRestore consists of two symptom-relieving drug candidates where the unique mechanism of action allows multiple indications – Alzheimer's disease, as well as cognitive disorders such as those associated with traumatic brain injury, sleep apnea and Parkinson's disease, as well as treatment for depression.

The **Alzstatin** platform focuses on developing disease-modifying and preventive drug candidates for early treatment of Alzheimer's disease.

Painless is the company's research platform in the field of pain and contains two projects: ACD440, which is a drug candidate in the clinical development phase for the treatment of neuropathic pain, and TrkA-NAM, which targets severe pain in conditions such as osteoarthritis.

AlzeCure® aims to pursue its own projects through preclinical research and development to an early clinical phase and is continually working on business development to find suitable out-licensing solutions or partnerships with other pharmaceutical companies.

FNCA Sweden AB is the company's Certified Adviser.

For more information, please visit www.alzecurepharma.com.

AlzeCure

150,000

It is estimated that around 150,000 people in Sweden live with dementia diseases, a figure that is expected to triple by 2050. Every year, around 25,000 people are affected, resulting in major care and healthcare costs for society.
The direct costs are estimated to be higher than those caused by cancer and cardiovascular diseases.

Financial information

October–December 2024

Figures in parentheses refer to the corresponding period of the previous year.

- Net sales during the period totaled SEK 0 thousand (0).
- Loss for the period totaled SEK -9,330 thousand (-9,756).
- Earnings per share, basic, totaled SEK -0.11 (-0.16).
- Cash flow from operating activities totaled SEK -7,565 thousand (-8,361).
- Total assets at the end of the period amounted to SEK 34,435 thousand (32,001).
- Cash and cash equivalents at the end of the period totaled SEK 31,498 thousand (29,100).

January–December 2024

Figures in parentheses refer to the corresponding period of the previous year.

- Net sales during the period totaled SEK 0 thousand (0).
- Loss for the period totaled SEK -35,234 thousand (-37,167).
- Earnings per share, basic, totaled SEK -0.46 (-0.60).
- Cash flow from operating activities totaled SEK -35,123 thousand (3,057).
- Total assets at the end of the period amounted to SEK 34,435 thousand (32,001).
- Cash and cash equivalents at the end of the period totaled SEK 31,498 thousand (29,100).
- No dividend is proposed.

Significant events

October–December 2024

- On October 28, the company presents new positive data in the TrkA-NAM pain project for osteoarthritis.
- On October 30, the company presents new anti-inflammatory data concerning NeuroRestore ACD856 at the Clinical Trials on Alzheimer's Disease conference (CTAD).

January–September 2024

- On January 29, the company selects a candidate drug and enters the next phase of development with TrkA-NAM ACD137 for the treatment of osteoarthritis and other severe pain conditions.
- On February 29, the company announces that the patent offices in China, India, South Africa, Israel, Hong Kong and Mexico have granted patents covering the company's clinical drug candidate ACD856, which is being developed for Alzheimer's and other cognitive impairment disorders.
- On March 26, the company's Board of Directors resolves on a new issue of shares of approximately SEK 52.8 million with preferential rights for existing shareholders. The rights issue is subject to approval by the Extraordinary General Meeting on April 25, 2024. The issue is guaranteed to approximately 63 percent through subscription commitments and guarantee commitments from existing owners and members of the company's management and Board of Directors, among others. To enable further capital injections, the Board of Directors may also exercise an overallotment option of up to approximately SEK 15.0 million.
- On March 26, the company announces that an Extraordinary General Meeting will convene on April 25, 2024.
- On April 10, the company announces that its Annual General Meeting will convene on May 14, 2024.
- On April 10, the company announces that Dr. Jan Lundberg, former head of research at Eli Lilly and AstraZeneca, is investing in AlzeCure and proposes that he be elected to serve on the company's Board of Directors.
- In April, the company receives new preclinical data for Neuro-Restore in inflammation, with relevance to Alzheimer's disease, and submits a new patent application for NeuroRestore ACD856.
- Jan Lundberg is elected to serve on the Board of Directors at the Annual General Meeting on May 14.
- On May 20, the company announces the final outcome of the rights issue with preferential rights for shareholders (the "Rights Issue") that ended on May 17, 2024. The issue raises approximately SEK 39.2 million for AlzeCure before issue expenses.
- In June, the company publishes a scientific article on the clinical Phase Ib results for ACD440 supporting the continued development of the lead drug candidate in the Painless platform in the European Journal of Pain.
- On June 14, the company's Board of Directors resolves on a directed share issue of 965,727 shares to Formue Nord Markeds-neutral A/S ("Formue Nord"), which has chosen to receive its agreed compensation as guarantor in shares.
- In July, the company carries out a directed share issue as a follow-up to a previously given subscription commitment and raises SEK 3.7 million.
- In July, the company publishes a new scientific article related to NeuroRestore ACD856 for the treatment of Alzheimer's and cognitive disorders.
- In August, the company presents new preclinical data for the lead drug candidate ACD137 (TrkA-NAM) at the international pain conference IASP in Amsterdam.

Significant events after the end of the period

- The company announces February 17, 2025, that they receive an EU grant for a Phase II clinical trial of NeuroRestore ACD856 for Alzheimer's disease.

See page 62 of the company's 2023 annual report for a list of definitions.

A word from the CEO

The fourth quarter of 2024 was yet another positive and eventful quarter for AlzeCure Pharma. During the quarter, we published and presented new positive preclinical findings from our clinical Alzheimer's project NeuroRestore, which we are preparing for Phase II clinical studies. Furthermore, in our second Alzheimer's project, Alzstatin, we opted to advance our latest molecule, ACD680, and prepare it for clinical trials. We also published new data from our pain project targeting knee osteoarthritis, TrkA-NAM. In preclinical models, we have shown that the analgesic effects of the candidate drug ACD137 are at least on par with the antibody Tanuzemab, while also exhibiting potential protective effects. These results are highly promising and we are very pleased with them. In February 2025 we were also awarded a €2.5 million grant from the European Innovation Council (EIC) Accelerator under the Horizon Europe program, with the potential to receive additional financing through the EIC Fund, subject to further due diligence and conditions being met. We are very proud and honored to receive this prestigious funding from the EIC Accelerator, which is both a significant financial contribution to the company and a recognition of the groundbreaking potential of ACD856. This grant will accelerate our clinical development and brings us closer to delivering a transformative therapy for Alzheimer's patients.

In the last quarter, we published and presented further preclinical data for our drug candidate NeuroRestore ACD856, which we are preparing for Phase II clinical studies in patients with Alzheimer's disease. Preclinical studies show that ACD856 can improve learning and memory function. The latest findings show that ACD856 also could have disease-modifying and neuroprotective effects, which are of significant value in treating Alzheimer's and other neurodegenerative diseases. These results indicate that with ACD856, we can also target inflammatory processes, which are a key element of disease progression in conditions such as Alzheimer's disease. The study was presented at the world-leading Alzheimer's conference CTAD (Clinical Trials in Alzheimer's Disease) in October[1)] and has led us to deepen our research collaboration with scientists at Karolinska Institutet.

Alzstatin, our disease-modifying and preventive treatment in tablet form for Alzheimer's disease, continues to be developed according to plan. The drug candidates in the platform, ACD680 and ACD679, are in preclinical development and are being prepared to enter clinical trials. Following a thorough evaluation of the generated data, including potency and safety findings, we have decided to proceed with ACD680 for further studies as an initial step. The collective results indicate that ACD680 has the potential to be a "Best-in-Class" molecule. Moreover, ACD680 is expected to have a longer patent term, until 2045, as well as an additional five years of exclusivity in the US, until 2050, which is highly valuable.

The compounds in the Alzstatin platform are "gamma-secretase modulators" (GSMs), which reduce production of the harmful amyloid-beta-42 protein that generates plaques in the brain. The biological process is considered a primary cause of Alzheimer's disease. Gamma-secretase modulators for the treatment of Alzheimer's have received growing attention during the year as the target mechanism has been validated by the Swiss pharmaceutical company Roche, which is also developing GSMs. Roche presented positive clinical Phase I data for its GSM, RG6289, and has now initiated a Phase II clinical trial, which has resulted in growing interest in our Alzstatin project from both other pharmaceutical companies and investors. Furthermore, interest in GSM as a class of drugs is on the rise, as they not only reduce plaque formation but also potentially enhance the brain's resilience.

Martin Jönsson, CEO

Our Painless platform, which includes the ACD440 and TrkA-NAM pain projects, also continues to make progress. With our TRPV1 antagonist ACD440, which we are primarily developing for local treatment of peripheral neuropathic pain (nerve injury pain), we have previously obtained positive clinical Phase IIa results in patients with chronic neuropathic pain. We have also conducted a Phase Ib clinical trial in nociceptive pain (tissue damage pain), in which, as in the Phase IIa study, we were also able to reduce the pain by about 50%. The results from these clinical studies have shown that ACD440, which is administered as a gel that is applied to the skin, demonstrates good suitability for further clinical development. We are now preparing for continued Phase II clinical trials with the compound.

Neuropathic pain is an area with great unmet medical need, especially with respect to finding alternatives to opioids, and we believe that ACD440 could significantly improve quality of life for patients suffering from this type of pain. Only one out of five patients is satisfied with their current treatment.[2] During the last quarter, we organized a seminar on neuropathic pain and ACD440 together with pain expert Dr. Rolf Karlström at Uppsala University and Uppsala University Hospital. If you want to know more, the seminar is available on our website and YouTube channel.[3]

Our second pain project, TrkA-NAM, focuses on arthritis of the knee. Over 300 million people suffer from the disease and the patient population is growing due to an aging population and obesity-related problems. The project continues to make good progress, and we conducted additional preclinical studies with favorable results during the year. Earlier this year, we selected a candidate drug for the project, ACD137, which we then advanced to safety and toxicology studies. The compound has powerful analgesic effects in several different preclinical models, indicating a wide range of uses for the compound. ACD137 has also been shown to have anti-inflammatory effects, which may further strengthen its pain-relieving properties, as well as potentially opening up other possible indications. In 2024 we also published and presented new data for ACD137 that demonstrated good efficacy in both neuropathic and nociceptive pain, which in turn indicates the broad potential of the project.

