EDISON

AlzeCure Pharma

Initiation of coverage

Well-balanced pipeline for Alzheimer's and pain

Pharma & biotech

AlzeCure is a pure play biotech focused on neurological disorders. The pipeline consists of three small-molecule platforms targeting Alzheimer's disease (AD) and pain. The NeuroRestore platform is focused on novel symptomatic treatment of AD (lead compound ACD856 is in Phase I), although there is a scientific rationale for disease modification potential as well. The Alzstatin platform (preclinical) is specifically aimed at modifying the course of AD and has a differentiated mechanism of action. We find the strategy to target both settings in AD, symptomatic and disease modifying treatments, to be a rational approach given the complex history of drug development in this vast indication. The third Painless platform, with two non-opioid assets for pain (lead ACD440 is in Phase Ib), complements the R&D pipeline well. We value AlzeCure at SEK729m or SEK19.3 per share.

Year end	Revenue (SEKm)	PBT* (SEKm)	EPS* (SEK)	DPS (SEK)	P/E (x)	Yield (%)
12/19	0.0	(50.9)	(1.35)	0.0	N/A	N/A
12/20	0.0	(71.4)	(1.89)	0.0	N/A	N/A
12/21e	0.0	(82.0)	(2.17)	0.0	N/A	N/A
12/22e	0.0	(86.1)	(2.28)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles and exceptional items.

Rational strategy to reach the 'high-hanging' fruit

Lead asset ACD856 (Phase I) from the NeuroRestore platform is a first-in-class cognitive enhancer for AD. ACD856 improves the signalling of neurotrophins, including nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), through positive modulation of the TrkA and TrkB. This is expected to improve cognitive function and memory. The second lead asset ACD440 (VR-1 antagonist for pain, Phase Ib) from the Painless platform is a topical drug for neuropathic pain, where pain control is a significant unmet need. Data are expected during 2021. AlzeCure is also working on its preclinical assets from the Alzstatin platform (oral γ-secretase modulator with disease modifying potential in AD) and another asset from the Painless platform (TrkA negative modulator) in major pain indications.

A balanced R&D pipeline led with competence

AlzeCure's R&D portfolio is a collection of small-molecule projects in two different, albeit not entirely unrelated, disease areas in neurology. The mechanisms of action of all compounds are also differentiated from closest comparable drugs. This strategy is backed by a highly competent management team, who hand-picked the projects based on their experience from large pharma. In our view, a well-balanced pipeline with a credible management is a great attraction for investors who prefer to rely on management's ability to diversify the company's assets (as opposed to a VC-like asset-centric investing style that requires specialised knowledge).

Valuation: SEK729m or SEK19.3 per share

We value AlzeCure at SEK729m or SEK19.3 per share, based on a risk-adjusted NPV analysis (cash of SEK112m at end Q420). Our valuation includes the two clinical stage assets, ACD856 for symptomatic treatment of AD and ACD440 for neuropathic pain. We currently do not value any other indications or projects in the preclinical stages, but will reconsider them if AlzeCure makes progress.

23 March 2021

Price	**SEK7.66**
Market cap	**SEK290m**
	SEK8.73/US$
Net cash (SEKm) at end-FY20	112.4
Shares in issue	37.8m
Free float	63%
Code	ALZCUR
Primary exchange	Nasdaq First North Growth
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	4.4	(16.6)	116.4
Rel (local)	(1.1)	(27.1)	26.1
52-week high/low	SEK11.60	SEK3.10	

Business description

AlzeCure Pharma is a clinical-stage biotech company based in Sweden focused on developing small molecule drugs for the treatment of Alzheimer's (symptomatic and disease modifying) and pain (neuropathic and osteoarthritic).

Next events

ACD440 Phase Ib data	Mid-2021
ACD856 Phase I SAD data	Mid-2021
ACD856 Phase I MAD data	H221
Filing for Phase IIa ACD440 study	H221

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EdisonTV executive interview

AlzeCure Pharma is a research client of Edison Investment Research Limited

Investment summary

Company description: Hand-picked projects for CNS and pain

AlzeCure Pharma is a clinical-stage biotech company based at the Novum Science Building associated with the Karolinska Institute in Stockholm, Sweden, with c 10 employees, who combined have over 100 years of experience from large pharma companies. The current management team formed part of AstraZeneca's neurology and pain division and were involved in the development of both symptomatic and disease-modifying drugs for AD. When AstraZeneca decided to focus on other indications, that team partnered with Professor Bengt Winblad (one of the world's most cited researchers in neurodegenerative diseases) at the Karolinska Institute in 2012. The Swedish Alzheimer's Foundation provided early funding and soon thereafter a commercial company was incorporated in 2016. Since then, it has raised c SEK100m in financing rounds and listed on Nasdaq First North Premier in November 2018. The IPO proceeds were c SEK200m (priced at SEK14 per share).

Valuation: SEK729m or SEK19.3 per share

We value AlzeCure at SEK729m or SEK19.3 per share (cash of SEK112m at end Q420, no debt; 12.5% discount rate). We modelled ACD856 (NeuroRestore) as a symptomatic AD drug with a cognition-improvement effect superior to that of existing generic AD drugs. We do not value Alzstatin program yet, but will reconsider once it will be close to or in the clinical development. Using the same model as for ACD856, but changing assumptions to a higher penetration rate and better pricing, we estimate potential peak sales for a Alzstatin disease-modifying AD drug could reach c $15bn (more details in the Valuation section). We include the clinical stage ACD440 asset from the Painless platform in our valuation, but similarly will reconsider TrkA- negative allosteric modulator (NAM) once it makes progress.

