# Annual Report 2021

# AlzeCure

#### INTRODUCTION

AlzeCure Pharma in brief3	
History4	
The year in brief5	
A word from the CEO6–7	

#### THE BUSINESS

AlzeCure's development & the path forward	1 8
Mission, Vision & Strategy	9
Business model	9
Market trends affecting AlzeCure10	–11
Alzheimer's disease12	-16
Pain	. 17
Research & Development 18	-19
Scientific advisors	. 20
Project portfolio	. 21
NeuroRestore 22	-23
Alzstatin 24	-25
Painless	-27
Shareholders & Share trend	. 28
Employees	. 29

## REPORT OF THE BOARD OF DIRECTORS & FINANCIAL STATEMENTS

Report of the Board of Directors 31–35
Multi-year overview35
Corporate governance report 36-40
Board of Directors and auditor 41-42
Senior executives
Financial reports 45
Income statement and
other comprehensive income 46
Balance sheet
Cash flow statement 48
Statement of cash flows 49
Notes 50–54
Signatures55
Audit report 56–57
OTHER
Definitions
Shareholder information 59

2022 Annual General Meeting...... 59

AlzeCure Pharma develops new drug therapies for the treatment of severe diseases and conditions that affect the central nervous system, such as Alzheimer's disease and pain, for which currently available treatment is extremely limited. AlzeCure® aims to pursue its own projects through preclinical research and development to an early clinical phase.

AlzeCure's three platforms

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



Painless – two projects: TrkA-NAM and ACD440, which both focus on

severe pain.

# AlzeCure Pharma in brief



AlzeCure<sup>®</sup> 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 and is developing several parallel drug candidates based on three research platforms: NeuroRestore<sup>®</sup>, Alzstatin<sup>®</sup> and Painless.

NeuroRestore consists of two symptomatic drug candidates where the unique mechanism of action allows multiple indications – Alzheimer's disease, as well as cognitive disorders associated with traumatic brain injury, sleep apnea and Parkinson's disease. The Alzstatin platform focuses on developing diseasemodifying and preventive drug candidates for early treatment of Alzheimer's disease and comprises two candidates.

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 solutions for outlicensing to other pharmaceutical companies.

### Strengths & Competitive advantages

AlzeCure considers itself to have a number of strengths and competitive advantages that increase the likelihood of success:

- An organization with extensive experience from industrial drug development in the field.
- Strong background in the genetically linked signaling pathways and biological systems of the indications, which supports the selected target mechanisms.
- The drugs are based on orally available small molecules, which allows for cost-effective long-term treatments.
- Drug development is driven by validated biomarkers and preclinical methods with good translatability to humans.
- An innovative, differentiated portfolio comprising both disease-modifying and symptomatic drug candidates for Alzheimer's and related diseases.
- Several indications and multiple candidates, which lead to risk diversification, not "a one trick pony."
- Strong safety profile in the drug candidates' mechanisms of action.

FNCA Sweden AB, +46(0)8 528 00 399 info@fnca.se, is the company's Certified Adviser. For more information, please visit www.alzecurepharma.se.

# History

### 2012

- The AlzeCure Foundation is formed in the fall in a collaborative effort between a group of prominent AstraZeneca researchers, Alzheimerfonden and Professor Bengt Winblad at Karolinska Institutet.
- The purpose of the organization is to develop new drugs and diagnostics for Alzheimer's and related diseases. When AstraZeneca closed its Alzheimer research operations in Södertälje, a strong need was noted to retain and further develop the important pharmaceutical research in the field of Alzheimer's in the region and in Sweden as a whole.
- A team of senior specialists in complementary fields of pharmaceutical research forms the scientific group that is the core of AlzeCure's operations.

### 2013-2015

- NeuroRestore is the first project when the Foundation initiates research and development at Novum, Karolinska Institutet in Huddinge, which becomes the natural hub for the operation.
- The project portfolio is developed and expanded in part through grants and funding from international grant programs such as the Alzheimer Drug Discovery Foundation and national funding sources such as Vinnova, Swedish Brainpower, Swelife, and Alzheimerfonden.

### 2016

 AlzeCure Pharma is founded because its main drug candidates are considered to have great commercial potential. The two project platforms in the company are NeuroRestore, the product of in-house research, while Alzstatin derives from AstraZeneca's research portfolio, where the project was launched on the initiative of AlzeCure's scientists.

### 2017

- Johan Sandin is appointed CEO for AlzeCure Pharma in February.
- In June, the company completes its first financing round to raise SEK 70 million before issue expenses.

#### 2018

- In July, the company completes its second financing round to raise SEK 40 million aimed at financing phase I studies for ACD855.
- Preclinical testing of ACD855 ends in July.
- IMPD (application to commence studies in humans) for the drug candidate ACD855 is submitted in October.
- The company is listed on Nasdaq First North Premier Growth Market in November.
- The necessary regulatory approvals to begin phase I studies for ACD855 are granted and the company begins dosing the first subjects in December.

#### 2019

- In March the company initiates a new drug project in the field of pain, TrkA-NAM.
- The company is represented at the International Conference on Alzheimer's & Parkinson's Diseases where it gives two presentations.
- In May the company chooses to refocus ACD855 from cognitive dysfunction to ocular indications and ACD856 becomes the primary drug candidate for cognitive dysfunction instead.
- At the annual general meeting on May 22, the company resolves to issue a warrant program aimed at its Board of Directors.
- In December the company obtains the necessary regulatory approvals to initiate the first clinical studies for the drug candidate ACD856 within the NeuroRestore platform. The company initiates the study shortly thereafter.

### 2020

- On January 7, the company in-licenses a new project, ACD440, which focuses on neuropathic pain and is in the clinical development phase.
- Martin Jönsson takes over as Chief Executive Officer on January 8, 2020. Martin has worked in the global pharmaceutical industry for more than 20 years, with extensive experience from various executive positions at both Ferring Pharmaceutical and Roche.
- Johan Sandin takes over the position of Chief Scientific Officer in January, which enables him to dedicate all of his time to research and development.
- Annigje van Es Johansson joins the management group in March as Head of Development & Chief Medical Officer and thereby steps down from the Board of Directors. This arrangement further strengthens the company in a period when it is developing and preparing to increase the number of clinical trials, in line with previously announced plans.
- At the annual general meeting on May 20, the company resolves to issue a warrant program aimed at its Board of Directors.
- In June the company presents favorable data from the first clinical trial with ACD856, which showed that it has a good pharmacokinetic profile with a significantly shorter half-life in humans than its predecessor, ACD855, and that the candidate is suitable for further clinical development as oral treatment of conditions such as Alzheimer's disease.
- In November the company receives approval from the regulatory authorities in Sweden to initiate a Phase I clinical trial with the drug candidate ACD856.
- In December the company receives approval to initiate a phase lb clinical trial with ACD440 in neuropathic pain.
- Favorable preclinical efficacy data for the pain project TrkA-NAM are obtained in December in an in vivo efficacy study.
- The company initiates the preclinical development phase with the drug candidate ACD857 in December.

### 2021

- In April, Associate Professor Märta Segerdahl Storck, MD/PhD, assumed the position of Chief Medical Officer (CMO). Dr. Segerdahl is responsible for the company's clinical development activities. She is also part of AlzeCure's management group.
- In April, positive and significant efficacy data were obtained slightly ahead of plan from the company's Phase Ib clinical trial with the drug candidate ACD440 for neuropathic pain. The drug candidate was also well tolerated as a topical treatment.
- Eva Lilienberg was elected to serve on AlzeCure's Board of Directors at the Annual General Meeting in May. Eva further strengthens the company with her broad international regulatory and commercial experience.
- In August, the company received approval from the Medical Products Agency to be able to further escalate the dose of ACD856 in the Phase I clinical trial (single ascending dose, SAD). The approval is based on the good tolerability of the drug candidate, which enables higher doses to be tested.
- In August, the company received approval from the regulatory authorities in Sweden to initiate a Phase I clinical trial (multiple ascending dose, MAD) for the drug candidate ACD856, with a focus on Alzheimer's disease.
- In October, the first study participant in the company's Phase I clinical trial (MAD) received a dose of the drug candidate ACD856.

# The year in brief

## Continued intensive research

### Significant events 2021

### Q1-Q2

- In April, Associate Professor Märta Segerdahl Storck, MD/PhD, assumed the position of Chief Medical Officer (CMO). Dr. Segerdahl is responsible for the company's clinical development activities. She is also part of AlzeCure's management group.
- In April, positive and significant efficacy data were obtained slightly ahead of plan from the company's Phase lb clinical trial with the drug candidate ACD440 for neuropathic pain. The drug candidate was also well tolerated as a topical treatment.
- Eva Lilienberg was elected to serve on AlzeCure's Board of Directors at the Annual General Meeting in May. Eva further strengthens the company with her broad international regulatory and commercial experience.

### Q3-Q4

- In July, a new article about ACD856 was published in the periodical "Cells," presenting the findings and describing the preclinical development of the compounds in the NeuroRestore platform. (Identification of Novel Positive Allosteric Modulators of Neurotrophin Receptors for the Treatment of Cognitive Dysfunction, Cells 2021 Jul23;10(8):1871.)
- New data supporting ACD856 for treatment of Alzheimer's disease were presented at the Alzheimer's Association International Conference (AAIC) 2021, which was held July 26–30 in Denver, Colorado, in the US.
- In August, the company received approval from the Medical Products Agency to further escalate the dose of ACD856 in the Phase I clinical trial (single ascending dose, SAD). The approval is based on

the good tolerability of the drug candidate, which enables higher doses to be tested.

- In August, the company received approval from the regulatory authorities in Sweden to initiate a Phase I clinical trial (multiple ascending dose, MAD) for the drug candidate ACD856, with a focus on Alzheimer's disease.
- In October, the first study participant in the company's Phase I clinical trial (MAD) received a dose of the drug candidate ACD856.
- The company presented the potential of the NeuroRestore project for treatment of depression at the European College of Neuropsychopharmacology (ECNP) 2021 conference, held October 2–5 in Lisbon, Portugal.

# Significant events after the end of the financial year

- The company receives feedback from the FDA that supports the continued clinical development program for ACD440, as well as preparations for the upcoming Phase II clinical trial.
- The Board of Directors approved a rights issue, subject to the approval of the Extraordinary General Meeting on March 1, 2022.
- The right issue was completed on March 22 and the company will receive SEK 48.5 million before issue costs.
- The company receives new indicative data from the ongoing clinical phase I MAD study with ACD856 showing that the substance reaches the brain, the target organ for the substance which is developed as a treatment for Alzheimer's disease.

### Multi-year overview

SEK thousand	2021	2020	2019	2018
Net sales	0	0	0	0
Operating profit/loss	-77,926	-71,579	-50,908	-35,893
Earnings for the year and comprehensive income	-77,781	-71,366	-50,858	-35,985
Earnings per share, basic (SEK)	-2.06	-1.89	-1.35	-1.58
Research expenses as a percentage of operating expenses (%)	85.0	86.3	87.7	92.8
Total assets	45,647	117,827	186,755	237,782
Cash and cash equivalents	41,741	112,434	182,499	234,549
Debt/equity ratio (%)	72,2	94.0	97.5	98.0
Average number of shares, basic	37,765,715	37,765,715	37,765,715	22,774,048
Average number of employees	11	8.0	4.0	1.5

AlzeCure has yet another positive and eventful year during which its operations progressed totally according to plan, with advances in all three of our project platforms: NeuroRestore, Alzstatin and Painless. During the last quarter we started a MAD Phase I clinical trial, which is AlzeCure's third clinical trial with ACD856, the company's leading drug candidate in the NeuroRestore platform, which focuses on Alzheimer's disease.

Martin Jönsson, CEO AlzeCure Pharma

# A word from the CEO

The year 2021 held many successes for AlzeCure. During the fourth quarter we started a MAD Phase I clinical trial, which is AlzeCure's third clinical trial with ACD856, the company's most advanced drug candidate in the Neuro-Restore platform, which focuses on Alzheimer's disease. We also submitted an application for a "pre-IND meeting" with the U.S. Food and Drug Administration (FDA) prior to a Phase II trial with the Painless project ACD440. In addition, favorable preclinical results were obtained for a new series of molecules for Alzstatin. In other words, the organization continued to deliver and make progress within our projects throughout 2021, and we look forward with great confidence to 2022. In light of these advances and ongoing value-creating activities, a rights issue raised capital to further strengthen AlzeCure.

AlzeCure continues to make good progress, especially in areas that have become increasingly relevant in 2021 and have drawn greater attention. Interest in Alzheimer's disease has continued to grow, which was particularly evidenced by the FDA's approval over the summer of a new and controversial antibody drug for the disease, Aduhelm<sup>™</sup> (aducanumab), the first new drug to be approved in 18 years. In 2022, we can expect additional antibody drugs for treatment of Alzheimer's to receive FDA approval.

Through its actions and announcements in 2021, the FDA has demonstrated its understanding of the great medical need in this area, as well as its support for the amyloid hypothesis: that the build-up of harmful amyloid beta in the brain plays a fundamental role in the onset and development of Alzheimer's disease.

The FDA decisions and the increased activity in the field of Alzheimer's are highly encouraging, both for patients and for AlzeCure with respect to interest from Big Pharma in our Alzheimer's projects. We see great benefits from our projects, which are based on small molecules that do not require invasive administration in the inpatient setting, but can be taken as a tablet at home. Small molecules can also be more easily designed for more efficient penetration of the blood-brain barrier and they are often simpler to produce and and therefore more cost-effective than biologics. Given that the dementia and Alzheimer's patient population – currently approximately 50 million patients worldwide – is expected to triple within the next 30 years, there will be high demand for cost-effective preventive therapies that avert damage to brain structures.

Our Alzstatin project platform aims to develop preventive disease-modifying treatments for Alzheimer's disease by reducing production of harmful amyloid-beta and thereby preventing accumulation of pathological amyloid in the brain. In the Alzstatin program we have preclinical studies that have shown that we can reduce the quantity of harmful amyloid-beta by 50 percent. The Alzstatin project ACD679 is currently in the preclinical development phase. Meanwhile, research continues in the ACD680 follow-up project. With multiple preclinical projects, we can ensure that we have the best possible compound when we move into clinical trials. In the fourth quarter, we also generated new positive preclinical data with a completely new series of molecules that are expected to be advantageous from a patent perspective.

ACD856, is our most advanced drug candidate in the innovative NeuroRestore platform with a primary focus on treatment of Alzheimer's disease to improve learning and to counteract memory and other cognitive problems. The SAD (Single Ascending Dose) clinical trial with ACD856 is evaluating tolerability and safety. During the third quarter, we received positive data in the study and applied to test even higher doses, which was granted by the Swedish Medical Products Agency. These studies are currently



underway, as is the MAD (Multiple Ascending Doses) Phase I clinical trial, in line with our communicated objectives. Our other drug candidate in the NeuroRestore platform, ACD857, is in the preclinical development phase. We plan to continue to develop this compound for an indication within the field of cognitive dysfunction, which also includes Alzheimer's.

We also see continued promising progress in our pain platform Painless, which consists of two projects, ACD440 and TrkA-NAM. ACD440 is a TRPV1 antagonist for topical use aimed at treating neuropathic pain. The project is based on discoveries that garnered the Nobel Prize in Physiology or Medicine in 2021. The groundbreaking discovery of TRPV1 and its link to pain perception is of great significance and we have used it in our ACD440 clinical program. Based on the positive results from the Phase Ib clinical trial of ACD440, which were obtained earlier than expected in 2021, we were able to report both positive pain relief effects and significant safety and tolerability results.

The neuropathic pain indication generates global pharmaceutical sales of USD 11 billion each year and annual growth is expected to be substantial, reaching over USD 25 billion by 2027 (Global-Data, 2021). Nevertheless, the medical need remains great. It is assessed that as many as 80 percent of patients with neuropathic pain today do not achieve adequate pain relief, which indicates the potential within the field and for our ACD440 project. Using this as a point of departure, in 2022 we intend to initiate a Phase II clinical trial with ACD440 among patients who suffer from chronic neuropathic pain. As part of the preparations, we submitted an application to the FDA for a pre-IND meeting in the fourth quarter, and the response we received provided good guidance for the project moving forward.

TrkA-NAM, our second pain project within the Painless platform, is aimed at treating severe pain conditions. One example is osteoarthritis of the knee, which is estimated to affect over 300 million people. After having obtained additional positive preclinical efficacy data in 2021, we are working on selecting a final drug candidate for the project. There are many potential indications for TrkA-NAM and the previous outlicensing deals made with TrkA-NAM molecules reveal great interest in the field, including the possibility of finding an alternative to opioids, which the US authorities are actively trying to replace. Already at this early stage, we have seen interest in the project from Big Pharma.

During the year we continued to have a strong focus on marketing communication and participated in several meetings and conferences. In 2021, we held symposia on our various project platforms, such as NeuroRestore and Painless. Together with Professor Maria Eriksdotter from Karolinska Institutet and others, we arranged a symposium in the autumn focusing on NeuroRestore. The symposia we arranged, which were very well received, have been recorded and are available on our website.

AlzeCure continued to deliver and make progress within our projects throughout 2021, and we look forward with great confidence to 2022.

During the year, we also published and participated in several publications, including abstracts and posters, at scientific congresses (AD/PD, IASP, AAIC and ECNP), as well as in scientific articles, including in the journal Cells, regarding our NeuroRestore platform and project ACD856<sup>1</sup>, and a publication related to Alzstatin (Gamma Secretase Modulator)<sup>2</sup>. These publications demonstrate the interest in and the scientific quality of the data we generate. We continue to work on reaching out to both private and institutional investors, as well as other pharmaceutical and research companies that may be interested in investing in or in-licensing our development projects, or alternatively in entering into a partnership.

