ERIK PENSER BANK

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Alzinova AB

Therapeutic Alzheimer's vaccine in the spotlight

A small company in an enormous market

Alzinova is a Swedish biopharma company in the clinical phase of developing a therapeutic vaccine and a monoclonal antibody targeting Alzheimer's disease. The company has identified a method to specifically target the toxic amyloid-beta oligomers in the brain – one of the underlying causes of Alzheimer's. Alzinova's leading drug candidate – the ALZ-101 vaccine – is currently undergoing a clinical ph Ib trial, with topline results for part A expected to be reported during Q4 2023. The company's other drug candidate – the ALZ-201 monoclonal antibody – is in preclinical studies in preparation for a ph Ib trial.

Alzheimer's – a widespread disease without a cure

The prevalence of dementia is some 50 million people worldwide, and Alzheimer's is the most common form of dementia, accounting for 60–70% of all cases. Alzheimer's causes great suffering for patients while also burdening healthcare systems with substantial costs. Its high prevalence, in combination with these elevated healthcare costs, leaves considerable market potential for drugs targeting Alzheimer's. The market for Alzheimer's treatments is expected to grow by a 20% CAGR until 2030. The key drivers behind this growth include an ageing global population, which leads to an increase in the occurrence of Alzheimer's, meaning the demand for effective therapies will continue to grow.

Blockbuster potential at high risk

We believe Alzinova has, thanks to its exciting vaccine and antibody drug candidate, the potential to become an important differentiated treatment for Alzheimer's patients. If Alzinova can take its lead drug candidate ALZ-101 to market with the help of a possible partner, the product has blockbuster potential, even with relatively narrow market penetration. A potential investor in Alzinova should thus be aware of the binary risk associated with an investment in biopharma, especially in the field of CNS (the central nervous system). This field has long been plagued by setbacks and failed studies, but the approval of lecanemab has sparked investor enthusiasm.

Note that the share price data, and thus valuation multiples, are as they appeared in the original report on 21 November.

Estimate changes

	23e	24e	25e
Total revenues	-	-	-

Coming events

Q4 - report	28 February 2024

Company details (SEKm)

Number of shares	45m
Market capitalisation	112
Net debt	-32
EV	80
Free float	81%
Daily trading volume, average	74k
Bloomberg Ticker	ALZ SS EQUITY

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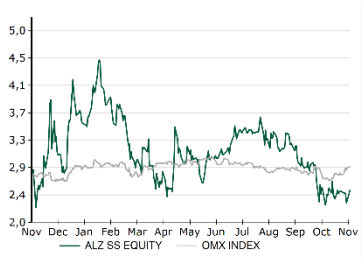
Forecasts (SEKm)

	2022	2023e	2024e	2025e
Net sales	0	0	0	0
Growth	N.m.	N.m.	N.m.	N.m.
EBITDA, adj.	-13	-14	-49	-69
EBIT, adj.	-13	-14	-49	-69
EPS, adj.	-0,4	-0,3	-1,1	-1,6
EPS growth, adj.	N.m.	N.m.	N.m.	N.m.
Equity per share	3,3	2,1	2,9	3,2
Dividend per share	0,0	0,0	0,0	0,0
EBIT margin	Neg.	Neg.	Neg.	Neg.
ROE, adj.	Neg.	Neg.	Neg.	Neg.
ROCE, adj.	Neg.	Neg.	Neg.	Neg.
EV/EBITDA	Neg.	-5,6x	-1,6x	-1,2x
EV/EBIT	Neg.	-5,6x	-1,6x	-1,2x
P/E, adj.	-6,9x	-7,9x	-2,3x	-1,6x
Price/book value	0,9x	1,2x	0,9x	0,8x
FCF yield	-30%	-27%	-59%	-77%
Net debt/EBITDA	2,4x	0,1x	0,4x	0,3x

Assessments

Potential	5
Risk	5
Financial position	2
History & track record	3
Share price	SEK 2,5

12-mth share price development



Conflicts of interest

	Yes	No
Market maker	✓	
Certified adviser		✓
Transactions, 12 mth		✓

Investment case

Alzinova is a biopharma company that focuses on Alzheimer's disease. This field has long been plagued by setbacks and failed studies, but the approval of lecanemab has sparked investor enthusiasm. We believe Alzinova has, thanks to its exciting vaccine and antibody drug candidate, the potential to become an important differentiated treatment for Alzheimer's patients. A ph II study with the vaccine candidate is anticipated to begin next year, which will be the first opportunity for it to show an effect on regulatory-relevant endpoints.

The prevalence of dementia is some 50 million people worldwide, and Alzheimer's is the most common form of dementia, accounting for 60–70% of all cases. Alzheimer's causes great suffering for patients while also burdening healthcare systems with substantial costs. Its high prevalence, in combination with these elevated healthcare costs, leaves considerable market potential for disease-modifying drugs targeting Alzheimer's. The market for Alzheimer's treatments is expected to grow by a 20% CAGR until 2030. The key drivers behind this growth include an ageing global population, which leads to an increase in the occurrence of Alzheimer's, meaning the demand for effective therapies will continue to grow. We model peak sales for the ALZ-101 candidate surpassing USD 4bn in 2035.

The company's technology – in particular the ALZ-101 vaccine – represents a new approach that requires fewer healthcare resources and offers the possibility to take a share in the so far less popular area of vaccines targeting Alzheimer's. Unlike other treatment methods, such as antibodies, it is likely only a few doses of a vaccine would be administered each year, rather than the need for administration as often as every other week. Moreover, it can be delivered to patients in an especially time- and price-effective manner thanks to a single injection at a primary care setting or at home by a nurse. Alzinova's vaccine thus holds the potential to reduce healthcare and societal costs compared with antibody therapies, creating opportunities for more patients to receive care.

The company's proprietary AβCC technology is unique and offers several advantages over other methods. Alzinova has identified a method that should be able to specifically target the toxic amyloid-beta oligomers in the brain, these being seen as one of the underlying causes of Alzheimer's. It has received positive feedback from meetings with both the FDA and the EMA ahead of the coming ph II study.

A potential investor in Alzinova should thus be aware of the binary risk associated with an investment in biopharma, especially in the field of CNS. At the same time, we judge the upside to be considerable given a positive outcome from this ph II study, possibly attracting a potential partnership. The company has already begun seeking a possible partner. Alzinova also has a skilled and experienced management team and a low burn rate. We see good possibilities for it to obtain fast track designation, which would facilitate the application process and future clinical development.

Company description

Alzinova is a Swedish biopharma company in the clinical phase of developing a therapeutic vaccine and a monoclonal antibody targeting Alzheimer's disease. The company's leading drug candidate – the ALZ-101 vaccine – is currently undergoing a clinical ph Ib trial, with topline results for part A expected to be reported during Q4 2023. The company's other drug candidate – the ALZ-201 monoclonal antibody – is in preclinical studies in preparation for a ph Ib trial.

Project	Indication	Preclinical	Ph Ib	Ph II	Ph III	Market
ALZ-101	Alzheimer's disease		Ongoing	Planned 2024+		2030E
ALZ-201	Alzheimer's disease	Ongoing	Planned 2024+			

Source: Company

Contents

Our valuation

We base our valuation of the company on four key factors: potential, financial position, risk, and history and track record.

- **Potential (5 points)**

Alzinova aims to address a major unmet medical need by developing an Alzheimer's treatment. Alzheimer's is an enormous market that has recently seen renewed hope of discovering several and more effective disease-modifying treatments. The market potential is substantial given the extensive burden on patients, the suffering of family members, and the elevated health economic costs. If Alzinova can take its lead drug candidate ALZ-101 to market with the help of a possible partner, the product has blockbuster potential, even with relatively narrow market penetration. The Alzheimer's field has historically seen few advances, but the latest in the market have yielded good returns and, more than anything, hope for a better future for Alzheimer's patients. Given this, we evaluate the potential for Alzinova at 5 points.

- **Risk (5 points)**

Material development risks persist as Alzinova is still at a relatively early stage and the path to the first complete readout of proof-of-concept data from a ph II study is not without obstacles. On top of this come operational and financial risks. Before year-end, we expect the readout of topline data from part A of the completed ph Ib study, which should provide more data on ALZ-101's safety and tolerability along with indications of its disease-modifying effect. We thus consider the risk level to be high and award 5 points for this.

- **Financial position (2 points)**

To judge the company's financial position, we consider its reported history. At the end of Q3, cash and cash equivalents totalled a little more than SEK 33m, which we believe is sufficient to prepare for the important ph II study in ALZ-101. The company does not have sufficient capital to conduct the study on its own, though. Alzinova needs to find a licensing partner, or it must take in further capital. The company has already initiated its search for a potential licensing partner. The costs associated with drug development are high and the Alzheimer's field, in particular, is one of the most expensive in which to conduct clinical studies owing to a demanding recruitment process and long follow-up times. We model capital raises to cover the financing needs for the coming ph II study, and we thus award the current financial position 2 points.

- **History and track record (3 points)**

Like other early-stage biopharma companies, Alzinova has a small but dedicated organisation. The board and management possess the necessary knowledge and expertise required to take a product all the way to market. We thus award 3 points to history and track record.

Probability assumptions

Below, we show the probability assumptions we have used in our model to value the company. Probability adjustments are primarily based on existing empirical data regarding the likelihood of a drug project reaching the market.

These adjustments should only be considered as a benchmarking exercise. As the company advances with its clinical development, there can be opportunities to apply for accelerated approval, for example, as well as the risk of further studies needing to be carried out. Alzheimer's has historically been a difficult area to research. More recently, two Alzheimer's players have seen their amyloid-beta products hit the market, bolstering the hypothesis behind amyloids and boosting confidence in the company's future market position. Moreover, as we believe the company will begin its ph II trial in 2024, at the earliest, we apply 99% likelihood of it moving from ph I to ph II. This data and our assumptions suggest that **the likelihood of ALZ-101 reaching the market is 12%**. We do not use probability adjustments for the company's other project, currently in the preclinical phase, or model future revenues from this.

Probability assumptions based on empirical neurological data

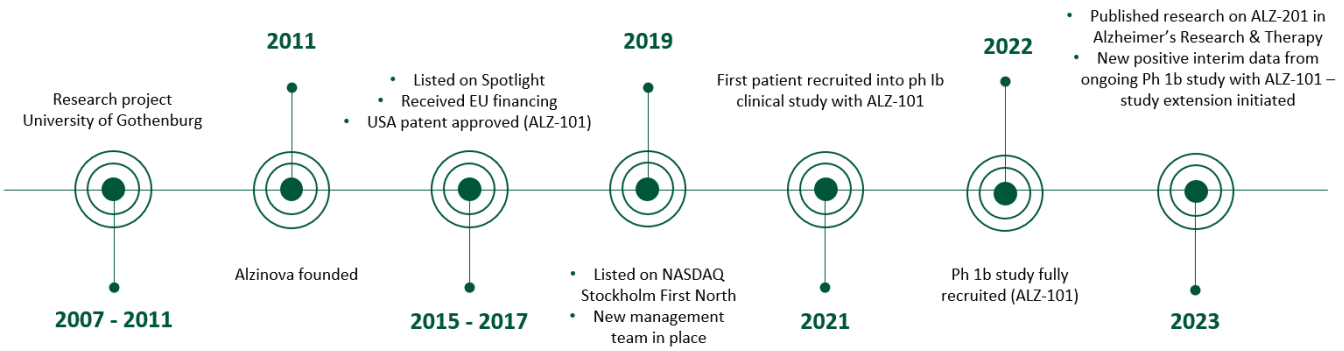
	Ph I to ph II	Ph II to ph III	Ph III to NDA/BLA	NDA/BLA to approval	Cumulative
Neurology	48%	27%	53%	87%	6%
Alzinova	**99%**	**27%**	**53%**	**87%**	**12%**

Source: BIO, QLS Advisors, EPB

History

Alzinova originates from a research project conducted at the University of Gothenburg. The company was founded by researchers in 2011 following their development of a unique technology platform, AβCC. Business angels and the holding company at the University of Gothenburg, GU Holding AB (now GU Ventures AB), provided startup capital and business development aid in its early years. In November 2015, Alzinova was listed via an IPO on Sweden's Spotlight Stock Market (previously known as AktieTorget). This new financing allowed the company to effectively approach the clinical phase and prepare for its first clinical ph Ib study of its main product, ALZ-101. Since March 2019, having undertaken a third capital raise, Alzinova trades as a public company on NASDAQ First North in Stockholm, Sweden (ticker: ALZ). The first clinical study with ALZ-101 started in 2021, and topline data from part A of this study will be released before year-end.

Timeline



Source: MFN, Company

Key events and share price development in recent years

Source: MFN

Share price development and expected news flow

The share price has, unlike those of a number of peer companies undertaking early clinical development, been relatively stable. The upturns have not been permanent and we believe additional clinical data is required for a more lasting effect on the share price.

In the near future, we expect data readout from part A of the company's clinical ph Ib study with ALZ-101, which will be the single most important event in the company's history so far. We expect that news regarding the other development project, ALZ-201, will have less of an effect on the share price.