Financials: Funded to key readouts

AlzeCure reports no income and in FY20 it reported SEK71.6m in operating loss, of which most (SEK62.4m) was booked as R&D expense. In FY19 the operating loss was SEK50.9m indicating that spending increased due to more R&D activities. We expect the spending to increase somewhat further in 2021 as both clinical trials are in full swing and forecast SEK82.0m in operating loss. Existing cash of SEK112m at the end of FY20 should provide funding into 2022. We note the existing budget is sufficient to reach the readouts from both clinical trials.

Sensitivities: Typical biotech risks apply

AlzeCure is exposed to the drug-development risks typically associated with pure play biotechs, namely clinical development delays or failures, IP protection, regulatory risks, competitor successes, partnering setbacks and financing and commercial risks. Its focus on developing drugs for AD could be considered higher risk, but also higher reward in our opinion. However, having projects that could have potential beyond AD does mitigate this risk to an extent. While AlzeCure has a sufficient cash runaway to complete the ongoing clinical trials for ACD856 and ACD440, additional funding will be required to progress these and facilitate the progression of preclinical candidates. As the company has guided, assets will likely need to be partnered at some point as later-stage CNS studies can be costly due to large populations and study duration, hence the ability to successfully negotiate a deal is a key sensitivity.

Three platforms, AD and pain are lead indications

AlzeCure has three platforms: NeuroRestore, Alzstatin and Painless (Exhibit 1). Assets within the two platforms targeting AD are wholly-owned. The Painless platform consists of two assets that are unrelated from the mechanism of action perspective. ACD440 (Painless) was in-licensed at rather beneficial terms (Exhibit 1 notes), while TrkA-NAM (Painless) is wholly-owned and has an interesting discovery history. Pharmacologically speaking, TrkA-NAMs have the opposite activity of NeuroRestore assets (which are TrkA/TrkB positive allosteric modulators or PAMs). AlzeCure somewhat serendipitously discovered these NAM molecules while working on NeuroRestore. Modulators help either activate or deactivate receptors via a separate site, so do not compete with inhibitors or agonists.

Two Phase I clinical trials are up and running with ACD856 and ACD440. The existing funding is sufficient to complete them, so the data readouts expected over the next 18 months will provide significant catalysts. In parallel, progression of preclinical assets can also be expected, which will add to the news flow. The company's overall strategy is to create value by advancing assets from early preclinical through to mid-stage clinical development and then to seek partnering deals.

Exhibit 1: AlzeCure's small-molecule R&D pipeline

Platform	Drug	Pharmacological class	Target indication(s)	Development stage	Current status and expected catalysts
NeuroRestore	ACD856	TrkA/TrkB PAM (oral)	Alzheimer's disease Parkinson's disease Traumatic brain injury Sleep disorders	Phase I	Wholly-owned. Phase I trial recently initiated after successful completion of a microdosing Phase 0 study in June 2020. Study is ongoing. Initial safety and tolerability data from SAD part of the study is expected by **mid-2021**, with MAD data by **end-2021**. In an extension phase, a separate signal detection study will be conducted to assess early cognitive effects of the compound, with data expected **during H222**.
	ACD857			Preclinical (late*)	Wholly owned. Progressed into late-stage in preclinical development as per December 2020 announcement. This compound could serve as a 'back-up' to ACD856 or AlzeCure could decide to strategically position its development for other indications, such as sleep disorders, traumatic brain injury or PD.
Alzstatin	ACD679	γ-secretase modulator (oral)	Alzheimer's disease	Preclinical (late*)	Wholly owned. ACD679 and ACD680 are currently progressing through pre-clinical development and updates on their progress can be expected during 2021.
	ACD680			Preclinical (early*)	
Painless	ACD440	VR-1 antagonist (topical)	Neuropathic pain	Phase Ib	In-licensed global rights from Acturum Life in January 2020; deal terms not disclosed, but there was no upfront payment and no milestone payments are due until the start of the Phase II trials. The oral formulation of this drug candidate underwent extensive development at AstraZeneca, but the company stopped the programme. AlzeCure is developing ACD440 as a topical reformulation meant to resolve certain safety issues with the oral version seen during the development at AstraZeneca. Phase Ib proof-of-mechanism data are **expected in mid-2021**.
	TrkA-NAM	TrkA NAM (oral)	Osteoarthritic pain	Preclinical (early*)	Wholly-owned. AlzeCure successfully completed preclinical efficacy studies in December 2020; a candidate drug is expected to be nominated **during H221**.

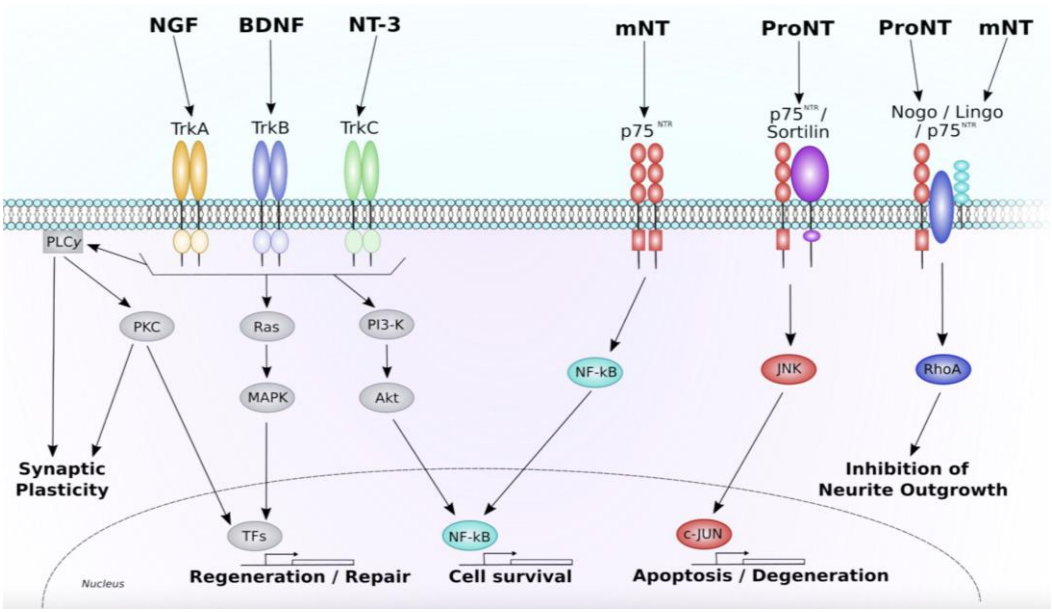
Source: Edison Investment Research, AlzeCure. Notes: SAD – single ascending dose, MAD – multiple ascending dose, PAM – positive allosteric modulator, NAM – negative allosteric modulator, TrkA – Tropomyosin receptor kinase A (also known as NTRK1), TrkB – Tropomyosin receptor kinase B (also known as NTRK2), VR1 – vanilloid receptor 1 (also known as TRPV1 or the capsaicin receptor). *Early preclinical stage implies compounds that are either in discovery or lead optimisation stages of development; late preclinical stage implies compounds that are undergoing the requisite safety and toxicology studies for IND submission to regulators.