> "The fourth quarter of 2024 was yet another positive and eventful quarter for AlzeCure Pharma. We published and presented new findings for both NeuroRestore ACD856 and TrkA-NAM ACD137. We also presented our projects at many events, including the world-leading Alzheimer's conference CTAD.
>
> Martin Jönsson, CEO

Interest in TrkA-NAM has risen as Asahi Kasei initiated a Phase IIb study with its candidate drug AK-1830, with the same target mechanism. TrkA-NAM is being developed to reduce peripheral NGF signaling and thus pain; because of the selective target mechanism of the molecules, TrkA-NAM is expected to maintain the good analgesic effects but without the side effects that NGF antibodies have previously demonstrated. This is validated by new preclinical data with ACD137 in an osteoarthritis model that we reported on in the fourth quarter. The results showed significant pain relief in both movement-induced and evoked pain, as well as a significant anti-inflammatory effect. The analgesic effect of ACD137 was as potent as that of the anti-NGF antibody Tanezumab, which has demonstrated significant and robust pain relief in patients in several clinical trials. ACD137 was also shown to have a protective effect against articular cartilage damage, showing a significant improvement in several structural parameters of cartilage and the knee joint, suggesting a protective effect on knee joint function in an osteoarthritis model.

We continue to focus on marketing communications and actively participate in various meetings and congresses to present our research to investors and potential partners. In November, we participated in events such as BIO-Europe, Europe's largest business development and partnership conference in the pharmaceutical industry. We continue to encounter growing interest from pharmaceutical companies and other stakeholders that may be interested in investing in or in-licensing our development projects, or alternatively in entering into a partnership.

Overall, we continued to make progress in all projects during the fourth quarter of 2024, with exciting new results that strengthen our position for the future. In collaboration with renowned institutions and scientists, both in Sweden and abroad, we produced exciting new results in our projects in 2024 that further strengthen the potential and improve our business development opportunities going forward. Backed by these positive results, and with research expenses and findings on track, I look forward to continuing to develop AlzeCure together with our partners and colleagues in 2025.

Stockholm, February 2025

Martin Jönsson

CEO of AlzeCure Pharma AB

AlzeCure has in February 2025 been awarded a €2.5 million grant from the European Innovation Council (EIC) Accelerator under the Horizon Europe program. In addition, the company has the potential to receive additional financing through the EIC Fund, subject to further due diligence and conditions being met.

"We are proud and honored to receive this prestigious funding from the EIC Accelerator, which recognizes ACD856's groundbreaking potential. This support will accelerate our clinical development and brings us closer to delivering a transformative therapy for Alzheimer's patients." Martin Jönsson.

1) Preclinical evidence for anti-inflammatory and immunomodulatory effects of NeuroRestore ACD856, a Trk-PAM in clinical development for the treatment of Alzheimer's disease, Parrado-Fernández, C., CTAD poster, October 2024. https://www.alzecurepharma.se/sv/wp-content/uploads/sites/3/2024/10/lp025-ctad-2024-acd856-poster.pdf
2) Finnerup et al; Pharmacotherapy for neuropathic pain in adults: systematic review, meta-analysis and updated NeuPSIG recommendations. Lancet Neurol. 2015; 14(2): 162–173
3) Seminar on neuropathic pain and ACD440 together with pain specialist Rolf Karlström, M.D., PhD and Assoc. Professor at Uppsala University: https://www.alzecurepharma.se/en/presentations-and-interviews/

Project portfolio

AlzeCure works with several research platforms:
NeuroRestore® and Alzstatin® – with a focus on Alzheimer's disease, where the leading drug candidate ACD856 is in the clinical development phase.
Painless – focuses on pain treatment and contains two projects: ACD440 in the clinical development phase and TrkA-NAM in preclinical phase.

There are several small-molecule drug candidates in the various platforms: two in NeuroRestore and one in Alzstatin. There are also two projects in the Painless platform. A diversified drug portfolio paves the way for other indications, such as cognitive dysfunction associated with Alzheimer's, traumatic brain injury, sleep disturbances, Parkinson's disease and depression, as well as for severe pain in conditions such as neuropathy and osteoarthritis.

- The NeuroRestore platform is developing a new generation of symptom-relieving drugs for the treatment of illnesses with cognitive dysfuntion, such as Alzheimer's disease. The target mechanism also has other potential indications, including depression and cognitive dysfuntion in Parkinson's disease, traumatic brain injury and sleep disorders. The leading drug candidate in the project, ACD856, is in the clinical development phase.
- Innovative disease-modifying and preventive oral drugs for Alzheimer's disease are under development within the Alzstatin platform. They are intended to enable simple administration of the drug and be more cost-effective. The drug candidate in the Alzstatin platform is in the preclinical development phase.
- The Painless platform includes two projects: TrkA-NAM ACD137 and ACD440, which both focus on severe pain conditions.
  - The drug candidate ACD440 was in-licensed in January 2020 and affects a specific biological mechanism; the 2021 Nobel Prize in Physiology or Medicine was awarded for the discovery of this mechanism.
    The compound is being developed for the treatment of neuropathic pain, a field with great unmet medical need. The project is currently in the clinical development phase.
  - The TrkA-NAM ACD137 project is aimed at treating other severe pain caused by disorders such as osteoarthritis, which today lacks sufficiently effective treatment. The project is currently in the preclinical phase.

AlzeCure's project portfolio

Platform	Candidate	Target	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
NeuroRestore	ACD856	Positive allosteric modulator (PAM) of Trk receptors	Alzheimer's disease Traumatic brain injury, Parkinson's disease, Sleep disorders, Depression					
NeuroRestore	ACD857	Positive allosteric modulator (PAM) of Trk receptors	Alzheimer's disease					
Alzstatin	ACD680	Gamma secretase modulator (GSM)	Alzheimer's disease					
Painless	ACD440	TrpV1 antagonist	Neuropathic pain					
Painless	ACD137	Negative Allosteric Modulator (NAM) of TrkA receptors	Osteoarthritis pain					

In progress Completed

For definitions of the phases, please see the AlzeCure Pharma website, www.alzecurepharma.com.

Project development

AlzeCure works with research and development of innovative and effective new small molecule drugs for treatment of diseases that affect the nervous system and the brain, with a focus on Alzheimer's disease and pain. The need for new treatments for these severe illnesses is great; for example, disease-modifying therapy for Alzheimer's is expected to be able to generate more than USD 15 billion* in annual sales.

The company is simultaneously developing three drug candidates based on the two research platforms NeuroRestore and Alzstatin, along with two projects within the Painless platform – TrkA-NAM and ACD440.

A diversified portfolio of drug candidates paves the way for other indications, such as cognitive dysfunction associated with traumatic brain injury, Parkinson's disease and sleep disorders. With its broad portfolio of assets and values, the company maximizes shareholder value by working in multiple indication areas where there is scientific support for the biological target mechanisms.

Neurology

Within NeuroRestore, a new generation of symptomatic drugs is being developed for the treatment of cognitive dysfunction (memory problems) in Alzheimer's disease. The NeuroRestore substances are known as Trk-PAMs, which stimulate specific signaling of the neurotrophins NGF (Nerve Growth Factor) and BDNF (Brain-Derived Neurotrophic Factor), which play an important role in normal neuronal function. The company initiated the first clinical trial with the primary drug candidate in NeuroRestore, ACD856, in late 2019. The study was completed on schedule in the second quarter of 2020. The results showed that ACD856 was well-suited for further clinical development, which led to the initiation of subsequent clinical trials, the SAD-study, according to plans in the end of 2020. In the third quarter of 2021 the MAD study was also initiated and both of these studies, which are part of the Phase I program for the drug candidate, have had the primary purpose of assessing safety and tolerability in humans. The MAD study, which was concluded according to plan in June 2022, showed that ACD856 has a good safety and tolerability profile in humans. Moreover, the results showed that the compound demonstrated good pharmacokinetic properties with rapid uptake in the body. In addition, ACD856 easily crosses the blood-brain barrier and can be measured in the spinal fluid; these important data support further clinical development work. Moreover, in September 2022 the company reported new EEG results from a planned exploratory analysis in the MAD study, which showed that ACD856 not only reaches the CNS, but also activates neuronal pathways in the brain, of relevance to both cognition and depression. ACD857 is in the research phase and also has the primary indication of cognitive dysfunction/Alzheimer's disease.

New preclinical data within the NeuroRestore platform have shown potential disease-modifying properties in this class of compounds. The findings show that both neurotrophins, NGF and BDNF, play important roles in retaining normal function and development in nerve cells, as well as in protecting them from damage, known as neuroprotective effects. Nerve cell death clearly correlates with functional impairment in Alzheimer's patients and no drugs with these protective effects are currently available on the market. The preclinical studies show that treatment with ACD856 results in increased survival for the nerve cells. Over the past two years, the studies have been complemented by additional data concerning the neuroprotective, regenerative and long-term effects of ACD856. The results indicate, among other things, that the substance can protect nerve cells against toxic Aβ42, the protein responsible for amyloid plaque formation in the brains of Alzheimer's patients. Moreover, data show that ACD856 increases the quantity of a specific protein that plays a key role in communication between nerve cells, which is severely affected in the disease. These important data, which highlight the potential of NeuroRestore as both a memory-improving and disease-modifying treatment, have been presented in publications and at a number of scientific conferences over the past two

* Source: Asher Mullard, Nature, June 8, 2021; Landmark Alzheimer's drug Approval.

1 **NeuroRestore® – the platform is developing a new generation of symptomatic drugs for the treatment of illnesses with cognitive disorders, such as Alzheimer's disease.**

2 **Alzstatin® – the platform develops innovative disease-modifying and preventive drugs for Alzheimer's disease.**

3 **Painless – two projects: TrkA-NAM and ACD440, which both focus on severe pain.**

"Diagnostics and biomarkers within the field of Alzheimer's are active fields of research, where key advances made in recent years have been of great importance for diagnostics, as well as for evaluating new drug candidates."