Events	Expected	Share price impact
Data readout – ph Ib study with ALZ-101 (part A)	Q4 2023	High
Further progress in project ALZ-201	-	Medium
Announced of non-dilutive financing solutions	-	High
Announcement of other capital raises	2024	High

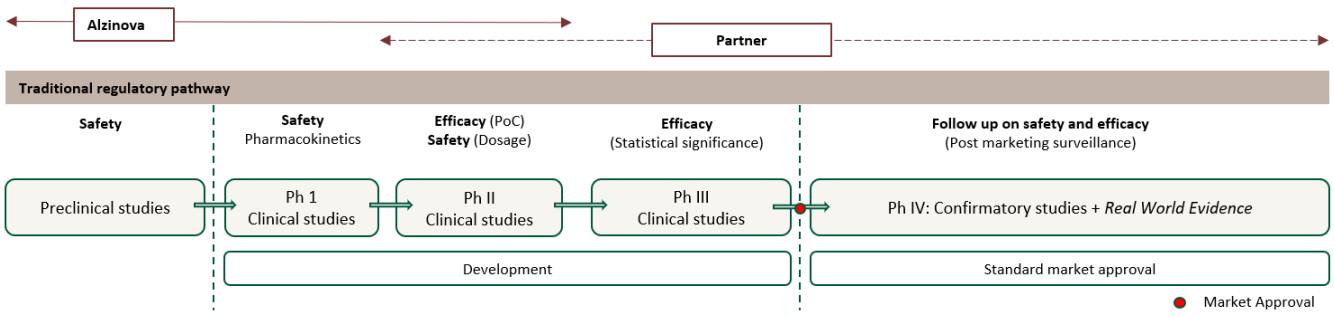
Source: EPB

Business strategy

A drug development company and its drug candidates must undertake all the traditional steps in the development process for registration, preclinical and clinical studies, and finally the approval process in the respective countries where the company wants to launch its products. The typical business strategy for smaller biopharma companies includes licensing and partnerships during the development phase. Companies often seek partnerships and collaborations with larger drugs companies, academic institutions, and other interested parties to gain access to resource, expertise, and financing.

Alzinova's aim is to run projects during clinical development to document that the drug candidates are safe and well-tolerated and also to gain proof-of-concept in patients with the disease. In practice, this means the company intends to successfully complete and report the clinical ph Ib – both part A and the extension (part B). Simultaneously, it is seeking partners. The next clinical study, ph II, is planned for 2024.

Drug development and the approval process



Source: Frontiers in Pharmacology, adapted from Detela & Lodge (2019)

As there is currently no approved therapeutic vaccine (aimed at curing or slowing down the disease in those already suffering) for Alzheimer's and very few approved disease-modifying treatments in the field (two antibodies in the US), the regulatory thresholds can be lowered through *fast track designation*.

Fast track designation is a process used for drug candidates that are expected to help those with serious illnesses. To obtain the designation, the drug candidate must be proven to help in a way that other medicines cannot. This can be applied to the development of many different drug candidates for serious diseases, including AIDS, Alzheimer's, cancer, epilepsy, and diabetes.

A company can apply for fast track designation at any point in the development process, using data from both clinical and preclinical studies. After an application has been sent in, the FDA has 60 days to respond, speeding up the process. Moreover, the drug development company can start to communicate with the FDA particularly early in the development process, often to ensure that all is running smoothly. They can also submit parts of the application before the whole has been completed to speed up potential authorisation.

Source: FDA, Applied clinical trials

Alzheimer's – a widespread disease

Alzheimer's is a complex neurological medical condition that primarily affects older people. It is characterised by a gradual worsening of cognitive abilities, including memory, reasoning, speech, and problem-solving. As it progresses, people with Alzheimer's can experience personality changes, disorientation, and difficulties in performing daily tasks. The exact cause of Alzheimer's is not fully understood, but it is associated with an accumulation of harmful protein deposits in the brain. There are currently only a few potential disease-modifying treatments for Alzheimer's and some symptomatic treatments, but still no cure for the time being. Alzheimer's has a profound effect on both sufferers and their families.

Dementia or Alzheimer's?

Dementia is an umbrella term referring to a set of symptoms related to a decline in cognitive function. Alzheimer's disease is a specific and common cause of dementia. In other words, **dementia** is a general term for numerous cognitive symptoms, while **Alzheimer's** is a specific disease that falls within the concept of dementia. There are other causes of dementia, such as vascular dementia, Lewy body dementia, and frontal lobe dementia, each with its own characteristics and causes.

A characteristic feature of Alzheimer's is the accumulation of harmful proteins in the brain. These proteins, namely amyloid-beta (Aβ) and tau, affect the brain, leading to a reduction in the number of neurotransmitters – chemical messengers that are essential for proper brain function.

Alzheimer's disease incidence is growing at an alarming rate as the global population ages. An estimated 50 million people globally have dementia, and Alzheimer's accounts for at least 60–70% of all cases of dementia. The number affected by dementia is expected to grow to 130 million worldwide by 2050 (*Alzheimer's Association, Alzheimer's Disease International*). Moreover, there are a considerable number of people whose Alzheimer's remains undetected or undiagnosed. Some sources cite around the same number of individuals with prodromal Alzheimer's (the period during which non-specific disease symptoms emerge) and an even larger number of people with preclinical Alzheimer's – characterised by normal cognition but with biomarkers consistent with Alzheimer's pathology.

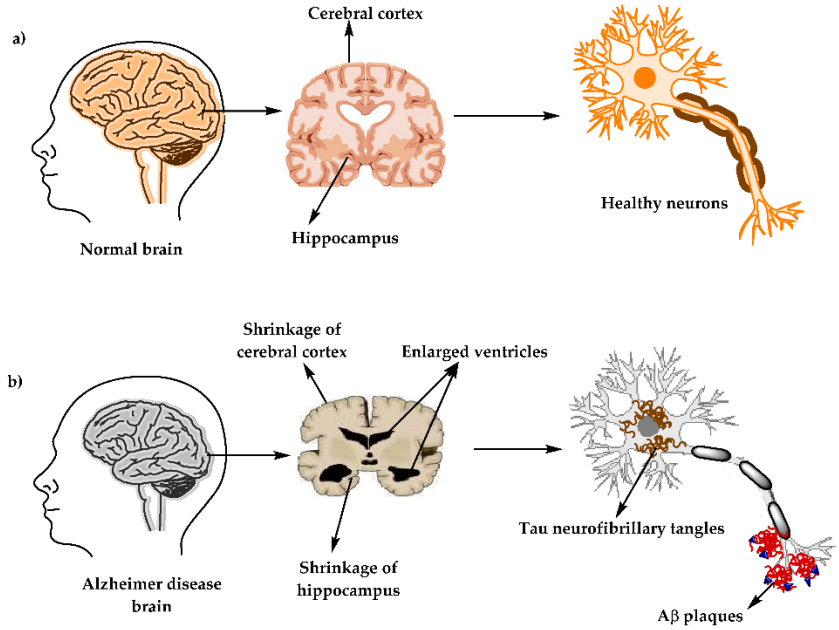
Biomarkers – measurable and quantifiable biological parameters (such as the level of a specific enzyme or hormone) that serves as an indicator of health-related assessments, such as disease risk, pathology, and its effects.

The brain of a healthy adult holds millions of nerve cells – neurons, each with long, branching extensions. These branches allow individual neurons to form connections with other neurons. At these connections, called synapses, information flows from one neuron and is taken up by another. The brain contains billions of these synapses. They allow signals to travel rapidly through the brain. These signals form the cellular basis for memories, thoughts, sensations, emotions, movements, and skills. Amyloid-beta is a protein that occurs in a healthy brain, but with Alzheimer's, small lumps form at the nerve fibres. The accumulation of amyloid-beta protein (or amyloid-beta plaque) and of an abnormal form of the tau protein inside neurons are two of several changes in the brain associated with Alzheimer's.

These changes can result from the damage to and destruction of neurons, called neurodegeneration. **Amyloid-beta** and **tau** play differing roles in Alzheimer's. Plaque and oligomers of amyloid-beta can harm neurons by disrupting neuron-to-neuron communication at the synapses. Tau inside the neurons can block the transport of nutrients and other molecules that are essential to the neurons' normal function and survival. Although the entire sequence of events with Alzheimer's remains unclear, amyloid-beta and tau are believed to play crucial roles in the course of the disease.

Other changes in the brain associated with Alzheimer's include inflammation and atrophy (reduced brain volume). The presence of toxic amyloid-beta and tau proteins is believed to also activate immune system cells in the brain called microglia. Microglia try to clear the toxic proteins and extensive debris from dead and dying cells. Chronic inflammation can occur when microglia cannot keep up with all that needs to be cleared. Atrophy is the result of cell loss. Normal brain function is further jeopardised by the brain's diminished ability to metabolise glucose, its key source of energy.

Healthy brain (a) vs brain affected by Alzheimer's (b)



Source: Molecules

Risk factors

The greatest risk factors for early-onset Alzheimer's are age and genetics – a family history of Alzheimer's, especially the E4 form of the apolipoprotein E (APOE) gene. Age is the more pertinent of the two – the risk of Alzheimer's dementia increases dramatically with age. Five per cent of those aged 65–74, 13% of people aged 75–84, and 33% of those aged 85 years or more have Alzheimer's dementia, according to the Alzheimer's Association. The ageing of the Baby Boomer generation will accelerate the number of Alzheimer's sufferers considerably. It is thus important to note that Alzheimer's dementia is not a normal part of ageing, and old age alone is not enough to cause Alzheimer's dementia.

Although age, genetics, and family history cannot be influenced, certain other risk factors can be changed or adjusted to reduce the risk of cognitive deterioration and dementia. Examples include physical activity, smoking, blood pressure, and diet. The Lancet Commission proposed that addressing modifiable risk factors can prevent or delay up to 40% of dementia cases.

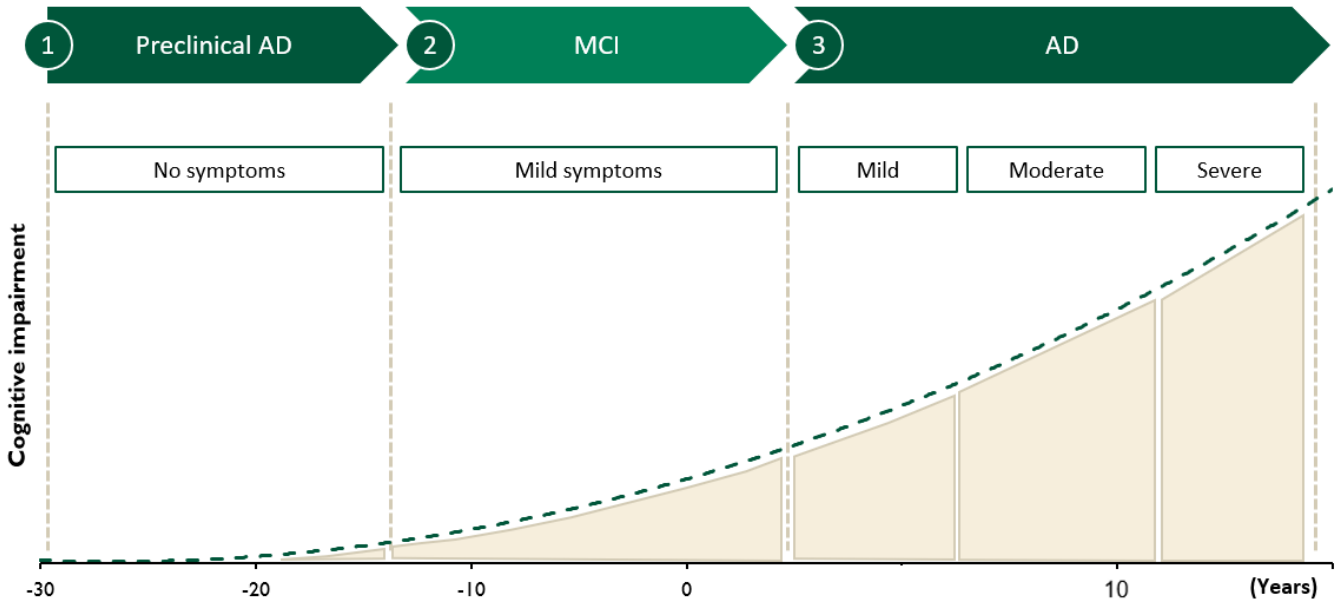
Disease progression

The disease is insidious and it is not possible to pinpoint its exact time of onset. As stated above, those affected typically experience increased memory problems and difficulties in planning and carrying out daily activities. Linguistic skills, time-awareness, and other cognitive functions worsen over time. Anxiety and worry are common symptoms and the disease pattern can also include delusion and behavioural changes. At an advanced stage, serious physical symptoms also occur.

Alzheimer's has a lengthy course that can extend over four to ten years, and sometimes even beyond that. The symptoms are difficult to detect in the early stages and the disease's progression cannot be stopped. The Alzheimer's timeline below shows three broad phases: preclinical Alzheimer's without symptoms, mild cognitive impairment (MCI) caused by Alzheimer's, and dementia caused by the disease, also known as Alzheimer's dementia. How long an individual is in each phase varies. This can be affected by age, genetics, gender, and other factors.

In its most recent annual report, Alzinova published an interview with a relative of an Alzheimer's patient, which can be found here.

Progression of Alzheimer's



Source: Nature, adapted from Alzheimer's Association

Diagnosis

The clinical picture of Alzheimer's varies – typically, those affected find it hard to pinpoint the exact time when their symptoms emerged. Self-diagnosis thus represents a major challenge. Common symptoms include memory problems, difficulty finding words, issues in performing daily activities, such as making a phone call or reading a newspaper, and problems with orientation. It is mainly the responsibility of primary care to make the first assessment of medical history, physical and mental status, and a basic laboratory investigation. A doctor will ask a series of questions that go beyond mere memory to assess cognitive abilities.