NeuroRestore platform: Primary value driver currently

AlzeCure's NeuroRestore platform comprises drugs (ACD856, ACD857 and ACD 855) designed to improve cognitive function in neurological disorders, but could also have the potential to show a disease modifying effect. These are novel, first-in-class, small molecule drugs that all exhibit the same mechanism of action: namely they enhance the signalling of neurotrophins, including NGF and BDNF through positive modulation of the TrkA and TrkB receptors, respectively. NGF and BDNF are part of the family of neurotrophin proteins that signal via tropomyosin receptor kinases

(TrkA, TrkB and Trk C) and the p75 neurotrophin receptor ($p75^{NTR}$); this signalling cascade helps to regulate neuronal survival, differentiation, neurogenesis and synaptic plasticity.

Exhibit 2: Highlights of the neurotrophin signalling cascade



Source: Houlton et al. (2019) Front. Neuro.

A variety of preclinical in vitro and in vivo models have established NGF/TrkA or BDNF/TrkB signalling as therapeutic target in numerous neurological disorders. However, the utility of using NGF or BDNF (recombinant or mimetics) as a systemically delivered drugs is limited due to their restricted ability to cross the blood-brain barrier, poor plasma stability and promiscuous binding across multiple receptors subtypes, which could have undesirable side effects. An approach to use small molecule TrkA and TrkB modulators, therefore, has gained interest. Based on the preclinical data so far presented by AlzeCure, ACD856 has overcome these limitations.

Having successfully completed a microdosing Phase 0 study for the lead compound ACD856 in June 2020, AlzeCure has initiated a Phase I trial with ACD856 in November 2020. The trial is currently recruiting patients and initial safety and tolerability data from single ascending dose (SAD) part of the study are expected by mid-2021, with multiple ascending dose (MAD) data by end-2021. In an extension phase, a separate signal-detection study will be conducted to assess early cognitive effects of the compound, with data expected during H222.

The Phase I trial will establish safety and tolerability, as well as confirm its pharmacokinetic (PK) profile. This latter will be particularly relevant, in our view, given predecessor compound ACD855 was initially developed as an AD drug. However, Phase I data indicated that a longer than expected half-life meant it would be unsuitable for a systemic, oral drug. In May 2019, the development was redirected to focus on eye diseases, while the back-up compound ACD856 was selected as the lead asset. We are reassured by the successful completion of the microdosing Phase 0 trial, following which the company reported that ACD856 has a suitable PK profile. ACD857 is another compound within the NeuroRestore platform that could be also used as a back-up compound or could be developed to address other relevant CNS indications where cognitive function is disturbed, such as certain sleep disorders, traumatic brain injury and Parkinson's disease (PD). The requisite IND enabling, preclinical studies started in December 2020.

During 2020, AlzeCure published preclinical data with ACD856 at the AAT-ADPD (March 2020) and at CTAD (November 2020) conferences that indicate a more optimal PK profile has been achieved with ACD856, which should be amenable to once-daily dosing. We highlight the preclinical data

disclosed at these conferences support the proposed development of ACD856 as a cognitive enhancing drug:

- **Broad cognitive enhancing effect**. AlzeCure's primary in vivo efficacy model has been a passive avoidance (PA) memory model (also known as fear conditioning). During these it has shown that ACD856 (0.3mg/kg) significantly and almost fully reverses scopolamine-induced memory impairments. Notably, this occurred when the drug candidate was administered either pre-training, post-training or pre-test, implying it can support three different cognitive modalities: memory acquisition, consolidation or retrieval.
- **Improvement of long-term memory.** Using the same PA memory model, ACD856 was able to improve long-term memory in old mice (20 months), which natively have age-related cognitive impairment. A significant improvement was noted 11 days after administration of ACD856 that is broadly in line with untreated young mice.
- **Enhancement of neurotransmitters.** In a microdialysis model ACD856 (10mg/kg) significantly increased the hippocampal levels of serotonin as well as increasing levels of dopamine and noradrenalin (not significant), when compared to vehicle. Furthermore, preclinical depression models (forced swim/Porsolt) showed a positive effect with ACD856, comparable to fluoxetine (Prozac).
- **Robust drug metabolism and pharmacokinetics (DMPK) profile.** AlzeCure reported ACD856 can achieve high CNS exposures and has a benign safety profile with no adverse events reported (in rats or mini-pigs) during dose-ranging or maximum tolerated dose (MTD) studies (up to 300mg/kg), suggesting it could have a broad dosing potential in humans.