Henrik Zetterberg, professor at Sahlgrenska University and collaboration partner in AlzeCure's Alzstatin GSM project.

years, including at the major international Alzheimer's conference CTAD in 2023. At the conference Eisai also presented the results of its Phase I clinical drug candidate E2511, which they are developing as a disease-modifying treatment for neurodegenerative diseases such as Alzheimer's. The compound has a similar target mechanism as ACD856, which strengthens the validation of the NeuroRestore platform. However, ACD856 has a broader effect profile than E2511 and, in addition to potential disease-modifying effects, also exhibits memory-enhancing and antidepressant effects, which the company sees as a clear differentiation.

In March 2024, the company presented new preclinical data on ACD856 demonstrating that the substance functions as a "biased" positive allosteric modulator (PAM), i.e. that the substance potentiates certain signaling pathways but not others, which means that the substance can have potent effects while maintaining a good safety profile. The results show that ACD856 can stimulate nerve cell growth, which is important for communication between nerve cells. In addition, the substance improves memory and learning ability in preclinical models. However, pain signaling is not affected, indicating a selective stimulation of specific signaling pathways.

In April 2024, the company reported that ACD856 also demonstrates anti-inflammatory properties both centrally in the brain and peripherally in the body with relief of clinical inflammatory symptoms in preclinical models and a reduction in several inflammatory markers. These new data indicate an opportunity to treat diseases with neuroinflammation, such as Alzheimer's disease, and that ACD856 may have a disease-modifying effect through its anti-inflammatory properties. A review article related to the preclinical findings with ACD856 was published in July 2024[1]. The company also presented new positive data on new anti-inflammatory and immunoregulatory effects of ACD856 at the major international Alzheimer's conference CTAD in late October 2024.

There is also strong scientific support for this target mechanism in depression. NeuroRestore compounds, such as ACD856, have demonstrated effects in preclinical models for depression, with data published in August 2023[2] and that were further supported by data in recently released articles in the prestigious journals Cell[3], Nature[4] and Science[5]. These studies show that several different classes of antidepressants appear to mediate their effects via BDNF/TrkB, further strengthening the link between BDNF and depression. AlzeCure has demonstrated in preclinical models that NeuroRestore compounds possess antidepressant effects and they also induce the release of neurotransmitters in the brain that are associated with depression.

In May 2023, AlzeCure reported that the European Patent Office had granted a patent for NeuroRestore, including ACD856. This patent has been validated in 33 territories across Europe, including Germany, France, the UK, Spain, Italy and Sweden. This achievement is yet another important step for ACD856, in light of the previously granted US patent for this substance. During the first quarter of 2024, patents were also granted for ACD856 in additional territories, including China, India, South Africa and Mexico, which is a key step in the effort to establish a comprehensive global patent portfolio for the NeuroRestore program. The new preclinical data on the anti-inflammatory properties of ACD856 also led to the submission of a new patent application in April 2024 for the drug candidate.

AlzeCure's disease-modifying research platform for Alzheimer's disease, Alzstatin, focuses specifically on reducing the production of toxic amyloid beta (Aβ42) in the brain. The substances in Alzstatin are known as gamma-secretase modulators (GSMs). Aβ plays a key pathological role in Alzheimer's disease and begins to accumulate in the brain years before clear symptoms develop.

The target mechanism in Alzstatin, gamma-secretase modulators (GSMs), is confirmed by previously reported study results, which we believe validate the amyloid hypothesis and thus Alzstatin's focus. At the CTAD conference in October 2023, Roche also presented Phase I clinical data for its GSM, and was able to demonstrate PoM in humans as well as a good safety profile for this class of compounds. They have now entered Phase II studies in 2024, which will further validate this target mechanism and help to chart a regulatory pathway forward for this class of compounds. Compared with the antibody therapies now coming to market, the small molecule compounds in the Alzstatin platform have several key differentiating features, including their ability to be designed to easily cross the blood-brain barrier and be produced more cost-effectively.

The drug candidate in the Alzstatin platform, ACD680, is in the preclinical phase and comes from a newly developed series of molecules that are expected to be advantageous from a patent perspective. New positive preclinical data on ACD680 were presented at the ADPD Alzheimer's and Parkinson's congress in late March 2023, in which the compound showed reductions of toxic Aβ42 by over 50% and good pharmacokinetic properties in vivo.

News in Q4

- In October, the company presents new positive data demonstrating both analgesic and anti-inflammatory effects in the TrkA-NAM pain project for osteoarthritis.
- The company also presents new preclinical data on the anti-inflammatory and immunoregulatory effects of NeuroRestore ACD856 at the Alzheimer's conference CTAD in October.

1) Forsell P, et al., Pharmaceuticals. 2024; 17(8):997.
2) Madjid N. et al., Psychopharmacol. 2023 Aug;240(8):1789-1804.
3) Casarotto PC. et al., Cell. 2021 Mar 4;184(5):1299-1313.
4) Moliner R. et al., Nat Neurosci. 2023 Jun;26(6):1032-1041.
5) https://www.science.org/content/article/psychedelic-inspired-drugs-could-relieve-depression-without-causing-hallucinations

Every 5 seconds someone in the world is diagnosed with Alzheimer's.

Pain

The Painless platform contains two projects aimed at developing new treatments for pain. Both projects involve non-opioids, which is important to emphasize, because of the inherent risk associated with opioids for abuse, overdose and secondary injuries – which has led to avoidance of opioids as first-line treatment for pain. Despite this treatment problem they are still frequently used, for which reason the need for new treatments that do not involve opioids is great.

In January 2020, a drug candidate in the clinical development phase aimed at treating neuropathic pain, ACD440 (TRPV1 antagonist), was in-licensed. This project is an important strategic in-licensing that strengthens the company's current clinical portfolio. The ACD440 project has its origins in Big Pharma and is based on strong scientific grounds. The 2021 Nobel Prize in Physiology or Medicine was awarded for the discovery of and insights into TRPV1, the biological system that serves as the basis for ACD440 and is central to temperature regulation and pain. The compound that is being developed as a gel for topical treatment has previously undergone clinical trials, but at that time as oral treatment. As planned, AlzeCure initiated a Phase Ib clinical trial of the drug candidate in late 2020, which was completed in April 2021 and showed positive proof-of-mechanism (POM) results, i.e. an analgesic effect in humans. The efficacy of ACD440 was clearly significant compared with placebo. The compound was also well tolerated as a topical gel on the skin, indicating good suitability for further clinical development as topical treatment for neuropathic pain conditions. Data from this study were published by the company in a scientific article in June 2024 in the European Journal of Pain. During the first quarter of 2022, the FDA provided feedback regarding the material and documentation submitted for a pre-IND meeting. The response was informative and in June 2022, the company initiated a Phase II trial with ACD440 in patients with peripheral neuropathic pain. This exploratory double-blind, placebo-controlled, randomized cross-over study aimed to evaluate the efficacy, safety and pharmacokinetics of the company's leading drug candidate in pain. AlzeCure reported positive top-line results from the study in May 2023, while the more detailed results from the study were presented at the international pain conference, EFIC, in September 2023. The patients, who were treated for 7+7 days in a cross-over design, ranged in age from 50–85 years and suffered from chronic neuropathic pain. Most of them were concurrently receiving alternative pain management therapies. Data from the study showed that ACD440 could demonstrate positive POM results in patients with chronic peripheral neuropathic pain; in other words, the drug candidate had an effect on the intended target mechanism. A clear and significant analgesic effect was observed in pain induced by cold and heat. This pain was reduced by about 50%, a significant and clinically relevant reduction. Temperature hypersensitivity is very common in the area of the skin where patients experience their neuropathic pain and is a major problem in daily life for these individuals. These positive POM results from this Phase II clinical trial were in line with previously reported Phase I results. Moreover, it was observed that ACD440, which is a topical gel that is applied to the skin in the painful area, was well tolerated and both the compound and the administration method demonstrate good suitability for further clinical development.

TrkA-NAM builds on the knowledge amassed and assets developed in the NeuroRestore platform, but with the purpose of developing new compounds that focus on providing pain relief in several conditions associated with severe pain. The goal of the project is to develop a small molecule "TrkA-negative allosteric modulator" that can reduce movement-induced and spontaneous pain in patients with painful osteoarthritis. The compounds in the platform block NGF-mediated signaling via TrkA receptors, a biological mechanism with strong genetic, preclinical and clinical validation with respect to its role in pain. In September 2022, AlzeCure presented results for a new compound, AC-0027838, which has been identified as a potent and selective negative modulator of NGF/TrkA signaling in cell-based analyses, at the IASP international pain conference. The results showed a potent analgesic effect in a nociceptive pain model. The data also show that the compound has a powerful anti-inflammatory effect, which can potentiate the analgesic effects in clinical contexts. Analysis of the inflamed tissue also demonstrated significant effects on CGRP, a relevant biomarker for inflammation and pain. The project selected a candidate drug, ACD137, in January 2024, and it is currently in the preclinical phase. In April the company reported that it had obtained new data in several different preclinical pain models showing clear and significant analgesic effects of ACD137, which were presented at the IASP World Congress on Pain in August 2024.

Nobel Prize

The 2021 Nobel Prize in Physiology or Medicine was awarded for Professor David Julius' discovery of TRPV1, the biological system that serves as the basis for ACD440 and is central to temperature regulation and pain.

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> "About 70-80 percent of patients with neuropathic pain do not adequately respond to current first-line treatment, and AlzeCure is developing its new intended treatment specifically for individuals in this group.

In October 2024, the company reported new preclinical data related to ACD137 in an osteoarthritis model. The results show significant pain relief in both movement-induced and evoked pain, as well as a significant anti-inflammatory effect. The analgesic effect of ACD137 is as potent as that of the anti-NGF antibody Tanezumab, which has demonstrated significant and robust pain relief in patients in several clinical trials. ACD137 was also shown to have a protective effect against articular cartilage damage, showing a significant improvement in several structural parameters of cartilage and the knee joint, suggesting a protective effect on knee joint function in an osteoarthritis model.