Typical tests used in primary care are the mini mental state examination (MMSE) and the Clock Test to assess memory function. More comprehensive assessments are made by occupational therapists, and specialist clinics often employ neuropsychological tests to objectively judge memory impairment and other cognitive issues. Such tests can help to objectively detect impairment to memory and other, higher-level cognitive functions early in the disease's progression. Although this can appear at an early stage, it is not possible to distinguish between Alzheimer's and other forms of dementia at this stage *(Alzheimerfonden – the Alzheimer's Fund in Sweden)*.

There are currently no specific blood tests that can diagnose Alzheimer's, but post-mortem analysis can offer insights into the condition of the brain. Changes in proteins like amyloid-beta and tau discovered post-mortem are important for diagnosis. Although an EEG can show the brain's basic rhythm, it cannot provide a specific Alzheimer's diagnosis.

Medical imaging techniques like PET cameras can be used to assess the brain's function and measure amyloid levels, helping to diagnose the disease early and evaluate the effect of various treatments.

Researchers are working on tests that can measure biological signs of the disease's progression in the brain. These, which include blood tests, can improve the accuracy of a diagnosis. They could also allow for diagnosis before symptoms even occur. Research shows there is also potential for tests based on capillary blood to detect Alzheimer's biomarkers.

Treatment

Today, there are few treatment alternatives – pharmacological and non-pharmacological options such as lifestyle changes and therapy. Symptom-relieving treatments for Alzheimer's are the most common medical options on the market in most western countries. One group of these drugs is the acetylcholinesterase inhibitors, sold under the brand names Reminyl, Exelon, and Aricept. Another type of drug is memantine. This relieves symptoms for a period, but it cannot affect disease progression in the long term.

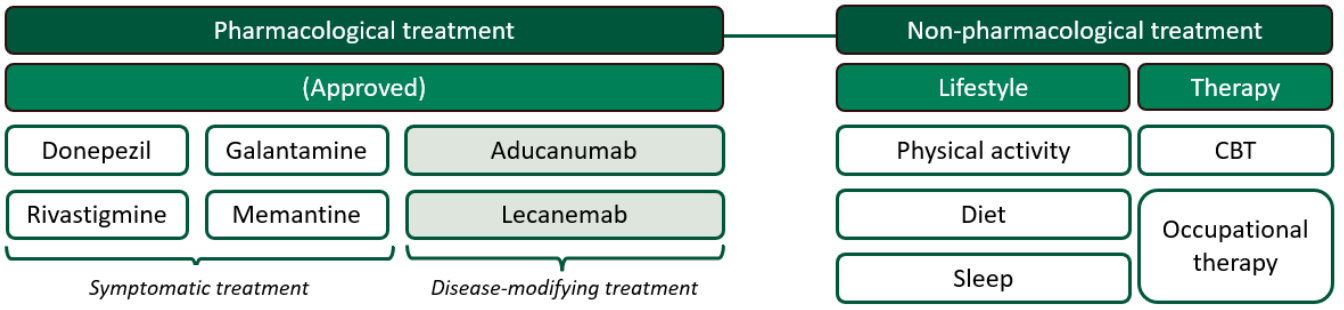
Researchers have spent several decades seeking treatments that can halt or cure Alzheimer's. Their research has been plagued by failure, however. In recent years, two new Alzheimer's treatments have been developed. The US market today features two disease-modifying alternatives: aducanumab and lecanemab. Lecanemab is a monoclonal antibody given via an intravenous drip that aims to halt disease symptoms and reduce the unhealthy accumulation of harmful protein lumps – amyloid plaque. The man behind the drug is Swedish professor Lars Lannfelt, who also founded BioArctic. Lecanemab was approved in the US this year, while a decision is expected in Europe before year-end.

What are the risks of the approved treatments?

Passive immunotherapy (administration of monoclonal antibodies against Aβ) brings increased risk of side effects, predominantly oedema and microbleeds, which are together referred to as ***amyloid-related imaging abnormalities*** (***ARIA***). ARIA is believed to occur on account of the immunological amyloid degradation triggered by the treatment. The impact of ARIA on patients is not clear-cut; these changes have been observed both with and without clinical symptoms.

Source: Janusinfo, Läkartidningen journal

A selection of Alzheimer's treatment alternatives

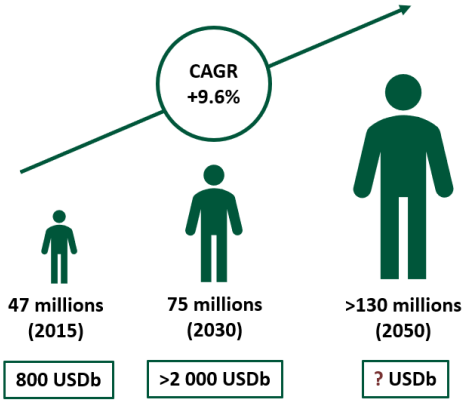


Source: Biomedicines

A common disease with a cost

Alzheimer's disease was officially listed as the sixth most common cause of death in the US in 2019. In 2020 and 2021, when COVID-19 became the third most common cause of death, Alzheimer's disease was pushed down to seventh place. The costs for health and medical care, especially long-term care, for those with Alzheimer's and other forms of dementia are considerable. Different sources claim that dementia care costs are around double that of cancer care, three times as much as cardiology care, and fourth times that of strokes. *Svenskt Demenscentrum* estimated that costs for dementia care in Sweden exceeded SEK 80bn in 2021, with the largest share of this spent on specialist care homes and home care services.

Global prevalence and societal costs for dementia



Source: Adapted from World Alzheimer Report (2015)

The costs for dementia care on a global basis are enormous. The annual global societal cost for dementia in 2019 was estimated at USD 1,300bn, and it is expected to rise to more than USD 2,000bn by 2030. Of this total estimated sum, just over USD 200bn (16%) was direct medical costs, USD 450bn (34%) was social costs (including long-term care), and USD 650bn (50%) was costs for informal care. This all represents significant stress for both healthcare systems and patients' families. Although most of those affected by dementia live in low- or middle-income countries, both the highest total costs and the highest costs per person are in high-income countries.

Quick facts about the health economic aspects of dementia

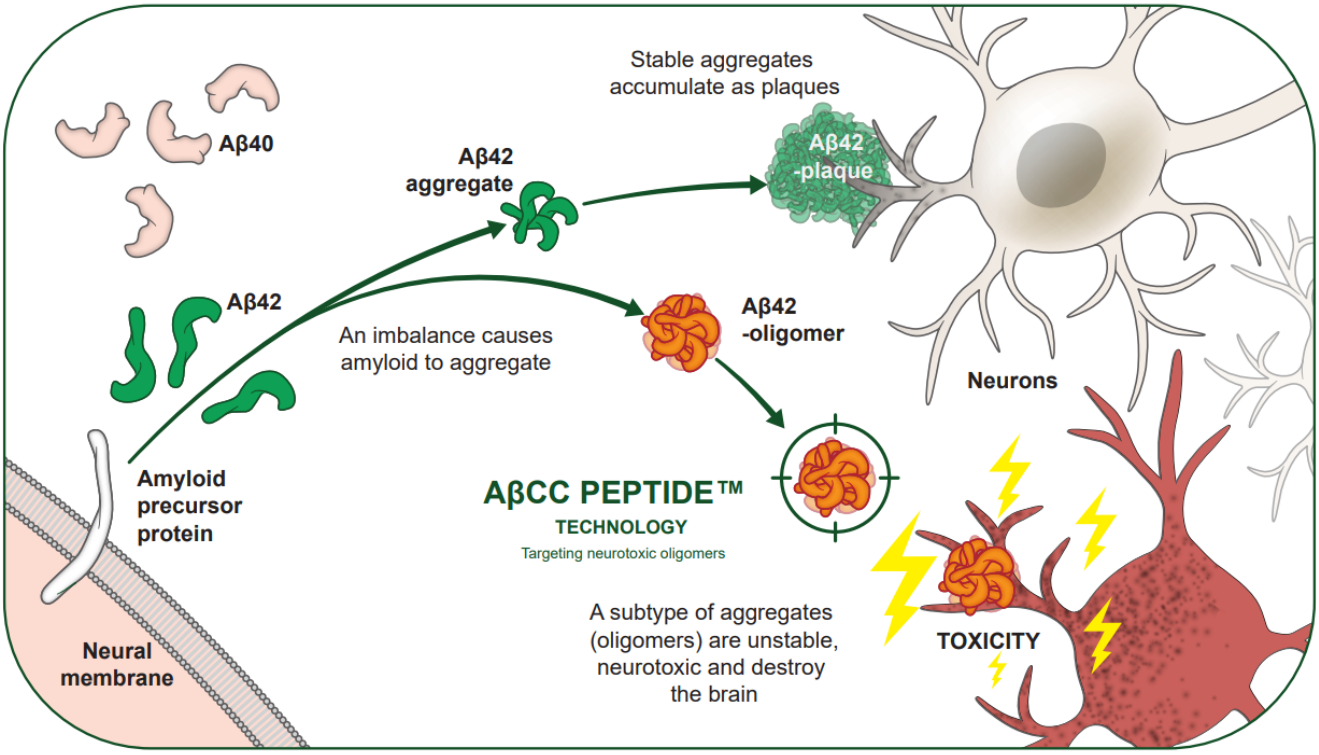
- The global economic costs for dementia were estimated at **USD 1,300bn in 2019**
- **61%** of those with dementia live in low- or middle-income countries, while **74%** of the costs stem from high-income countries
- **Informal care accounts for some 50%** of global costs
- More than **11 million Americans** care for a family member or friend with Alzheimer's dementia, a contribution to the nation that is worth **USD 340bn**
- Dementia care is expected to require more than **one million extra care workers** in 2020–2030 – more staff than are in any other occupation in the entire US.

Source: Alzheimer's Association, Alzheimer's & Dementia

ALZ-101

Alzinova is developing an alternative therapeutic oligomer-specific vaccine. What does this mean? Vaccines stimulate the body's immune system, protecting an individual from a disease. As stated earlier, when Aβ molecules clump together, this forms unstable deposits, called plaques. In addition, oligomers also form. Oligomers differ structurally from plaque and are especially toxic to brain cells. Vaccination with ALZ-101 activates the body to produce its own antibodies, specifically targeting toxic accumulations of Aβ oligomers in the brain. The treatment method is particularly specific and is expected to also bring with it lower risk of side effects like bleeding and oedema.

Aβ plaque, oligomers, and their damaging effect on nerve cells



Source: Company

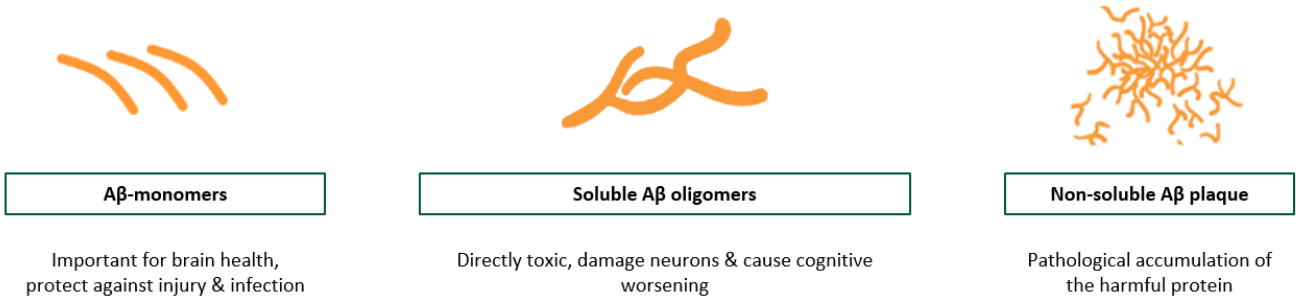
Vaccine candidate ALZ-101 is undergoing clinical development. A ph Ib study in Alzheimer's patients was initiated in Q3 2021 and fully recruited by December 2022. Based on the positive interim data, the company decided in May 2023 on an extension of the ongoing clinical study. Topline data from part A of the study will be presented during Q4 2023.

Unlike other treatment methods, such as antibodies, it is likely only a few doses of a vaccine would be administered each year, rather than the need for administration as often as every other week. Moreover, it can be delivered to patients in an especially time- and price-effective manner thanks to a single injection at a primary care setting or at home by a nurse. Treating patients with antibody therapy significantly increases the societal costs, leading to fewer patients receiving care. Alzinova's vaccine thus holds the potential to reduce healthcare and societal costs compared with antibody therapies, creating opportunities for more patients to receive care.

What role do oligomers play?

Smaller accumulations of Aβ proteins are called oligomers. As stated before, oligomers differ structurally from plaque and are especially toxic for brain cells.

Monomers, oligomers, and plaque



Source: J Mol Science, Alzheon

It has been known for many years that Aβ oligomers are particularly harmful to the nervous system compared with monomers and fibrillary forms of peptides. Their presence in an affected brain has a stronger link to the severity of the disease than the plaque load itself. These oligomers thus represent an especially attractive target for future immunotherapy.

Although oligomers differ structurally from monomers and fibrils, many common structural features are shared by all forms of peptides. Immunotherapy thus tends to focus on all peptide types. It is technically challenging to develop antibodies and vaccines specifically targeting oligomers. This is because oligomers are difficult to isolate since Aβ is in constant equilibrium with different soluble and insoluble aggregate states.

Alzinova's proposed solution to this problem is based on its **AβCC peptide technology**, which comprises stabilised oligomers, allowing for the development of therapies that react only with the toxic oligomers rather than with plaque.