I am pleased and proud to report that in 2021, the AlzeCure team of dedicated, motivated and ambitious employees continued to make good progress. We continue to have several promising projects under development within fields with great unmet medical need, which is incredibly satisfying and motivating. We view the growing interest in the field of Alzheimer's and interest in AlzeCure as a company as an acknowledgement that we are on the right path and we continue to be confident about the future.

In light of the successful developments during the year and the planned studies for our development projects, the Board of Directors decided to raise capital, with the aim of further strengthening AlzeCure and facilitating accelerated value creation for our shareholders. The funds from the rights issue will primarily be used to develop our drug candidates in all research platforms in order to achieve some of the important development goals set for the projects: initiation of a Phase IIa clinical trial with ACD440 regarding neuropathic pain, and advancement of development of the TrkA-NAM pain program and the ACD680 Alzheimer's project to preclinical safety tests.

I would like to take this opportunity to wish you a good 2022 with hopes of many advances for AlzeCure.

Stockholm April 2022 Martin Jönsson

Feb;26(3):880-892.

# Nobel Prize

ACD440 is a TRPV1 antagonist for topical use aimed at treating neuropathic pain. The project is based on discoveries by Professor David Julius, which garnered the Nobel Prize in Physiology or Medicine in 2021.

1) Dahlström M et al. Identification of Novel Positive Allosteric Modulators of Neurotrophin Receptors for the Treatment of Cognitive Dysfunction. Cells. 2021 Jul 23;10(8):1871.

2) Weber TA et al. y-Secretase modulators show selectivity for y-secretase-mediated amyloid precursor protein intramembrane processing. J Cell Mol Med. 2022

# AlzeCure's development & the path forward

AlzeCure Pharma develops new drug therapies for the treatment of severe diseases and conditions that affect the central nervous system, such as Alzheimer's disease and pain, for which currently available treatment is extremely limited. AlzeCure<sup>®</sup> aims to pursue its own projects through preclinical research and development to an early clinical phase.

AlzeCure's two innovative small molecule platforms in neurology, NeuroRestore® and Alzstatin®, as well as our latest pain projects, TrkA-NAM and ACD440, are all making good progress in their development. The company has the explicit goal of developing new therapies for Alzheimer's disease and pain – severe disorders affecting the nervous system and for which there is currently no effective treatment. In Alzheimer's we are working on therapies aimed at both symptomatic relief and prevention, where our two unique project platforms focus on two key findings related to the disease: the accumulation of amyloid in the brain and the disruption of normal nerve cell function that leads to the symptoms of the disease. In the field of pain we focus on both nociceptive and neuropathic pain.

AlzeCure has two of its drug candidates in clinical trials. A diversified portfolio of drug candidates that act on central signaling pathways in the brain also opens up for other indications such as cognitive dysfunctions in traumatic brain injury, sleep disturbances and Parkinson's disease.

#### Important milestones for 2022

In 2022, AlzeCure intends to work to meet the following milestones in order to achieve its vision to become a leading neuroscientific research and development company that provides great value to patients, relatives and society:

- Initiation of Phase IIa clinical trial with ACD440 regarding neuropathic pain.
- Present the results from the clinical phase la MAD (multiple ascending dose) study regarding ACD856, a drug candidate focused on AD.
- Advancing the TrkA-NAM pain program toward preclinical safety tests.
- Advancing the development of ACD680, a drug candidate focused on prevention of Alzheimer's disease, toward preclinical safety tests.

#### Important milestones for 2022



### Patents

A strong patent portfolio is crucial for successful commercialization of our projects.

AlzeCure Pharma has an active patent strategy and has established a broad portfolio of patents and patent applications for the projects. It includes seven different patent families. Four of them are approved patents in different territories, while three have reached the stage where the application has been submitted to all of the current major pharmaceutical markets, including the US, EU, Japan and China, as well as territories that are potential major pharmaceutical markets in the future. An application for the ACD440 topical product was submitted in May 2021. Patent applications covering ACD856 are waiting in 19 territories. If they are granted, the resulting patents could provide protection until February 2039 and possibly longer in areas where extensions are available.

The company believes that there is good potential to achieve global protection for its drug candidates. AlzeCure believes that by having more applications in this field, flexibility increases with respect to future partnerships.

AlzeCure plans to expand the patent portfolio within the key areas with additional applications in 2022.

# Mission, Vision & Strategy

#### Mission

We are resolved in our commitment to provide hope and relief to patients and their families by developing innovative, groundbreaking drugs in the fields of Alzheimer's disease, pain and other severe diseases.

#### Vision

Our vision is to become a leading neuroscientific research and development company that creates great value for patients and society.

# **Business model**

AlzeCure<sup>®</sup> 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 developing several parallel drug candidates based on three research platforms: NeuroRestore<sup>®</sup>, Alzstatin<sup>®</sup> and Painless.

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 solutions for outlicensing to other pharmaceutical companies.

AlzeCure continually evaluates possibilities for future collaboration agreements and commercial licensing agreements with leading pharmaceutical companies that can contribute R&D, manufacturing, commercialization and geographical reach to enhance the value of the Company's drug platforms and drug candidates.

### Strategy

AlzeCure Pharma's strategy is to develop a broad portfolio of symptomatic, disease-modifying and preventive drugs for Alzheimer's, pain and other serious illnesses through work based on the following four guidelines:

- The right patient: Focusing on genetically, clinically and pathologically defined diseases to increase the ability of clinical effect.
- The right mechanism: The treatment acts on genetically associated signaling pathways in Alzheimer's disease and other indications.
- The right clinical design: The clinical studies are based on validated biomarkers and preclinical methods with good transfer to humans.
- The right treatment: Small molecule drugs that penetrate the blood brain barrier (BBB) and which are designed for safe, efficacious long-term treatments.



### Drugs based on small molecules

AlzeCure's drug candidates are based on small molecules, which offer several advantages over biologics:

- Small molecules can be designed to provide better permeability across the blood-brain barrier than biologics, and are therefore well suited for treatment of diseases of the brain.
- Small molecules can be given as oral treatment, in tablet form, which is both convenient and costeffectively advantageous for the patient compared with invasive intravenous injections, which must often be administered by care providers.
- Small molecules are less expensive to produce than biologics, which could potentially provide price-related advantages, for example with respect to long-term treatment of chronic diseases.



Illustrative comparison between biological and small molecule drugs.

# 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 trillion and is expected to 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 diseasemodifying 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. Three other antibody therapies targeting amyloid pathology have also recently been 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.

# 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. In 2018, over 64 percent of all new drugs approved by the FDA came from small research and development companies.

#### Development related to diagnostics & biomarkers

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). A spinal fluid test is an invasive procedure in which spinal fluid is drawn for analysis. 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 correct 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, heart disease 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 opiates for treatment of pain. Consequently, there is currently a high unmet medical need for new, non-opiate treatments in this field.

#### **Biomarkers**

AlzeCure is working closely with leading researchers in the field of biomarkers, such as Professor Henrik Zetterberg, who is considered to be a world authority in the field. Using measurable markers, often biological molecules such as proteins, changes can be detected in the disease scenario, but the effects of treatment can also be assessed. Hlin Kvartsberg, who earned her PhD in a joint doctoral program at AlzeCure and Sahlgrenska Academy at the University of Gothenburg, was awarded a prize in 2020 for her thesis on new biomarkers in the disease. The company intends to use these advances in diagnostics and thereby ensure that the right patients in the right phase of disease are included in the clinical phases. Including the right patient population will increase the likelihood of success. "Diagnostics and biomarkers within the field of Alzheimer's is an active field of research, where key advances made in recent years have been of great importance for diagnostics, as well as for evaluating new drug candidates."

> Professor Henrik Zetterberg University of Gothenburg; University College of London

# Alzheimer's disease

Alzheimer's is the most common form of dementia, with around 60–70 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.

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 (A $\beta$ ) 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 A $\beta$  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.





Today, growing sums are being invested in medical research in Alzheimer's due to the extensive human suffering, and the costs to healthcare and society are considerable. Total global costs for dementia-related illnesses were estimated at around USD 1 trillion, which is expected to triple by 2050. The lack of effective symptomatic treatments and efficacious treatments that slow or prevent the course (disease-modifying) of the disease represent an urgent medical need. The few approved drugs sold in today's 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<sup>™</sup> (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 lecanemab and donanemab were submitted to the FDA during the autumn. Taken together, this trend reveals an accessible regulatory pathway for drugs within the field, thereby leading to growing interest in research into new drugs for Alzheimer's disease.

#### 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

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.

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.

#### 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 of both cholinesterase inhibitors and NMDA inhibitors 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. In addition to these drugs, there is also an approved amyloid beta antibody treatment in the United States. In June 2021, the FDA approved a new drug for Alzheimer's disease in the US, Aduhelm™ (aducanumab).

AlzeCure's NeuroRestore® and Alzstatin® platforms act in a completely different manner in their treatment of the disease than the drugs 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. **))** The socioeconomic costs of Alzheimer's disease are currently very high. At the individual level, of course, the problems the disease causes for patients and their families are most important. Currently there is no effective medication for the disease, for which reason there is a high unmet medical need for both new symptomatic and disease-modifying drugs within this important area.

Professor Bengt Winblad, Karolinska Institute

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 treatment 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 middleincome countries compared with high-income countries



# 50%

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 so severe that they require treatment.

# 10 million

Every year about 10 million people suffer from TBI worldwide. The global market for treatment of TBI is expected to grow from SEK 970 billion in 2017 to SEK 1,350 billion in 2024.



# 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

More than 900 million people worldwide suffer from sleep apnea, the majority of whom are undiagnosed. 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 so severe that they 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 suffer from 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.

"We develop drugs to help treat one of the few common disorders that currently lack effective treatment."

## 50 million

As previously mentioned, Alzheimer's is the most common form of dementia, and worldwide around 50 million people is estimated to be living with dementiarelated diseases, a figure that is expected to rise to 82 and 152 million sufferers by the years 2030 and 2050 respectively.

## 150,000

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 are estimated to be higher than those caused by cancer and cardiovascular diseases.



### About Alzheimerfonden

Alzheimerfonden (the Swedish Alzheimerfonden) is the only fundraising organization in Sweden that focuses solely on grants for research on Alzheimer's disease and other dementia diagnoses. Annual research grants from Alzheimerfonden are crucial for conducting research projects in this field in Sweden. Major research advances have been made in recent times, but more resources are needed to succeed in finding a drug to cure or to slow the progress of the disease. Alzheimerfonden does not receive any government grants; its activities are funded entirely by donations from private individuals and businesses. Swedish Alzheimer's research is cutting-edge and many Swedish researchers are world leaders at the forefront of the field. A substantial increase in funding is therefore crucial so that projects can be conducted more optimally and make faster progress.

Alzheimerfonden also engages in extensive public outreach initiatives through seminars, articles, participation in discussions, etc. The organization also supports relatives in various ways, such as in the case of young relatives with parents who suffer from cognitive impairment. Alzheimerfonden provides annual grants to healthcare workers who want to pursue postgraduate programs in the fields of cognitive impairment care and dementia care for nurses and doctors, as well as for occupational and physical therapists, since we believe that such care should be provided by well-educated staff.

Alzheimerfonden will continue to pursue efforts to be a leading organization in the field of Alzheimer's and our aim is to contribute to pioneering new initiatives in research and care. The formation of the AlzeCure research foundation is one such initiative.

> Please support Alzheimerfonden in its activities with a donation via www.alzheimerfonden.se

# Diagnosed with Alzheimer's and became an ambassador



In the summer of 2019, Anders Granqvist was only 52 years old when he was diagnosed with Alzheimer's disease. Anders and his wife Madeleine have chosen to be open about the illness and are now becoming ambassadors for Alzheimerfonden. "Many people just withdraw. It's better to stand up and let people know that we need effective medicines. The more people who do so, the faster that research will make progress," says Anders.

In the summer of 2019, after extensive workup, Anders received the devastating news at the clinic for cognitive disorders at Karolinska University Hospital. He was only 52 years old and the doctor stood there and told him that he had early-onset Alzheimer's disease. One year later, the family, which also includes two children, began to adapt to the new reality by moving to a new home. They had already sold their beloved single-family home in Nacka and would trade it for an apartment better suited to their new lifestyle, with different financial circumstances and Anders' need to be close to the gym, grocery store and municipal transportation when he could no longer drive. Since Anders receiving the diagnosis, everything he had previously exceled at – working with computers and practical things around the house – had begun to fail. You have to take it for what it is. There is not much to do about it. It's just a matter of bracing yourself and doing what you want to do. It's about doing the best you can yourself ", Anders answers the question of what his life is like.

# Pain

Pain, both acute and chronic, afflicts millions of people around the world. 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. An example of chronic nociceptive pain that lasts for more than 3–6 months is pain from osteoarthritis.

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 opiates as first-line treatment for pain. Despite this treatment problem they are still frequently used, for which reason the need for new non-opiate treatments is great.

# Woman suffering from postherpetic neuralgia after developing shingles:

"When I was diagnosed, and if someone had told me then, that – this is what you'll have to live with – then I'd have done something really crazy. This has really destroyed a large part of my life. I can tolerate a lot of pain, I've had breast cancer surgery, received chemotherapy and never complained, but this is horrendous. I've just received a new treatment, but I don't think it helps at all. " Britt.

# 600 million

Neuropathic pain affects a total of approximately 7–8 percent of the adult population, which means about 600 million people worldwide.

# USD 25 billion

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.

**))** One in five people in the population suffers from chronic pain that requires treatment. Living with pain is incredibly stressful for the patient, both physically and mentally. One of three patients seek medical care because of pain. The available treatments are not sufficiently effective and are often associated with addiction problems. There is great potential for a new drug here, especially with a favorable side effect profile and without risk of addiction. Dr. Märta Segerdahl, CMO

# Research & Development

AlzeCure<sup>®</sup> engages in research and development of innovative and effective novel small molecule drugs for 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 four drug candidates based on the two research platforms NeuroRestore<sup>®</sup> and Alzstatin<sup>®</sup>, along with two projects in the "Painless" pain platform – TrkA-NAM and ACD440.

- Within NeuroRestore, a new generation of symptomatic drugs is being developed for the treatment of cognitive dysfunction (memory disorders) in Alzheimer's disease.
- Within Alzstatin, disease-modifying and preventive drugs for early treatment of Alzheimer's patients are being developed.
- TrkA-NAM is a project in research phase aimed at developing a new treatment for severe pain in conditions such as osteoarthritis.
- ACD440 is a drug candidate in the clinical development phase aimed at treating neuropathic pain and was in-licensed in January 2020.

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

#### Neurology

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, with results showing that ACD856 was well-suited for further clinical development. Consequently, continued clinical trials could be initiated at the end of 2020, also according to plan. The results of the "SAD" study (Single Ascending Dose) in August 2021 showed that the compound was well tolerated in humans. In the third quarter of 2021 the MAD study (Multiple Ascending Dose) was also initiated and both of these studies, which are part of the phase I program for the drug candidate, have the primary purpose of assessing safety and tolerability in humans.

# 50 million

In the US alone, an estimated 50 million adults live with chronic or severe pain, and more people suffer from pain than diabetes, heart disease and cancer combined.

# 70%-80%

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.



**11** Neurotrophins such as NGF and BDNF play a key role in the normal function of the brain and new therapies focused on these biological systems can offer exciting new opportunities for treatment of neurodegenerative diseases such as Alzheimer's disease. Our preclinical studies in the field demonstrate potent efficacy in several different relevant models, which supports continued development in the field.

Professor Maria Eriksdotter, Karolinska Institutei

ACD857 is in the research phase and also has the primary indication of cognitive dysfunction/Alzheimer's disease. At the end of 2020, the drug candidate entered into the next development phase, which aims to assess the preclinical safety profile before clinical trials can begin.

AlzeCure's disease-modifying research platform for Alzheimer's disease, Alzstatin, focuses on reducing the production of toxic amyloid beta (A $\beta$ ) in the brain. A $\beta$  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 is confirmed by previously reported study results, which we believe validate the amyloid hypothesis and thus Alzstatin's focus.

The goal is to develop a tablet preparation that will be easily administered within the healthcare system.

The leading drug candidate within Alzstatin, ACD679, is in preclinical phase and alongside this work, the development of an additional drug candidate (ACD680) is in progress to ensure that the company has the best compound for clinical studies.

#### Pain

The Painless platform contains two projects aimed at developing new treatments for pain. Both projects involve non-opiates, which is important to emphasize, because of the inherent risk associated with opiates for abuse, overdose and secondary injuries – which has led to avoidance of opiates as first-line treatment for pain. Despite the problems with opiates they are still frequently used, for which reason the need for new non-opiate treatments is great. In January 2020, a drug candidate in the clinical development phase aimed at treating neuropathic pain, ACD440, 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 data, 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. The company is now planning further Phase II trials.

TrkA-NAM builds on the knowledge amassed and assets developed in the NeuroRestore platform, but with the aim of developing new compounds that focus on providing pain relief in 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 project, which is in the research phase, has strong preclinical and clinical validation. The company received the first positive preclinical efficacy data during the latter part of 2020 and is actively working on the development of a drug candidate for preclinical safety studies. Th de ba Ne

The company is simultaneously developing four drug candidates based on the two research platforms NeuroRestore<sup>®</sup> and Alzstatin<sup>®</sup>.

The company is developing two projects within the "Painless" pain platform – TrkA-NAM and ACD440.