Market trends affecting AlzeCure®

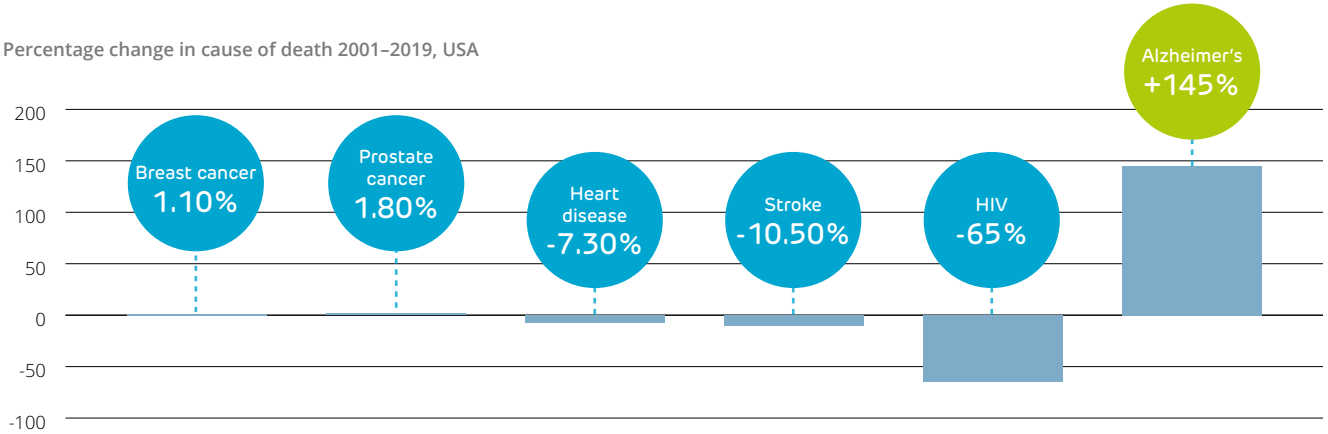
Increased social costs for Alzheimer's and other neurodegenerative diseases.
Costs associated with Alzheimer's and other neurodegenerative diseases are sharply rising and account for a substantial burden on the public healthcare system. The global cost to society for dementia is estimated at more than USD 1.3 trillion and is expected to almost triple over the next 30 years. These burgeoning costs increase the need for disease-modifying and/or preventive treatments appreciably.

Increased need for treatment due to an aging population
Old age is the greatest risk factor in dementia-related illnesses such as Alzheimer's, but also for pain problems. Life expectancy is anticipated to rise globally as a result of improving living standards and improved health care.

New treatment for Alzheimer's disease targeting amyloid plaques receives FDA approval
An antibody therapy (Aduhelm™) targeting amyloid pathology received approval in the US in June 2021 as the first disease-modifying treatment for Alzheimer's disease through the FDA's Accelerated Approval process. The approval is based on a "surrogate endpoint," in this case the reduction of beta-amyloid in the brain. Two other antibody therapies targeting amyloid pathology were also granted "Breakthrough Therapy Designation" status, giving them access to the FDA's other fast track processes, which could lead to a significantly faster pathway to market for drugs in this important area.

Amyloid-based therapeutics show positive effects on cognitive function in Alzheimer's patients and receive full market approval
Leqembi (lecanemab), one of the above-mentioned antibody therapies targeting amyloid pathology, was reported in September 2022 in a pivotal Phase III study to have achieved its efficacy milestones, with significant positive effects on functional and cognitive decline, as well as a reduction in the quantity of amyloid plaque in the brain. These Phase III results, which support the amyloid hypothesis, have served as the basis for the full market approval received from the FDA on July 6, 2023. Furthermore, yet another of the above-mentioned antibody therapies, Donanemab, received full marketing authorization in the US in July 2024, further validating the amyloid hypothesis. As a result, there is growing interest in research into other new drugs for the treatment of Alzheimer's disease, such as drugs that attack symptoms in other ways (NeuroRestore), as well as those (such as Alzstatin) that attack amyloid formation early in the course of disease, and that can be administered as tablets – unlike antibody treatment, which is administered intravenously. Drugs such as NeuroRestore and Alzstatin can also potentially be given in combination with existing therapy.

Percentage change in cause of death 2001–2019, USA



The mortality rate for Alzheimer's disease has risen sharply, while several other causes of death have fallen.

Major pharmaceutical companies are allocating investments in CNS-related illnesses to specialized research projects.
An increasing number of major pharmaceutical companies are starting investment funds aimed at smaller research companies and drug companies, as this is where a great deal of innovation takes place. The trend favors smaller R&D companies as opportunities for licensing agreements concerning the research, development and commercialization of drug candidates are increasing.

Development related to diagnostics & biomarkers for Alzheimer's disease
Significant progress has been made in this field through intensive work, including recent findings that a combination of blood-based biomarkers and simple cognitive tests have very high sensitivity for detection of Alzheimer's disease at an earlier stage. Currently, Alzheimer's disease is mainly diagnosed through clinical examination, including a lumbar puncture combined with tests of cognitive ability and brain imaging (PET). PET diagnostics is a nuclear medicine imaging method used to identify differences between healthy brains and brains in patients with Alzheimer's. There is a great need to be able to correctly diagnose Alzheimer's in order to include a relevant population in clinical trials to develop drugs for the disease, and the development that is taking place in the field, including in blood-based biomarkers, entails significant progress for the area.

Great need for new pain treatments
In the US alone, an estimated 50 million adults live with chronic or severe pain, and more people suffer from pain than diabetes, cardiovascular diseases and cancer combined. Data from Europe show similar results and the health and socioeconomic costs are estimated at 3–10 percent of gross domestic product in Europe. Regarding the efficacy of currently available drugs in the field, for example, approximately 80 percent of patients with neuropathic pain do not respond adequately to current treatment. Because of the risk of abuse, overdose and secondary injuries, there is also an effort to avoid opioids for treatment of pain. Consequently, there is currently a high unmet medical need for new, non-opioid treatments in this field.

Alzheimer's disease

Alzheimer's is the most common form of dementia, with around 60–80 percent of all dementia cases stemming from this illness. It is a deadly disease that has a huge impact on sufferers and their relatives alike. Yet despite this, there is currently a lack of preventive and disease-modifying treatments in the global market.

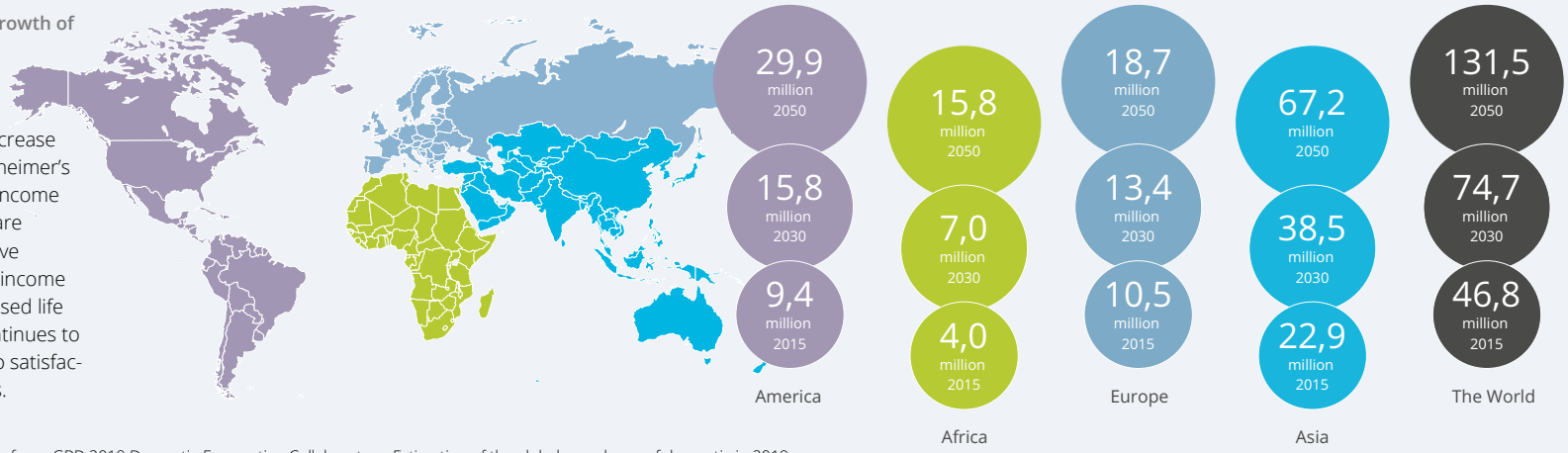
Alzheimer's disease is a neurodegenerative disease, which is a collective term for various conditions in which the nerve cells of the brain gradually deteriorate and eventually die. Nerve cells have very limited regeneration and damage to them therefore becomes clear and crucial for the functionality of the nervous system. Nerve cell death in the brain in connection with Alzheimer's manifests through a variety of symptoms, such as impaired memory, as well as difficulties finding words, expressing oneself and understanding. Difficulties with the concept of time are also common. Eventually, sufferers experience orientation problems in their surroundings, and difficulties reading, writing and counting or managing practical tasks. Some have problems with perception and difficulty in recognizing what they see, and reasoning and planning become more difficult. With the passage of time, sufferers become more and more dependent on help from relatives and/or care services. Because a characteristic of the disease is its gradual onset, it can be difficult to identify when the problems actually began. Symptoms may also vary from person to person.

Alzheimer's is the most common form of dementia, with around 60–80 percent of all dementia cases stemming from this illness. Even though it is a deadly disease that has a huge impact on both sufferers and their relatives, currently no preventive or disease-modifying treatments are available. The disease starts with amyloid beta (Aβ) protein beginning to clump in the brain, which ultimately form the amyloid plaques so characteristic of the illness. These have a negative impact on nerve cell function and lead, inter alia, to reduced levels of important neurotransmitters in the brain. These neurotransmitters, such as acetylcholine and glutamate, are necessary for nerve cells to communicate with each other and for the normal operation of the brain. With time, the ability of nerve cells to survive also deteriorates and they die.

The reasons that some individuals develop the disease while others do not are as yet unknown, but it is clear that accumulations of Aβ amyloid in the brain play a central part in Alzheimer's. The most common risk factors for developing Alzheimer's are old age and genetic proclivity. The disease may appear early, between the ages of 40 and 65 for the hereditary form, but is most common after 65. The course of disease begins many years before the brain suffers from widespread nerve cell death and the patient shows clinical symptoms. A person diagnosed with Alzheimer's disease lives for an average of four to eight years after being diagnosed.