Comparison of Alzinova's unique method with other Alzheimer's treatments

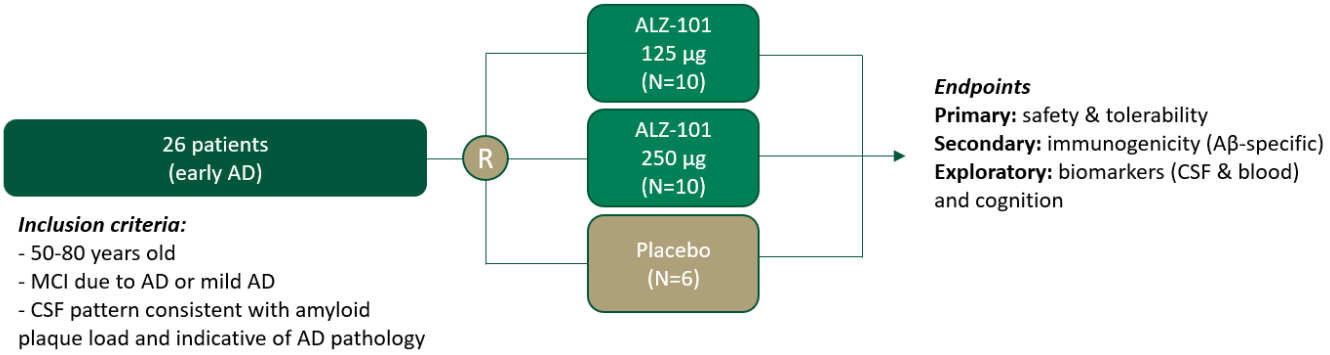
ALZ-101	Other actors
⊕ **Targeted** treatment that specifically targets and neutralizes the toxic peptides (so-called oligomers)	⊖ Target **larger accumulations of amyloid-beta**
⊕ **Active therapy** – a vaccine that stimulates the body to produce its own antibodies against oligomers	⊖ **Non-specific** treatments which are not specifically targeting and neutralizing the toxic oligomers
⊕ **Fast, effective and uncomplicated treatment** without long and expensive hospital stays	⊖ Often complicated treatments that require frequent hospital visits
⊕ **Potentially reduces the risk of serious side effects**	⊖ **Potentially serious side effects**
⊕ Treatment can start **early** in the disease to prevent progression	⊖ **Unlikely to be sufficiently effective**

Source: Company

Clinical ph Ib study with ALZ-101

The high point next year will be the company's most important milestone so far: reporting of the topline results from part A of the clinical double-blinded, randomised, placebo-controlled ph Ib study. Part A of the study was conducted over 20 weeks, with four doses of ALZ-101 at two strengths (125 and 250 µg) or placebo in weeks 0, 4, 8, and 16, with follow-up for 48 weeks.

The design of the clinical ph Ib study



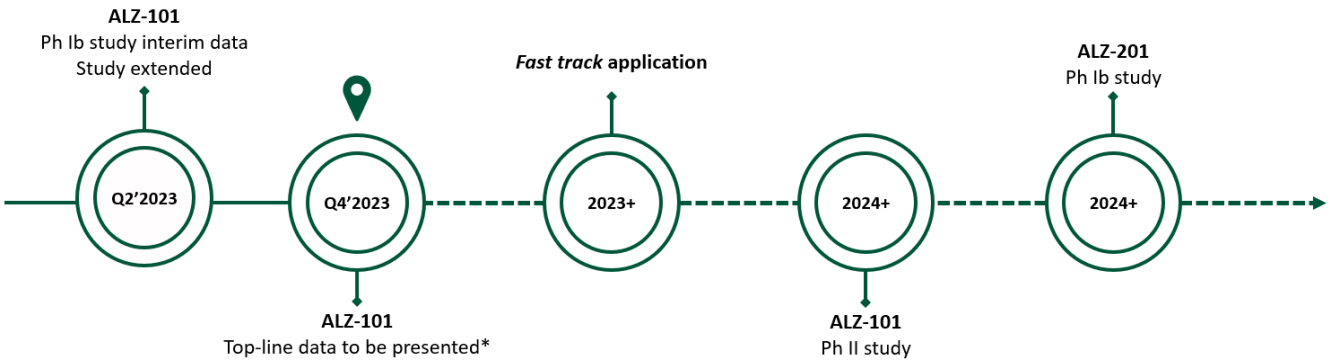
Source: Company

In May 2023, the company announced that a second interim analysis had been conducted and showed positive data with continued good safety and tolerability as well as a clear immunological result. That is to say, specific antibodies had been formed after dosing with ALZ-101. Based on this positive second interim data analysis, Alzinova decided on an extension (part B) of the study. As part of the extension, all the patients will be offered treatment with the highest dose of ALZ-101. The first patient was dosed in May and the last in the extension is expected to receive their final dose in early 2024. Results from the extension should provide the company with valuable information on the long-term effect of ALZ-101 and further strengthen Alzinova's position both when approaching potential partners and the regulatory authorities.

In addition, the company held a pre-IND meeting with the FDA and has received positive feedback on its planned development programme with ALZ-101. The EMA has also provided a positive response to the future planning for the ALZ-101 programme. Such preparation lays the ground for the planned ph II study and means the company can start making ready to include European study centres for its future trials.

The company has started actively looking for a potential licensing partner. It plans to continue the search for a licensing partner and to prepare for a ph II study alongside advancing its other development project with ALZ-201.

Timeline from the company



**Full analysis and a report are expected to be presented in early 2024.*

Source: Company

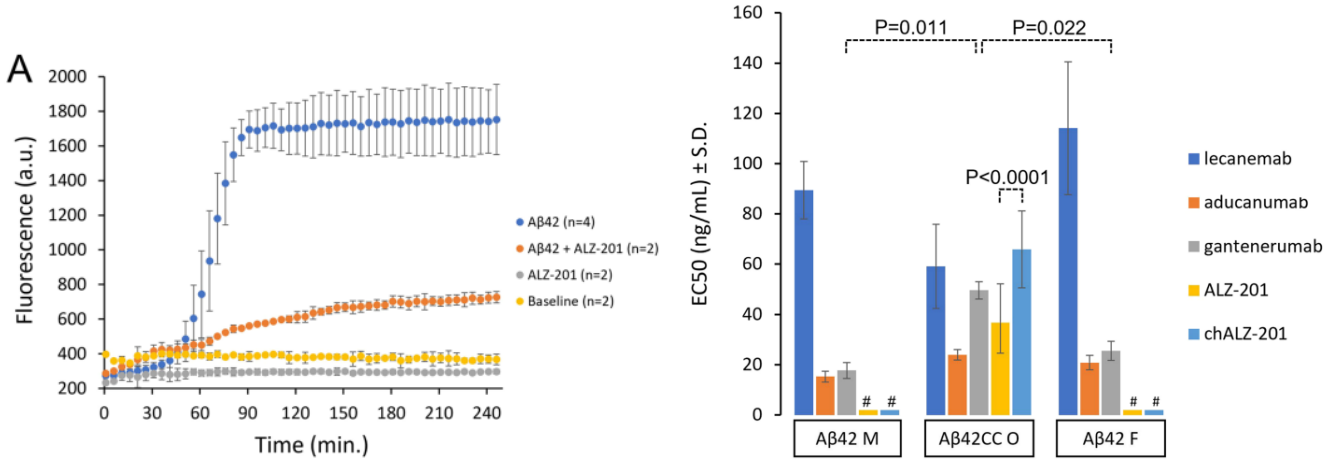
The company's other drug candidate – ALZ-201

Using the same technology, Alzinova is also developing the ALZ-201 antibody, which is currently in preclinical development. ALZ-201 is a monoclonal antibody obtained from mice immunised with ALZ-101 developed to specifically target and neutralise the toxic form of the amyloid-beta peptide – oligomers. The ALZ-201 antibody does not bind to other, harmless forms of amyloid-beta, such as fibrils and plaque, which has been shown in preclinical studies on human material. The company is currently developing a humanised version of ALZ-201 in preparation for a clinical ph Ib study in Alzheimer's patients. This is expected to start in 2024 at the earliest.

Preclinical results suggest that a small amount of Aβ42 oligomers account for the chief toxic effect in Alzheimer's, and that specificity for this is probably necessary to achieve a good therapeutic effect from an antibody treatment. These results support the argument that ALZ-201 has the potential to stop or hinder the progressive cognitive deterioration seen in Alzheimer's sufferers. Passive immunotherapy with ALZ-201 can be further developed as an effective complement and a disease-modifying alternative to the ALZ-101 therapeutic vaccine.

The drug candidate was noted in Alzheimer's research & therapy in 2022. ALZ-201 was shown to have had a positive physiological and protective impact on mouse neurones in a post-mortem Alzheimer's brain extract. Its specificity indicated that a particular type of soluble Aβ42 oligomer can account for much of the neurotoxicity seen with Alzheimer's. This critical attribute highlighted the potential of ALZ-201 as a new drug candidate that can achieve a clinically therapeutic effect on Alzheimer's, according to the article.

Examples from the article: binding analysis of ALZ-201 (left) and comparison with other treatments (right)



*__Left__: binding analysis of ALZ-201; __right__: analysis of how well the different drug candidates bind to Aβ monomers (M), oligomers (O), and fibrils (F). # Indicates that no binding was detected in the tests. Note that a lower signal indicates a stronger binding.

Source: Alzheimer's Research & Therapy

During 2022, Alzinova presented at CTAD – an annual Alzheimer's conference. The conference focused on clinical development of new drug candidates for Alzheimer's treatment. Alzinova's CSO Anders Sandberg summarised the development project in a poster presentation. This covered the progress of the ALZ-201 monoclonal antibody and its unique binding profile versus other drug candidates under development. The data showed that ALZ-201 differs markedly from lecanemab, aducanumab, and gantenerumab in that it binds specifically to oligomers alone. Thanks to this targeted bonding profile, ALZ-201 is believed to have a robust neutralising effect on the toxic form of amyloid-beta extracted from the brains of deceased Alzheimer's patients.

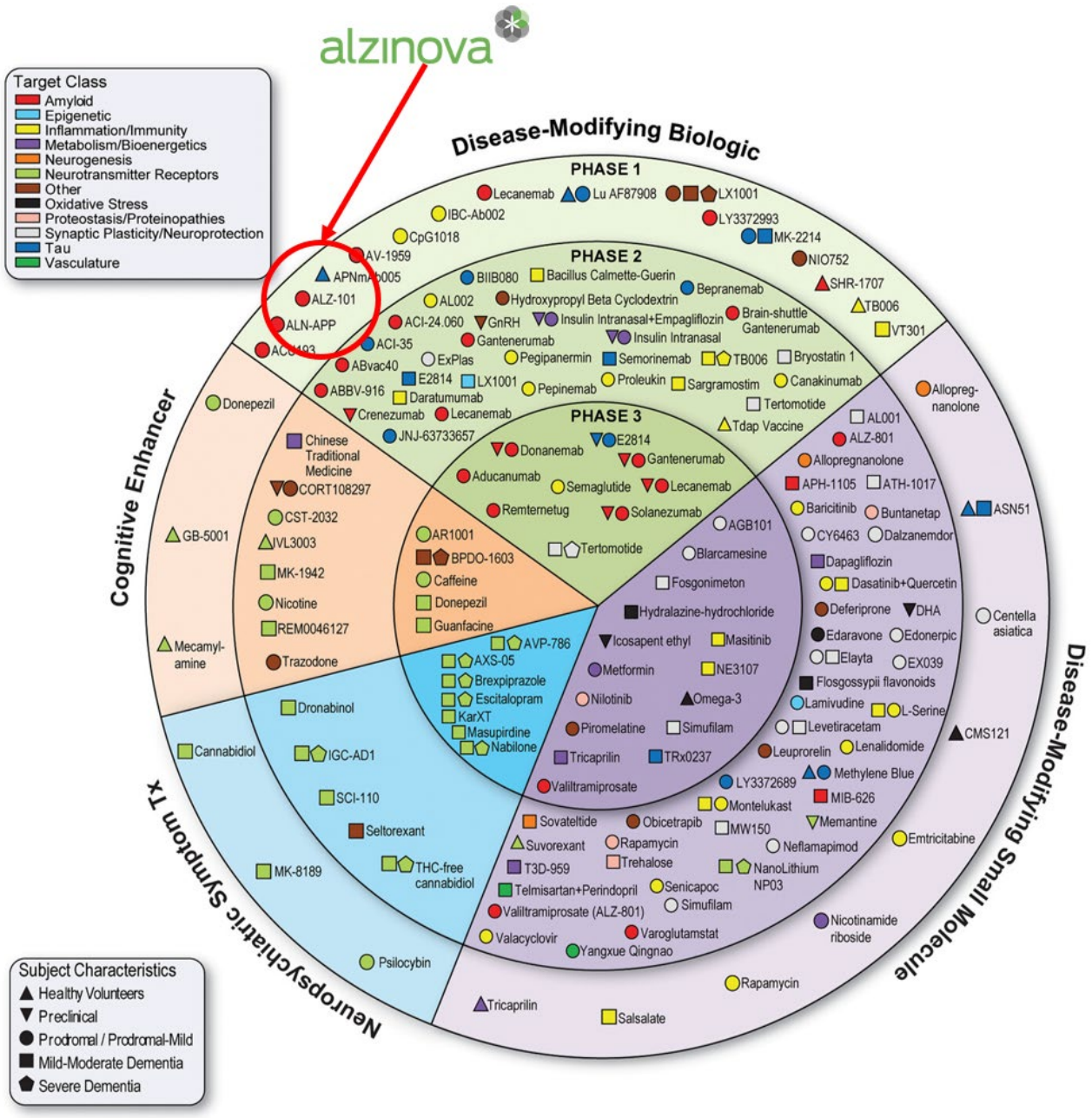
As the project is in the preclinical phase, we do not include it in our revenue forecasts.