# 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.



Copyrights to BBVA Foundation Frontiers of Knowledge Awards



# Scientific advisors

AlzeCure cooperates with leading researchers and key opinion leaders in the field to ensure that we gain access to the latest advice and findings and optimally design our preclinical and clinical studies. These collaborations have also resulted in publications and a doctoral thesis that was awarded a prize for best PhD thesis at Sahlgrenska Academy.



### Professor Bengt Winblad

#### Karolinska Institutet, Stockholm, Sweden

Professor at Karolinska Institutet in Stockholm and one of the world's most cited researchers in neurodegenerative diseases. In 2016, Professor Winblad was the recipient of the Life-Time Achievement Award from the US-based Alzheimer's Association for his invaluable contributions to Alzheimer's research. Professor Winblad is also the recipient of the Swedish Brain Foundation's Jubilee Award.



#### Professor Henrik Zetterberg

University of Gothenburg and University College London, UK Professor of neurochemistry, Chief physician at Sahlgrenska University Hospital and Professor at University College London (UCL). Professor Zetterberg is also chair of the Swedish Alzheimer's Foundation Scientific Council and is a leading global authority in the field of biomarkers related to neurodegenerative diseases.



#### Professor Peter Snyder

#### University of Rhode Island, USA

Vice President of Research and Economic Development and Professor of Biomedical Sciences at the University of Rhode Island, Kingston, RI. Professor Snyder has extensive experience with leading positions in the field of Neuroscience, including at Pfizer, where he led the development of new compounds for the treatment of schizophrenia and Alzheimer's disease. He is also Senior Associate Editor for Alzheimer's & Dementia: The Journal of the Alzheimer's Association.



#### Associate Professor John Harrison

#### Alzheimer Center, VUmc, Amsterdam, Netherlands

Associate Professor at Alzheimer Center VU Medical Center in Amsterdam and visiting professor at the Institute of Psychiatry, Psychology & Neuroscience at King's College London. Dr. Harrison has more than 20 years of experience in successfully integrating cognitive testing into drug development programs. He has worked with more than 40 drug development organizations in recent years, including 8 of the current Fortune top 10 pharmaceutical companies.



### Dr. Rolf Karlsten

#### University Hospital, Uppsala, Sweden

MD, specialist in anesthesiology and pain management. PhD in pain research 1994. Previously worked as head of Medical Science with a main focus on pain projects in major pharmaceutical companies. Currently head of the Interdisciplinary Pain Center at Uppsala University Hospital, which covers all types of acute and chronic pain conditions.



#### Professor Sven Ove Ögren

#### Karolinska Institutet, Stockholm, Sweden

Professor at Karolinska Institutet, Sweden. Recognized scientist in the field of Neuropsychology with extensive experience in drug development – project leader for two drug products developed from concept to market in the CNS area. More than 400 publications in the field of neuropsychiatry and cognition.

# Project portfolio

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

There are several drug candidates in the various platforms: two candidates in NeuroRestore and two candidates in Alzstatin, as well as two projects that remain in the Painless platform. A diversified portfolio of drug candidates paves the way for other indications, such as cognitive disorders associated with Alzheimer's, traumatic brain injury, sleep apnea and Parkinson's disease, as well as for severe pain in conditions such as neuropathy and osteoarthritis.

- The NeuroRestore platform is a new generation of symptomatic drugs for the treatment of illnesses with cognitive disorders, such as Alzheimer's disease. The target mechanism also has other potential indications, including depression and cognitive disorders in Parkinson's disease, traumatic brain injury and sleep disorders.
- Innovative small molecule disease-modifying and preventive 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 Painless platform includes two projects: TrkA-NAM and ACD440, which both focus on severe pain.
- 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 project is aimed at treating severe pain caused by disorders such as osteoarthritis, which today lacks sufficiently effective treatment. The project is currently in the research phase.

### AlzeCure's project portfolio<sup>1</sup>

Platform	Candidate	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
NeuroRestore	ACD856	Alzheimer's disease Sleep disorders/ Traumatic brain injury Parkinson's disease					
Neu	ACD857	Alzheimer's disease					
atin	ACD679	Alzheimer's disease					
Alzstatin	ACD680	Alzheimer's disease					
less	ACD440	Neuropathic pain					
Painless	Trka-NAM	Osteoarthritis pain					

In progress

Completed

1) For definitions of the phases, please see the AlzeCure Pharma website, www.alzecurepharma.se

# **NeuroRestore**<sup>®</sup>

In Alzheimer's disease, the nerve cells cease functioning as they should, which leads to a deterioration of memory and learning. AlzeCure has identified drug-like compounds that stimulate neurotrophic signaling pathways, thereby strengthening nerve cell function and improving memory.



NeuroRestore is a platform of symptomatic drug candidates for diseases where cognitive ability is impaired, such as Alzheimer's.

NeuroRestore stimulates several important signal pathways in the brain, which among other things leads to improved cognition. In preclinical studies with NeuroRestore, we have been able to demonstrate that our drug compounds not only boost communication between nerve cells but also improve cognitive ability.

The drug candidates in NeuroRestore stimulate signaling of neurotrophins, the most well-known of which is Nerve Growth Factor (NGF) and Brain Derived Neurotrophic Factor (BDNF). These neurotrophins are important for maintaining nerve cell function and communication, which are impaired with cognitive disorders. BDNF plays an important role for nerve cell function and communication in the areas of the brain that are essential for our cognitive ability, such as the hippocampus, located in the temporal lobe. In addition, special "cholinergic neurons" in the basal forebrain depend on NGF to maintain their biological function, but also to survive. Loss of cholinergic neurons in the basal forebrain, as well as dysfunction of normal neuron function and communication in the hippocampus, are early signs of Alzheimer's and correlate with cognitive impairment. The drug candidates in the NeuroRestore platform strengthen the signaling of these two important neurotrophins, which results in improved memory and learning – something that AlzeCure has been able to demonstrate in several different preclinical models.

The levels of NGF and BDNF are disrupted in many diseases and signaling is reduced. This reduced function impairs both communication between the contact surfaces at nerve ends and the function in neurons, which gives rise to cognitive impairment.

There is also genetic support for this target mechanism – a genetic variation of BDNF in humans, leading to a reduction in BDNF secretion, is involved in cognitive impairment related to both neurodegenerative processes seen in Alzheimer's and Parkinson's disease, but also in other cognitive indications such as traumatic brain injury and sleep disorders. AlzeCure also considers there to be a potential for adding further indications based on the specific target mechanism. There is also strong scientific support for this target mechanism in depression. NeuoRestore compounds have



Neurotrophins such as BDNF and NGF bind to Trk receptors on the cell surface and mediate important effects such as strengthening communication between neurons and protecting against injury. NeuroRestore strengthens the dysfunctional signaling that exists in this system in diseases such as Alzheimer's.



AlzeCure has strategically chosen to work on development of small molecule drug candidates – not only to be able to develop effective and safe products, but also to be able to offer medications in tablet format.



demonstrated efficacy in preclinical models for depression, which has been further supported by data in a recently published article in the highly respected publication Cell<sup>1</sup>.

In the preclinical trials, ACD856, the leading drug candidate in the NeuroRestore platform, has been able to demonstrate that it can strengthen signaling in the intended pathway and improve cognitive ability. Among other things, the compound has been able to show that it can reverse age-induced memory impairment and strengthen the effect of existing drugs (acetylcholinesterase inhibitors), which AlzeCure views as a competitive advantage.

AlzeCure started the first clinical trial with ACD856 in December 2019. The study was completed on schedule in the second quarter of 2020, with results showing that ACD856 was well-suited for further clinical development. Continued clinical trials were initiated in late 2020, also according to plan. The results of the SAD study in August 2021 showed that the compound was well tolerated

in humans. 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 the primary purpose of assessing safety and tolerability in humans.

After completed phase I studies, the company plans to carry out a signal detection study for ACD856 in order to be able to evaluate signals of efficacy for the drug candidate at an early stage of the development process. If an early effect is found, validation of the target mechanism will be strengthened and the potential of licensing agreements regarding ACD856, or the entire NeuroRestore platform, will increase considerably.



AlzeCure's primary drug candidates within Neuro-Restore – ACD856 and ACD857 – act as BDNF/NGF signaling enhancers. The biological mechanism that the compounds affect enable their use in several different diseases in which the same signal pathway is disrupted. These indications include:

- Cognitive impairments linked to:
- Alzheimer's disease
- Parkinson's disease
- TBI and other head injuries
- Sleep disruptions
- Complications from major surgery
- Depression

1) Casarotto et al., Antidepressant drugs act by directly binding to TRKB neurotrophin receptors, Cell (2021)

# Alzstatin®

Our disease-modifying research platform, Alzstatin, consisting of both disease-modifying and preventive drug candidates, focuses on reducing the production of toxic amyloid beta (Aβ) in the brain. Aβ plays a key pathogenic role in Alzheimer's and begins to accumulate in the brain years before clear symptoms develop.

Platform	Candidate	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
atin	ACD679	Alzheimer's disease					
Alzstatin	ACD680	Alzheimer's disease					

### Did you know that 60–70 percent of all dementia cases have Alzheimer's disease as the underlying cause?

#### Amyloid-beta

The brain consists of about 100 billion nerve cells (neurons) that are interconnected in an intricate network and are vital for brain function and survival. Autopsies of the brains of Alzheimer's patients show abundant amounts of amyloid (AB) plagues, the accumulation of which is assessed to have a major impact on the course of disease. AB plagues consist of an accumulation of AB peptides, which are formed and secreted by nerve cells in the brain. A $\beta$  is a family consisting of 30–43 building blocks (AB30 – AB43); Of these building blocks, AB42 is the main component in AB plaque. AB42 is particularly "sticky" and has a strong tendency to form clumps. This process is complex and the AB peptide accumulates in smaller aggregates, oligomers and protofibrils, which then form the building blocks of fibrils that form AB plaques. In Alzheimer's disease, the nerve cells are surrounded by these AB aggregates, which affects the communication ability and function of the nerve cells, which in turn leads to them withering and eventually dying. Exactly how AB causes nerve cells to die at the molecular level is not yet known. Much of the data suggest that the ill health of the nerve cells leads to accumulations of another protein, tau, inside the cells and that taken together, this leads to the death of the cells. A clear hereditary connection can be seen in about 1 percent of all Alzheimer's cases. The heredity component involves specific

mutations in any of three specific genes, all of which are directly involved in A $\beta$  peptide production. The common denominator among all these mutations is that they affect the A $\beta$  peptide itself, or its production (relatively more A $\beta$ 42), in a way that accelerates build-up of A $\beta$  plaques, thereby demonstrating the central role that A $\beta$  plays in Alzheimer's, while making this peptide and the amyloid process the most validated disease process in Alzheimer's today.

Major advances in research during the 2000s have made it possible to follow the amyloid process in living individuals over time. A large number of such studies have shown that AB plagues begin to accumulate up to 20 years before symptoms appear and that it more or less reaches its peak and decreases in further growth once the symptoms of the disease begin to become apparent. When clinical symptoms occur, the structure of the brain has begun to change because of diseased nerve cells that have contracted and nerve cells that have died. The brain has literally begun to decrease in size. Several previous clinical trials with AB-targeted drugs in patients with relatively advanced Alzheimer's have failed. Given the new knowledge about how early AB builds up and is stored in the brain, it is likely that these candidates were tested too late in the disease, during a phase when AB had already played most of its pathogenic role. New clinical studies in the field, in which AB-targeted drugs have been administered earlier

in the course of disease, have been able to demonstrate clinical efficacy in patients, thereby strengthening the validity of this target mechanism.

It is clear that A $\beta$ -amyloidosis is a causative agent of hereditary familial Alzheimer's disease, as described above. More and more comparative studies, where the A $\beta$  process in sporadic Alzheimer's has been compared with familial Alzheimer's, show a similar structure of A $\beta$  in sporadic disease, though it usually occurs later in life. These research data strongly suggest that A $\beta$  accumulation also plays a crucial pathological role in sporadic Alzheimer's, which accounts for about 99 percent of cases in Alzheimer's disease.

The drug candidates in the Alzstatin platform are "gammasecretase modulators" (GSM) and affect the function of the enzyme gamma secretase. Gamma secretase acts like a pair of scissors and snips Aβ42 out from a longer protein known as APP. The sticky Aβ42 peptide, which over time forms clumps of so-called oligomers and fibrils that ultimately form the amyloid plaques in the brain so characteristic of Alzheimer's. Mutations in gamma secretase that lead to a relative increase in Aβ42 peptide is the cause of hereditary Alzheimer's disease. This demonstrates the role of Aβ42 in the progression of the disease and is, together with mutations in the Aβ-peptide itself, the strongest known genetic link to Alzheimer's disease. The candidates in the Alzstatin platform affect enzyme function so that it instead snips out shorter forms of the AB peptide, AB37 and Aβ38, which in addition to their not being sticky and not forming aggregates, may also have a restrictive effect on the formation of AB42 aggregates. This means the drug candidates in the Alzstatin platform have two separate but synergistic effects that together contribute to a stronger anti-amyloidogenic – and thus more potent - disease-modifying effect.

The program also benefits from a drug based on small molecules, which enables oral administration (tablets), low production costs and good penetration of the blood-brain barrier.

We have shown in preclinical tests that the modulation of gamma secretase leads to a reduction of up to 50 percent in the production of Alzheimer-related AB42 without affecting other signaling important for cells. The project is further confirmed by positive findings made in the recently published clinical patient studies with BAN2401, Aducanumab, Donanemab, och Lecanemab/BAN2401, which we believe validate the amyloid hypothesis as a treatable and clinically relevant pathological mechanism.

Major advances have also been made in the field of diagnostics with new blood-based tests, providing a cost-effective means of screening high-risk populations and thus identifying the right

patients in the presymptomatic phase of the disease for upcoming clinical studies and future treatments.

The leading drug candidate within Alzstatin, ACD679, is currently in the preclinical development phase. Alongside this compound, the development of an additional drug candidate is in progress (ACD680) to ensure that the company has the best compound for clinical studies. The program is also differentiated by a drug based on small molecules, which enables oral administration (tablets), low production costs and good penetration of the blood-brain barrier.



the formation of shorter fragments that prevents the aggregation effect

AB42 slowly accumulates to form an aggregate growing from monomers to oligomers, fibrills and ultimately plague. Research has not yet identified what in these processes, or which molecular form, is most harmful to nerve cells and causes the disease to progress. Thus we consider the best treatment alternative is to reduce the production of AB42 as this will reduce all forms of amyloid aggregates and is therefore likely to affect and hinder the progression of the disease. GSM has a directly opposite effect on Aβ compared to the mutations that cause the disease in the hereditary forms of Alzheimer's.



# Painless

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 other conditions such as osteoarthritis.

Platform	Candidate	Indication	Research phase	Preclinical phase	Phase I	Phase II	Phase III
less	ACD440	Neuropathic pain					
Painless	Trka-NAM	Osteoarthritis pain					

#### ACD440

ACD440 is a TRPV1 antagonist that is in the clinical development phase, and the company's aim is to develop a new topical local treatment for neuropathic pain. The drug candidate, which was an important strategic in-licensing carried out in January 2020, fits well into the company's existing pipeline and strengthens the clinical portfolio.

The 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 has previously undergone Phase I clinical trials, in which both good tolerability and early positive signals of efficacy were observed. The mechanism of action of the project is via TRPV1 receptors, which have a key role in pain signaling, and ACD440 has been shown in preclinical trials to have an effect on both nociceptive and neuropathic pain. The compound has previously undergone extensive preclinical safety studies and since the compound is being developed for local use, systemic exposure can be kept very low, while the concentration of the compound locally can be kept high for maximum analgesic effect.

Nociceptors are stimulated by heat, acid and strong food, which can lead to feelings of pain. Despite the differences in these stimuli, a single target protein expressed in these pain-sensing nerve cells responds to them all. The molecular target is the TRPV1 receptor, which is expressed in sensory neurons and is upregulated in the skin of individuals with certain types of neuropathic pain. Consequently, there is strong scientific support for local treatment with this type of target mechanism. Neuropathic pain is associated with impaired quality of life and current treatments rarely provide adequate pain relief. In all, an estimated 7–8 percent of the adult population worldwide suffers from pain with neuropathic elements, corresponding to about 80 million individuals in the US, Europe and Japan alone. Over half of these patients do not respond to current first-line treatment and it is specifically toward this group of individuals that AlzeCure is aiming its new intended treatment.

As planned, AlzeCure initiated a Phase Ib clinical trial of the drug candidate in late 2020, which was presented in April 2021 and showed positive proof-of-mechanism data, i.e. an analgesic effect in humans. The efficacy of ACD440 was clearly significant compared with placebo. It 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. The company is now planning further Phase II trials.

About 50 percent of patients do not respond to current first-line treatment and it is specifically toward this group of individuals that AlzeCure is aiming its new intended treatment.





#### TrkA-NAM

The TrkA-NAM project, which is in the research phase, is aimed at treatment of pain and has strong preclinical and clinical validation.

For the TrkA-NAM drug project, we have leveraged our knowledge concerning the underlying biology for the NeuroRestore platform in order to develop new compounds that focus on providing pain relief in 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 global osteoarthritis market is expected to reach USD 11.0 billion by 2025, from USD 7.3 billion in 2020. Growth in this market is driven by factors such as the increasing occurrence of osteoarthritis, the growing aging population, and an increase in the number of sports injuries.

Over 240 million people worldwide suffer from painful and activity-limiting osteoarthritis of the hip or knee. Many patients experience insufficient pain relief or side effects with current treatment, which today usually consist of NSAIDs or opiates, and there is a great need for more effective and better tolerated drugs in this field. In addition, there is a risk of abuse and development of tolerance even with short-term use of opiodes.