Geographic distribution and expected growth of prevalence of dementia

The figure shows the expected growth in the number of cases of dementia between 2015 and 2050. The largest increase in number of cases of dementia and Alzheimer's is expected to occur in low and middle-income countries (LMIC), since these countries are expected to demonstrate a higher relative improvement in quality of life than high-income countries (HIC), which leads to an increased life expectancy. The need for treatment continues to be very high since there are currently no satisfactory treatment options for such patients.



* Updated with figures based on estimated growth from: GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health. 2022 Jan 6:S2468-2667(21)00249-8.

Today, growing sums are being invested in medical research in Alzheimer's due to the extensive human suffering and considerable costs to healthcare and society. Total global costs for dementia-related illnesses are estimated to exceed USD 1.3 trillion, which is expected to nearly triple by 2050. The lack of effective symptom-relieving treatments and efficacious treatments that slow or prevent the course (disease-modifying) of the disease have led to an urgent medical need. The few approved drugs sold in today's global market have only a limited symptom-relieving effect and entail problematic side effects. Thus there is a very urgent medical need for new symptomatic and disease-modifying treatments. A disease-modifying therapy for Alzheimer's is considered capable of generating more than USD 15 billion in annual sales.

In June 2021, the FDA approved a new Alzheimer's drug in the US, Aduhelm™ (aducanumab), for which one year of treatment costs about USD 28,000. Subsequently, three additional antibody drugs for the treatment of Alzheimer's disease received "Breakthrough Therapy Designation" from the FDA. This status provides access to FDA's other "fast track" processes. Applications for approval of two of these drugs were also submitted to the FDA. One of these, the antibody drug Leqembi (lecanemab), received full approval from the US Food and Drug Administration (FDA) in July 2023, after receiving conditional approval in January 2023. One year of treatment costs about USD 26,500. Another antibody drug, Donanemab, received full market approval in the US in July 2024. This approval demonstrates an accessible regulatory pathway for drugs within the field and has led to growing interest in research into new drugs for Alzheimer's disease. The results of the studies with these new Alzheimer's drugs have also validated the amyloid hypothesis – that Aβ plays a central role in the development of the disease in Alzheimer's patients.

Symptoms

Usually, the first signs of Alzheimer's are impaired memory, difficulties in finding words, expressing oneself and understanding. Difficulties with the concept of time are also common. Eventually, sufferers experience orientation problems in their surroundings, and difficulties reading, writing and counting or managing practical tasks. Some have problems with perception and difficulty in recognizing what they see, and reasoning and planning become more difficult. With the passage of time, sufferers become more and more dependent on help from relatives and/or care services. Because a characteristic of the disease is its gradual onset, it can be difficult to identify when the problems actually began. Symptoms may also vary from person to person.

Prevalence

As previously mentioned, Alzheimer's is the most common form of dementia, and worldwide over 50 million people were estimated to be living with dementia-related diseases in 2020, a figure that is expected to rise to 82 and 152 million sufferers by the years 2030 and 2050 respectively. Geographical distribution and the anticipated increase in dementia is shown in the figure above.

It is estimated that around 150,000 people in Sweden are living with dementia diseases, a figure that is expected to double by 2050. Every year, around 25,000 people are affected, resulting in major care and healthcare costs for society. The direct costs in Sweden are greater than those caused by cancer and cardiovascular diseases.

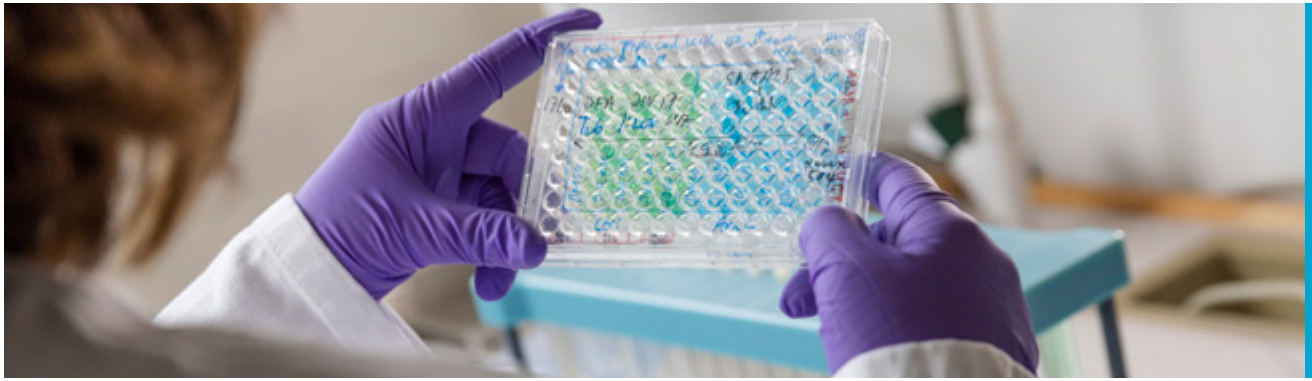
Treatment

On the global market there are currently two different classes of approved symptomatic drugs for the treatment of Alzheimer's disease to improve cognition and memory function.

- Cholinesterase inhibitors: The drug allows the neurotransmitter acetylcholine to work longer in the brain and thus boost nerve cell communications. The drug primarily provides symptom relief, rather than slowing the course of disease.
- NMDA inhibitors: The drug affects glutamate signaling, which plays an important part in nerve cell communications.

However, the effect of the above treatment methods is usually limited and associated with side effects. The most common side effects are gastrointestinal symptoms, including nausea, diarrhea and stomach pain. Other common side effects are problems associated with the heart, high blood pressure, dizziness and headache. The need for new drugs with better symptom-relieving effect and fewer side effects is thus urgent.

AlzeCure's NeuroRestore® and Alzstatin® platforms act in a completely different manner in their treatment of the disease than the drug classes described above. NeuroRestore seeks to improve communication between nerve cells by strengthening the signaling of neurotrophins such as BDNF and NGF, so that memory function is improved in the patient while also avoiding difficult side effects. Alzstatin is aimed at preventing or delaying the very occurrence of the illness by reducing production of toxic amyloid in the brain and thereby preventing the formation of amyloid aggregates such as oligomers and plaque in the brain.



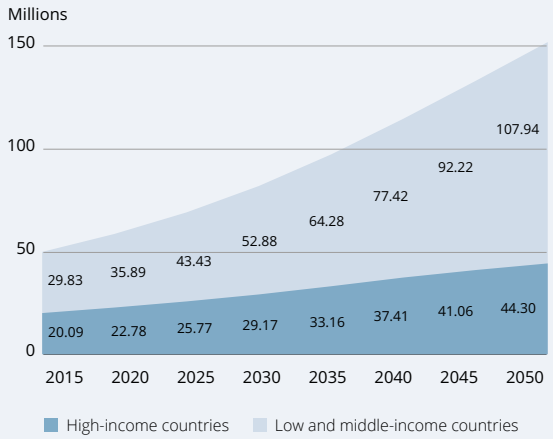
"I am so grateful that AlzeCure is running a project on gamma-secretase modulators (GSMs). There is so much genetic and biochemical data to support this approach, which could be a true primary prevention drug for Alzheimer's.

Henrik Zetterberg, professor at Sahlgrenska University and partner in AlzeCure's Alzstatin GSM project.

> The socioeconomic costs of Alzheimer's disease are currently very high. At the individual level, the problems the disease causes for patients and their families are of course the most important. Currently there is no effective medication for the disease, and subsequently there is a high unmet medical need for both new symptomatic and disease-modifying drugs within this important area.
>
> Professor Bengt Winblad, Karolinska Institutet

The figure below shows the expected growth in the number of cases of dementia between 2015 and 2050*. The largest increase in number of cases of dementia and Alzheimer's is expected to occur in low and medium income countries (LMIC), since these countries are expected to demonstrate a higher relative improvement in quality of life than high-income countries (HIC), which leads to an increased life expectancy. The need for novel therapies continues to be very high since there are currently no satisfactory treatment options for such patients.

The number of individuals with dementia in low and middle-income countries compared with high-income countries



Source: World Alzheimer Report 2015, Alzheimer's Disease International.

Other diseases with cognitive dysfunction

There are several other diseases in which cognitive functions such as memory function and learning are affected; in addition to the classic neurodegenerative diseases such as Alzheimer's and Parkinson's disease, other indications include sleep disorders and traumatic brain injury. The cognitive dysfunction in these indications could be addressed by drug candidates from the NeuroRestore platform.

Sleep apnea

Globally, over 900 million people are estimated to be affected by sleep apnea. A Swedish population study shows that 50 percent of women between the ages of 20 and 70 have mild sleep apnea and that 6 percent suffer from sleep apnea that is severe enough to require treatment. The condition occurs in particular with overweight and high blood pressure. As the population gradually becomes more overweight, the incidence of sleep apnea is also expected to increase. There is also a hereditary component associated with the condition. One consequence of suffering from sleep apnea is that the patient suffers from extreme fatigue, since the body reflexively wakes up when breathing stops. The body also suffers oxygen insufficiency since breathing is absent for long periods and the body does not get a chance to recover. This fatigue also leads to impaired cognitive ability. The patients' symptoms are somewhat similar to Alzheimer's, since memory function, learning and other cognitive abilities are negatively impacted by sleep apnea.

Traumatic brain injury (TBI)

Traumatic brain injury (TBI) is caused by external trauma where the nerve cells in the brain are immediately damaged. TBI is a major global health and socioeconomic problem and is a common cause of death, especially among young adults, and can cause lifelong injuries among those who survive. Every year about 10 million people are diagnosed with TBI worldwide. In North America, TBI affects about 1.7 million individuals annually, with total medical costs of more than SEK 600 billion. The global market for treatment of TBI is expected to grow from SEK 970 billion in 2017 to SEK 1,350 billion in 2024. The two most common causes of TBI are traffic accidents and falls. The majority of other causes of cases of TBI are violence or work or sports-related. The increase in TBI is due in part to the increased use of vehicles in low and middle-income countries.

TBI has been shown to increase the risk of developing dementia-related diseases, such as Alzheimer's disease and other neurodegenerative diseases, such as Parkinson's disease. Studies show that a person who sustains a TBI is at an approximately 24 percent increased risk of suffering from dementia.