NGF dysregulation a hallmark of cognitive decline

Loss of synaptic function is one of the hallmarks of AD and strongly correlates with the cognitive decline that occurs during disease progression. It has been extensively highlighted that the accumulation of toxic protein aggregates, such as Aβ oligomers/plaques or tau tangles, play a significant role in this neuronal degeneration through triggering toxic inflammatory responses (Koffie et al, 2011; Pepeu and Giovannini, 2017). More specifically, the loss of cholinergic neurons is a cardinal feature of AD, as evidenced by three of the FDA approved drugs, which all aim to correct cholinergic tone through inhibition of acetylcholinesterase. These cholinergic neurons are lost extensively in the basal forebrain and hippocampus and are strongly dependent on NGF for neuronal survival, with evidence indicating that Aβ can disrupt NGF metabolism. (Pepeu and Giovannini, 2017; Latina et al, 2017). Hence the view is that ACD856, which can positively modulate TrkA, could in theory correct this dysregulated NGF signalling and slow the cognitive decline. We highlight two seminal clinical studies that, despite their limitations, highlight interest in the area, as the settings in these trials were fairly complicated:

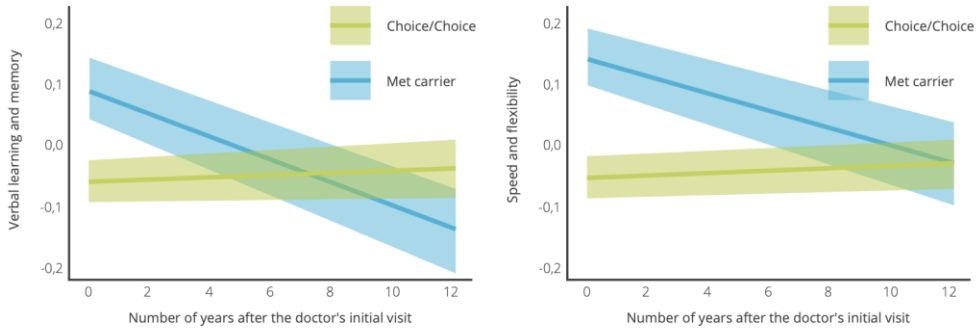
- **NGF infusions.** In a small investigator-led study, three patients with AD were treated with NGF via continuous infusions (intracerebroventricular). This was associated with a slight improvement in cognition for two patients, but this benefit was outweighed by the induction of back pain and weight loss, which was attributed to the NGF infusion. We also note a subsequent study was conducted using stereotactic implants that released NGF and had better outcomes. Needless to say, both are highly invasive and significantly different to AlzeCure's approach.
- **NGF gene therapy.** In a Phase I trial, eight patients with mild AD were treated with an ex vivo gene therapy, where autologous fibroblasts modified to express NGF were transplanted into the basal forebrain. This resulted in improvements in the rate of cognitive decline (MMSE and ADAS-cog). Post-mortem findings subsequently showed a trophic response to NGF, which stimulated growth of cholinergic neurons. However, a subsequent Phase II trial (sham controlled) conducted by Ceregene/Sangamo used an in vivo approach (where the therapy was

administered directly into patients' brains). The results from this trial showed no significant differences compared to placebo and the project was discontinued.

Boosting BDNF could also provide a disease modifying effect

ACD856's ability to also positively modulate TrkB provides it with an additional mechanism of action since BDNF has also been closely linked with the worsening of cognition in AD. BDNF is a polymorphic gene meaning that more than one allele occupies the gene's location (eg genes that control hair colour are polymorphic, hence the wide range of colour pattern). The majority of polymorphisms are silent and they do not alter the function of a gene. In the BDNF case, a genetic single nucleotide polymorphism is found to occur that causes a slight change in the BDNF protein sequence (Val66Met). This specific polymorphism has been shown to result in a reduction of BDNF secretion in the hippocampus (Egan et al, 2003). Exhibit 3 highlights results from a longitudinal study of the Wisconsin Registry for Alzheimer's Prevention, in which patients underwent BDNF genotyping and cognitive assessments. Carriers of the BDNF-Val66Met polymorphism occurred in c 30% of the population and exhibited a more severe decline in both verbal learning/memory (Exhibit 3 left, p = 0.002) and speed/flexibility (right, p = 0.02), compared to BDNF Val/Val homozygotes.

Exhibit 3: BDNF-Val66Met is associated with a worsening of cognitive decline



Source: AlzeCure Pharma, adapted from Boots *et al.* (2017) Neurology

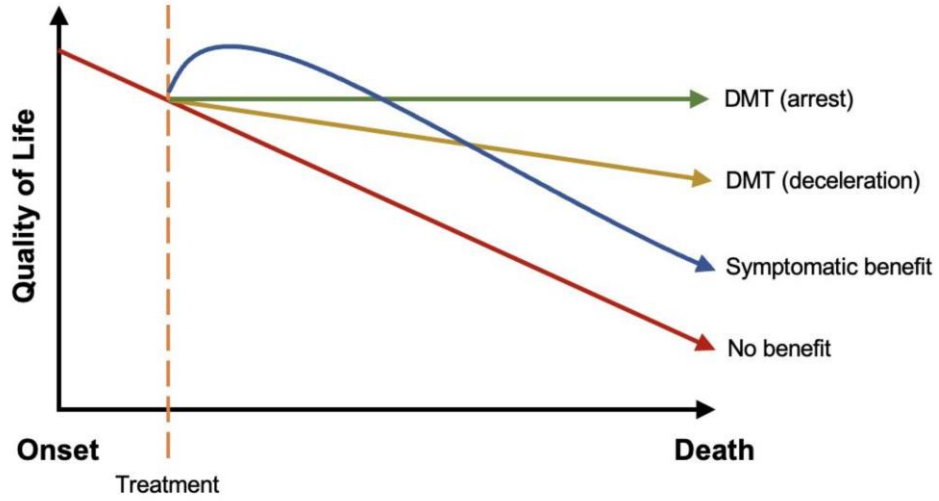
Findings from a separate study of the Dominantly Inherited Alzheimer Network (DIAN) have further supported the BDNF-Val66Met polymorphism theory. Preclinical AD patients carrying BDNF-Val66Met exhibited worse memory performance. Especially notable from this study was the finding that carriers had lower hippocampal glucose metabolism and increased cerebrospinal fluid (CSF) levels of tau and p-tau, suggesting the BDNF-Val66Met polymorphism could exacerbate AD pathogenesis downstream of Aβ. The authors concluded: 'strategies designed to increase CNS BDNF levels may be a viable therapeutic alternative or addition to those which seek to reduce the neurotoxic effects of Aβ' (Lim et al, 2016; Rogaeva and Schmitt-Ulms, 2016). In our view, this indicates that ACD856 could even have a disease modifying effect for AD.