Over the past decade, a number of anti-NGF antibodies have been developed and used in several clinical trials to treat painful osteoarthritis. The first positive study was with Tanezumab, which showed a potent analgesic effect in osteoarthritis of the knee in a phase II clinical trial, which has been followed by several phase III clinical trials for various pain indications. However, a small number of patients who received anti-NGF antibodies developed side effects, which has put the brakes on further development of these drugs.

A small-molecule drug with a mechanism that generates the same favorable effects as anti-NGF-antibodies, but without the side effects observed for them, would have great market potential. A selective TrkA-negative allosteric modulator meets these criteria.

As previously mentioned, the target mechanism has been strongly validated by both preclinical and clinical data, and Alze-Cure's unique compounds differentiate themselves with their selective effect on relevant signaling pathways to achieve optimal pain relief without inducing side effects. In addition, the TrkA-NAM compounds are small molecules, which facilitates administration for patients (tablets) while contributing to more cost-effective treatment. Moreover, the product is non-opioid, an important consideration with respect to gaining future regulatory approval from authorities, including the FDA.

AlzeCure currently has a promising series of chemical compounds in research phase. The company received positive preclinical efficacy data during the latter part of 2020 and is actively working on the development of a drug candidate for preclinical safety studies.

The team at AlzeCure has many years of research experience in the fields of neuorology and pain. This project is an excellent example of leveraging synergies between the projects and maximizing shareholder value.

# Shareholders & Share trend

### The share

The share has traded on Nasdaq First North Premier Growth Market under the name ALZCUR since November 28, 2018. On December 31, 2021, the number of shares in the company totaled 37,765,715.

#### Share-related compensation programs

In 2019 the company launched an incentive program with warrants aimed at some members of the Board of Directors. A total of 110,000 warrants were issued: 35,000 warrants went to Thomas Pollare and 25,000 warrants each went to Annigje van Es Johansson, Ragnar Linder and Pirkko Sulila Tamsen.

The warrants, which were issued at the market price as of May 22, 2019, entitle the holder to subscribe for shares during the period June 15–30, 2022. 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 22, 2019. For more information, please see the minutes from the AGM of May 22, 2019.

In 2020 the company also launched an incentive program, this time with warrants aimed at the Chief Executive Officer. A total of 300,000 warrants were issued. The warrants, which were issued at the market price based on an external valuation as of May 20, 2020, entitle the holder to subscribe for shares during the period June 15, 2023 – July 5, 2023. 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 20, 2020. For more information, please see the minutes from the AGM of May 20, 2020.

The total dilutive effect is 1 percent as of the closing date.

### Owners as of December 31, 2021

The ten largest owners as of December 31, 2021	Number of shares	Share capital and votes
BFCM P/C BFCM Sweden Retail LT	4,503,265	11.9%
FV Group AB	2,000,000	5.3%
AlzeCure Discovery AB	1,710,000	4.5%
Sjuenda Holding AB	1,578,600	4.2%
Nordnet Pensionsförsäkring AB	1,444,866	3.8%
SEB-Stiftelsen	1,400,000	3.7%
Futur Pension	1,091,700	2.9%
Thomas Pollare	881,877	2.3%
Stein Grimsvik	875,600	2.3%
Pontus Forsell	873,643	2.3%
10 largest owners	16,359,551	43.3%
Other	21,406,164	56.7%
TOTAL	37,765,715	100%

Trend for AlzeCure's share price in 2021.

#### Share price SEK



D Interest in AlzeCure continued in 2021 and the number of shareholders continued to increase.

Martin Jönsson, CEO

# Employees

The AlzeCure<sup>®</sup> organization, which comprises research, development and the management group, possesses more than 100 years of joint experience from global pharmaceutical companies. Parts of the company's current management group was formerly part of AstraZeneca's neurology and pain research unit where they were involved at the center of research and development of both symptomatic and disease-modifying drugs for the treatment of Alzheimer's disease. The organization was further strengthened during the year. During the year we actively worked to develop and consolidate our mission, vision and core values. We have also met patient organizations, such as the Alzheimer's Foundation, at Team Days, which has further increased our motivation and passion for what we do.





The organization is a major asset for the company and together possesses long and extensive experience and expertise within the field. The ability to design additional projects and make progress has been demonstrated many times. Moreover, this is done with passionate drive, with a focus on innovation and collaboration.

# Report of the Board of Directors & financial reports

#### REPORT OF THE BOARD OF DIRECTORS

& FINANCIAL STATEMENTS	
Report of the Board of Directors3	1–35
Multi-year overview	35
Corporate governance report3	6-40
Board of Directors and auditor 4	1-42
Senior executives4	3-44
Financial reports	45
Income statement and other	
comprehensive income	46
Balance sheet	47
Statement of change in equity	48
Cash flow statement	49
Notes 5	
Signatures	55
Audit report 5	6-57
OTHER	
Definitions	50
Shareholder information	
2022 Annual General Meeting	59

# Report of the Board of Directors

The Board of Directors and the Chief Executive Officer of AlzeCure Pharma AB (publ), corp. ID no. 559094–8302, hereby present the annual report for the financial year 2021.

The annual report has been prepared in Swedish crowns (SEK) and rounded to the nearest thousand unless otherwise indicated. Figures within parentheses refer to the corresponding period for the previous financial year.

#### The business

#### Information about the business

AlzeCure Pharma AB (publ), hereinafter as AlzeCure<sup>®</sup>, was founded on November 22, 2016 and is domiciled in Stockholm.

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 and is developing several parallel drug candidates based on three research platforms: NeuroRestore®, Alzstatin® and Painless.

NeuroRestore consists of two symptomatic drug candidates where the unique mechanism of action supports treatment of multiple indications, including Alzheimer's disease, as well as cognitive disorders associated with traumatic brain injury, sleep apnea and Parkinson's disease. The Alzstatin platform focuses on developing disease-modifying and preventive drug candidates for early treatment of Alzheimer's disease and comprises two candidates. 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 carries out its research in its own laboratories located at Novum at Karolinska Institutet in Huddinge.

#### Development of the business

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 outlicensing solutions with other pharmaceutical companies.

#### Research and development

AlzeCure engages in 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.<sup>1</sup>

The company is simultaneously developing four 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 disorders associated with Alzheimer's, traumatic brain injury, sleep disturbances and Parkinson's disease, as well as for severe pain in conditions such as neuropathy and osteoarthritis.

- The NeuroRestore platform is a new generation of symptomatic drugs for the treatment of illnesses with cognitive disorders, such as Alzheimer's disease. The target mechanism also has other potential indications, including depression and cognitive disorders in Parkinson's disease, traumatic brain injury and sleep disorders.
- Innovative disease-modifying and preventive drugs for Alzheimer's disease are under development within the Alzstatin platform.
- The Painless platform includes two projects: TrkA-NAM 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 project is aimed at treating severe pain caused by disorders such as osteoarthritis, which today lacks sufficiently effective treatment. The project is currently in the research phase.

With its broad portfolio of projects, the company maximizes shareholder value by working in multiple indication areas where there is scientific support for the biological target mechanisms. Within NeuroRestore, a new generation of symptomatic drugs is being developed for the treatment of cognitive dysfunction (memory disorders) in Alzheimer's disease. 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, with results showing that ACD856 was well-suited for further clinical development. Continued clinical trials were initiated in late 2020, also according to plan. 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 the primary purpose of assessing safety and tolerability in humans. ACD857 is in the research phase and also has the primary indication of cognitive dysfunction/Alzheimer's disease.

AlzeCure's disease-modifying research platform for Alzheimer's disease, Alzstatin, focuses on reducing the production of toxic amyloid beta (A $\beta$ ) in the brain. A $\beta$  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 is confirmed by previously reported study results, which we believe validate the amyloid hypothesis and thus Alzstatin's focus.

The leading drug candidate within Alzstatin, ACD679, is in preclinical phase and alongside this work, the development of an additional drug candidate (ACD680) is in progress to ensure that the company has the best compound for clinical studies.

The need for these types of treatments is great and diseasemodifying therapy for Alzheimer's is expected to be able to generate more than USD 15 billion in annual sales.

<sup>1)</sup> Fierce Pharma, Despite controversy, Biogen's Aduhelm is already generating enthusiasm among doctors: survey, 2021

AlzeCure's Painless platform contains two projects aimed at new treatments for pain. Both projects involve non-opiates, which is important to emphasize, because of the inherent risk associated with opiates for abuse, overdose and secondary injuries – which has led to avoidance of opiates as first-line treatment for pain. Despite the problems related to opiates they are still frequently used, for which reason the need for new non-opiate treatments is great.

In January 2020, a drug candidate in the clinical development phase aimed at treating neuropathic pain, ACD440, 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 data, i.e. an analgesic effect in humans. The efficacy of ACD440 was clearly significant compared with placebo. It 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. The company is now planning further Phase II trials.

TrkA-NAM builds on the knowledge amassed and assets developed in the NeuroRestore platform, but with the aim of developing new compounds that focus on providing pain relief in 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 project, which is in the research phase, has strong preclinical and clinical validation. The company received the first positive preclinical efficacy data during the latter part of 2020 and is actively working on the development of a drug candidate for preclinical safety studies.

Activities are supported by continuous access to important knowledge, unique ideas and the latest technology. AlzeCure consists of a very experienced team of industrial pharmaceutical

developers with extensive experience within the fields of CNS and pain, and a scientific network comprising world-leading expertise in neurodegenerative diseases in both preclinical and clinical research. This proximity to, and integration of, clinical expertise in AlzeCure enables the development of new methods for testing therapeutic concepts and allowing the early clinical testing of new treatment methods.

#### Significant events during the year

- In April, Associate Professor Märta Segerdahl Storck, MD/PhD, assumed the position of Chief Medical Officer (CMO). Dr.
  Segerdahl is responsible for the company's clinical development activities. She is also part of AlzeCure's management group.
- In April, positive and significant efficacy data were obtained slightly ahead of plan from the company's Phase Ib clinical trial with the drug candidate ACD440 for neuropathic pain. The drug candidate was also well tolerated as a topical treatment.
- Eva Lilienberg was elected to serve on AlzeCure's Board of Directors at the Annual General Meeting in May. Eva further strengthens the company with her broad international regulatory and commercial experience.
- In July, a new article about ACD856 was published in the periodical "Cells," presenting the findings and describing the preclinical development of the compounds in the NeuroRestore platform. (Identification of Novel Positive Allosteric Modulators of Neurotrophin Receptors for the Treatment of Cognitive Dysfunction, Cells 2021 Jul23;10(8):1871.)
- New data supporting ACD856 for treatment of Alzheimer's disease were presented at the Alzheimer's Association International Conference (AAIC) 2021, which was held July 26-30 in Denver, Colorado, in the US.
- In August, the company received approval from the Medical Products Agency to further excalate the dose of ACD856 in the Phase I clinical trial (single ascending dose, SAD). The approval is based on the good tolerability of the drug candidate, which enables higher doses to be tested.
- In August, the company received approval from the regulatory authorities in Sweden to initiate a Phase I clinical trial (multiple

ascending dose, MAD) for the drug candidate ACD856, with a focus on Alzheimer's disease.

- In October, the first study participant in the company's Phase I clinical trial (MAD) received a dose of the drug candidate ACD856.
- The company presented the potential of the NeuroRestore project for treatment of depression at the European College of Neuropsychopharmacology (ECNP) 2021 conference, held October 2–5 in Lisbon, Portugal.

# Significant events after the end of the financial year

- The company received feedback from the FDA that supports the continued clinical development program for ACD440, as well as preparations for the upcoming Phase II clinical trial.
- On March 1, an Extraordinary General Meeting was held during which a rights issue was approved.
- The right issue was completed on March 22 and the company will receive SEK 48.5 million before issue costs.

#### Revenue and profit/loss

During 2021, net sales totaled SEK 0 thousand (0), and the company is not expected to generate any revenues before its products have progressed further in their development phases.

The operating loss for the year totaled SEK –77,926 thousand (–71,579). The company's research activities have developed steadily and thus also its expenses. In 2021, research expenses increased by 7 percent compared with 2020, which is according to plan. The company continued to dedicate considerable effort to its patent portfolio in 2021.

During the year administrative expenses totaled SEK -11,265 thousand (-9,375). The increase is mainly attributable to an increased focus in 2021 on communications and investor relations to increase the visibility for the company.

AlzeCure's earnings for the financial year totaled SEK -77,781 thousand (-71,366). Earnings per share totaled SEK -2.06 (-1.89).

### Liquidity and financial position

At the end of the year, equity was SEK 32,974 thousand (110,755) and the debt/equity ratio was 72.2 percent (94.0).

Cash and cash equivalents at the end of the period totaled SEK 41,741 thousand (112,434).

In the opinion of the Board of Directors and the Chief Executive Officer, AlzeCure's financial position is sufficiently strong to run the key projects forward to create great value for the shareholders. The Board of Directors continuously reviews the company's longterm financing to ensure continued development. The opportunity to re-prioritize within existing projects exists to secure the business going forward. See also Significant events after the end of the financial year. Because the operation is currently in a precommercial stage with no sales revenues, the board has resolved to propose to the AGM that no dividend be paid to shareholders in 2022.

#### Cash flow and investments

Cash flow from operating activities including changes in working capital for the year totaled SEK -70,639 thousand (-69,508).

Cash flow from investing activities totaled SEK -54 thousand (-671), mainly attributable to investments in laboratory equipment.

Cash flow from financing activities totaled SEK 0 thousand (114) for the year. In 2020 warrants were issued.

### Personnel

During the year, work continued building and preparing AlzeCure's organization for the future. The company had twelve (nine) employees on the closing date. The organization is still relatively small, but the company is also working with a large and talented network of consultants who are dedicated to AlzeCure.

### Share-related remuneration

The company has two incentive programs for a total of 410,000 warrants issued on the closing date, with a potential dilutive effect of 1%. Other than these warrant programs, the company has not established any share-based incentive programs or other out-

standing securities that can be translated into equity, warrants or other share-related financial instruments. For more information, see the heading "Incentive program" below.

# Guidelines for remunerations to senior executives

The Annual General Meeting on May 20, 2020 resolved to adopt guidelines for remuneration to the CEO and other senior executives. AlzeCure Pharma shall offer a total compensation package at market levels that enables skilled senior executives to be recruited and retained. Remuneration to the CEO and other senior executives may consist of basic salary, variable remuneration, other benefits and pension. The basic salary forms the basis of the total remuneration and shall be proportionate to the executive's responsibilities and authority. The variable remuneration must not exceed an amount equal to six months' salary for the executive concerned. The variable remuneration is based on performance in relation to individually defined qualitative and quantitative measures, and also on the performance of the company relative to targets set by the Board of Directors. Pensionable pay consists only of basic salary.

The notice period shall be at least three months if employment is terminated on the initiative of the senior executive and between three and twelve months if terminated by the company. No severance pay is due on termination of employment. Any share and sharerelated programs shall be decided by the general meeting of shareholders. Allocations will be made in accordance with the resolutions passed by the general meeting. Other than as follows from employment contracts as described above, the senior executives are not entitled to any benefits after their employment/duties have ended.

The CEO's remuneration shall be set and approved by the Board of Directors. Remuneration to other senior executives shall be set by the CEO, who shall present a proposal to the Board of Directors for approval. The Board of Directors shall be entitled to deviate from the above guidelines for remuneration of senior executives if there is particular reason to do so.

Compensation to the CEO consists of a fixed monthly salary; see also note 6. All pension commitments must be based on defined contributions. Agreements under market terms between the company and representatives from the Board and management group are in place. See also note 6.

### Nomination Committee

AlzeCure Pharma's nomination committee for the 2022 Annual General Meeting was appointed in accordance with the principles adopted by the Annual General Meeting on May 17, 2021 and consists of:

- William Gunnarsson, appointed by BFCM P/C BFCM Sweden Retail LT
- Bo Rydlinger, appointed by FV Group AB
- Liselotte Jansson, appointed by AlzeCure Discovery AB
- Thomas Pollare (Chairman of the Board)

Prior to the 2022 Annual General Meeting, the nomination committee shall prepare resolutions on election and remuneration issues and, where appropriate, procedural issues for the next nomination committee.

### Environment

AlzeCure is actively engaged in reducing any negative environmental impact and to develop as a sustainable company. As the company does not have any product sales it has no environmental impact in this regard; its focus instead is to exercise responsibility in its purchases of goods and services and its use of energy and transportation.

### Work of the Board of Directors

The company's Board comprises four members including the Chairman, who were elected at the general meeting to serve until the end of the 2022 AGM. In 2021 the Board met twelve times. The Board is responsible for matters such as setting objectives and strategies, ensuring the adoption of procedures and systems for evaluating objectives; the ongoing evaluation of the company's financial performance and position, and evaluating its operational management. The Board follows written rules of procedure that are revised and adopted at the statutory annual board meeting. The rules of procedure govern such things as Board practice, the Board's functions and the distribution of work between the Board and the CEO, and where appropriate between the Board and various committees.

#### The share and ownership structure

The share has traded on Nasdaq First North Premier Growth Market under the name ALZCUR since November 28, 2018. On December 31, 2021, the number of shares in the company totaled 37,765,715.

All shares are ordinary shares and have equal rights to the company's profit, and each share entitles the holder to one vote at the AGM. At the AGM, each shareholder is entitled to vote the full number of shares, owned or represented, without limitation to the number of votes. BFCM P/C BFCM Sweden Retail LT is the only shareholder that has a proportion of shares and votes larger than 10 percent. Their holding was 11.7 percent as of December 31, 2021.

#### Incentive program

In 2019 the company launched an incentive program with warrants aimed at some members of the Board of Directors. A total of 110,000 warrants were issued: 35,000 warrants went to Thomas Pollare and 25,000 warrants each went to Annigje van Es Johansson, Ragnar Linder and Pirkko Sulila Tamsen.