The symptoms of TBI may be both physical and mental, and vary depending on the severity of the injury. Common symptoms include memory loss, headache, fatigue, sleep difficulties, concentration difficulties and mood swings. Depression during or after TBI is common. Within one year, half of all people with TBI suffer from depression, and within seven years, two thirds are affected.

Parkinson's disease

Parkinson's disease is a chronic and progressive neurodegenerative disease. The diagnosis is based on the patient having a combination of motor symptoms, such as tremors, mobility impairment, muscle stiffness, and balance and walking difficulties. The symptoms occur mainly as a result of a gradual loss of dopamine-containing nerve cells in the brain. In addition to the motor problems, impairment of cognitive functions such as memory and attention are also common.

Common cognitive problems include difficulties with:

- Attention and concentration.
- Planning such as organizing an eventful day.
- Following complicated conversations and the ability to solve complex problems.
- Being able to quickly formulate thoughts.
- Remembering events or special details, but where clues often guide the memory back.

Dementia associated with Parkinson's disease is not an uncommon type of dementia, accounting for about 1.5–3 percent of all dementia cases.

Pain

Pain, both acute and chronic, afflicts millions of people around the world.
A high proportion of primary care physician visits are due to pain-related conditions.

A Swedish survey found that nearly 30% of patients seen by primary care physicians had a pain-related condition, and about half of these cases involved some form of chronic pain[1]. A WHO study involving 15 primary care centers in various regions of the world found that 22% of patients experienced persistent pain[2]. An estimated 25% to 30% of individuals with chronic pain face significant difficulties in areas such as employment, sick leave, healthcare utilization, perceived care needs and daily life. The societal cost of back pain alone in the Netherlands was estimated at 1.7% of gross domestic product (GDP)[3], with similar findings reported in other countries. According to a report by the Swedish Agency on Health Technology Assessment and Assessment of Social Services, the total economic cost of severe chronic pain was estimated at SEK 85 billion in 2003[4].

Pain can be categorized in different ways, but one of the most common is nociceptive versus neuropathic pain.

Nociceptive pain is the result of activity in signaling pathways caused by tissue damage. Nociceptive pain is usually acute and develops in response to a specific situation, such as postsurgical pain and pain associated with sports injuries. It tends to disappear when the affected body part heals. One example of chronic nociceptive pain that lasts for more than 3–6 months is pain from osteoarthritis.

The body contains specialized nerve cells, which in turn have sensors known as nociceptors. They react to stimuli that can injure the body, such as extreme heat or cold, pressure, pinching and chemicals. These warning signals are then transmitted along the nervous system to the brain. This happens very quickly in real time, such as quickly pulling away hands after touching a hot oven, or not putting weight on an injured ankle.

Neuropathic pain is pain resulting from dysfunction in or direct damage to the nervous system. Neuropathic pain is almost always chronic. Chronic pain is a disabling disease that affects every aspect of the patient's life, which includes the ability of the individual to work and engage in social and leisure activities. Neuropathic pain affects a total of approximately 7–8 percent of the adult population, which means about 600 million people worldwide. People with certain diseases, such as diabetes and HIV, suffer from neuropathic pain to a greater extent; about 25 and 35 percent of patients with these conditions, respectively, experience neuropathic pain.

Peripheral neuropathic pain results from various types of damage to the nerve fibers, such as toxic, traumatic, metabolic, infection-related, or compressional injuries. Common symptoms are painful tingling or itching that can be described as a stabbing or burning pain, including a sensation of getting an electric shock. Patients may also experience allodynia (pain caused by a stimulus that usually does not cause pain) or hyperalgesia (increased pain from a stimulus that normally provokes pain). Examples of conditions associated with neuropathic pain are painful peripheral neuropathy caused by conditions such as diabetes, painful postherpetic neuralgia (shingles), neuropathic pain induced by chemotherapy and/or direct injury to the nerve.

Osteoarthritis – "wear and tear arthritis" – can affect all joints of the body, but most common are the knees, hips, back and shoulders. It was previously believed that this pain was due entirely to local inflammation. It is now known that other mechanisms are involved, and that the pain is primarily nociceptive in nature. Osteoarthritis pain also affects most aspects of the patient's life; in addition to the severe pain itself, it limits mobility and the ability to work, while also making it difficult to engage in leisure activities and a social life. Physical exercise can only help to a limited extent, while existing drug treatments have only a small effect on the pain and should not be given to patients with conditions such as cardiovascular or lung disease. Therefore there is a great need for new effective drugs for the treatment of osteoarthritis pain.

Prevalence

An estimated 50 million adults in the US suffer from chronic pain that requires treatment. More Americans currently suffer from pain than diabetes, heart disease and cancer combined. The data from Europe show similar results and health and socioeconomic costs are estimated at 3–10 percent of gross domestic product in Europe.

The neuropathic pain market is characterized by high unmet medical need in all indications and in all major markets, where only 20–30 percent of patients respond to existing treatments. The patient population is expected to continue to grow, due to factors such as an aging population, an increased incidence of type 2 diabetes, and a growing number of cancer survivors who were previously treated with chemotherapy. The global market for neuropathic pain was valued at about USD 11 billion in 2020 and is expected to grow to USD 25 billion by 2027.

Treatment

There is currently a major medical need for several different severe pain conditions. For example, about 70–80 percent of patients with neuropathic pain do not experience adequate pain relief with existing treatments. Because of the risk of abuse, overdose and secondary injuries, nowadays doctors avoid prescribing opioids as first-line treatment for pain. Despite this treatment problem they are still frequently used, for which reason the need for new treatments that do not involve opioids is great.

1) Hasselström J, et al. Prevalence of pain in general practice. Eur J Pain 2002; 6:375–385.
2) Gureje O, et al. Persistent pain and well-being: A World Health Organization study in primary care. JAMA 1998; 280: 147–151.
3) van Tulder MW, et al. A cost-of-illness study of back pain in the Netherlands. Pain 1995; 62: 233–240.
4) SBU report 2006. Methods of treating chronic pain. A systematic review. Stockholm: Swedish Agency on Health Technology Assessment and Assessment of Social Services (SBU). SBU report no. 177/1+2. ISBN 91-85413-08-9. www.sbu.se.

Comments on the report

Financial overview

SEK thousand	Oct.–Dec. 2024	Oct.–Dec. 2023	Jan.–Dec. 2024	Jan.–Dec. 2023
Net sales	0	0	0	0
Operating profit/loss	-9,576	-10,034	-36,144	-38,262
Earnings for the period and comprehensive income	-9,330	-9,756	-35,234	-37,167
Earnings per share, basic (SEK)	-0.11	-0.16	-0.46	-0.60
Research expenses as a percentage of operating expenses (%)	68.4	70.0	68.2	72.1
Cash flow from operating activities	-7,565	-8,361	-35,123	3,057
Total assets	34,435	32,001	34,435	32,001
Cash and cash equivalents	31,498	29,100	31,498	29,100
Debt/equity ratio (%)	76.0	74.3	76.0	74.3
Average number of shares, basic	88,295,200	62,087,012	77,151,550	62,087,012
Average number of employees	11	10	11	11

See the definitions below.

Revenue and profit/loss

The company had no net sales during the period, which is in line with earlier periods and according to plan.

The operating loss for the fourth quarter of 2024 totaled SEK -9,576 thousand (-10,034). The operating loss for full-year 2024 totaled SEK -36,144 thousand (-38,262). The company continued to conduct research in the fourth quarter of 2024, with steady progress according to plan. Research expenses accounted for 68.4 percent (70.0) of operating expenses in the fourth quarter and a total of 68.2 percent (72.1) for the full year. More information about research at AlzeCure can be found in the "Project Portfolio" and "Project Development" sections of this report.

Administrative expenses this quarter were on a par with such expenses during the same period the previous year. The total for the period January to December is somewhat higher, since the company plans to continue to focus on communication and business development, including internationally. Operating profit/loss is in line with the plan the company had for 2024.

Other operating income for Q4 totaled SEK 142 thousand (45) and includes, in addition to exchange rate gains, a government grant of SEK 30 thousand, as well as certain invoiced consulting services. Other operating income for full-year 2024 was SEK 463 thousand (147), including SEK 300 thousand in grants received.

Other operating expenses mainly consist of exchange rate losses and totaled SEK -55 thousand (-40) for the fourth quarter, and SEK -153 thousand (-104) for the period January to December.

The company had 11 (11) employees on the closing date.

Earnings per share, basic, totaled SEK -0.11 (-0.16) for the fourth quarter, and SEK -0.46 (-0.60) for full-year 2024.

Financial position

At the end of the period, equity was SEK 26,185 thousand (23,774) and the debt/equity ratio was 76.0 percent (74.3). Cash and cash equivalents at the end of the period totaled SEK 31,498 thousand (29,100). The company carried out a rights issue in May 2024 that raised SEK 39.2 million before issue expenses, along with a directed share issue in June, that time to Formue Nord Markedsneutral A/S which chose to receive its agreed compensation as guarantor in shares. The directed share issue totaled SEK 1.6 million. An additional directed share issue was carried out in July as a follow-up to a previous subscription commitment and the company then received SEK 3.7 million before issue expenses.

The company's available funds and equity as of December 31, 2024 are not deemed to be sufficient to cover the liquidity needed to conduct the identified possible activities for the next 12 months. Financing risk continues to be high as a result of the current financial climate and geopolitical turmoil. The Board of Directors continuously reviews the company's long-term financing to ensure its continued progress. Existing projects can be reprioritized as an option to ensure future operations.

At the Annual General Meeting on May 17, 2023, the company launched another incentive program with 500,000 warrants aimed at the company's Chief Executive Officer. For more details, please see "Share-related compensation programs" in the report.

As of the closing date of December 31, 2024, a total of 500,000 warrants were issued. This gives a dilution effect of 0 percent on the closing date.

Cash flow and investments

Cash flow from operating activities including changes in working capital for the fourth quarter of 2024 totaled SEK -7,565 thousand (-8,361). For the period January to December 2024, the corresponding cash flow totaled SEK -35,123 thousand (3,057). The previous year's positive figure is mainly attributable to the receivable that arose in the 2022 accounts relating to the issue proceeds, which were not settled until January 2023.

Cash flow from investing activities totaled SEK -124 thousand (0) during the fourth quarter and the corresponding figure for full-year 2024 is SEK -124 thousand (7). Historically, the company has mainly invested in laboratory equipment, and this year is no exception.