Symptomatic versus disease modifying therapies

The consensus in Alzheimer's is that disease modifying therapy (DMT) would represent a breakthrough. However, since there are no such drugs and development of DMTs has been spectacularly unsuccessful, a clear definition of what constitutes DMT and how it differs from symptomatic therapy is also lacking (J Cummings and N Fox, 2017). According to the recent EMEA guidance document, 'symptomatic improvement is defined as a treatment effect that does not change the overall course of the disease', whereas 'a disease modifying therapy is one which delays the underlying pathological or pathophysiological disease processes', which would correlate with 'a significant effect on adequately validated biomarkers'. The choice of biomarker as well as the type of analysis is left open.

Disease modification can be understood as different outcomes that range from cure to slowing of the natural course of the disease and increasing patient survival. This concept is shown in Exhibit 4. Until more data become available for ACD856, it is unclear if AlzeCure will be attempting to show a disease modifying effect. Data expected from the Phase I extension cohort during H222 will look initially for a signal that ACD856 has a cognitive enhancing effect. We believe biomarker data will likely be required to show ACD856 has a disease modifying potential.

Exhibit 4: Symptomatic versus DMT



Source: Edison Investment Research

The revenue potential of new entrants in the AD market would depend on the benefit relative to the currently approved symptomatic drugs. This could range from direct competition with existing drugs if efficacy is similar, to a market disruptor with a multibillion-dollar potential if the drug modifies the progression of the disease. There could also be a variety of scenarios in between these extremes, in our view:

- second-line symptomatic treatment after existing cognitive enhancers stop working,
- first-line therapy if the symptomatic benefit is more pronounced that that achieved with current standard of care,
- additional symptomatic benefit in combination with existing standard of care, or
- if a disease modifying effect is proven, it would likely quickly become standard of care.

Four pharmacologic treatments have been approved by major regulators and are established in clinical practice that can moderately improve symptoms. However, these do not slow AD's progression nor improve patient survival. These are acetylcholinesterase inhibitors: donepezil, rivastigmine and galantamine, which are the standard first-line therapy and the only approved drugs for mild disease. Memantine (NMDA receptor antagonist) is approved for moderate to severe disease but is often used off-label in mild disease as well. Treatment options vary widely across geographies.

Exhibit 5: Symptomatic treatments approved for mild AD

Class	MoA	Product	Company	Proprietary status	Peak sales (pa)
Acetylcholinesterase inhibitors	Inhibit the enzyme that breaks down acetylcholine in the synaptic cleft (acetylcholinesterase) to increase the amount of acetylcholine available at the synapse for cholinergic neurotransmission	Aricept (donepezil)	Pfizer, Eisai	Generic	$3.9bn (2009)
		Exelon (rivastigmine)	Novartis	Generic	$1.1bn* (2011)
		Razadyne (galantamine)	Johnson & Johnson, Takeda	Generic	$0.5bn (2008)
NMDA receptor antagonists	Memantine reduces the amount of glutamate receptor activation and excitotoxic glutamatergic neurotransmission	Namenda (memantine)	Allergan, Lundbeck, Daiichi Sankyo, Merz, Hanmi Pharmaceutical	Generic	$1.2bn (2014)
		Namenda XR (memantine extended release formulation)	Allergan, Merz, Adamas Pharmaceuticals	Generic	$0.8bn (2015)

Source: Evaluate Pharma, Edison Investment Research. Note: *Includes sales from Exelon Patch.

With regards to market size, currently the trend of ageing populations and the increasing prevalence of AD is mostly offset by the increasing use of lower-priced generics, as branded drug protection expires. However, due to a high unmet need and the vast patient population, any new, effective drug could disrupt the market. In our view, any new disease modifying drug would have a realistic potential to reach annual peak sales that are a multiple of the current combined sales of all generic AD drugs (in the Valuation section we show a scenario where a disease modifying drug could reach $15bn in peak sales). We note that Institute for Clinical and Economical Review (ICER) is due to publish a draft report on 5 May 2021 that will assess the comparative clinical effectiveness and value of aducanumab, and might better define pricing expectations for DMTs in AD.

Competitive landscape for NeuroRestore

From our research, we believe that AlzeCure has a first-in-class molecule with ACD856. Although we have identified a variety of developmental drugs with similar mechanisms of action to ACD856, we do not currently believe there to be anything that we would consider a direct competitor.

ATH-1017, a small molecule designed to increase HGF/Met activation, which can be viewed as a similar neurotrophin signalling cascade to NGF/TrkA and BNDF/TrkB, has also been implicated in the cognitive decline associated with AD and PD. Athira Pharma is developing it as a daily, subcutaneous injection and recently initiated two Phase II–III clinical trials in patients with mild-to-moderate AD. Based on its interactions with the FDA, Athira believes the Phase II/III LIFT-AD trial may provide registrational data if key secondary efficacy endpoints are meet (ADAS-Cog and ADAS-CGIC). Athira was valued at c $760m as of 16 March 2021.