The warrants, which were issued at the market price as of May 22, 2019, entitle the holder to subscribe for shares during the period June 15–30, 2022. The issue price for newly subscribed shares totaled 150 percent of the volume-weighted average closingprice 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 22, 2019, which gave a cash price of SEK 6.50 per share. The incentive program also presumes that the Board is active in the company. For more information, please see the minutes from the AGM of May 22, 2019.

In 2020 the company also launched an incentive program, this time with warrants aimed at the Chief Executive Officer. A total of 300,000 warrants were issued. The warrants, which were issued at the market price based on an external valuation as of May 20, 2020, entitle the holder to subscribe for shares during the period June 15, 2023 – July 5, 2023. 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 20, 2020, which gave a cash price of SEK 7.40 per share. The incentive program also presumes that the Chief Executive Officer is active in the company. For more information, please see the minutes from the AGM of May 20, 2020.

The total dilutive effect is 1% as of the closing date.

### Owners as of December 31, 2021

The ten largest owners as of December 31, 2021	Number of shares	Share capital and votes
BFCM P/C BFCM Sweden Retail LT	4,503,265	11.9%
FV Group AB	2,000,000	5.3%
AlzeCure Discovery AB	1,710,000	4.5%
Sjuenda Holding AB	1,578,600	4.2%
Nordnet Pensionsförsäkring AB	1,444,866	3.8%
SEB-Stiftelsen	1,400,000	3.7%
Futur Pension	1,091,700	2.9%
Thomas Pollare	881,877	2.3%
Stein Grimsvik	875,600	2.3%
Pontus Forsell	873,643	2.3%
10 largest owners	16,359,551	43.3%
Other	21,406,164	56.7%
TOTAL	37,765,715	100%

#### Activities and prospects

2021 was yet another extremely intense year for AlzeCure, which further developed and expanded its three research platforms and its portfolio. This enables better opportunities for proceeding all the way to patients and the market, as well as the potential for more indications in addition to Alzheimer's, such as cognitive disorders related to Traumatic Brain Injury (TBIs), Parkinson's and sleep apnea, as well as pain. The company has two drug candidates in clinical development phase.

At the beginning of 2020 ACD440, a drug candidate in the clinical development phase aimed at treating neuropathic pain, was in-licensed. The 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. Neuropathic pain is often associated with greatly impaired quality of life and current treatments rarely provide adequate pain relief. In all, an estimated 7–8 percent of the adult population worldwide suffers from pain with neuropathic elements, corresponding to about 25 million individuals in the US, Europe and Japan alone.

AlzeCure intends to continue its activities and holds the opinion that the company's projects have great market potential. The company has no revenues and is dependent on external financing to safeguard continued operation until the projects begin to generate revenues. AlzeCure is continually working on business development to find suitable outlicensing solutions with other pharmaceutical companies. 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 outlicensing solutions with other pharmaceutical companies.

#### Risks and uncertainties

Commercial risks

In addition to financial risks, commercial risks are primarily linked to research and development efforts. Drug development in general is risky and capital-intensive.

The risks involved in the R&D necessary for a drug candidate to gain authority approval for use as a drug are many and include product development delays, higher-than-anticipated expenses, failure of the drug candidates to meet efficacy expectations and unexpected or undesirable side effects.

The pharmaceutical industry is characterized by global competition, rapid technological development and extensive investment requirements. There are competitors with significant financial resources and there is a risk that competitors develop drugs that have a negative impact on the company's competitive situation.

When a drug is approved, there is still a risk that national or international sales fail to meet expectations and the product does not become commercially successful. A drug's market acceptance and sales are dependent on a number of factors including product characteristics, clinical documentation and outcomes, competing products, distribution channels, availability, price, subsidies/reimbursements, and sales and marketing initiatives. These circumstances can have a negative effect on AlzeCure's future operations, financial position and profitability.

The COVID-19 pandemic is still underway and the company has taken the necessary measures to protect its employees and limit any negative impact on the company's operations. The company continues to closely monitor the situation, even though the restrictions have been lifted.

We will all be affected by the turmoil in the world right now, though exactly how cannot be said at this time.

*Financial risks and procedures for asset management* See note 13 for comments on the financial risks.

#### Multi-year overview

SEK thousand	2021	2020	2019	2018
	Jan. 1, 2021 -Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020	Jan. 1, 2019 -Dec. 31, 2019	Jan. 1, 2018 -Dec. 31, 2018
Net sales	0	0	0	0
Operating profit/loss	-77,926	-71,579	-50,908	-35,893
Earnings for the year and comprehensive income	-77,781	-71,366	-50,858	-35,985
Earnings per share, basic (SEK)	-2.06	-1.89	-1.35	-1.58
Research expenses as a percentage of operating expenses (%)	85.0	86.3	87.7	92.8
Total assets	45,647	117,827	186,755	237,782
Cash and cash equivalents	41,741	112,434	182,499	234,549
Debt/equity ratio (%)	72,2	94.0	97.5	98.0
Average number of shares, basic	37,765,715	37,765,715	37,765,715	22,774,048
Average number of employees	11,0	8.0	4.0	1.5

For definitions of key performance indicators, see note 17.

# Proposed disposition of the company's earnings

The following earnings are at the disposal of the Annual General Meeting:

#### SEK thousand

Accumulated profit/loss	-169,031
Share premium reserve	278,842
Profit/loss for the year	-77,781
	32,030

The Board of Directors and Chief Executive Officer propose that earnings be distributed as follows:

#### SEK thousand

to be carried forward	32,030
	32.030

#### **Dividend policy**

AlzeCure is currently in an expansive growth phase where any capital surpluses in the operation are invested in the operation and/or acquisitions. To date, the company has not allocated any dividends to its shareholders since the formation of the company. In light of this, AlzeCure has not adopted any dividend policy.

The company's earnings and position in general are shown in the income statement and balance sheet, as well as the cash flow statement with notes.

# Corporate governance report

#### Overview

AlzeCure Pharma AB (AlzeCure<sup>®</sup>) is a Swedish public limited liability company governed by Swedish law, primarily the Swedish Companies Act (2005:551), the Swedish Annual Accounts Act (1995:1554) and internal rules and regulations. Because the company's shares are traded on Nasdaq First North Premier Growth Market, the company also complies with Nasdaq First North's regulatory framework, the Swedish Corporate Governance Code (the Code) and pronouncements by the Swedish Securities Council concerning best practices on the Swedish stock market.

As a rule, the Code is not applicable to companies whose shares are admitted to trading on a so-called multilateral trading facility (such as Nasdaq First North Growth Market); however, since July 1, 2018 the Code applies to companies whose shares are admitted to trading in the Premier segment at Nasdaq First North Growth Market. While the Code specifies a higher standard of good corporate governance than the minimum requirements of the Swedish Companies Act, companies are not obliged to comply with all of the rules in the Code as it provides leeway to deviate from the rules on the condition that all such deviations and the chosen alternative solutions are described and that the reason for the deviations are explained in the corporate governance report under the so-called comply-or-explain principle.

#### Shareholders

AlzeCure's share is listed on Nasdaq First North Premier Growth Market. Share capital as of December 31, 2021 amounted to SEK 944,000 distributed over 37,765,715 shares, each with a quota value of SEK 0.025. BFCM P/C BFCM Sweden Retail LT was the largest individual shareholder as of December 31, 2021 and represented 11.9 percent of the shares. They were also the only shareholder who, as of the closing date, had a shareholding in the company that represented at least one tenth of votes for all shares in the company.

All shares are ordinary shares and have equal rights to the company's profit, and each share entitles the holder to one vote at the AGM. At the AGM, each shareholder is entitled to vote the full

number of shares, owned or represented, without limitation to the number of votes.

### Annual General Meeting (AGM)

Shareholders exercise their voting rights at the AGM. The AGM must be held within six months of the end of each financial year.

Shareholders exercise their right to decide on the company's affairs at the AGM. Shareholders exercise their voting rights on key issues such as the approval of income statements and balance sheets, the appropriation of the company's profit or loss, the discharge from liability of Board members and the CEO, the election of Board members and auditors, and compensation to the Board and auditors.

Extraordinary shareholders' meetings may be convened in addition to the AGM. In accordance with AlzeCure's articles of incorporation, notice convening the AGM is announced through the Official Swedish Gazette (Post- och Inrikes Tidningar) and by making the notice available on the company's website. At the same time, an advertisement informing that notice has been given must be placed in the Swedish business daily, Dagens Industri. According to the company's articles of incorporation, the AGM must be held in Stockholm, Sweden.

### Right to attend the AGM

Shareholders who are registered directly in the shares ledger kept by Euroclear Sweden AB six working days before the AGM and who have notified the company of their intention to participate in the AGM not later than the date specified in the notice to attend the AGM, have the right to participate in the AGM and to vote the number of shares they hold. Shareholders whose shares are registered in the name of a nominee or trustee must register their shares with Euroclear in their own name for the right to participate in the AGM. Such registration may be temporary. Shareholders may participate in the AGM in person or by proxy, but by no more than two persons. Shareholders are usually able to register for the AGM in a number of different ways, described in more detail in the notice to attend.

### Initiatives from shareholders

Shareholders who wish to have a matter addressed at the AGM are required to submit a request in writing to the Board. Usually, the request must be received by the Board no later than seven weeks before the AGM.

### 2021 Annual General Meeting

AlzeCure's Annual General Meeting was held on May 17, 2021. In addition to the customary agenda items, the AGM resolved the following:

- to reelect Thomas Pollare, Ragnar Linder and Ellen Donnelly, and to elect Eva Lilienberg, as board members until the end of the next AGM. Pirkko Sulila Tamsen declined reelection;
- to reelect Thomas Pollare as Chairman of the Board until the end of the next AGM;
- to reelect registered auditors Grant Thornton Sweden AB as the company auditor;
- that a fee be paid in the amount of SEK 200,000 to the Chairman of the Board and SEK 100,000 to each of the other Board members who are not employees of the company;
- that the auditors fee be paid against approved invoice;
- to approve the Board's remuneration report in accordance with Chapter 8. Section 53 a of the Swedish Companies Act; and
- to authorize the Board to resolve on the new issue of shares, warrants and/or convertibles on one or more occasions before the next AGM, with or without deviation from shareholders' preferential rights, that involves the issue, subscription or conversion to a number of shares corresponding to a maximum dilution of 20 percent of the total number of shares in the company at the time of the resolution. The new issues can be carried out with or without a provision regarding contribution in kind, set-off or other provisions referred to in Chapter 13, Section 5, first paragraph 6, Chapter 14, Section 5, first paragraph 6 and Chapter 15, Section 5, first paragraph 4, of the Swedish Companies Act. The purpose of the authorization is to increase the company's financial flexibility and the Board of Directors' scope of action.
#### 2022 Annual General Meeting

The Annual General Meeting will be held on Tuesday, May 17, in Stockholm. Notice convening the AGM will be announced through the Official Swedish Gazette (Post- och Inrikes Tidningar) and by making the notice available on the company's website. At the same time, an advertisement informing that notice has been given will be placed in the Swedish business daily, Dagens Industri.

Shareholders who wish to have an issue addressed at the AGM must submit a written request to the Board well in advance of the AGM. The Board may be contacted by letter at: Board of Directors, AlzeCure Pharma AB, Hälsovägen 7, 141 57 Huddinge, or by e-mail to: info@alzecurepharma.com

#### Nomination Committee

The 2019 AGM resolved to establish a nomination committee tasked with preparing resolutions prior to AGMs on matters concerning elections and fees and, where appropriate, procedural matters for the next nomination committee, and to establish instructions for said committee's work. The nomination committee must comprise the three largest shareholders as of September 30 in terms of votes, and who wish to participate in the nomination committee's work.

## Instructions concerning the work and composition of the nomination committee

The Chairman of the Board must contact the company's three largest shareholders in terms of votes according to a transcript of Euroclear Sweden AB's shares ledger on September 30, and allow each to appoint a representative, who together with the Chairman of the Board, will constitute the nomination committee. Should any of them not exercise the right to appoint a member, the right to appoint such a member will be transferred to the next biggest shareholder in terms of votes who does not already have the right to appoint a member to the nomination committee. This procedure must continue until the nomination committee comprises three members excluding the Chairman of the Board. Unless otherwise agreed, the member representing the biggest shareholder in terms of votes must be appointed chairman of the nomination committee. The Chairman of the Board may not be chairman of the nomination committee.

The Chairman of the Board must convene the nomination committee's first meeting and also, as part of the nomination committee's work, present to it the conditions regarding the work of the Board and the requirement for special skills etc. that may be of importance for the nomination committee's work.

The names of nomination committee members must be published as soon as the nomination committee is appointed, but no later than six months before the next AGM. The nomination committee's term of office runs from the date when its composition is made public until such time as a new nomination committee is appointed.

If any change in the company's ownership structure takes place after September 30 but before the nomination committee's complete motions have been made public, and if a shareholder, who following this change has become one of the company's three biggest shareholders in terms of votes, expresses a wish to the nominating committee chairman to become a member of said committee, the shareholder has the right to appoint an additional member to the nomination committee. Furthermore, the nomination committee may resolve that a member, who in terms of votes has become significantly smaller than the third biggest company shareholder in terms of votes, must resign from the nomination committee if this is deemed appropriate.

If a member of the nomination committee resigns during the term of office or if said member is prevented from fulfilling the assignment, the nomination committee must urge the shareholder who appointed the member to appoint a new member within a reasonable time. Should any shareholder not exercise the right to appoint a new member, the right to appoint such a member will be transferred to the next biggest shareholder in terms of votes who has not already appointed, or who has declined the right to appoint, a member to the nomination committee. Changes to the composition of the nomination committee must be made public as soon as they take place.

The nomination committee must put forth proposals on the matters listed below for presentation to the AGM for resolution:

- proposed chairman of the meeting,
- proposed Board of Directors,
- proposed Chairman of the Board
- proposal for board fees and their distribution between the Chairman and other members of the Board,
- proposals for fees to members of the remuneration and audit committees (where applicable),
- proposed auditors
- proposed fees to auditors and to the extent considered necessary, proposals for amendments in current nomination committee regulations.

No fee shall be paid to the members of the nomination committee. These instructions are applicable until the AGM resolves otherwise.

#### Nomination committee for the 2022 Annual General Meeting

The company's nomination committee for the 2022 Annual General Meeting consists of:

- William Gunnarsson, appointed by BFCM P/C BFCM Sweden Retail LT
- Bo Rydlinger, appointed by FV Group AB
- Liselotte Jansson, appointed by AlzeCure Discovery
- Thomas Pollare (Chairman of the Board)

## Guidelines for remunerations to senior executives

The guidelines shall apply to employment contracts entered into after this decision on guidelines, and to any changes made to existing terms after this decision. The 2020 Annual General Meeting resolved to adopt the following guidelines for remuneration of senior executives:

AlzeCure Pharma shall offer a total compensation package at market levels that enables skilled senior executives to be recruited and retained. Remuneration to the CEO and other senior executives may consist of basic salary, variable remuneration, other benefits and pension. The basic salary forms the basis of the total remuneration and shall be proportionate to the executive's responsibilities and authority. The variable remuneration must not exceed an amount equal to six months' salary for the executive concerned. The variable remuneration is based on performance in relation to individually defined qualitative and quantitative measures, and also on the performance of the company relative to targets set by the Board of Directors. Pensionable pay consists only of basic salary. Pension benefits shall be offered on market terms in relation to what applies to corresponding executives in the market.

The notice period shall be at least three months if employment is terminated on the initiative of the senior executive and between three and twelve months if terminated by the company. No severance pay is due on termination of employment. Any share and share-related programs shall be decided by the general meeting of shareholders. Allocations will be made in accordance with the resolutions passed by the general meeting. Other than as follows from employment contracts as described above, the senior executives are not entitled to any benefits after their employment/duties have ended.

The CEO's remuneration shall be set and approved by the Board of Directors. Remuneration to other senior executives shall be set by the Chief Executive Officer. The Board shall follow up and evaluate the application of the guidelines and current compensation structures and compensation levels in the company. The Board of Directors shall be entitled to deviate from the above guidelines for remuneration of senior executives if there is particular reason to do so.

#### Board of Directors

The responsibilities of AlzeCure Pharma's Board are governed by the Swedish Companies Act and the articles of incorporation. According to the Swedish Companies Act, the Board of Directors is responsible for administration and organization, which means it is responsible for such things as establishing objectives and strategies, ensuring that procedures and systems for evaluating objectives are in place; the ongoing evaluation of the company's financial performance and position, and evaluating its operational management. The Board is also responsible for ensuring that the annual accounts and, where appropriate, consolidated financial statements and interim reports are prepared in a timely manner. The Board also appoints the CEO. Board members are elected annually at the AGM for the period up until the end of the next AGM. According to the company's articles of incorporation, the Board must comprise no fewer than three and no more than ten members without alternates.

#### Chairman of the Board

The Chairman of the Board is elected by the Board or where appropriate by the AGM; the Chairman bears particular responsibility for the management of the work of the Board and ensuring that such work is well organized. The Chairman of the Board is also responsible for ensuring the Board evaluates its work annually and that the Board is provided with information sufficient to enable its work to be performed effectively.

The Chairman of the Board is also responsible for ensuring that the Board is provided with satisfactory documentation in support of its work, and for contacts with shareholders on ownership matters and for conveying the views of the owners to the Board.

#### Board procedures

In addition to the provisions of the Swedish Companies Act, the Board follows written rules of procedure that are revised annually and adopted by the Board at the statutory annual board meeting held following the AGM in which elections to the Board have taken place. The rules of procedure govern e.g. the allocation of assignments and responsibilities between the board, the Chairman of the Board and the CEO and it specifies the procedure for the CEO's financial reporting.