The state of play in Alzheimer's – 2023

As stated above, there are several well-documented mechanisms in the research into the physiological and pathological basis for Alzheimer's. These include Aβ deposition, abnormal phosphorylation of tau protein, decreased acetylcholine activity, etc. A key theme in ongoing Alzheimer's research is the continued development of drugs that can remove amyloid plaques from the brain. Researchers believe that removing amyloid plaque from the brain can hinder the progress of Alzheimer's disease. The starting point for these mechanisms is, among others, the amyloid cascade hypothesis. Removal of amyloid-beta has been the most studied mechanism in the field.

However, it has been impacted by several failures, and only one drug candidate has reached as far as accelerated approval and one to full approval in the US. Unfavourable results from study after study have prompted a debate regarding how key amyloid-beta is to the disease's progression. Meanwhile, a number of projects have been based on the tau hypothesis. Below, we look at the most discussed drugs that have recently been approved or are on their way to approval in the largest markets – the US and Europe. We also show the drug development pipeline in Alzheimer's.

Drug development pipeline in Alzheimer's



Source: Traditional research & Clinical interventions (2023)

Immunotherapy targeting Aβ has been shown as a possible way to hinder Alzheimer's progression. There are two treatment principles for such therapy: inducing the immune system to produce its own antibodies (active immunisation), or direct injection of foreign antibodies (passive immunisation).

As of the start of 2023, there were 187 ph I, II, or III studies ongoing, evaluating 141 unique Alzheimer's treatments. A total of 36 drug candidates were being investigated in 55 ph III studies, while 99 ph II and 33 ph I studies were registered. The most common being studied were disease-modifying therapies, accounting for 78% of all ongoing studies. Among these, 22 studies focused on Aβ and 13 on tau. We see a less competitive landscape within vaccines than in the general Aβ area. Of the 20 studies conducted over the past 20 years, only four were completed and several were suspended. Full data is hard to locate from several of these, while a number of projects fell dormant. Currently, we can see only three direct competitors to Alzinova's ALZ-101.

A selection of clinical studies with Alzheimer's vaccines

Drugs	Immunogen/ peptide region	Sponsor	Study Population	Administration	NCT Number	Phases	Status	Start Date	Completion Date
AADvac1	Tau fragment sequence (294–305) KDNIKHVPGGGS	Axon Neuroscience SE	Mild to moderate AD	Subcutaneous	NCT01850238	Phase I	Completed	May 2013	Mar 2015
		Axon Neuroscience SE	Mild AD	Subcutaneous	NCT02579252	Phase II	Completed	Mar 2016	Jun 2019
ACI-35.030	Phosphorylated-Tau	AC Immune SA	Early AD, tauopathy	NA	NCT04445831	Phase I / Phase II	Active, not recruiting	Jul 2019	Oct 2023
ABvac40	Multiple repeats of short C terminal Aβ (x-40)	Araclon Biotech S.L.	Mild cognitive impairment, very mild AD	Subcutaneous	NCT03461276	Phase II	Active, not recruiting	Feb 2018	Dec 2022
ACC-001	Aβ (1–7) peptide	Pfizer	Mild to moderate AD	Intramuscular	NCT00959192	Phase II	Completed	Aug 2009	Jan 2013
		Pfizer	Mild to moderate AD	Intramuscular	NCT01238991	Phase II	Terminated	Dec 2010	Dec 2013
		Pfizer	Mild to moderate AD	Intramuscular	NCT00752232	Phase II	Completed	Dec 2008	Jul 2012
		Pfizer	Mild to moderate AD	Intramuscular	NCT00960531	Phase II	Terminated	Jul 2009	Dec 2013
		JANSSEN	Mild to moderate AD	Intramuscular	NCT01284387	Phase II	Completed	Jan 2011	Feb 2014
AFFITOPE AD01	Synthetic N terminal Aβ mimotope	Affiris AG	Mild to moderate AD	Subcutaneous	NCT00495417	Phase I	Completed	Jul 2007	Aug 2009
AFFITOPE AD02	Synthetic N terminal Aβ mimotope	Affiris AG	Mild to moderate AD	Subcutaneous	NCT00633841	Phase I	Completed	Feb 2008	Sep 2009
ALZ-101	Soluble oligomeric Aβ	Alzinova AB	Early AD	Intramuscular	NCT05328115	Phase I	Recruiting	Sep 2021	Jul 2023
CAD106	Aβ (1–6) peptide	Novartis	AD	Subcutaneous	NCT01023685	Phase II	Completed	Dec 2009	Feb 2012
		Novartis	AD	Subcutaneous	NCT00956410	Phase II	Completed	Sep 2009	Jun 2011
		Novartis	Mild AD	Intramuscular	NCT01097096	Phase II	Completed	Mar 2010	Dec 2012
Lu AF20513	Engineered mixed-peptides with Aβ (1–12) repeats and tetanus toxin sequences	H. Lundbeck A/S	Mild AD	NA	NCT03819699	Phase I	Terminated	Dec 2018	Jun 2019
UB 311	Aβ (1–14) peptide	United Biomedical	Mild to moderate AD	Intramuscular	NCT00965588	Phase I	Completed	Feb 2009	Apr 2011
		United Neuroscience Ltd.	Mild AD	Intramuscular	NCT02551809	Phase II	Completed	Oct 2015	Aug 2018
		United Neuroscience Ltd.	Mild AD	Intramuscular	NCT03531710	Phase II	Terminated	Aug 2018	Oct 2019
V950	Aβ40	Merck Sharp & Dohme LLC	AD	Intramuscular	NCT00464334	Phase I	Completed	Mar 2007	Jan 2012

Source: Neuroscience and biobehavioral reviews (2023)

A handful of the competitors in the vaccine field

Company	Project	Specificity	Ph (2023)
AC Immune	ACI-24	F, O, M	Ph I/IIb
Araclon Biotech GRIFOLS	ABvac40	F,M	Ph IIa
vaxxinity	UB311	F,O,M	Ph IIa
alzinova	**ALZ-101**	**O**	**Ph Ib**

*F = fibrils, O = oligomers, M = monomers

Source: EPB

AC Immune – vaccine candidates for both Aβ and tau

AC Immune is a biopharma company based in Switzerland, with a subsidiary in the US. The company is developing two types of vaccines against Alzheimer's – ACI-24 (anti-Aβ) and ACI-35 (anti-tau). We consider the Aβ-focused programme a clear competitor to ALZ-101. A completed ph I/IIb study (EudraCT 2008-006257-40) showed that the ACI-24 vaccine was not immunogenic, after which the company amended the formulation and administration path in its successor, ACI-24.060. Based on the preclinical results, immunisation with ACI-24.060 is expected to provide **a broad immune response to Aβ**. Drug candidate ACI-24 is currently undergoing a ph Ib/II trial.

Araclon Biotech – vaccine candidate for Aβ

Araclon Biotech, a Spanish biotech company fully owned by Grifols, focuses on Alzheimer's research. Its clinical ph II study, AB1601 (NCT03461276), showed that its vaccine candidate ABvac40 was safe, well-tolerated, and immunogenic. A high concentration of antibodies were seen in plasma across the whole study, and ABvac40 demonstrated a sufficient safety profile regarding ARIA-E, ARIA-H, and aseptic meningo-encephalomyelitis during the 36–42-month follow-up period. ABvac40 does not target oligomers, instead binding only to the shorter Aβ40 peptide that most believe has only a minor effect on the course of the disease compared with the more toxic Aβ42. Final study results, including exploratory endpoints, will be published during Q4 2023.

United Biomedical – Vaxxinity's UB311

United Biomedical is a multinational biopharma company with its roots in the US. Its Vaxxinity subsidiary is developing UB311, a vaccine candidate targeting Aβ. The clinical ph I and ph IIa studies showed that UB-311 is well-tolerated in early Alzheimer's patients given repeat dosing over three years, with a safety profile comparable with placebo and only a few isolated cases of amyloid-related side effects. Moreover, it demonstrated an immunological result. However, the candidate is not oligomer-specific but binds to fibrils, oligomers, and monomers. The FDA has awarded UB-311 Fast Track Designation.

The big guns in AD treatment and research

Passive immunisation – with non-body antibodies – is the treatment type that has been in the spotlight for the past two years. In June 2021, the FDA approved the first new Alzheimer's drug since the 1990s: aducanumab has been developed by NeurImmune and inlicensed by Biogen. Earlier in the year, the agency approved another antibody treatment, the Swedish-developed monoclonal antibody lecanemab – the result of a strategic research collaboration between BioArctic and Eisai. Eisai has been responsible for the development and regulatory interactions for lecanemab globally, working alongside Biogen on marketing and commercialisation of the product, with Eisai as the ultimate decision-maker.

Another success in the field this year has come from Eli Lilly. The company announced positive results from a ph III study with drug candidate donanemab. The results showed that the drug slows down the cognitive decline in early-stage Alzheimer's. We could thus shortly see a third approval of a new Alzheimer's treatment. The situation in Europe differs to that in the US, as no disease-modifying Alzheimer's treatments have been approved by the EMA medicines agency. The registration process for lecanemab is ongoing in Europe.

Aducanumab, lecanemab, and donanemab all reduce the amount of plaque, with some slowing down of the disease's progress as a result. There was also earlier some hope regarding Roche's drug candidate gantenerumab. After the readout of its ph III study did not meet expectations, the project was abandoned in December 2022.

Comparison of the three most talked-about drug candidates

	Aducanumab Intravenous infusion	Donanemab Intravenous infusion	Lecanemab Intravenous infusion
Indication	Early AD	Early AD	Early AD
Effect on cognition (CDR-SB scale)		29%	26%
Blood-brain barrier penetration	Low (1,5%)	Low (0,1%)	Low (0,3%)
Brain swelling	35%	24%	13%

Source: EPB

Lecanemab – Biogen & Eisai

The FDA had previously approved lecanemab via its *Accelerated Approval* process, based on the positive results from a ph IIb study. Traditional authorisation was based on the results of CLARITY-AD, a ph III study that registered 1,795 patients who received either lecanemab (10 mg/kg) or placebo every other week via intravenous infusion. This study achieved all primary and secondary endpoints and demonstrated a 26% reduction in clinically proven cognitive decline on the CDR-SB scale *(Clinical Dementia Rating)* after 18 months of treatment. Life quality analysis, using the EQ-5D-5L and QOL-AD scales, also showed an average improvement of 50% over the 18 months.

The most common side effects included ARIA. Given these safety concerns, the FDA included a *black box warning* for ARIA in lecanemab's prescription information. This explained that lecanemab can cause ARIA and stated that genetic testing for ApoE-e4 should be carried out ahead of treatment. Patient monitoring should include regular MR scans of the brain, three during the first 14 weeks of treatment. Caution should be exercised when considering the use of lecanemab for patients taking anticoagulants. Patients in Europe cannot yet access this new treatment. Treatment with lecanemab is currently undergoing a full evaluation by the EMA, following the submission of a marketing authorisation application in January 2023.

***Black box warning* – what is that?**

A black box warning is a label on prescription medication that warns patients and caregivers about important safety considerations, such as serious side effects or life-threatening risks. Also known as a black label warning or a boxed warning, it is named for the black border around the warning text on a medicine's packaging, label, and other descriptive documentation.

Aducanumab – Biogen & Eisai

Aducanumab has undergone two clinical ph II trials, with a demonstrated improvement in patients in these studies. Despite the controversy, the FDA approved aducanumab in the US in mid-2021 for use in patients with mild Alzheimer's. Tolerability and safety for the treatment are currently being evaluated and aducanumab is not widely used. Approvals in Europe and Japan remain under evaluation. The FDA's approval is dependent upon Biogen conducting further studies. The first was launched at the end of July, at the Alzheimer's Association International Congress. The ICARE-AD study will follow 6,000 Americans for ten years. The study has no control group receiving placebo.

Donanemab – Eli Lilly

Earlier this year, Eli Lilly presented data from its TRAILBLAZER-ALZ 2 ph III study with 1,736 patients. Topline data showed that the primary endpoint was achieved: treatment with donanemab slowed down the clinical disease progression significantly. The evaluation was carried out using the global cognitive and functional scale (iARDS), which showed a 19–22% reduction for all participants receiving donanemab compared to the placebo group. The reduction on the CDR-SB scale was 29%.

In terms of the drug's safety, amyloid-related imaging abnormalities (ARIA) were the treatment's most common side effects in the study. ARIA occurred across the entire class of amyloid-plaque-clearing antibody therapies, these findings being consistent with other investigative therapies in the same class. Occurrences of ARIA and infusion-related reactions were consistent with the earlier TRAILBLAZER ALZ study. While many cases of ARIA are transient or asymptomatic, ARIA can prove serious, even leading to death in some cases.

In the donanemab treatment group, cerebral swelling (ARIA-E) was reported in 24% of TRAILBLAZER-ALZ 2 participants. Micro bleedings in the brain were seen in 31% of participants receiving donanemab, compared with just over 14% of placebo participants. Only a little over 2% of patients in the study experienced the severe form of ARIA. Eli Lilly expects an FDA decision by the end of 2023.