Cash flow from financing activities totaled SEK 0 thousand (0) for the fourth quarter of 2024. For full-year 2024, cash flow from investing activities totaled SEK 37,645 thousand (459). This item represents the proceeds from the rights issue carried out in May and the directed share issues carried out in June and July. The rights issue raised a total of SEK 39,172 thousand for the company, with SEK 32,410 thousand after issue expenses. The directed share issue in June to one of the guarantors of the rights issue raised an additional

SEK 1,642 thousand for the company, less issue expenses of SEK 11 thousand. The directed share issue in July raised SEK 3,740 thousand before issue expenses, which totaled SEK 136 thousand. This results in a net capital injection of SEK 37.6 million. The positive figure from the previous year is mainly due to a credited issue expense, attributable to the issuance in the fourth quarter of 2022, as well as the issue of a new incentive program aimed at the CEO.

Accounting policies and valuation principles

General information and compliance with IAS 34

The company's year-end report has been prepared in accordance with IAS 34 Interim Financial Reporting, with consideration for the exceptions and additions to IFRS stated in RFR 2. AlzeCure Pharma AB (publ) is domiciled in Stockholm.

No expenses during the period have been deemed to meet the requirement for capitalization according to IAS 38. The company's research has not yet advanced far enough for capitalization.

Significant accounting policies and valuation principles

This year-end report has been prepared in compliance with the accounting policies and valuation principles applied in the company's most recent annual report.

Significant estimates and assumptions

When preparing interim reports, the Board and the CEO must, in accordance with the applicable accounting policies and valuation policies, make certain estimates, assessments and assumptions that affect the recognition and valuation of assets, provisions, liabilities, income and expenses. The outcome may deviate from these estimates and assessments and will very rarely amount to the same sum as the estimated outcome.

The estimates and assessments made in the interim report, including the assessment of the main causes of uncertainty, are the same as those applied in the most recent Annual Report.

Key ratios and definitions

Earnings per share: net sales for the period divided by the average number of shares during the period.
Debt/equity ratio: equity, and where applicable untaxed reserves (less deferred tax), in relation to total assets.
Research expenses as a percentage of total operating expenses: Research expenses divided by operating expenses, which include research expenses, administrative expenses and other operating expenses. Research expenses include the company's direct expenses relating to research activities such as expenditures for personnel, material and external services.

Significant risks and uncertainties

The company develops drug candidates and activities will always involve regulatory, market and financial risks. Financing risk is deemed to have increased as a result of the current financial climate and geopolitical turmoil. Financing risk refers to the ability to finance projects to the point of commercialization. The company manages this through timely preparations for raising capital. See also the "Going concern" section below. Otherwise, no significant changes regarding those risks and uncertainty factors took place during the period compared with those presented in the most recent annual report.

The geopolitical situation in the world is very uncertain, and it is difficult to say how it may affect the company's development. The company currently has no transactions or activities associated with Russia.

The general economy, both domestically and internationally, will continue to be a challenge for all companies going forward. The company is very cost conscious and continues to focus on prioritizing activities.

Related party transactions

During the second quarter of 2022, a consulting agreement was signed, on arm's-length terms, with the company Tegnér Biotech Consulting AB, which is owned by Board member Ragnar Linder. The agreement covers consulting services related to business development. During the period January to December 2024 the fee for consulting services totaled SEK 21 thousand, of which SEK 5 thousand was charged to the fourth quarter.

Going concern

A rights issue and two directed share issues were carried out during the period January to September 2024, raising SEK 44.6 million before issue expenses for the company. Consequently, the Board of Directors and the Chief Executive Officer hold the opinion that AlzeCure's financial position has been strengthened in order to advance the key projects and generate great shareholder value. However, the Board's assessment is that cash and cash equivalents and equity as of December 31, 2024 are not sufficient to ensure the operation of the identified potential activities for the next 12 months. Financing risk continues to be high as a result of the current financial climate and geopolitical turmoil. The Board of Directors continues to review the company's long-term financing to ensure its continued development. Existing projects can be reprioritized as an option to ensure future operations.

Reconciliation of alternative performance measures

SEK thousand	Oct.–Dec. 2024	Oct.–Dec. 2023	Jan.–Dec. 2024	Jan.–Dec. 2023
Research expenses as a percentage of total operating expenses:				
Research expenses	-6,648	-7,056	-24,981	-27,707
Administrative expenses	-3,015	-2,983	-11,473	-10,598
Other operating expenses	-55	-40	-153	-104
Total operating expenses	**-9,718**	**-10,079**	**-36,607**	**-38,409**
Research expenses as a percentage of total operating expenses:	**68.4%**	**70.0%**	**68.2%**	**72.1%**
Debt/equity ratio (%) December 31, 2024:				
Total equity at end of period	26,185	23,774	26,185	23,774
Total assets at end of period	34,435	32,001	34,435	32,001
Debt/equity ratio (%):	**76.0%**	**74.3%**	**76.0%**	**74.3%**

The share, share capital & ownership structure

The share

The share has traded on Nasdaq First North Premier Growth Market under the name ALZCUR since November 28, 2018. In the second quarter, a rights issue was carried out that caused the number of shares to increase by 23,042,461 to a total of 85,129,473 shares. Share capital increased from SEK 1,552,175.30 to SEK 2,128,236.825. In the second quarter, a directed share issue to Formue Nord Markedsneutral A/S was conducted, as they had guaranteed part of the AlzeCure's rights issue that ended on May 17, 2024, and wished to receive their agreed compensation as guarantor in shares. As a result, the number of shares increased by 965,727 to a total of 86,095,200 shares. Share capital increased from SEK 2,128,236.825 to SEK 2,152,380. In July, an additional directed share issue was carried out as a follow-up to a previous subscription commitment and the number of shares in the company then increased by 2,200,000 to a total of 88,295,200 shares. Share capital increased from SEK 2,152,380 to SEK 2,207,380.

Share-related compensation programs

In 2023, the company provided an incentive program with warrants aimed at the Chief Executive Officer. A total of 500,000 warrants were issued. The warrants, which were issued at the market price based on an external valuation as of May 17, 2023, entitle the holder to subscribe for shares during the period July 1, 2026 – August 1, 2026. The issue price for newly subscribed shares totaled 150 percent of the volume-weighted average closing price for the company's shares on the Nasdaq First North Premier Growth Market during the 10 trading days preceding the Annual General Meeting on Wednesday, May 17, 2023. For more information, see the minutes from the Annual General Meeting.

The total dilutive effect of the incentive programs is 0 percent on the closing date.

Financial calendar

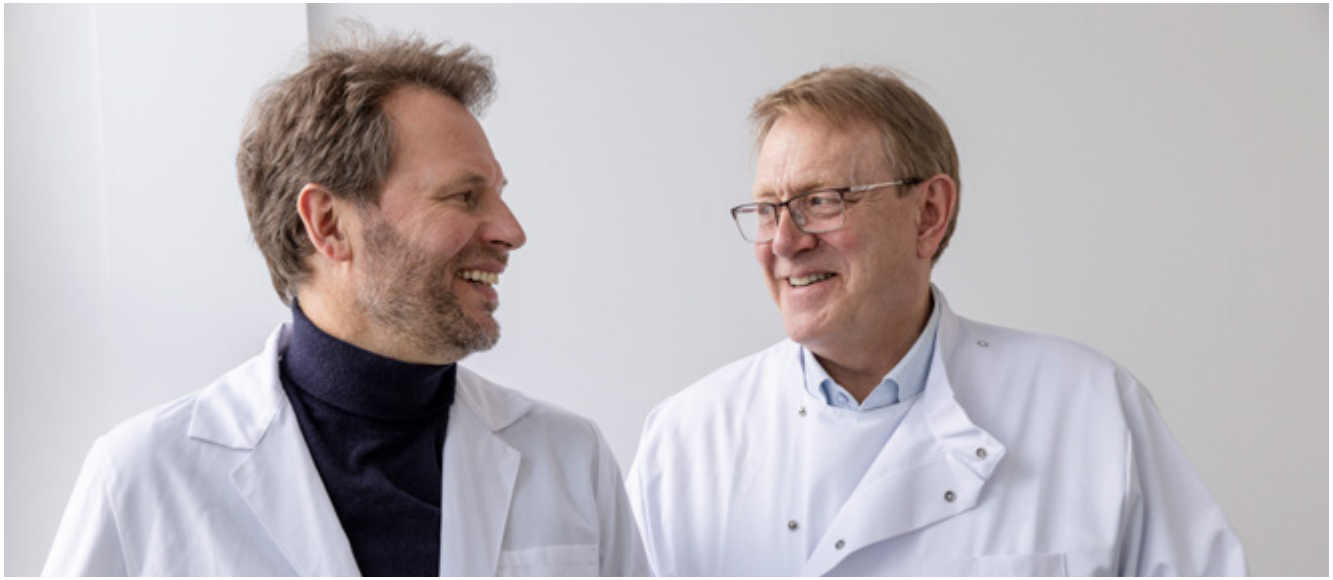
Annual Report 2024	April 3, 2025
Interim report Q1, January–March 2025	May 5, 2025
Annual General Meeting	May 14, 2025
Interim report Q2, April–June 2025	August 26, 2025
Interim report Q3, July–September 2025	November 11, 2025

Nomination Committee

AlzeCure Pharma's nomination committee for the 2025 Annual General Meeting was appointed in accordance with the principles adopted by the Annual General Meeting on May 22, 2019 and consists of: William Gunnarsson, appointed by BWG Invest Sàrl, Rolf Karlsson, appointed by FV Group AB, Peter Thelin, appointed by Sjuenda Holding AB and Thomas Pollare (Chairman of the Board).

Owners as of December 31, 2024

The 10 largest owners as of December 31, 2024	Number of shares	Share capital and votes
BWG Invest Sàrl	13,120,942	14.9%
Sjuenda Holding AB	6,912,752	7.8%
FV Group AB	6,600,000	7.5%
SEB-Stiftelsen	3,429,999	3.9%
Avanza Pension	2,989,581	3.4%
Nordnet Pensionsförsäkring AB	2,947,427	3.3%
Thomas Pollare	2,272,126	2.6%
Futur	2,060,496	2.3%
AlzeCure Discovery AB	1,710,000	1.9%
Acturum Life AB	1,478,872	1.7%
10 largest owners	**43,522,195**	**49.3%**
Other	44,773,006	50.7%
TOTAL	**88,295,200**	**100%**



The Board's assurance

The Board of Directors and the CEO hereby certify that this interim report provides a true and fair view of the company's operations, position and results and describes significant risks and uncertainties facing the company.