At the first Board meeting, the Board also sets forth and adopts instructions for the CEO. The Board's work is evaluated on an ongoing basis.

The Board meets according to an annual schedule laid down in advance. In addition to these meetings, further meetings may be arranged to address issues that cannot be referred to a scheduled meeting. In addition to Board meetings, the Chairman of the Board and the CEO maintain a dialog concerning the management of the company.

#### Board committees

Based on its size and composition, the Board has decided that the duties and assignments of a remuneration committee and audit committee are best performed by the Board as a whole, and has accordingly decided not to appoint any special committees.

#### Compensation to Board members

Compensation to the company's board members is resolved by the shareholders' meeting. The AGM of May 17, 2021 resolved that until the next AGM, a fee be paid in the amount of SEK 200,000 to the Chairman of the Board and SEK 100,000 to the other board members who are not employees of the company.

Independent in

BOARD OF DIRECTORS Name	Assignment	Attendance at Board meetings	Elected	Holdings, shares <sup>1</sup>	Holdings, warrants	relation to the company and company management	Independent major owners
Thomas Pollare	Chairman	12/12	2017	881,887	35,000	No	Yes
Ragnar Linder	Board member	12/12	2017	30,429	25,000	Yes	Yes
Ellen Donnelly	Board member	10/12	2018	-	-	Yes	Yes
Eva Lilienberg	Board member	9/9	2021	-	-	Yes	Yes
Pirkko Sulila Tamsen <sup>2</sup>	Board member	3/3	2018	21,000	25,000	Yes	Yes

1) Refers to own holding and that of physical related parties and legal persons.

2) Member of the Board of Directors until May 17, 2021.

#### Composition of the Board

The company's Board comprises four members including the Chairman, who were elected at the general meeting to serve until the end of the 2022 AGM. All members were elected by the AGM held May 17, 2021. The Board met twelve times in 2021. The attendance of individual members at meetings is shown in the table below. All of the meetings during the year followed approved agendas that were provided, together with documentation for each agenda item, to Board members prior to Board meetings. The CEO participates in Board meetings but has no vote. Each scheduled Board meeting includes a review of the current business situation, the company's economic performance and financial position and the outlook for the rest of the year. See pages 41–42 for a description of the members of the Board of Directors.

#### The CEO and other senior executives

The CEO is appointed by, and is subordinate to, the Board of Directors and bears primary responsibility for the company's day-to-day administration and its daily operations. The CEO must comply with the Board of Directors' guidelines and instructions. The distribution of assignments between the Board of Directors and the CEO is set forth in the Board's rules of procedure and the CEO's instructions. The CEO is also responsible for preparing reports and compiling information from management prior to Board meetings and presents materials at Board meetings.

According to the instructions for financial reporting, the CEO is responsible for such in AlzeCure and must therefore ensure that the Board of Directors is provided with sufficient information to enable it to evaluate AlzeCure's financial position on an ongoing basis.

The CEO must keep the Board of Directors continuously informed of developments in the company's operations, sales trends, earnings and financial position, the liquidity and credit situation, important business events and other circumstances that the Board is aware of that cannot be regarded as insignificant for the company's shareholders (such as material disputes and the termination of agreements essential to the company and other significant circumstances affecting operations) Company management, headed by the CEO of the company, consists of people in charge of key business areas at AlzeCure. The CEO and other senior executives are presented in greater detail on pages 43–44.

## Remuneration and employment terms for the CEO and other senior executives

The Board decides on compensation to the CEO, and the CEO decides on conditions for other senior executives and employees.

Compensation to senior executives who are employees can consist of a basic salary, pension and other benefits. Periods of notice and compensation in the event of termination are individual and governed by the applicable employment contract. Compensation to the CEO consists of a fixed monthly salary, as well as a variable potential compensation beginning in 2021. The notice period is six months for the CEO and 12 months if terminated by the company. Under his employment contract, the CEO has the right to compensation from the company amounting to the difference between the CEO's salary at the time the contract is terminated and any new salary the CEO receives during a period of 12 months from the time the contract is terminated. However, this compensation may not amount to more than 60 percent of the monthly salary the CEO received from the company. AlzeCure's employment agreements include provisions under which all intellectual property rights developed by an employee as part of his or her employment will accrue to AlzeCure. The company's employment agreements contain restrictions on competition.

Other than as described above, no senior executive has the right to compensation after termination of employment.

For more information about remuneration to the CEO and senior executives, see note 6.

#### Share-related compensation programs

The company launched an incentive program with warrants aimed at some members of the Board of Directors. A total of 110,000 warrants were issued to: Thomas Pollare, 35,000 warrants, Annigje van Es Johansson, 25,000 warrants, Ragnar Linder, 25,000 warrants and Pirkko Sulila Tamsen, 25,000 warrants. The warrants, which were issued at the market price as of May 22, 2019, entitle the holder to subscribe for shares during the period June 15, 2022 – June 30, 2022. The issue price for newly subscribed shares will total 150 percent of the volume-weighted average closing price for the company's shares on Nasdaq First North Premier during the 10 trading days preceding the Annual General Meeting on May 22, 2019. For more information, please see the minutes from the AGM of May 22, 2019.

In 2020 the company also launched an incentive program, this time with warrants aimed at the Chief Executive Officer. A total of 300,000 warrants were issued. The warrants, which were issued at the market price based on an external valuation as of May 20, 2020, entitle the holder to subscribe for shares during the period June 15, 2023 – July 5, 2023. 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 20, 2020. For more information, please see the minutes from the AGM of May 20, 2020. The total dilution effect is 1%.

#### Audit

The company's statutory auditor is appointed by the AGM. The auditor must examine the company's annual report, its accounting records and the administration of the Board of Directors and the Chief Executive Officer. Following the end of each financial year, the auditor must submit an auditor's report to the AGM. According to the company's articles of incorporation, it must have one or two auditors and no more than one alternate auditor.

Grant Thornton Sweden AB (Box 7623, SE 103 94 Stockholm, Sweden) has been the company's auditor since 2017, with Camilla Nilsson as auditor-in-charge since 2019. Camilla Nilsson is an Authorized Public Accountant and a member of FAR, the Swedish Institute of Authorized Public Accountants.

Resolutions concerning compensation to auditors are passed by the general meeting. The AGM of May 17, 2021 resolved that the auditor's fee be paid against approved invoice. For more information about remuneration to auditors, see note 5.

#### Internal controls

The company has decided not to set up any special function for internal control; instead this task is carried out by the Board of Directors as a whole. Each year, the Board evaluates the need to establish a special internal audit department.

The Board of Directors bears overall responsibility for internal controls. Provisions in the Swedish Companies Act and the Swedish Annual Accounts Act require the inclusion of information about the most important features in AlzeCure's system for internal control and risk management in the company's Corporate Governance Report. In order to maintain good internal control, the Board has established a number of policy documents such as the Board's rules of procedure, the CEO instruction, instructions for financial reporting, and an information and communications policy.

Internal control includes control of the company's organization, procedures and actions. The aim is to ensure reliable and accurate financial reporting; that the company's financial reporting is performed in compliance with the law and applicable accounting standards and that other requirements are met.

The internal control system also seeks to monitor compliance with the company's guidelines, principles and instructions. Furthermore, the protection of the company's assets and the appropriate and cost-effective use of the company's resources are also monitored. Internal control is also carried out by monitoring by means of the implemented information and business management systems, and by analyzing risks. A review of financial statements and reporting paths takes place at every Board meeting.

See pages 41–44 for more information about the composition of the Board of Directors and the management group.



# Board of Directors and auditor

According to the company's articles of incorporation, the Board must comprise no fewer than three and no more than ten members with no alternates. The Board currently comprises four members with no alternates. The Board members were elected to serve until the end of the 2022 AGM.



#### THOMAS POLLARE

Born: 1953

Chairman of the Board and Board member since 2017.

Education/experience: Thomas Pollare holds an M.D. from Karolinska Institutet and a Ph.D. from Uppsala university. He was previously a partner in the Venture Capital company 3i. He has held VP positions at both Pharmacia Corp and Schering-Plough Inc. He has been responsible for the market approval of several pharmaceutical products in various therapeutic areas and which generated billions in annual sales. He has previous experience of board work in both start-up companies and private equity investments.

**Current assignments:** Chairman of the Board and CEO of Oncolution AB. Chairman of the Boards of AC Intressenter AB, Sinfonia Biotherapeutics AB, AlzeCure Discovery AB, Stiftelsen AlzeCure and A3P Biomedical AB. Member of the boards of SSI Diagnostics Holding A/S och Psilox AB. Alternate member of the board of BioWorks Thechnologies AB.

**Completed assignments (past five years):** Chairman of the boards of BioWorks Technologies AB, QuiaPEG Pharmaceuticals AB and QuiaPEG Pharmaceuticals Holding AB. Member of the boards of Pharmaceuticals Sales & Development Sweden AB, Cereno Scientific AB, Premacure Holding AB, Premacure AB, Xellia Pharmaceuticals ApS, Centro Gamma Knife Santiago S.a.P Chile, Gamma Knife Center Ecuador S.APT and GammaKnife Center Indonesia.

Holdings: 881,887 shares and 35,000 warrants

Dependent in relation to the company and company management, but independent in relation to the company's largest shareholders.



#### RAGNAR LINDER

Born: 1953

Board member since 2017.

Education/experience: Ragnar Linder has a Master of Science degree in Chemical Engineering from KTH Royal Institute of Technology. Ragnar is a co-founder of Pygargus, a research company in the field of real-world evidence, which was bought by IMS Health (currently IQVIA) in 2013 and in which Ragnar has held senior positions ever since. He has also held several senior positions in Amgen Nordic (CEO), Aventis, HMR and Hoechst. Ragnar has also been a member of the boards of several biotech, pharmaceutical and CRO companies. Today, Ragnar is an independent consultant.

**Current assignments:** Member of the board of Pharmacolog i Uppsala AB and 3 D Trace AB.

**Completed assignments (past five years):** Senior Principle, Iqvia Inc. and member of the board of R. Linder Holding AB.

Holdings: 30,429 shares and 25,000 warrants.

Independent in relation to the company, company management, and the company's major shareholders.



#### **ELLEN DONNELLY**

Born: 1974

Board member since 2018.

Education/experience: Ellen Donnelly has a Ph.D. from Yale University Medical School (USA). Ellen has previously held various executive positions in clinical development, project management, research and strategy at Pfizer. Prior to joining Pfizer, Ellen held various positions in American biotechnology and management consultancy companies. Ellen was recently CEO of Modus Therapeutics, a Swedish biotech company that focuses on sickle cell diseases.

Current assignments: CEO, Abliva AB.

**Completed assignments (past five years):** CEO of Modus Therapeutics Holding AB (publ) and Modus Therapeutics AB. CEO, Epigenetics Division of Juvenescence; CEO, Souvien Therapeutics.

#### Holdings: No holdings.

Independent in relation to the company, company management, and the company's major shareholders.



#### **EVA LILIENBERG**

Born: 1956 Board member since 2021.

Education/experience: Eva Lilienberg holds an M.Sc. in pharmaceutical sciences. Eva has broad international regulatory and commercial experience. She also has solid experience of drug development from various senior management positions at Merck, Sharp & Dohme (MSD), with a focus on New Products/Regulatory Affairs, and has led international teams with the aim of optimizing development programs to ensure that pharmaceutical products are approved, reimbursed and commercially viable. Eva has worked actively with regulatory bodies such as the FDA and the EMA. She has also held various positions at international pharmaceutical companies such as Astra, Draco (now AstraZeneca) and HMR (now Sanofi) and has worked as a consultant at several small and medium-sized pharmaceutical companies. Eva has been certified as a Board member by Styrelseakademien.

**Current assignments:** Consultant and CEO of Kapitel Tre AB. Board member of the Regulatory Affairs section of the Swedish Society of Pharmaceutical Sciences.

**Completed assignments (past five years):** Service Area lead/Principal Consultant for drug development project at NDA Regulatory Services AB.

Holdings: No holdings.

Independent in relation to the company, company management, and the company's major shareholders.

#### AUDITOR

The company's statutory auditor is appointed by the AGM. According to the company's articles of incorporation, it must have one or two auditors and no more than one alternate auditor.

Grant Thornton Sweden AB (Box 7623, SE 103 94 Stockholm, Sweden) has been the company's auditor since 2017, with Camilla Nilsson as auditor-in-charge since 2019. Camilla Nilsson, born 1973, is an Authorized Public Accountant and a member of FAR, the Swedish Institute of Authorised Public Accountants.

# Senior executives

The management group includes the following people:



#### MARTIN JÖNSSON

Born: 1968

CEO since January 8, 2020

Education/experience: Martin Jönsson holds an M.Sc. in business from the University of Lund, and has also studied at the University of Freiburg, Germany and the University of Ottawa, Canada. Martin Jönsson has more than 20 years of experience in the global pharmaceutical industry and has held several senior positions, with experience in business development, marketing, sales, alliance management and medical affairs. Previous employers include Roche and Ferring Pharmaceuticals.

#### Current assignments: None.

**Completed assignments (past five years):** Senior positions in a variety of fields at Ferring Pharmaceuticals, including business area manager for several therapeutic areas.

Holdings: 102,000 shares and 300,000 warrants.



#### JOHAN SANDIN

**Born:** 1970

CEO 2017–2019, CSO from January 8, 2020.

Education/experience: Johan Sandin holds a Ph.D. from Karolinska Institutet with a focus on neuropharmacology and has substantial international academic and industrial experience. He has previously worked at AstraZeneca, where he held scientific, project and executive positions in charge of in vitro biology, in vivo pharmacology and biochemical biomarkers within the CNS field.

**Current assignments:** Member of the board and CEO at Sandin Pharma Consulting AB. Member of the board and deputy CEO at ArgusEye AB. Member of the boards of AC Intressenter AB and Sinfonia Biotherapeutics AB. CEO of AlzeCure Discovery AB.

Completed assignments (past five years): None.

Holdings: 850,000 shares.

Name	Position	Employed/ worked for AlzeCure	Holdings, shares <sup>1</sup>
Martin Jönsson	Chief Executive Officer	2020	102,000
Johan Sandin	Chief Scientific Officer	2017	850,000
Birgitta Lundvik	CFO	2017	75,000
Pontus Forsell	Head of Research & Discovery	2017	853,642
Märta Segerdahl	Head of Development	2021	-
Annigje van Es Johansson (through February 2021)	Head of Development	2018	82,000

1) Refers to own holding and that of physical related parties and legal persons.



#### **BIRGITTA LUNDVIK**

Born: 1967

CFO since 2017.

Education/experience: Birgitta Lundvik holds an M.Sc. in business from Uppsala University and an eMBA in finance from the Stockholm School of Economics, Sweden. Birgitta Lundvik has more than 25 years of experience from software development, life science and real estate companies. She has been involved in several M&A projects and has broad experience of venture capital companies.

**Current assignments:**Chairman of the Board of HERAccount AB. Member of the board and CEO of Enable – Finance & Business Development in Sweden AB. Board member of Brf Arken. Alternate member of the board of Helander & Lundvik Ekonomikonsulter AB and Balanced Competence Uppsala Redovisningsbyrå AB.

**Completed assignments (past five years):** Secretary and Treasurer of Favro North America Inc. Deputy chairman of Swedsoft. Chair of the board of LobSor Pharmaceuticals AB. Member of the board and CEO of Hansoft Technologies AB. CEO of Favro AB and Nonna Holding AB.

Holdings: 75,000 shares.



#### PONTUS FORSELL

Born: 1967

Head of Research & Discovery, engaged as a consultant since 2017, employed since 2019.

Education/experience: Pontus Forsell holds a PhD in Medical Biochemistry & Biophysics from Karolinska Institutet, Sweden.Pontus Forsell has more than 20 years of experience from several biotech and pharmaceutical companies, such as Biolipox, Orexo, Merck and AstraZeneca, in project and management positions.He is an expert in early phase drug development within the disease areas neurology, analgesia and inflammation, as well as respiratory diseases.

**Current assignments:** Member of the Board and CEO of Research, Education & Training AB (RETAB).

Completed assignments (past five years): None. Holdings: 853,643 shares.



#### MÄRTA SEGERDAHL

Born: 1956

Head of Development, employed April 1, 2021.

**Education/experience:** Märta Segerdahl is holds an MD, a PhD, and is an associate professor, trained at Karolinska Institutet. Märta has board certification in anesthesia, intensive care and pain medicine. Märta has substantial international, academic and industrial experience in the field of CNS and pain. Following 25 years in clinical medicine, she joined AstraZeneca in 2006, and since then has worked within the global pharmaceutical industry at Grünenthal, Lundbeck and Asarina Pharma, where she has held senior positions in translational medicine, external collaborations and clinical development within the field of CNS.

**Current assignments:** Member of the board and CEO at MS Medical Consulting AB. Board member and Vice President of Christian Storck Management AB.

**Completed assignments (past five years):** Senior positions at Lundbeck A/S, Asarina Pharma Apse.

Holdings: No shareholdings.