Several other trials are ongoing with donanemab. One study, TRAILBLAZER-ALZ 3, is investigating whether donanemab treatment can delay or prevent the development of Alzheimer's. Another, called TRAILBLAZER-ALZ 4, is comparing donanemab treatment with that of another anti-amyloid drug – aducanumab.

Remternetug – Eli Lilly

Remternetug is another type of amyloid-targeting immunotherapy drug. It is also being developed by Eli Lilly, the maker of donanemab. Like donanemab, it is intended to treat early-stage Alzheimer's patients. Remternetug has been described by several sources as a second-generation immunotherapy, as it targets the same type of amyloids as donanemab, but hopefully with a better performance. It is also administered to patients in a different manner: an injection into subcutaneous fat. Other immunotherapies being developed for Alzheimer's are given via intravenous drip. This requires that patients visit a clinic to receive the medication and such visits can take up to an hour.

A larger ph III study with remternetug (TRAILRUNNER-ALZ 1) began in August 2022 to test the effectiveness and safety of remternetug in a larger group of people with mild Alzheimer's. The study is expected to conclude during 2025.

Challenges in the Alzheimer's field

Alzheimer's is a research field with a history of failures. A comeback – in the form of two approvals in the US (Aduhelm® and Leqembi®) – and a further potential approval on the horizon (donanemab), together with ongoing studies, give hope and optimism for the future, though. Advances in Alzheimer's drug development would provide incredibly high returns on investments – proof of this was seen in autumn 2022, when several Alzheimer's-related companies' share prices shot up after Eisai released positive data on lecanemab.

Given the **high risk and previous lack of commercial success** associated with CNS drug development, many pharma companies have drastically cut their investments in CNS diseases over the past 20 years. The Alzheimer's field has been under-financed but has seen wind in its sails in recent years thanks to the approval of Leqembi® (lecanemab).

Moreover, **clinical Alzheimer's studies cost more per patient** than trials in other therapeutic areas, with 50–70% of the costs spent on patient screening. It is challenging to recruit to Alzheimer's studies and patient attrition is high as the studies are often lengthier than in other therapeutic areas, while patients are usually older and have high co-morbidity.

Co-morbidity

The existence of concurrent or additional medical conditions at first diagnosis, or the specific condition under investigation. Comorbidity can affect not only a patient's capacity to function, but also their survival.

Side effects of the approved treatments are uncomfortable and, in many cases, severe. Traditional symptom-alleviating treatment drugs can cause side effects like diarrhoea, vomiting, and stomach pain. Among the new antibody treatments, ARIA is the most serious side effect – the above-mentioned Leqembi® is sold in the US with a black box warning for just this reason.

Alzheimer's **is often diagnosed at the later stages**, when substantial brain damage has already occurred. There are also many **questions regarding the amyloid cascade hypothesis**. Some sources claim that the amount of amyloid plaque in the brain has little to no correlation to the extent of dementia and that the localisation of plaque does not correlate with the disease phenotype. There are even many people with large amounts of plaque in the brain who do not have major cognitive impairment. Researchers continue to debate the extent to which amyloid plaque directs the course of the disease.

Moreover, there is the **problem with animal models**. Animal models for Alzheimer's cannot fully replicate the human disease, making it challenging to translate the results from preclinical research into effective human treatments.

The ageing global population is exacerbating the occurrence of Alzheimer's. This demographic challenge highlights the urgency in developing effective treatments and preventative strategies, despite the difficulties mentioned above. We believe Alzinova is in a solid position to handle these challenges.

The market for Alzheimer's treatments

The Alzheimer's market is expected to grow by a CAGR of 20% in 2020–2030 and to reach just over USD 14bn in the eight largest markets (8MM – the US, France, Germany, Italy, Spain, the UK, Japan, and China), according to the latest report from GlobalData (2023). Other sources indicate a market size of up to USD 11bn. Key factors driving this growth include an ageing global population, prompting an increase in occurrences of Alzheimer's, and, in particular, the entry of disease-modifying therapies (DMTs) into the market.

Market size in value terms (USDm)

Product	Company	2022	2023e	2024e	2025e	2026e	2027e	2028e
Leqembi	Eisai		87	528	1 353	2 443	3 368	4 246
Donanemab	Eli Lilly			544	1 007	1 467	1 746	2 057
ANAVEX 2-73	Anavex Life Sciences					1 127	1 360	1 202
ACI-24	Undisclosed partner sales							768
LY3372993	Eli Lilly				281	406	488	572
PRX012	Prothena						92	270
SAGE-718	SAGE Therapeutics					24	124	249
KarXT	Karuna Therapeutics				13	62	134	220
ACI-24	AC Immune			39	70	95	138	166
AL002	Alector				10	43	67	137
Other		747	654	614	598	652	813	971
Total		**747**	**741**	**1 726**	**3 332**	**6 319**	**8 330**	**10 860**

Source: Evaluate Pharma

Deals in the Alzheimer's field

According to the WHO's World Alzheimer Report, the target is to double the output of global research into Alzheimer's in 2017–2025. The field remains severely under-financed, but there seems to be light at the end of the tunnel. Licensing business in Alzheimer's recovered in 2020 and 2021, according to IQVIA, but the situation for partnerships once again faced challenges in 2022–2023, owing to the tough climate for financing. However, there has been much activity in the field – for example, the clinical development discussed above. But it is not only drug development in the spotlight. During 2020, Pfizer collaborated with IBM on developing an AI model to predict Alzheimer's in healthy humans before symptom development, and in 2021, Genentech announced a co-operation with Winterlight Labs on speech-based digital biomarkers.

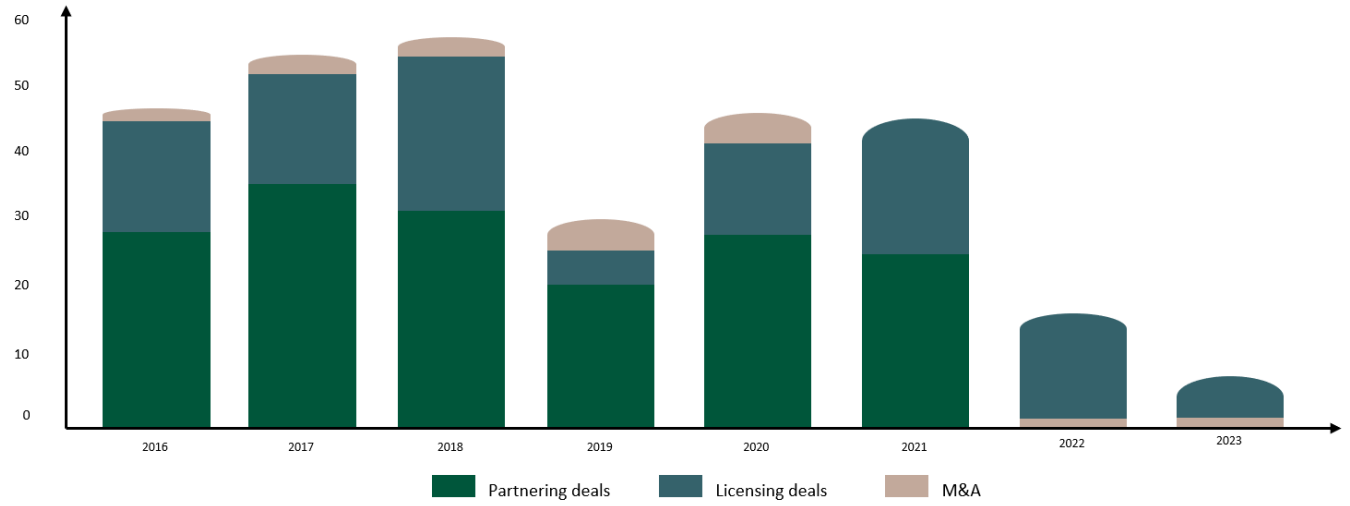
Selected licensing deals in Alzheimer's in 2018–2021

Date	Total value	Company	Mechanism/field
25-08-2021	USD 3bn	Roche & Shape Therapeutics	RNA platform for gene therapy
27-02-2020	USD 2.7bn	Biogen & Sangamo Therapeutics	-
20-03-2018	USD 2.3bn	Prothena & Celgene	Anti-tau antibody
02-07-2021	USD 2.2bn	GSK & Alector	Monoclonal antibodies
29-07-2020	USD 2.1bn	UCB & Roche	Monoclonal antibodies
12-12-2018	USD 1.8bn	Eli Lilly & AC Immune	Tau aggregation inhibitors
01-11-2018	USD 1.2bn	Sanofi & Denali Therapeutics	RIPK1 inhibitors
05-01-2018	USD 1.1bn	Takeda & Denali Therapeutics	ATV platform

Source: IQVIA

Most Alzheimer's drug development deals in 2016–2021 were either partnerships or licensing. During 2022–2023, the number of deals was 22, with a mean contract value of USD 470m. In our model, we forecast Alzinova making a licensing deal when its ph II study is completed, but there are also opportunities for the company to sign a deal before that – both before and during an ongoing ph II study. It has already begun seeking a possible partner. We include a deal value of just over USD 500m in our model.

Alzheimer's deals in 2016–2023



Source: IQVIA, Evaluate Pharma

Addressable population and sales forecasts for ALZ-101

We estimate the number of Alzheimer's patients at 6.7m in the US and 10.7m in Europe (including non-EU countries), with these numbers increasing by 4% and 2%, respectively, every year. Moreover, we expect that some 45% of these patients are diagnosed and offered treatment. This constitutes the addressable population for ALZ-101 in our model. We are aware of the large number of unrecognised cases when it comes to diagnosing Alzheimer's, and also that the disease can be categorised into different phases. The aforementioned ph Ib study targeted treatment of early-stage Alzheimer's. We choose to look at the entire diagnosed Alzheimer's population based on the data available to us. We forecast peak sales surpassing USD 4bn in the US and Europe in 2035.

Revenue estimates (non-risk-adjusted)

		2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035
USA														
AD prevalence (millions)	4%	6,7	6,9	7,2	7,4	7,7	8,0	8,2	8,5	8,8	9,1	9,5	9,8	10,2
Patients receiving treatment	45%	3,0	3,1	3,2	3,3	3,5	3,6	3,7	3,8	4,0	4,1	4,3	4,4	4,6
									START					**PEAK**
Launch curve									*0,05*	*0,20*	*0,40*	*0,70*	*0,85*	*1,00*
Market penetration	5%								0%	1%	2%	4%	4%	5%
Patients treated with ALZ-101									0,01	0,04	0,08	0,15	0,19	0,23
Price	10 000 USD								10 000	10 000	10 000	10 000	10 000	10 000
Price adjustment	2%								0%	0%	0%	0%	0%	0%
Sales (USDm)									**96**	**397**	**823**	**1 492**	**1 876**	**2 286**
Europe														
AD prevalence (millions)	2%	10,7	10,9	11,4	11,6	11,8		12,3	12,5	12,7	13,0	13,2	13,5	13,7
Patients receiving treatment	45%	4,8	4,9	5,1	5,2	5,3		5,5	5,6	5,7	5,8	6,0	6,1	6,2
									START					**PEAK**
Launch curve									*0,05*	*0,20*	*0,40*	*0,70*	*0,85*	*1,00*
Market penetration	5%								0%	1%	2%	4%	4%	5%
Patients treated with ALZ-101									0,01	0,06	0,12	0,21	0,26	0,31
Price	7 500 USD								7 500	7 500	7 500	7 500	7 500	7 500
Price adjustment	2%								0%	0%	0%	0%	0%	0%
Sales (USDm)									**105**	**430**	**876**	**1 563**	**1 934**	**2 318**
Total sales (USDm)									**201**	**827**	**1 700**	**3 055**	**3 810**	**4 604**

Source: EPB

We forecast that ALZ-101's market penetration of this addressable population reaches 5% in both the US and Europe. We believe the product will be approved in 2030 at the earliest, by which time there will be several approved treatments, making it hard to grab a larger market share. Effectiveness of the treatment will be crucial for market penetration, while the method of administration will also play a key role. The vaccine is administered in a far more cost-efficient manner and requires fewer healthcare resources compared with antibody treatments, for example, which today must be administered as an intravenous infusion. Higher market penetration is thus possible. We use the latest approved Alzheimer's treatment – lecanemab – when considering price setting. According to different sources, a per patient prescription for lecanemab costs USD 19,500 a year, including USD 11,000 in personal expenses. Our forecasts are thus highly dependent on the chosen market penetration level and the price when the product reaches the market. Below, we present a scenario analysis with the impact of market penetration and price on peak sales for ALZ-101.