Huddinge, Thursday, February 27, 2025

Thomas Pollare
Chairman of the Board

Eva Lilienberg
Board member

Ragnar Linder
Board member

Jan Lundberg
Board member

Janet Hoogstraate
Board member

Martin Jönsson
Chief Executive Officer

This report has not been reviewed by the company's auditors.

For more information, please see www.alzecurepharma.com or contact:
Martin Jönsson, CEO, info@alzecurepharma.com

FNCA is the company's Certified Adviser.
FNCA Sweden AB, info@fnca.se

Income statement and other comprehensive income

SEK thousand	Oct.–Dec. 2024	Oct.–Dec. 2023	Jan.–Dec. 2024	Jan.–Dec. 2023
Net sales	0	0	0	0
Operating expenses				
Research expenses	-6,648	-7,056	-24,981	-27,707
Administrative expenses	-3,015	-2,983	-11,473	-10,598
Other operating income	142	45	463	147
Other operating expenses	-55	-40	-153	-104
Operating profit/loss	**-9,576**	**-10,034**	**-36,144**	**-38,262**
Profit/loss from financial items				
Interest income and similar profit/loss items	246	278	929	1,102
Interest expenses and similar profit/loss items	0	0	-19	-7
Loss after financial items	**-9,330**	**-9,756**	**-35,234**	**-37,167**
Earnings for the period and comprehensive income	**-9,330**	**-9,756**	**-35,234**	**-37,167**
Earnings for the period per share, basic, SEK	-0.11	-0.16	-0.46	-0.60
Earnings for the period per share, diluted, SEK	-0.11	-0.16	-0.46	-0.60
Average number of shares, basic	88,295,200	62,087,012	77,151,550	62,087,012
Average number of shares, diluted	88,295,200	62,087,012	77,151,550	62,087,012

Balance sheet

SEK thousand	Dec. 31, 2024	Dec. 31, 2023
ASSETS		
Non-current assets		
Intangible fixed assets		
Project rights	17	17
Total intangible fixed assets	**17**	**17**
Tangible fixed assets		
Equipment, tools and installations	207	376
Total tangible fixed assets	**207**	**376**
Total non-current assets	**224**	**393**
Current assets		
Current receivables		
Trade receivables	35	0
Other current receivables	1,735	1,469
Prepaid expenses and accrued income	943	1,039
Total current receivables	**2,713**	**2,508**
Cash and bank balances	**31,498**	**29,100**
Total current assets	**34,211**	**31,608**
TOTAL ASSETS	**34,435**	**32,001**

SEK thousand	Dec. 31, 2024	Dec. 31, 2023
EQUITY AND LIABILITIES		
Restricted equity		
Share capital	2,207	1,552
Total restricted equity	**2,207**	**1,552**
Unrestricted equity		
Share premium reserve	399,430	362,440
Accumulated profit/loss	-340,218	-303,051
Profit/loss for the year	-35,234	-37,167
Total unrestricted equity	**23,978**	**22,222**
Total equity	**26,185**	**23,774**
Current liabilities		
Trade payables	2,685	2,687
Other current liabilities	314	592
Accrued expenses and deferred income	5,251	4,948
Total current liabilities	**8,250**	**8,227**
Total liabilities	**8,250**	**8,227**
TOTAL EQUITY AND LIABILITIES	**34,435**	**32,001**

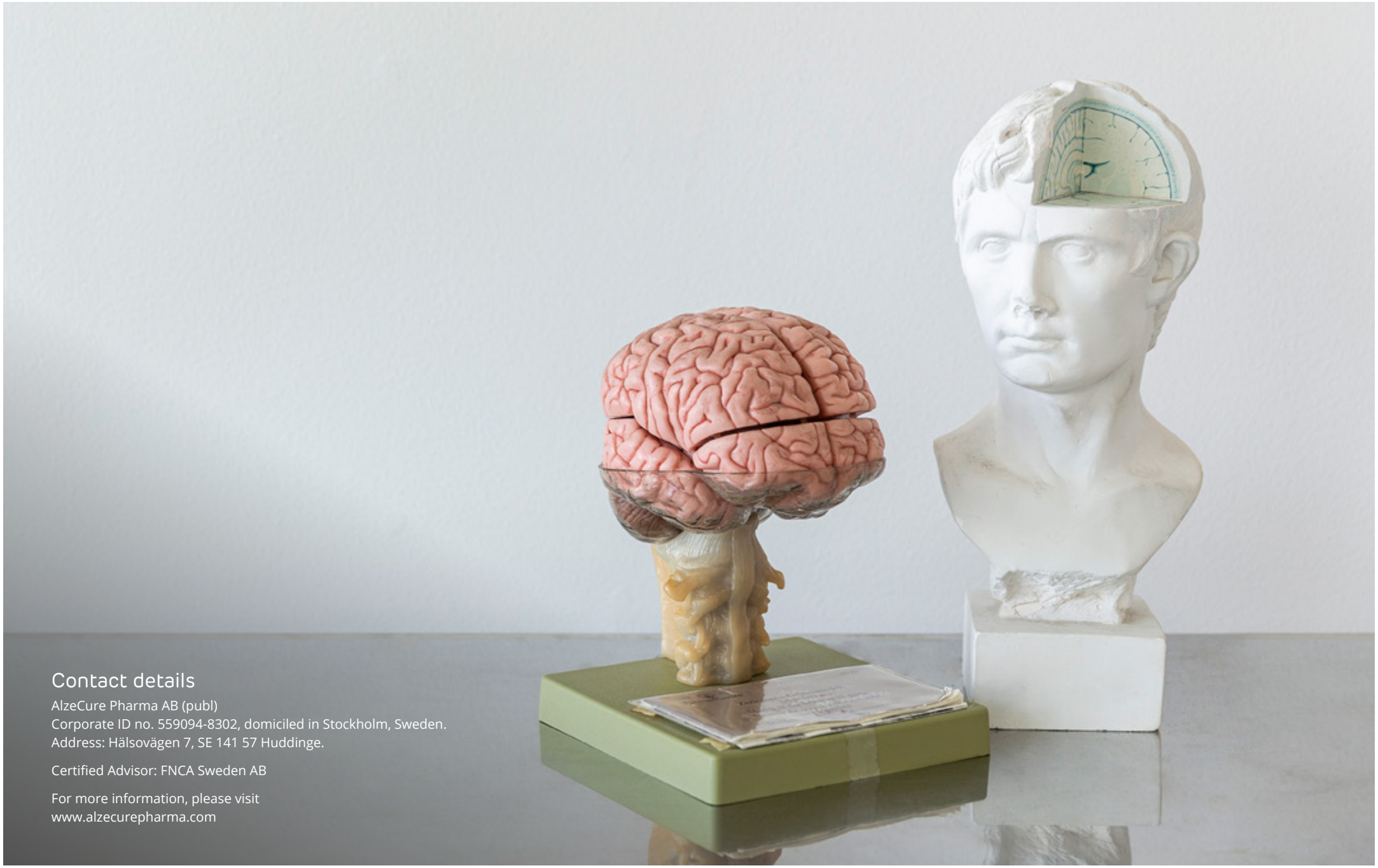
Statement of change in equity

SEK thousand	Share capital	Share premium reserve	Accumulated profit/loss	Profit/loss for the year	Total equity
Opening balance January 1, 2023	**1,552**	**361,981**	**-246,812**	**-56,239**	**60,482**
Appropriation of earnings			-56,239	56,239	0
Rights issue					0
Issue expenses		39			39
Warrants 2023/2026		420			420
Earnings for the year and comprehensive income				-37,167	-37,167
Closing balance December 31, 2023	**1,552**	**362,440**	**-303,051**	**-37,167**	**23,774**

Opening balance January 1, 2024	**1,552**	**362,440**	**-303,051**	**-37,167**	**23,774**
Appropriation of earnings			-37,167	37,167	0
Rights issue	576	38,596			39,172
Issue expenses		-6,762			-6,762
Directed share issue	24	1,618			1,642
Issue expenses		-11			-11
Directed share issue	55	3,685			3,740
Issue expenses		-136			-136
Earnings for the year and comprehensive income				-35,234	-35,234
Closing balance December 31, 2024	**2,207**	**399,430**	**-340,218**	**-35,234**	**26,185**

Cash flow statement

SEK thousand	Oct.–Dec. 2024	Oct.–Dec. 2023	Jan.–Dec. 2024	Jan.–Dec. 2023
Operating activities				
Operating loss before financial items	-9,576	-10,034	-36,144	-38,262
Adjustment for items not included in cash flow, etc.				
Depreciation and amortization	51	110	293	476
Interest received	246	278	929	1,102
Interest paid	0	0	-19	-7
Cash flow from operating activities before changes in working capital	-9,279	-9,646	-34,941	-36,691
Statement of change in working capital				
Change in trade receivables	6	0	-35	0
Change in current receivables	498	-76	-170	41,875
Change in trade payables	1,208	772	-2	-2,158
Change in current operating liabilities	2	589	25	31
Net cash flow from operating activities	**-7,565**	**-8,361**	**-35,123**	**3,057**
Investing activities				
Acquisition of tangible fixed assets	-124	0	-124	0
Repayment of financial fixed assets	0	0	0	7
Cash flow from investing activities	**-124**	**0**	**-124**	**7**
Financing activities				
Issues	0	0	44,554	420
Issue expenses	0	0	-6,909	39
Cash flow from financing activities	**0**	**0**	**37,645**	**459**
Cash flow for the period	**-7,689**	**-8,361**	**2,398**	**3,523**
Cash and cash equivalents at beginning of period	39,187	37,461	29,100	25,577
Cash and cash equivalents at end of period	**31,498**	**29,100**	**31,498**	**29,100**



Contact details

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Certified Advisor: FNCA Sweden AB

For more information, please visit
www.alzecurepharma.com

AlzeCure