PharmatrophiX recently completed a Phase IIa proof-of-concept trial for its $p75^{NTR}$ modulator LM11A-31, which again can be considered to work in a similar manner. We understand that the trial was completed in June 2020 and an analysis was expected Q420 but data have not yet been published.

Exhibit 6: Landscape of neurotrophin signalling enhancers

Company	Drug	Pharmacological class	Target indication(s)	Development stage	Notes
Small molecule					
AlzeCure	ACD856	TrkA/TrkB PAM (oral)	Alzheimer's disease*	Phase I	Phase I initiated Jan 2021, SAD data are expected mid-2021, MAD data by end-2021 and initial efficacy data H222
Athira	ATH-1017 (NDX-1017)	HGF/Met (subcutaneous)	Alzheimer's disease	Phase II/III and Phase II	Phase II/III LIFT-AD trial started in Sep 2020, headline data are expected end-2022. Phase II ACT-AD trial start in Nov 2020, headline data are expected early 2021
			Parkinson's disease	Phase II (IND pending)	IND filing expected during H121 with the Phase II trial potentially initiating by end 2021. Based on the prior Phase Ia/b data in AD, no Phase I trial in PD patients is expected prior to initiating this Phase II.
PharmatrophiX	LM11A-31	$p75^{NTR}$ modulator (oral)	Alzheimer's disease	Phase I/II	Phase I/II trial initiated in Feb 2017, LPLV occurred June 2020 and data analysis of Phase IIa was expected in Q420, data not published
	LM22A-4	TrkB partial agonist (intranasal)	-	Preclinical	Current status of development unknown.
Other					
Sangamo/ Ceregene	CERE-110 (AAV2-NGF)	NGF gene therapy (intracranial injection)	Alzheimer's disease	Phase II	Phase II completed in 2015 but the programme discontinued in AD, presumably due to a lack of efficacy.
Mimetogen	tavilermide (MIM-D3)	NGF mimetic (ocular)	Dry eye disease	Phase III	Phase III MIM-728 trial completed enrolment in March 2020, headline data are expected Q420.
Dompe	Oxervate (cenegermin)	Recombinant NGF (ocular)	Neurotrophic keratitis	Approved (FDA and EMA)	Also in clinical development in other ocular indications – dry eye disease (Phase II) and glaucoma (Phase I).

Source: Edison Investment Research, AlzeCure. Note: PAM – positive allosteric modulator, NAM – negative allosteric modulator, TrkA – Tropomyosin receptor kinase A (also known as NTRK1), TrkB – Tropomyosin receptor kinase B (also known as NTRK2). *Could also be developed for PD, traumatic brain injury and sleep disorders.

Alzstatin: Novel way to tackle Abeta

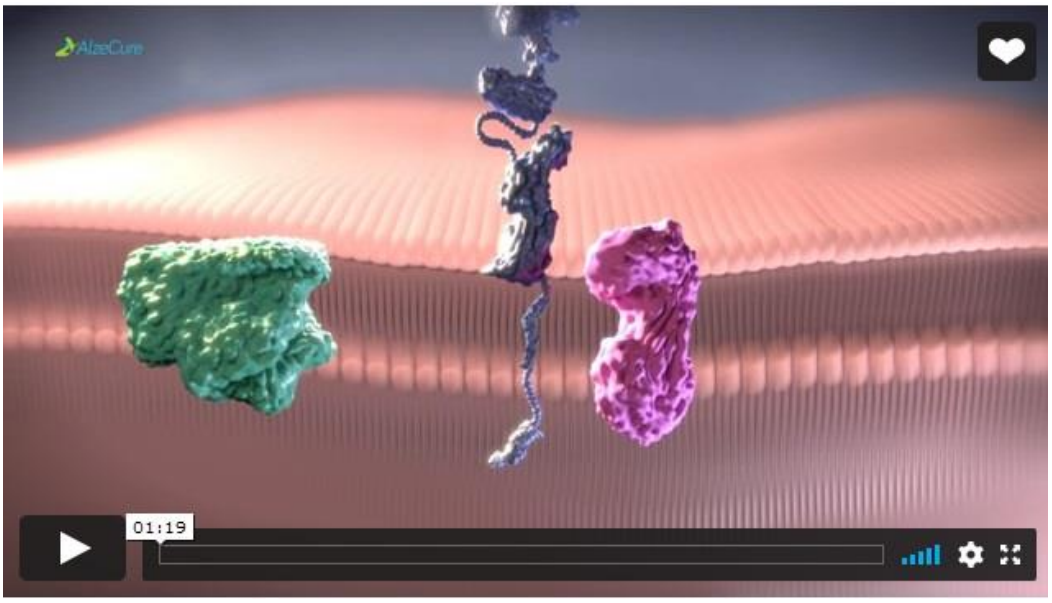
The traditional amyloid hypothesis postulates that Aβ protein is the causative factor in AD. However, this has been a subject of much debate over the last decade, with multiple clinical trial failures of Aβ-targeting therapies seemingly vindicating the scepticism. As the science evolved, a rather simplistic view that removing Aβ plaques should lead to improvement has changed too. More recent theory updates focus on so called toxic forms of Aβ.

Drug candidates from the Alzstatin platform have potential as disease modifying drugs for AD, in our view, although both projects (ACD679 and ACD680) are in an early stage of development. These have a distinctly different mechanism from the Aβ-targeting antibodies, such as Biogen's aducanumab, which have recently captured the attention of investors. These are small molecules capable of modulating γ-secretase, a target involved upstream in the production cascade of toxic Aβ-aggregates. Modulation of γ-secretase produces shorter, less toxic Aβ-peptides whilst not changing overall levels of Aβ. This is a novel approach where modulation rather than full inhibition of γ-secretase is expected to circumvent the safety issues previously found by large pharma with γ-secretase inhibitors. Given that safety issues have plagued the development of full γ-secretase targeting agents in the past, establishing a clean safety profile will be important. So, preclinical and Phase I safety data for ACD679 and ACD680 will be a meaningful catalyst for AlzeCure, in our view.