Sensitivity analysis: the impact of price and market penetration on ALZ-101 peak sales in the US and Europe (USDm)

US					
	2%	**4%**	**5%**	**10%**	**15%**
USD 5,000	457	914	1 143	2 286	3 429
USD 7,500	686	1 371	1 714	3 429	5 143
USD 10,000	914	1 829	2 286	4 571	6 857
USD 12,500	1 143	2 286	2 857	5 714	8 571
USD 15,000	1 371	2 743	3 429	6 857	10 286

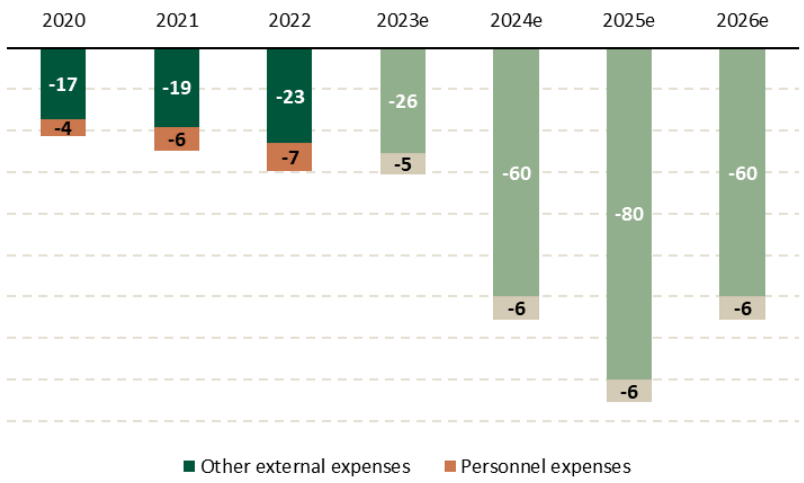
Europe					
	2%	**4%**	**5%**	**10%**	**15%**
USD 1,000	124	247	309	618	927
USD 2,500	309	618	773	1 546	2 318
USD 7,500	927	1 855	2 318	4 637	6 955
USD 10,000	1 236	2 473	3 091	6 182	9 273
USD 12,500	1 546	3 091	3 864	7 728	11 591

Source: EPB

Financial position and overall forecasts

Alzinova is in the early development stage and has thus not reported any revenues yet. Operating expenses in 2022 rose somewhat compared with 2021, and we expect them to increase considerably from the initiation of the clinical ph II study with ALZ-101 and also the clinical ph Ib study with ALZ-201. We believe operating expenses will comprise R&D costs for the respective development programmes, overheads, and fixed costs and other external costs for consultancy work, etc. We model no revenues until 2026, with revenues subsequently stemming from one-off payments, milestones, and royalties from future potential partners.

Cost profile: historical figures and forecasts



Source: EPB

Cash and cash equivalents totalled just over SEK 33m at the end of Q3. Given the current cost profile and a planned clinical study, we expect the company will need to secure additional financing to undertake the planned ph II study. The company itself believes it can use cash to finance the preparatory part of the planned study. Development expenses for Alzheimer's drugs far surpass most estimates in other therapeutic areas – for example, studies require a rigorous screening process and long follow-up period. Bearing that in mind, we include capital raises in our model.

So far, the company has taken in SEK 199m through rights and directed issues and a warrant programme.

Year		(SEKm)*
2015	Rights issue	17
2015	Directed issue	5,0
2016	Warrant programme	14
2018	Rights issue	30
2018	Directed issue	15
2019	Warrant programme (management)	2
2020	Warrant programme (management)	0,3
2020	Rights issue	50
2020	Directed issue	3
2022	Warrant programme	3
2022	Rights issue	34
2023	Warrant programme	26
Total		**199**

**before issue costs*

Source: Company

Valuation of peer companies

As Alzinova is not yet profitable, we do not consider the recognised key performance indicators as particularly relevant in a relative valuation. Instead, we use technology value (EV) to evaluate Alzinova versus other Alzheimer's companies at a similar development stage. We also consider the number of active projects. In Sweden, there is only one peer company – AlzeCure – which develops Alzheimer's treatments. AlzeCure has a symptom-alleviating candidate ACD856 (NeuroRestore platform) in ph I and a disease-modifying candidate ACD679 in preclinical, plus another preclinical candidate – ACD860 (Alzstatin platform). We have also selected three US companies that clearly show the value differences between the Swedish and US markets. Companies in ph I are valued far higher, even though none of their projects have been approved and none of the companies have turned profitable.

Alzinova even trades at a discount to AlzeCure Pharma. We believe this stems from the previous delays to the ph Ib study and as AlzeCure is running projects across two indications: Alzheimer's and pain relief.

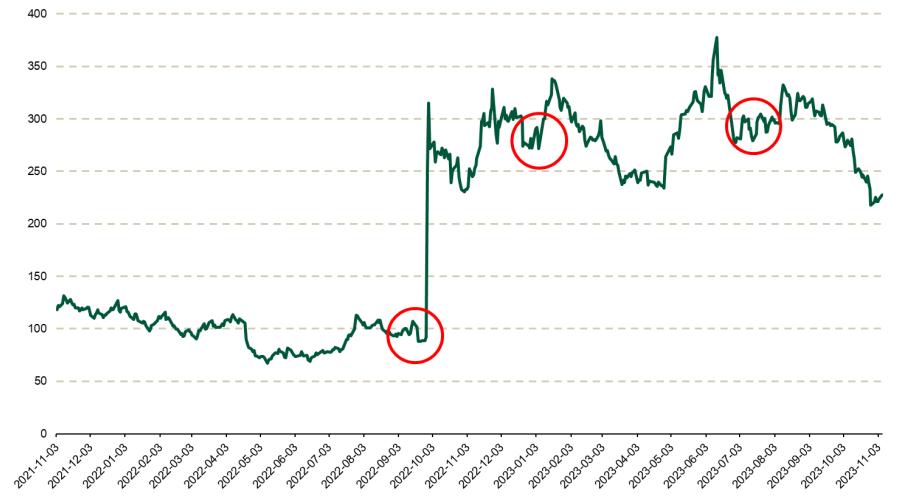
Company	Share price	Market cap (SEKm)	EV (SEKm)	EBIT (SEKm)	# of projects	Leading project
AlzeCure Pharma	4	261	216	-42	6	Ph I*
AC Immune	30	2481	1560	-813	9	Ph I/II
Acumen Pharmaceuticals	24	1382	-182	-552	1	Ph I
Alzamend Neuro	21	135	118	-162	5	Ph II
Alzinova	**2**	**106**	**70**	**-16**	**2**	**Ph Ib**
Average		**873**	**356**			
Median		**261**	**118**			

**Ph I project in AD*

Source: FactSet (3 November 2023)

Looking at the potential development of a company with a project that has gone all the way to market – BioArctic – the picture is much more encouraging. In September 2022, BioArctic announced that lecanemab had reached both primary and secondary endpoints in the CLARITY-AD study, prompting a share price hike. Then, in January 2023, lecanemab received accelerated approval, followed by full FDA approval in July. The share price movements in BioArctic have stabilised since the major news in September 2022, but shareholders have seen substantial returns despite the share price normalising during 2023. Alzinova has a long way to go to take ALZ-101 or ALZ-201 all the way to market, but if it succeeds with this, the potential for great returns is enormous.

BioArctic's share price (2021–2023)



Comparison BIOA & ALZ Company	Share price	Market cap (SEKm)	EV (SEKm)	EBIT (SEKm)	Leading project
BioArctic B	223	19 620	18 584	280	Godkänd produkt
Alzinova	2	106	70	-16	Fas Ib

Source: FactSet (6 November 2023)

Risks

Clinical development risk

In terms of companies in early clinical development, the greatest risk is always that they fail in their planned clinical studies or do not receive approval to begin such studies. There is also a risk that the authorities do not approve an application for clinical studies or to advance further with ongoing studies. Both preclinical and clinical studies are associated with considerable uncertainty, as well as risks with their timing or results. We believe the likelihood of such risks is high, as for other R&D companies in relatively early development stages.

Risks related to patient recruitment or delays

The Alzheimer's field is known for its lengthy follow-up periods for clinical studies. This entails risk with both patient recruitment and delays. We do not yet know the design of the planned ph II study with ALZ-101, but it is likely to include more than 150 patients. Alzinova has previously experienced delays with its ph Ib study, which is a common problem for clinical studies in general. We consider the risks associated with this as high.

Risks related to key staff

The company has a compact management structure and is highly dependent on key executives. If it were to lose some of its key staff, this would damage the company's future development.

Commercialisation risk

The company has not yet commercialised any projects, such as via licensing deals, partnerships, or through its own development, or launched any drugs. It thus has not made any sales or generated any revenues.

Financial risks

Owing to the company's current cash position, it will, in our view, need to take in capital to run its business, unless it signs a licensing deal. There are no guarantees that it can raise the necessary capital at favourable terms, or that it can raise any such capital at all. Should it not manage to raise this capital, there is a risk to its continued operation. We believe the risk associated with its financial position is elevated in the short term.

Other risks

Other risks include those regarding the competitive environment. The changing legislative landscape also poses a risk. We consider the risks associated with these as medium-high.

Ownership structure and management

The largest shareholder in Alzinova in terms of capital and votes is Maida Vale Capital AB at 15.15%. Then come Avanza Pension with 7.24% and Nordnet Pension with 5.01% of each.

Shareholder	Number of shares	Capital (%)
Maida Vale Capital AB	6 747 686	15,15%
Avanza Pension AB	3 223 681	7,24%
Nordnet Pension AB	2 229 751	5,01%
Patrik Ahlvin	1 004 750	2,26%
Sara Gjertz	877 303	1,97%
Total for five largest shareholders	14 083 171	31,63%
Total for all shareholders	**44 531 265**	**100%**

Source: Company

Board of directors

Julian Aleksov – Chair

Board member since 2023. He has more than 25 years' experience in finance and international business development in the pharma and tech industries, including at Oasmia Pharmaceutical AB, and has been an investor and entrepreneur in several business areas, primarily drug development. Currently, board member at Maida Vale Capital AB and Hunterhex AB. Independent in relation to the company and its management, but not to major shareholders.

Anders Blom – board member

Board member since 2021. He has more than 25 years' experience of international economics and business development in the pharma and medtech industries. This includes as a partner and CEO at risk capital firm Nexttobe AB and as an executive VP and CFO at Oasmia Pharmaceutical AB (plc). Previous board experience from Hansa Biopharma AB (plc), Biolamina AB, Delta Projects AB, and Selego AB, among others. Currently, chair of the board at Maida Vale Capital AB, Terranet AB, Rosland Nordic AB, and others. Independent in relation to the company and its management, but not to major shareholders.

Per-Göran Gillberg – board member

Board member since 2020. He has 35 years' experience in the pharma industry. This includes pharmacology and neuropharmacology at Kabi, Kabi Pharmacia, Pharmacia & Upjohn, and at Pharmacia, AstraZeneca, and Albireo. Founder of Albireo AB and current board member at Dicot AB. Independent in relation to the company, its management, and major shareholders.

Clas Malmeström – board member

Board member since 2015. Doctor of the neurological clinic and laboratory for clinical immunology at Sahlgrenska University Hospital, Gothenburg. Since 2001, he has led research into multiple sclerosis (MS) at the hospital's MS centre and at Gothenburg University's institute for clinical neuroscience. Beyond academic research, he has taken part in several clinical drug development tests in MS led by Biogen-Idec, Merck, Novartis, Roche, and Sanofi, several of which have resulted in today's standard MS treatments. Independent in relation to the company, its management, and major shareholders.

Carol Routledge – board member

Board member since 2018. She is an R&D and drug development expert with more than 30 years' experience at pharma and biotech companies, with a focus on drug acquisition and profiling of NCE biology. This includes management within pharma research and development in several therapeutic areas, such as immunoinflammatory diseases and neuroscience. Previously a fund manager of a semi-philanthropic dementia fund and research manager and CEO of EDoN. Currently, Chief Medical and Scientific Officer at Small Pharma. Independent in relation to the company, its management, and major shareholders.

Anders Waas – board member

Board member since 2018. He has held several senior management positions at Astra, AstraZeneca, CV Therapeutics, Actogenics, and Tikomed AB. His previous experience lies in leadership, business development, and drug development. Currently, chair of the board at Transmed Gothenburg AB, Sobrera Pharma AB, Sortina Pharma AB, Iscaff Pharma AB, OligoNova Accelerate AB, and SiMSen Diagnostics AB. Independent in relation to the company and its management, but not to major shareholders.

Lena Degling Wikingsson – board member

Board member since 2020. She has 25 years' experience in the pharma industry. This includes regulatory questions and the development of biological drugs and vaccines at Dilafor, Avaris AB, Independent Pharmaceutica AB, SBL Vaccines, Accuro Immunology, and Läkemedelsverket (Swedish Medical Products Agency). Currently, CEO of Dilafor AB and chair of the board at Simplexia AB and Dilafor Incentive AB, board member at XNK Therapeutics AB. Independent in relation to the company, its management, and major shareholders.

Management

Kristina Torfgård – Chief Executive Officer

CEO since 2019. She has 30 years' experience of drug development having held key roles in the pharma and biopharma industries. Previously worked with R&D at AstraZeneca at both early and late stages and worked at Albireo AB/ Pharma Inc as VP Clinical & Regulatory Affairs and VP Global Project Head. Currently, a board member at GU Ventures.

Anders Sandberg – Chief Scientific Officer

Chief Scientific Officer since 2015. One of Alzinova's founders and was CEO during a transition period. He has extensive experience of protein research with an emphasis on protein stability and folding. Since 2007, he has worked with neurotoxic peptide aggregates, leading to the development of ALZ-101 and ALZ-201. He is also the co-inventor of Alzinova's AβCC technology, and he has been a deputy board member since 2011.

Håkan Skogström – Chief Financial Officer

Chief Financial Officer since 2020. He has more than 25 years' experience in senior financial management in the shipping sector. Previously, CFO and CEO at a privately owned Swedish shipping company with international operations, which he helped build, and CFO of Safe at Sea AB.

Kirsten Harting – Chief Medical Officer

Chief Medical Officer since 2023. She has more than 30 years' experience of medicine, clinical studies, and drug development, along with business development and launching products on the market at Lundbeck, Pfizer, ALK, and Novo Nordisk, among others.