# Financial Reports

# Income statement and other comprehensive income

SEK thousand	Note	2021	2020
Net sales		0	0
Operating expenses	6.7		
Research expenses		-66,715	-62,356
Administrative expenses	5	-11,265	-9,375
Other operating expenses	4	554	660
Other operating expenses		-500	-508
Operating profit/loss		-77,926	-71,579
Profit/loss from financial items			
Interest income and similar profit/loss items		146	214
Interest expenses and similar profit/loss items		-1	-1
Loss after financial items		-77,781	-71,366
Earnings for the year and comprehensive income	8	-77,781	-71,366
Earnings for the period per share, basic (SEK)		-2.06	-1.89
Earnings for the period per share, diluted (SEK)		-2.06	-1.89
Average number of shares, basic		37,765,715	37,765,715
Average number of shares, diluted		38,175,715	38,050,715

# Balance sheet

SEK thousand	Note	Dec. 31, 2021	Dec. 31, 2020
ASSETS			
Non-current assets			
Intangible fixed assets			
Project rights	9	17	17
Total intangible fixed assets		17	17
Tangible fixed assets			
Equipment, tools and installations	10	1,422	1,944
Total tangible fixed assets		1,422	1,944
Financial fixed assets		7	7
Total non-current assets		1,446	1,968
Current assets			
Current receivables			
Advance to supplier		0	703
Trade receivables		0	8
Other current receivables		1,539	2,349
Prepaid expenses and accrued income		921	365
Total current receivables		2,460	3,425
Cash and bank balances	12	41,741	112,434
Total current assets		44,201	115,859
TOTAL ASSETS		45,647	117,827

SEK thousand	Note	Dec. 31, 2021	Dec. 31, 2020
EQUITY AND LIABILITIES			
Restricted equity	11		
Share capital		944	944
Total restricted equity		944	944
Unrestricted equity	11		
Share premium reserve		278,842	278,842
Accumulated profit/loss		-169,031	-97,665
Profit/loss for the year		-77,781	-71,366
Total unrestricted equity		32,030	109,811
Total equity		32,974	110,755
Current liabilities			
Trade payables		5,971	3,966
Other current liabilities		319	199
Accrued expenses and deferred income	14	6,383	2,907
Total current liabilities		12,673	7,072
Total liabilities		12,673	7,072
TOTAL EQUITY AND LIABILITIES		45,647	117,827

# Statement of change in equity

SEK thousand	Share capital	Share premi- um reserve	Accumulated profit/loss	Profit/loss for the year	Total equity
Opening balance January 1, 2020	944	278,728	-46,807	-50,858	182,007
Appropriation of earnings			-50,858	50,858	0
Warrant program		114			114
Earnings for the year and comprehensive income				-71,366	-71,366
Closing balance December 31, 2020	944	278,842	-97,665	-71,366	110,755
Opening balance January 1, 2021	944	278,842	-97,665	-71,366	110,755
Appropriation of earnings			-71 366	71 366	0

Closing balance December 31, 2021	944	278,842	-169,031	-77,781	32,974
Earnings for the year and comprehensive income				-77,781	-77,781
Appropriation of earnings			-/1,366	/1,366	0

# Cash flow statement

SEK thousand	2021	2020
Operating activities		
Operating loss before financial items	-77,926	-71,579
Adjustment for items not included in cash flow:		
Depreciation and amortization	576	495
Interest received	146	214
Interest paid	-1	-1
Cash flow from operating activities before changes in working capital	-77,205	-70,871
Statement of change in working capital		
Change in trade receivables	8	8
Change in other current receivables	957	-969
Change in trade payables	2,005	969
Change in other current receivables	3,596	1,355
Cash flow from operating activities	-70,639	-69,508
Investing activities		
Acquisition of tangible fixed assets	-54	-671
Cash flow from investing activities	-54	-671
Financing activities		
Warrant program	0	114
Cash flow from financing activities	0	114
Cash flow for the year	-70,693	-70,065
Cash and cash equivalents at beginning of year	112,434	182,499
Cash and cash equivalents, Dec. 31	41,741	112,434

## Notes

#### **NOTE 1** General information

#### **General information**

This annual report concerns the Swedish company AlzeCure Pharma AB (publ), corporate ID number 559094-8302. The company is registered and domiciled in Stockholm, Sweden. The company was formed on November 22, 2016 and its shares have been listed on the Nasdaq First North Premier Growth Market since November 28, 2018. The company's address is Hälsovägen 7, SE 141 57 Huddinge.

#### The nature of the business

AlzeCure Pharma AB (publ), hereinafter as AlzeCure®, was founded on November 22, 2016 and is domiciled in Stockholm.

AlzeCure is a Swedish pharmaceutical company engaged in innovative small molecular drug research with a primary focus on Alzheimer's disease and pain. The company is listed on Nasdaq First North Premier Growth Market and is developing four drug candidates based on the two research platforms, NeuroRestore® and Alzstatin®. The company also has two projects in the field of pain, TrkA-NAM and ACD440. The ADC440 project was acquired in January 2020. AlzeCure carries out research in laboratories located at Novum at Karolinska Institutet in Huddinge.

FNCA Sweden AB, +46(0)8 528 00 399 info@fnca.se, is the company's Certified Adviser. For more information, please visit www.alzecurepharma.se.

#### **NOTE 2** Accounting policies and valuation principles

### General Information, compliance with IFRS and the going concern principal

This annual report has been prepared in accordance with International Financial Reporting Standards (IFRS) issued by the International Accounting Standards Board (IASB) as adopted by the European Union (EU) with the restrictions arising from the Swedish Annual Accounts Act and RFR 2 Accounting for legal entities. AlzeCure Pharma does not constitute a group.

AlzeCure has only one line of business and only operates in Sweden. The chief operating decision maker is the Chief Executive Officer. The company is not anticipated to have any direct revenues until its products are launched on the market or licensed for external production. Consequently, segment reporting is not relevant.

The annual accounts have been drawn up under the proviso that the company conducts its business according to the going concern principle.

New and amended standards currently known are not expected to affect the company's financial reports in any material way.

The Annual Report for AlzeCure Pharma AB (publ) for the financial year ending on December 31, 2021 has been approved by the Board of directors and Chief Executive Officer and will be presented to the Annual General Meeting on May 17, 2022 for adoption.

The annual report was prepared using the accruals concept and based on cost. Monetary amounts are expressed in Swedish crowns (SEK), which is the company's accounting currency, and rounded to the nearest thousand unless otherwise indicated.

Non-current assets and non-current liabilities consist in all material respects of amounts that are expected to be recovered or settled more than twelve months from the closing date. Current assets and current liabilities consist in all material respects of amounts that are expected to be recovered or settled within twelve months of the closing date.

#### Currency translation

Foreign currency transactions are translated into the accounting currency at the exchange rate prevailing on the transaction date. Monetary assets and liabilities in foreign currency are translated to the accounting currency at the exchange rate prevailing on the closing date.

Exchange rate differences that arise from translations are reported under profit/loss for the year. Exchange-rate gains and losses on operating receivables and liabilities are reported under operating profit/loss while exchangerate gains and exchange-rate losses on financial receivables and liabilities are reported as financial items.

#### Revenue

Because the company conducts operations that to date have only included pharmaceutical research, it has not yet entered into any agreements with customers and thus does not report any revenues.

#### Other income - Reporting public subsidies

Public subsidies are reported at fair value. Subsidies received intended for covering costs are reported under Other operating income during the period in which the costs eligible for subsidy arise.

#### Operating expenses

Operating expenses are reported under profit/loss when the service is used or when the event has occurred.

Research expenditures are reported as expenses under Research expenses as they arise. Thus the item Research expenses includes expenditures for research aimed at obtaining new scientific or technical knowledge.

#### Borrowing costs

Borrowing costs are expensed in the period during which they occur and are reported under Interest expenses and similar profit/loss items. Financial expenses consist primarily of interest expenses on loans and exchange rate losses. The company currently has no borrowing costs.

#### Employee benefits

#### Current compensation

Liabilities for salaries, compensation and paid absence whose settlement is expected within 12 months of the financial year, are reported as current liabilities in the amount that is expected to be paid when the liabilities are settled, without regard to discounting.

Expenses for current compensation are reported as the services are performed by the employees.

#### Pensions

The company's pension commitments only include defined contribution plans. A defined contribution pension plan is one where the company pays fixed premiums to a separate juridical entity. The company has no legal or constructive obligation to pay further contributions if the juridical entity lacks sufficient assets to pay all the employee benefits associated with the employees' service during the current or prior periods. Thus the company has no additional risk.

#### Income tax

Income tax consists of current tax and deferred tax. Income tax is reported in the income statement except when the underlying transaction is reported in equity, in which case the associated tax effect is reported under equity.

Current tax is tax that must be paid or received in respect of the current year by applying the tax rates that were enacted, or announced, as of the closing date. Adjustments of current tax attributable to prior periods are also reported under current tax.

As yet, the company does not meet requirements for capitalizing deferred tax assets on tax losses.

#### Non-current assets

The carrying amount of an intangible asset or tangible fixed assets is removed from the balance sheet when the asset is retired or disposed of or when no future economic benefits are anticipated from the use or retirement/disposal of the asset. Gains and losses that arise from the disposal or retirement of an asset consist of the difference between the sales price and the asset's carrying amount less deductions for direct selling expenses. Profit and loss are reported as other operating income/expense.

#### Intangible fixed assets

Intangible fixed assets consist of project rights in respect of NeuroRestore and are reported at cost as the project is not yet concluded. Cost includes expenditures directly attributable to the acquisition of the asset.

Intangible fixed assets that have a limited useful life are depreciated systematically over the asset's estimated useful life. Useful life is tested at every balance sheet date and adjusted as necessary. Depreciation commences upon completion. When the depreciable amounts of the assets are determined, the asset's residual value is taken into account where applicable.

Development expenditures are capitalized when they meet the criteria under IAS 38, i.e. when research proceeds to development and the total work is estimated to reach significant amounts. Otherwise, development expenditures are expensed as normal operating expenses. The most important criteria for capitalization are that the development's end product has demonstrable future earnings, cost-saving or cash flow potential and that there are technological and financial conditions for completing development work once started. The company's research has not advanced far enough to be capitalized. The company currently only has acquired intangible assets.

#### Tangible fixed assets

Tangible fixed assets are reported at cost after deductions for accumulated depreciations and any impairments. Cost includes the purchase price and expenditures directly attributable to an asset in order to bring it to the position and condition necessary for use in accordance with the purpose of the acquisition.

Tangible fixed assets that have a limited useful life are depreciated systematically over the asset's estimated useful life. Useful life is tested at every balance sheet date and adjusted as necessary. The estimated useful life of the company's tangible fixed assets is five years. Depreciation commences upon completion. When the depreciable amounts of the assets are determined, the asset's residual value is taken into account where applicable.

#### Impairment charges

Assets are considered for impairment whenever events or changes in circumstances indicate that the asset's carrying amount may not be recoverable. An impairment loss is reported in the amount by which the asset's carrying amount exceeds its recoverable value. The recoverable value is the asset's fair value less selling expenses or its value in use, whichever is the higher. When calculating value in use, the estimated future cash flows are discounted to present value at a discount rate before tax that reflects current market assessments of the time value of money and the risks associated with the asset.

When assessing the need to recognize impairment, assets are grouped at the lowest levels at which there are in all material respects independent cash-flows (cash generating units). Assets previously impaired are tested on the closing date to see if a reversal is necessary.

#### **Financial instruments**

#### Reporting and valuation at initial recognition

Financial assets and liabilities are reported when the company becomes party to an agreement in respect of the financial instrument's agreed conditions. The carrying amount is a reasonable approximation of fair value.

Financial assets are removed from the statement of financial position/ balance sheet when the contractual rights in respect of the financial asset expire, or when the financial asset and all significant risks and benefits are transferred. A financial liability is removed from the statement of financial position/balance sheet when it is extinguished, i.e. when it is discharged, canceled or expires.

#### Classification and valuation of financial assets upon initial recognition

Trade receivables that do not include a significant financing component are initially measured at fair value adjusted for transaction expenses (where appropriate).

In 2021, which is included in the financial report, the company only reports financial assets that are categorized as measured at amortized cost. This is consistent with the measurement in 2020.

#### The classification is determined by:

- the company's business model for the administration of the financial asset, and
- theproperties of the contractual cash flows from the financial asset

Financial assets are measured at amortized cost if the assets meet the following criteria and are not recognized at fair value through profit or loss:
they are held within the framework of a business model whose objective is to hold the financial assets and collect the contractual cash flows, and
the contractual conditions for the financial assets give rise to cash flows that are only payments for the capital amount and interest on the outstanding principal.

All revenues and expenses in respect of the financial assets reported in the income statement are classified as interest income or interest expenses.

#### Subsequent valuation

#### Financial assets measured at amortized cost

Following initial recognition, financial assets are measured at amortized cost by using the effective interest method. Discounting is omitted if the effect is insignificant. The company's cash and cash equivalents, trade receivables and most other receivables belong to this category of financial instruments.

#### Impairment of trade receivables

The company uses the simplified method when reporting trade receivables and shows anticipated credit losses for the remaining term. This is where the anticipated shortcomings in contractual cash flows are found given the risk of nonpayment at some time during the lifetime of the financial instrument. When calculating, the company uses its historical experience, external indications and forward-looking information to calculate the anticipated credit losses with the aid of a provision matrix. Because they have common credit attributes, the company assesses the impairment of trade receivables collectively where the receivables are grouped based on the number of overdue days.

#### Classification and measurement of liabilities

The company's financial liabilities include trade accounts payable and other liabilities. Financial liabilities are initially measured at fair value adjusted for transaction expenses. Following initial recognition, financial liabilities are measured at amortized cost using the effective interest method.

#### Cash and cash equivalents

Cash and cash equivalents only include bank balances.

#### **Contingent liabilities**

A contingent liability is reported when there is a possible obligation that arises from past events and whose existence is confirmed only by the occurrence of one or more uncertain future events or when there is an obligation that is not reported as a liability or provision because it is not likely that an outflow of resources will be required.

#### Equity, reserves and dividends

#### Equity in the company consists of the following items:

- Share capital representing the nominal value of issued and registered shares.
- Share premium reserve including equity premiums obtained on new share issues. Any transaction expenses associated with the new share issue are deducted from the share premium reserve taking into account any income tax effects.
- Profit or loss brought forward, i.e. all retained earnings or losses for the current and prior periods.

Transactions with the company's owners, such as shareholder contributions and dividends, are reported separately in equity.

#### Cash flow statement

The cash flow statement was prepared according to the indirect method. The reported cash flow includes only those transactions that entail receipts or payments. The company classifies available bank deposits as cash and cash equivalents.

#### **NOTE 3** Significant estimations and uncertainties in assessments

#### Significant estimates

Preparing the financial statements in accordance with IFRS taking into account relief rules in RFR2, requires company management to make estimations, assessments and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, revenues and expenses. Actual outcomes may deviate from these estimations.

#### Uncertainties in assessments

The estimations and assumptions are evaluated on an ongoing basis. Changes in estimations are reported in the period in which the change is made if the change only affects that period, or in the period in which the change is made and future periods if the change affects both the current and future periods.

The demarcation between research expenses and development expenses constitutes a source of uncertainties in estimations and entails a significant risk of substantial adjustment to the value of an asset or liability during the coming financial year. Apportioning research and development phases in new development projects, and determining whether or not the requirements for capitalizing development expenses have been met, requires estimations.

An important part of this estimation takes place when the company proceeds from a research phase to a development phase, which is where the demarcation difficulty comes into focus. Because the company's operation as yet focuses solely on research, there is currently no need for such an estimation.

Another source of uncertainty lies in estimating the extent to which deferred tax assets can be reported based on an estimation of the likelihood of the company's future taxable revenues against which the deferred tax asset can be exercised. Accordingly, the company has not reported any deferred tax assets.

#### **NOTE 4** Other operating expenses

	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Exchange rate gains	217	443
Government assistance, etc., received	-	81
Other operating expenses	337	136
Total	554	660

#### **NOTE 5** Remuneration to auditors

	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Grant Thornton Sweden AB		
Audit assignment	160	159
Audit activities in addition to the audit assignment	40	40
Total	200	199

#### **NOTE 6** Salaries, other remuneration and social security expenses

	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Average number of employees		
Women	7	5
Men	4	3
Total	11	8

## Salaries, remuneration, social security contributions and pension expenses

2,190	1,715
8,176	5,375
10,366	7,090
511	398
1,610	1,108
2,419	1,853
4,540	3,359
	8,176 <b>10,366</b> 511 1,610 2,419

#### Board members and senior executives

	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Number of Board members on closing date		
Women	2	2
Men	2	2
Total	4	4

#### Number of CEOs and other senior

executives		
Women	2	2
Men	3	3
Total	5	5

### Information regarding compensation to the Board and senior executives, 2021

Name	Assignment	Basic salary/fee	Pension expense	Total
Thomas Pollare	Chairman of the Board	179	-	179
Eva Lilienberg <sup>1</sup>	Board member	58	-	58
Ragnar Linder	Board member	90	-	90
Ellen Donnelly	Board member	90	-	90
Pirkko Sulila Tamsen <sup>2</sup>	Board member	31	-	31
Martin Jönsson	CEO	1,577	511	2,088
Other senior exec- utives		5,840	891	6,731
Total		7,865	1,402	9,267

Member of the Board of Directors beginning on May 17, 2021.
 Member of the Board of Directors until May 17, 2021.

### Information regarding compensation to the Board and senior executives, 2020

Name	Assignment	Basic salary/fee	Pension expense	Total
Thomas Pollare	Chairman of the Board	150	-	150
Annigje van Es Johansson <sup>1</sup>	Board member	13	-	13
Ragnar Linder	Board member	75	-	75
Ellen Donnelly	Board member	75	-	75
Pirkko Sulila Tamsen	Board member	75	-	75
Martin Jönsson	CEO	1,200	398	1,598
Other senior executives	5	5,476	704	6,180
Total		7,064	1,102	8,166

1) Member of the Board of Directors until March 2, 2020.

#### Related party transactions

"Related parties" refers to all members of the Board and senior executives and their family members. The guiding principles for what constitutes related party transactions are set forth in IAS 24.