The Alzstatin platform has recently gained significant attention, primarily due to external factors; namely, the upcoming US FDA decision on whether it will approve Biogen's aducanumab for AD, which has pushed the amyloid hypothesis back into focus. Should the FDA approve Biogen's aducanumab, it will be a landmark decision in Alzheimer's research, making it the first new AD drug

approved in c 20 years and more importantly the first disease modifying drug. As described below, the data, however, were rather mixed, so the stakes for Biogen are high.

Exhibit 7: Alzstatin explained



Source: AlzeCure

A short review of the current status of Aβ theory

In short, the traditional amyloid hypothesis postulates that insoluble Aβ oligomers/plaques are the key neurotoxic culprit in AD and drugs targeting these could have a disease modifying effect. Vast resources in the industry have been aimed at intervening in the amyloid cascade to prevent or slow these toxic effects, however, no drugs have yet been successfully developed and approved. Aβ-targeting antibodies has been extensively pursued and we highlight three notable examples that are still being actively developed:

- **Aducanumab** (Biogen, Eisai) is a monoclonal antibody designed to selectively bind to aggregated forms of Aβ that is currently under FDA review with a PDUFA decision date set for 7 June 2021. Approval would broadly be considered as controversial due to mixed data in the Phase III EMERGE and ENGAGE trials and the negative outcome from the advisory committee (AdComm) meeting on 6 November 2020. The AdComm outcomes are non-binding, so the drug could still be approved, when the vast patient population with minimal treatment options is taken in the consideration. An approval would be a landmark event and a significant catalyst for the AD research field in general.
- **Lecanemab** (BioArctic, Eisai, Biogen) is more commonly known as BAN2401. This monoclonal antibody was designed to bind soluble Aβ-protofibrils and many would argue it is currently the second most advanced asset after aducanumab. Based on Phase IIb data, the pivotal Phase III Clarity AD trial initiated during March 2019 and is investigating the drug in early symptomatic patients. Headline 18-month efficacy data are expected in H122. A second Phase III trial (AHEAD 3-45) in pre-symptomatic patients started in July 2020.
- **Donanemab** (Eli Lilly) is a monoclonal antibody that targets a modified form of Aβ (pyroglutamated) that is considered to play a key role in the aggregation process through acting as a seed. Eli Lilly recently reported positive data from its Phase II TRAILBLAZER-ALZ trial, using a relatively new composite score (iARDS) from its primary endpoint. Additional data were presented at the International Conference on Alzheimer's and Parkinson's Diseases, AD/PD 2021, 9–14 March 2021, which showed treatment resulted in improvements in cognitive decline across several notable clinical endpoints, albeit only the novel iARDS endpoint showed a

statistically significant change. The adverse event rate of ARIA-E (brain oedema), characteristic to the class, was significantly higher at 27% in the treatment arm versus 1% in the placebo arm and could be a concern. Phase II TRAILBLAZER-ALZ 2 data are anticipated in 2023.

We have highlighted these three Aβ-targeting agents as they are the most advanced assets still being actively developed. Notable historical Phase III failures include: solanezumab (Eli Lilly), bapineuzumab (Pfizer, Janssen), gantenerumab (Roche, MorphoSys) and crenezumab (Roche, AC Immune).

Upstream targets in the amyloid cascade have also become a focus, namely β-secretase (BACE) and γ-secretase, which are two enzymes that process amyloid precursor protein (APP) into the Aβ monomer units that aggregate and result in the build-up of toxic Aβ-oligomers/plaques. As per the traditional amyloid hypothesis, inhibition of these upstream processes should prevent the formation of Aβ aggregates, pathological progression and the worsening of symptoms. BACE inhibitors were viewed as having great potential and many large pharma players had heavily invested in this strategy. However, 2018 alone saw three BACE inhibitors failing Phase III studies: verubecestat (Merck), atabecestat (Janssen) and lanabecestat (Eli Lilly, AstraZeneca).

Similarly, γ-secretase inhibitors were initially viewed as having a good potential, but failed to meet expectations, particularly with Eli Lilly's semagecstat casting a shadow of safety concerns on the class. Semagacestat's Phase III IDENTITY trials stopped prematurely in August 2010 due to the drug apparently worsening disease progression. We note one causal factor that was been attributed to this has been the high dose used in the trials resulted in sustained, complete inhibition of γ-secretase. Beyond processing APP into smaller Aβ monomer units, γ-secretase is thought to play a critical role in processing other important proteins such as Notch. It is thought that impairment of Notch signalling results in negative cognitive effects. The question that therefore remains is whether AlzeCure's approach with Alzstatin, modulating rather than inhibiting γ-secretase, can spare critical signalling pathways like Notch and circumvent the safety issues previously found with semagacestat, but still maintain a similar effect on reducing downstream levels of toxic Aβ aggregates.

γ-secretase modulation: A differentiated approach

The question that therefore remains is whether AlzeCure's approach with Alzstatin, modulating rather than inhibiting γ-secretase, can circumvent the safety issues previously found, but still maintain a similar effect on reducing downstream levels of toxic Aβ aggregates. Not all Aβ monomer units are equal and it is thought the longer units ($Aβ_{1-40}$ and AB_{1-42}) are more susceptible to aggregation, whereas shorter fragments ($Aβ_{1-37}$ and $Aβ_{1-38}$) are less prone to this, less neurotoxic and could in fact have an anti-amyloidogenic effect (Boy et al, 2019). The Alzstatin programme has been derived from and built on learning management took from an analogous programme at AstraZeneca, which generated compounds that achieved this: modulating γ-secretase to produce shorter, less toxic Aβ-peptides while not changing overall levels of Aβ and sparing Notch signalling. Worth noting is that in familial AD, mutations in the γ-secretase complex result in virtually the opposite effect of Alzstatin's compounds. Familial AD is characterised by an early onset (between 30 and 60 years of age) and is inheritable.