Sebastian Hansson – Business Development Director

Business Development Director since 2023. He has 15 years' experience of pharma R&D and clinical development, CROs and GMP production of APIs (active pharmaceutical ingredients). Previously COO at SWIPP AB, project leader and key account manager at Polypeptide Group and head of business development at Solve R&C. Currently, board member at Bulb Intelligence AB, Tyto Competitice Intelligence Solutions AB, and Scientific Intelligence Consulting Öresund AB.

Stefan Pierrou – Development Project Director

Development Project Director since 2021. He has 25 years' experience in drug discovery and development. Previously, he has worked as a preclinical research manager and clinical project leader, and he has held several project-leading and management roles in R&D at AstraZeneca. Currently, CEO of ESP Life Science Consulting AB.

Patents and market protection

Both the company's development projects are based on the patented AβCC technology. ALZ-101 and ALZ-201 are patented through two patent families, as shown below.

Stable Aβ monomers and oligomers (ALZ-101)			
Region/country	**Patent no.**	**Status**	**Expires**
Australia	2009236699	Approved	14 April 2029
Europe*	2262526	Approved	14 April 2029
Japan	5817060	Approved	14 April 2029
Japan	6128450	Approved	14 April 2029
India	292362	Approved	14 April 2029
Canada	2721156	Approved	14 April 2029
China	ZL200980122412.X	Approved	14 April 2029
US	9688734	Approved	2 January 2030
US	10023622	Approved	14 April 2029
US	10138281	Approved	14 April 2029
Anti-oligomer antibodies (ALZ-201)			
Europe**	2683738	Approved	7 March 2032
US	9062102	Approved	30 July 2032

* Belgium, Switzerland, Lichtenstein, Czechia, Germany, Denmark, Spain, Finland, France, UK, Croatia, Ireland, Italy, Norway, Netherlands, Poland, and Sweden

**Switzerland, Germany, France, UK, Ireland, Luxembourg, Monaco, Netherlands, and Sweden

Source: Company

The patents for ALZ-101 expire in 2029 in most regions, posing a challenge for the company. Managing a short patent lifespan can be challenging for a biopharma company, but there are several strategies to maximise the value of intangible assets and ensure continued progress. For example, it could explore combination therapies that could provide a unique therapeutic advantage and also extend the patent protection and market exclusivity. Reformulation of an existing drug can lead to a new patent and thus also extend market exclusivity. In certain regions, the regulatory authorities offer supplementary protection certificates (SPCs) or patent extension for particular biomedical products.

Alzinova is working on further development of its patent portfolio. Earlier in 2023, the company handed in a new patent application for an evolved form of ALZ-201. If Alzinova receives a patent approval, the expected patent lifespan should extend to at least 2044. A clear strategy for further developing the patent portfolio is an essential factor in both ongoing and future partnership negotiations.

Appendix

Appendix 1: Glossary

Aβ or amyloid-beta – a peptide (part of a protein) created by the body that binds together in the brain and is a likely cause of Alzheimer's disease.

Amyloid fibrils – misfolded proteins that form aggregates.

Apolipoprotein E (ApoE) genotype – in around 20% of cases, Alzheimer's can be attributed to genetic polymorphism (sequence variation) in the APOE gene. Apolipoprotein E (ApoE) is a glycoprotein produced primarily by the liver and central nervous system. ApoE is found on the surface of lipoprotein particles and is important for the transport and absorption of blood fats. Dysfunctional ApoE can lead to increased plasma levels of cholesterol and triglycerides. There are three relevant allelic variants: ApoE3, EpoE4, and EpoE2. The E4 allele in particular suggests a greater risk of developing Alzheimer's. The E4 allele is also associated with increased cholesterol values and an increased risk of cardiovascular diseases.

ARIA – amyloid-related imaging abnormalities – identified with the help of MR scans, ARIA is, in most cases, seen as swelling in one or several regions of the brain (ARIA-E) or micro bleeding in the brain (ARIA-H). The impact of ARIA on patients is not clear-cut; these changes have been observed both with and without clinical symptoms.

EEG (electroencephalography) – a scan of the brain's electrical activity.

EMA (European Medicines Agency) – the EMA protects and promotes public health and animal health through the evaluation and monitoring of drugs in the EU and EES countries.

FDA (US Food and Drug Administration) – protects public health by ensuring that drugs, biological products, medtech products, foodstuffs, cosmetics, and radiation-emitting products fulfil fundamental safety requirements. In certain cases, the FDA must approve the sale of a product in the US market, while other products need only satisfy requirements for their manufacturing, marketing, and distribution.

Prodromal phase or prodromal stage – the period when initial signs or the first indications of a disease (prodromal symptoms) are noticed.

Spinal fluid test or lumbar puncture (LP) for post-mortem analysis – a diagnostic method for several conditions with neurological symptoms.

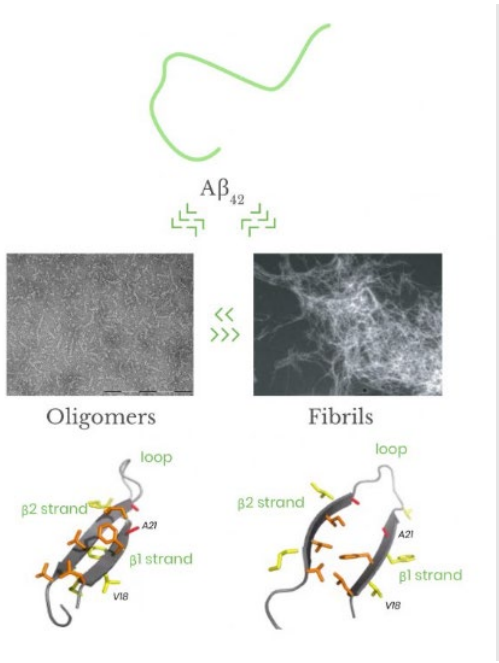
Appendix 2: Oligomer-specific immunotherapy – AβCC peptide technology

Alzinova's drug candidates are based on the company's proprietary AβCC peptide technology. The technology involves the covalent restriction of the Aβ peptide to ensure it forms only the soluble Aβ toxins (oligomers/protofibrils) that play a central role in the disease process.

By introducing a strategically placed covalent (a disulphide bond), it stabilises the oligomer structure and prevents the change in conformation that is needed for fibril formation. This results in an accumulation of Aβ42CC as stable and homogeneous oligomers.

The stabilised AβCC oligomers have the unique property of stimulating the immune system to produce antibodies that can differentiate between oligomers and less toxic forms of peptides, such as fibrils and monomers. This technology sets Alzinova in a unique position to isolate large quantities of synthetic mimetic Aβ42 oligomers that can be used as antigens in the development of immunotherapy.

Aβ peptide in aggregate as oligomers or fibrils



Source: Company

Appendix 3: Amyloid cascade hypothesis

The amyloid cascade hypothesis is the most widely accepted theory regarding the emergence of Alzheimer's. The hypothesis is based on amyloid-beta peptides (Aβ) aggregating in the brain, these accumulations in the form of oligomers and plaque disturbing the communication between nerve cells, resulting in nerve cell death in Alzheimer's. There is substantial evidence supporting this hypothesis in the form of genetic studies, neuropathological discoveries, neurochemical findings, and the results of experiments and newly FDA-approved treatments. Despite this, debate regarding the hypothesis continues. Some people appear to be able to cope with relatively large levels of Aβ plaque in the brain without showing clear cognitive symptoms, which adds to the discussions regarding the validity of the hypothesis.

Amyloid-beta is formed after cleavage from the parent APP molecule by the enzymes ß- and y-secretase. If a-secretase cleaves instead of y-secretase, no Aß is formed. After Aß is produced, soluble dimers, oligomers and protofibrils, plus insoluble plaque, are formed, accumulating between nerve cells. The relationship between Aß plaque and tau neurofibrillary tangles is unclear, but Aß pathology appears to lead to tau pathology. New research shows that Aß oligomers and protofibrils are particularly toxic for the brain, and they are believed to be the peptide forms causing the disease.

Income statement

	2020	2021	2022	2023e	2024e	2025e
Other operating income	15	17	17	16	16	16
Total revenues	**15**	**17**	**17**	**16**	**16**	**16**
Gross profits	**15**	**17**	**17**	**16**	**16**	**16**
General administrative costs	-4	-6	-7	-5	-6	-6
Other operating costs	-17	-19	-23	-26	-60	-80
EBITDA	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
EBITDA, adjusted	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
EBITA, adjusted	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
EBIT	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
EBIT, adjusted	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
Profit/loss before tax	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
Profit/loss before tax, adjusted	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
Net income	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
Net income, adjusted	**-6**	**-8**	**-13**	**-14**	**-49**	**-69**
Revenue growth	-	*16%*	*-4%*	*-2%*	*0%*	*0%*
Gross margin	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
EBIT margin, adjusted	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
EPS, adjusted	*-0,41*	*-0,48*	*-0,40*	*-0,32*	*-1,11*	*-1,56*
EPS growth, adjusted	-	*N.m.*	*N.m.*	*N.m.*	*N.m.*	*N.m.*

Source: Alzinova AB, EPB

Cash flow analysis

	2020	2021	2022	2023e	2024e	2025e
EBIT	-6	-8	-13	-14	-49	-69
Changes in working capital	0	-2	3	0	0	0
Cash flows from operating activities	**-6**	**-10**	**-10**	**-14**	**-49**	**-69**
Investments in intangible fixed assets	-15	-17	-17	-16	-16	-16
Cash flows from investment activities	**-15**	**-17**	**-17**	**-16**	**-16**	**-16**
Free cash flows	**-21**	**-27**	**-27**	**-30**	**-66**	**-86**
Rights issues / buybacks	53	0	37	0	85	85
Other items	-10	0	-7	0	0	0
Cash flows from financing activities	**43**	**0**	**30**	**0**	**85**	**85**
Cash flows	**22**	**-27**	**3**	**-30**	**19**	**-1**
Net debt	**-56**	**-29**	**-32**	**-2**	**-21**	**-21**

Source: Alzinova AB, EPB

Balance sheet

	2020	2021	2022	2023e	2024e	2025e
ASSETS						
Other intangible assets	44	62	78	95	111	127
Total fixed assets	**44**	**62**	**78**	**95**	**111**	**127**
Other current assets	1	1	1	1	1	1
Cash and cash equivalents and short-term investments	56	29	32	2	21	21
Total current assets	**56**	**30**	**33**	**3**	**22**	**22**
TOTAL ASSETS	**101**	**92**	**112**	**97**	**133**	**149**
EQUITY AND LIABILITIES						
Equity	96	88	106	91	127	143
Total equity	**96**	**88**	**106**	**91**	**127**	**143**
Other long-term liabilities	1	1	1	1	1	1
Total long-term liabilities	**1**	**1**	**1**	**1**	**1**	**1**
Trade payables	2	2	3	2	2	2
Other current liabilities	2	1	2	3	3	3
Total current liabilities	**4**	**2**	**5**	**5**	**5**	**5**
TOTAL EQUITY AND LIABILITIES	**101**	**92**	**112**	**97**	**133**	**149**

Source: Alzinova AB, EPB

Growth and margins

	2020	2021	2022	2023e	2024e	2025e
Revenue growth	-	N.m.	N.m.	N.m.	N.m.	N.m.
EBITDA growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
EBIT growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
EPS growth, adjusted	-	N.m.	N.m.	N.m.	N.m.	N.m.
Gross margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBITDA margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBITDA margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EBIT margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Profit margin, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Source: Alzinova AB, EPB

Profitability

	2020	2021	2022	2023e	2024e	2025e
ROE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROCE, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
ROIC, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.

Source: Alzinova AB, EPB

Capital efficiency

	2020	2021	2022	2023e	2024e	2025e
Total current liabilities / total expenses	19%	10%	18%	17%	8%	6%
Working capital / total revenues	-23%	-7%	-24%	-26%	-26%	-26%
Capital turnover rate	0,2x	0,2x	0,2x	0,2x	0,1x	0,1x

Source: Alzinova AB, EPB

Financial position

	2020	2021	2022	2023e	2024e	2025e
Net debt	-56	-29	-32	-2	-21	-21
Equity asset ratio	95%	96%	95%	94%	95%	96%
Net debt/equity ratio	-0,6x	-0,3x	-0,3x	0,0x	-0,2x	-0,1x
Net debt / EBITDA	8,6x	3,8x	2,4x	0,1x	0,4x	0,3x

Source: Alzinova AB, EPB

Share data

	2020	2021	2022	2023e	2024e	2025e
EPS	-0,41	-0,48	-0,40	-0,32	-1,11	-1,56
EPS, adjusted	-0,41	-0,48	-0,40	-0,32	-1,11	-1,56
FCF per share	-1,34	-1,72	-0,83	-0,68	-1,47	-1,92
Dividend per share	0,00	0,00	0,00	0,00	0,00	0,00
Equity per share	6,09	5,61	3,26	2,05	2,85	3,21
Number of shares at year-end, m	15,8	15,8	32,4	44,5	44,5	44,5
Number of shares after dilution, average	15,8	15,8	32,4	44,5	44,5	44,5

Source: Alzinova AB, EPB

Valuation

	2020	2021	2022	2023e	2024e	2025e
P/E, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Price/book value	1,3x	1,1x	0,9x	1,2x	0,9x	0,8x
P/FCF	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
FCF yield	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
Dividend yield	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
Payout ratio, adjusted	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%
EV/Sales	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV/EBITDA, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV/EBIT, adjusted	Neg.	Neg.	Neg.	Neg.	Neg.	Neg.
EV	65	73	58	80	80	80
Share price	7,7	6,4	2,8	2,5	2,5	2,5

Source: Alzinova AB, EPB

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