The Chairman and Board members are paid a fee in accordance with the AGM's resolution. The AGM of May 21, 2021 resolved that the Chairman of the Board would receive a fee in the amount of SEK 200,000 and that other Board members who are not employees of the company, will receive a fee in the amount of SEK 100,000 each. Board members are not entitled to any benefits after they have left the Board.

Compensation to senior executives who are employees can consist of a basic salary, pension and other benefits. Periods of notice and compensation in the event of termination are individual and governed by the applicable employment contract. The notice period is six months for the CEO and 12 months if terminated by the company. Under his employment contract, the CEO has the right to compensation from the company amounting to the difference between the CEO's salary at the time the contract is terminated and any new salary the CEO receives during a period of 12 months from the time the contract is terminated. However, this compensation may not amount to more than 60 percent of the monthly salary the CEO received from the company. In 2020 an incentive program was provided with warrants aimed at the Chief Executive Officer. AlzeCure's employment agreements include provisions under which all intellectual property rights developed by an employee as part of his or her employment will accrue to AlzeCure. The company's employment agreements contain restrictions on competition.

Other than as described above, no senior executive has the right to compensation after termination of employment. In 2021, the company was not party to related party transactions that are singly or jointly of material importance for the company other than those described above.

#### **NOTE 7** Expenses classified by type

	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Personnel costs	-15,208	-10,929
Consultancy costs	-50,092	-52,034
Laboratory materials etc.	-4,129	-2,929
Patent expenses	-2,901	-1,838
Depreciation and amortization	-576	-495
Other	-5,574	-4,014
Total	-78,480	-72,239

<b>NOTE 8</b> Tax on profit for the year		
	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Current tax	-	-
Deferred tax	_	_
Total	-	_

#### Reconciliation of effective tax

-77.781	
.,,,01	-71,366
16,023	15,272
	16,023

Tax effect of:		
Non-deductible expenses	-7	-11
Deferred tax assets unrecognized	16,030	15,283
Total	16,023	15,272

Tax losses amount to SEK 254,181 thousand. However, it is uncertain how large a part will remain after future changes in ownership and those already made. There is no question of there being a need to report any deferred tax assets for these items, as the company will most likely continue making losses in the coming year.

#### **NOTE 9** Project rights

	Dec. 31, 2021	Dec. 31, 2020
Opening cost	17	17
Cost for the year	-	-
Closing accumulated cost	17	17
Closing residual value according to plan	17	17

#### **NOTE 10** Equipment, tools and installations

	Dec. 31, 2021	Dec. 31, 2020
Opening cost	2,841	2,170
Cost for the year	54	671
Closing accumulated cost	2,895	2,841
Opening depreciation	-897	-402
Depreciation for the year	-576	-495
Closing accumulated depreciation	-1,473	-897
Closing residual value according to plan	1,422	1,944

All depreciation is included in the item Research expenses.

NOTE 11 Equity		
Number of shares	Dec. 31, 2021	Dec. 31, 2020
At the beginning of the period	37,765,715	37,765,715
At the end of the period	37,765,715	37,765,715

At the end of the year the company has 37,765,715 shares, with a quota value of SEK 0.025.

In 2019 the company launched an incentive program with warrants aimed at some members of the Board of Directors. A total of 110,000 warrants were issued: 35,000 warrants went to Thomas Pollare and 25,000 warrants each went to An van Es Johansson, Ragnar Linder and Pirkko Sulila Tamsen. The dilution effect is less than 0.03%. The warrants, which were issued at the market price as of May 22, 2019, entitle the holder to subscribe for shares during the period June 15–30, 2022. 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 22, 2019. For more information, please see the minutes from the AGM of May 22, 2019.

In 2020 the company also launched an incentive program, this time with warrants aimed at the Chief Executive Officer. A total of 300,000 warrants were issued. The warrants, which were issued at the market price based on an external valuation as of May 20, 2020, entitle the holder to subscribe for shares during the period June 15, 2023 – July 5, 2023. 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 20, 2020. For more information, please see the minutes from the AGM of May 20, 2020.

The total dilutive effect is 1% on the closing date.

#### **NOTE 12** Pledged assets and contingent liabilities

There are no pledged assets other than a blocked bank account in the amount of SEK 50 thousand (50) for warranties, and the Board has not identified any contingent liabilities

### **NOTE 13** Financial risk management and the company's asset management procedures

The company's activities expose it to various financial risks such as market risk (including currency risk in cash flow), credit risk and liquidity risk.

Market risk consists mainly of currency risks. The company collaborates with international parties and has some exposure to fluctuations in different currencies, in particular GBP, USD and EUR. Currency risk arises through future business transactions and the carrying amount of assets and liabilities. The company's net exposure in foreign currencies is limited because of the current scope of its operations.

The credit risk for cash and cash equivalents is considered to be negligible as the counterparties for the company's bank balances are reputable banks with high credit ratings from external evaluators.

Financing risk constitutes the ability to finance projects to commercialization. The company manages this by the timely preparation of new share issues.

Liquidity risk is where the company cannot meet its obligations. The company manages this risk by constantly monitoring cash flow to reduce liquidity risk and ensure its ability to pay.

The objective of asset management is to ensure that operations are financed through equity.

#### **NOTE 14** Accrued expenses and deferred income

	Dec. 31, 2021	Dec. 31, 2020
Accrued vacation pay	1,607	919
Accrued social security expenses, payroll tax	1,534	904
Accrued expenses, external services	3,242	1,084
Total	6,383	2,907

#### **NOTE 15** Significant events after the end of the financial year

On March 1, an Extraordinary General Meeting was held during which a rights issue was approved. The right issue was completed on March 22 and the company will receive SEK 48.5 million before issue costs.

No significant events leading to adjustments have occurred between the closing date and the date of approval of this report.

#### **NOTE 16** Approval of the annual report

The company's annual report for the financial year Jan. 1, 2021 to Dec. 31, 2021 was approved by the Board of Directors and the Chief Executive Officer on April 6, 2022.

#### **NOTE 17** Definitions KPI

#### Key performance indicator definitions

#### Net sales

Revenues from the sale of goods and services in the main operation during the current period.

#### Equity/assets ratio

Equity and 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 such as expenditures for personnel, material and external services.

#### Reconciliation of alternative performance measures

SEK thousand	Jan. 1, 2021 –Dec. 31, 2021	Jan. 1, 2020 –Dec. 31, 2020
Research expenses as a percentage of total operating expenses		
Research expenses	-66,715	-62,356
Administrative expenses	-11,265	-9,375
Other operating expenses	-500	-508
Total operating expenses	-78,480	-72,239
Research expenses as a percentage of total operating expenses (%):	85.0	86.3
Debt/equity ratio (%):		
Total equity at end of period	32,974	110,755
Total assets at end of period	45,647	117,827
Debt/equity ratio (%):	72.2	94.0

# Signatures

Stockholm April 06, 2022

Thomas Pollare Chairman of the Board Eva Lilienberg Board member

Ragnar Linder *Board member*  Ellen Donnelly Board member

Martin Jönsson Chief Executive Officer

Our auditor's report was submitted on April 6, 2022 Grant Thornton Sweden AB

> Camilla Nilsson Authorized auditor

# Audit report

To the general meeting of the shareholders of Alzecure Pharma AB Corporate identity number 559094-8302

#### Report on the annual accounts

#### Opinions

We have audited the annual accounts of Alzecure Pharma AB for the year 2021 except for the corporate governance statement on pages 36–44. The annual accounts of the company are included on pages 30–55 in this document.

In our opinion, the annual accounts have been prepared in accordance with the Annual Accounts Act and present fairly, in all material respects, the financial position of Alzecure Pharma AB as of 31 December 2021 and its financial performance and cash flow for the year then ended in accordance with the Annual Accounts Act. Our opinions do not cover the corporate governance statement on pages 36–44. The statutory administration report is consistent with the other parts of the annual accounts.

We therefore recommend that the general meeting of shareholders adopts the income statement and balance sheet.

#### **Basis for Opinions**

We conducted our audit in accordance with International Standards on Auditing (ISA) and generally accepted auditing standards in Sweden. Our responsibilities under those standards are further described in the "Auditor's Responsibilities" section. We are independent of Alzecure Pharma AB in accordance with professional ethics for accountants in Sweden and have otherwise fulfilled our ethical responsibilities in accordance with these requirements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions.

#### Other Information than the annual accounts

This document also contains other information than the annual accounts and is found on pages 1–29, 58–60. The renumeration report for the financial year 2021, which will be submitted after the date of this auditor's report, also constitutes of other information. The Board of Directors and the Managing Director are responsible for this other information.

Our opinion on the annual accounts does not cover this other information and we do not express any form of assurance conclusion regarding this other information. In connection with our audit of the annual accounts, our responsibility is to read the information identified above and consider whether the information is materially inconsistent with the annual accounts. In this procedure we also take into account our knowledge otherwise obtained in the audit and assess whether the information otherwise appears to be materially misstated.

If we, based on the work performed concerning this information, conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

## Responsibilities of the Board of Directors and the Managing Director

The Board of Directors and the Managing Director are responsible for the preparation of the annual accounts and that they give a fair presentation in accordance with the Annual Accounts Act. The board of Directors and the Managing Director are also responsible for such internal control as they determine is necessary to enable the preparation of annual accounts that are free from material misstatement, whether due to fraud or error.

In preparing the annual accounts, the Board of Directors and the Managing Director are responsible for the assessment of the company's ability to continue as a going concern. They disclose, as applicable, matters related to going concern and using the going concern basis of accounting. The going concern basis of accounting is however not applied if the Board of Directors and the Managing Director intends to liquidate the company, to cease operations, or has no realistic alternative but to do so.

#### Auditor's responsibility

Our objectives are to obtain reasonable assurance about whether the annual accounts as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinions. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs and generally accepted auditing standards in Sweden will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these annual accounts. As part of an audit in accordance with ISAs, we exercise professional judgment and maintain professional skepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the annual accounts, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinions. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of the company's internal control relevant to our audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the company's internal control.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by the Board of Directors and the Managing Director.
- Conclude on the appropriateness of the Board of Directors' and the Managing Director's use of the going concern basis of accounting in preparing the annual accounts. We also draw a conclusion, based on the audit evidence obtained, as to whether any material uncertainty exists related to events or conditions that may cast significant doubt on the company's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the annual accounts or, if such disclosures are inadequate, to modify our opinion about the annual accounts. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause a company to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the annual accounts, including the disclosures, and whether the annual accounts represent the underlying transactions and events in a manner that achieves fair presentation.

We must inform the Board of Directors of, among other matters, the planned scope and timing of the audit. We must also inform of significant audit findings during our audit, including any significant deficiencies in internal control that we identified.

## Report on other legal and regulatory requirements

#### Opinions

In addition to our audit of the annual accounts, we have also audited the administration of the Board of Directors and the Managing Director of Alzecure Pharma AB for the year 2021 and the proposed appropriations of the company's profit or loss.

We recommend to the general meeting of shareholders that the profit be appropriated in accordance with the proposal in the statutory administration report and that the members of the Board of Directors and the Managing Director be discharged from liability for the financial year.

#### **Basis for Opinions**

We conducted the audit in accordance with generally accepted auditing standards in Sweden. Our responsibilities under those standards are further described in the "Auditor's Responsibilities" section. We are independent of Alzecure Pharma AB in accordance with professional ethics for accountants in Sweden and have otherwise fulfilled our ethical responsibilities in accordance with these requirements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinions.

### Responsibilities of the Board of Directors and the Managing Director

The Board of Directors is responsible for the proposal for appropriations of the company's profit or loss. At the proposal of a dividend, this includes an assessment of whether the dividend is justifiable considering the requirements which the company's type of operations, size and risks place on the size of the company's equity, consolidation requirements, liquidity and position in general.

The Board of Directors is responsible for the company's organization and the administration of the company's affairs. This includes among other things continuous assessment of the company's financial situation and ensuring that the company's organization is designed so that the accounting, management of assets and the company's financial affairs otherwise are controlled in a reassuring manner. The Managing Director shall manage the ongoing administration according to the Board of Directors' guidelines and instructions and among other matters take measures that are necessary to fulfill the company's accounting in accordance with law and handle the management of assets in a reassuring manner.

#### Auditor's responsibility

Our objective concerning the audit of the administration, and thereby our opinion about discharge from liability, is to obtain audit evidence to assess with a reasonable degree of assurance whether any member of the Board of Directors or the Managing Director in any material respect:

- has undertaken any action or been guilty of any omission which can give rise to liability to the company, or
- in any other way has acted in contravention of the Companies Act, the Annual Accounts Act or the Articles of Association.

Our objective concerning the audit of the proposed appropriations of the company's profit or loss, and thereby our opinion about this, is to assess with reasonable degree of assurance whether the proposal is in accordance with the Companies Act.

Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with generally accepted auditing standards in Sweden will always detect actions or omissions that can give rise to liability to the company, or that the proposed appropriations of the company's profit or loss are not in accordance with the Companies Act.

As part of an audit in accordance with generally accepted auditing standards in Sweden, we exercise professional judgment and maintain professional scepticism throughout the audit. The examination of the administration and the proposed appropriations of the company's profit or loss is based primarily on the audit of the accounts. Additional audit procedures performed are based on our professional judgment with starting point in risk and materiality. This means that we focus the examination on such actions, areas and relationships that are material for the operations and where deviations and violations would have particular importance for the company's situation. We examine and test decisions undertaken, support for decisions, actions taken and other circumstances that are relevant to our opinion concerning discharge from liability. As a basis for our opinion on the Board of Directors' proposed appropriations of the company's profit or loss we examined whether the proposal is in accordance with the Companies Act.

### The auditor's examination of the corporate governance statement

The Board of Directors is responsible for the corporate governance statement on pages 36–44 and that it has been prepared in accordance with the Annual Accounts Act. Our examination of the corporate governance statement is conducted in accordance with FAR's auditing standard RevU 16 The auditor's examination of the corporate governance statement. This means that our examination of the corporate governance statement is different and substantially less in scope than an audit conducted in accordance with International Standards on Auditing and generally accepted auditing standards in Sweden. We believe that the examination has provided us with sufficient basis for our opinions.

A corporate governance statement has been prepared. Disclosures in accordance with chapter 6 section 6 the second paragraph points 2-6 of the Annual Accounts Act and chapter 7 section 31 the second paragraph the same law are consistent with the other parts of the annual accounts and consolidated accounts and are in accordance with the Annual Accounts Act.

Stockholm, April 6, 2022

Grant Thornton Sweden AB

Camilla Nilsson Authorized Public Accountant

# Definitions

Term	Definition
AlzeCure, AlzeCure Pharma or the company	AlzeCure Pharma AB
Amyloid-beta	A peptide that is the main component in the plaque found in the brains of Alzheimer's patients
Antibody	Protein used by the body's immune system to detect and render harmless foreign substances
BDNF	Brain Derived Neurotrophic Factor
Biomarker	Measurable indicator of a biological state
BBB, blood-brain barrier	Connected capillary pathways in the brain that protect brain tissue
CNS	Central nervous system
Fibrils	Small, thread-like structures that occur in and around cells About one nanometer thick and made up of proteins or polysaccharides
GBP	Pounds Sterling
GSM	Gamma secretase modulator
In vitro	Biological process, outside organisms, in test tubes or cell cultures
In vivo	Biological process occurring in animals or humans
Clinical studies/trials	Drug testing performed in humans

Term	Definition
Cognition	The brain's ability to receive, store and process, as well as to produce information
Drug candidate	A drug under development that has not yet received market approval
Monomers	A monomer is the initial molecule in polymerization where mono- mers combine to form long molecule chains called polymers.
NAM	Negative Allosteric Modulator
NGF	Nerve Growth Factor
NSAID	Non-steroidal anti-inflammatory drugs
Oligomers/protofibrils	Molecular chain of several monomers
Peptide	Molecule comprising amino acids
Preclinical studies	Studies carried out in a lab environment (not in humans)
SEK	Swedish crowns
ТВІ	Traumatic brain injury
TrkA	Tropomyosin receptor kinase A
USD	US dollar

# Shareholder information

Financial calendar 2022	Date
Interim report Q1, January – March 2022	May 5, 2022
Annual General Meeting	May 17, 2022
Interim report Q2, April-June 2022	August 25, 2022
Interim report Q3, July-September 2022	November 10, 2022

All financial reports are available on the AlzeCure website, www.alzecurepharma.com

#### For additional information about AlzeCure, please contact: AlzeCure Pharma AB (publ) Corporate ID no. 559094-8302, domiciled in Stockholm, Sweden. Address: Hälsovägen 7, SE 141 57 Huddinge. info@alzecurepharma.com

FNCA Tel: +46(0)8-528 00 399, info@fnca.se is the company's Certified Advisor

# 2022 Annual General Meeting

The Annual General Meeting will be on May 17. The Board of Directors has decided that the Annual General Meeting shall be held without presence of either shareholders, proxies and/or external parties and that the shareholders shall have the opportunity to vote by mail.

To have the right to participate at the Annual General Meeting shareholders must:

- be recorded as a shareholder in the share register maintained by Euroclear Sweden AB as of May 9, 2022
- no later than May 16 sent in the postal voting form which can be found on the company's website.

For complete information about the 2022 Annual General Meeting, please see the notice which will be posted on the AlzeCure website www.alzecurepharma.com.

#### Contact details

AlzeCure Pharma AB (publ) Corporate ID no. 559094-8302, domiciled in Stockholm, Sweden.

Address: Hälsovägen 7, SE 141 57 Huddinge Tel: +46(0)8-528 00 399,

Certified Advisor: FNCA Sweden AB, info@fnca.se

For more information, please visi www.alzecurepharma.com