We note others have also pursued this concept and conducted clinical studies, but none of these programmes seem to be active anymore:

- **PF-06648671** (Pfizer) underwent several Phase I studies and was reported to be safe and well tolerated in healthy patients (young and elderly), with favourable changes in $Aβ_{1-37/38}/Aβ_{1-40/42}$ ratios. We understand this was discontinued as part of Pfizer's portfolio prioritisation in January 2018.

- **BMS-932481** (Bristol-Myers Squibb) – Phase I data were reported in July 2016 and again showed favourable changes in $A\beta_{1-37/38}/A\beta_{1-40/42}$ ratios, but development was discontinued due an insufficient safety margin with an increase in liver enzymes noted at therapeutic doses.
- **NGP 555** (NeuroGenetic Pharmaceuticals, private) has undergone Phase I SAD and MAD studies in healthy volunteers. In January 2017 this was reported to be well tolerated and showed favourable change in $A\beta_{1-37}/A\beta_{1-40/42}$ ratios, but the current status of development is unknown.

ACD679 and ACD680 are progressing through pre-clinical development and updates on their progress can be expected during 2021. These assets are aiming for the disease modifying effect in AD, which is the 'holy grail' indication in a major CNS indication. We do not value the Alzstatin programme yet because of its early stage, but once the assets reach clinical development, value creation can be rapid.

Painless: Two different approaches for pain

Ongoing evolution of assets within the Painless platform will further diversify AlzeCure's pipeline and, in our view, de-risks the investment case as the market opportunity for these innovative, non-opioid based analgesics could be significant. The platform currently consists of in-licensed asset ACD440, which is being developed as a topical treatment for neuropathic pain (Phase Ib), and TrkA-NAM for osteopathic pain (early preclinical).

ACD440: A 'hot' prospect

ACD440 is a topical vanilloid receptor 1 (VR-1) antagonist currently in a Phase Ib trial. The VR-1, more commonly known as TRPV1 or the capsaicin receptor, has been a well-established target for the treatment of pain and has been implicated in the transduction of pain (nociceptive, inflammatory or neuropathic). In fact, topical capsaicin has been used as a homeopathic remedy for more than a century with the presumption that the ability to induce persistent receptor activation (a burning sensation) results in receptor desensitization and induction of an analgesic effects. We note several capsaicin-based topical treatments (Qutenza, Zacin and Axsain) are approved by regulators and prescribed for the treatment of pain associated with a variety of conditions, including postherpetic neuralgia, diabetic peripheral neuropathy and osteoarthritic pain.

The roots of this program stem back to AstraZeneca, which originally discovered and developed the compound as an oral drug in various pain indications. In January 2020, it was in-licensed from Acturum Life, which acquired rights to the drug-candidate when taking over the research sites in Södertälje, Sweden, previously occupied by AstraZeneca. We note the oral formulation of this had undergone extensive development at AstraZeneca but was discontinued. We understand this was related to the undesirable side effects resulting from systemic exposure, which appear to be a side effect of the class, but also coincided with when AstraZeneca exited from CNS research. Looking at a broader picture, extensive efforts have been made into developing VR-1 antagonists by various other companies (Amgen, Abbott, GSK, Merck/NeuroGen, Glenmark/Eli Lilly), but all of them were stopped in early clinical development, likely due to the same undesirable side effects resulting from systemic, oral exposure. Namely, hyperthermia and impairment of noxious heat sensation. Such high interest could be a result of the highly lucrative and large pain indications (osteoarthritis, dental pain, migraine).

ACD440 is a topical reformulation of the AstraZeneca's original compound, which we believe could be a solution to the undesirable side effects, while retaining the efficacy seen in the oral formulation trials. In January 2021, AlzeCure initiated a relatively inexpensive (SEK10–15m) placebo-controlled Phase Ib trial, conducted in 24 healthy volunteers, for ACD440. We anticipate safety and tolerability to be reported during mid-2021, as well as some proof-of-mechanism data, which could act to

validate the topical reformulation and its use in neuropathic pain. Thereafter, Alzecure has guided that preparations for a Phase IIa trial could start in H221 to enable trial initiation in 2022, which would give a better sense of the forms of neuropathic pain it will target. As ACD440 is in-licensed, we understand the initiation of a Phase IIa for ACD440 will trigger payment of an undisclosed milestone to Acturum Life, however, the deal terms have been described as very attractive by AlzeCure.

The potential indication currently is neuropathic pain, which is a symptom of a broad group of different underlying conditions. The key characteristic of this indication is the fact that this is a vast population of patients (diabetic nephropathy, herpetic neuralgia, cancer chemotherapy, autoimmune conditions, etc). Another key characteristic is the fact that in less than half of the patients pain control is unsatisfactory, so the unmet need is high (Sommer and Gruccu, 2017).

TrkA NAM: Differentiated from large pharma approach

AlzeCure's TrkA-NAM program stems from the high throughput screening efforts that generated compounds in the NeuroRestore platform, where it discovered selective negative allosteric modulators (NAM) for the TrkA receptor (note that the NeuroRestore programme has positive modulators, PAMs). Pharmacologically, these can be viewed as having inhibitory activity on NGF/TrkA neurotrophic signalling, which has been implicated to play a role in the pathogenesis of inflammatory pain (Skeratt et al, 2016).

Although a different mechanism of action, large pharma have committed significant resources to develop anti-NGF targeting antibodies for pain, with Pfizer/Lilly's tanezumab undergoing c 21 and Regeneron/Teva's fasinumab around seven Phase III trials. Development of these has been complicated, however, and safety concerns have plagued this class, with the FDA placing a clinical hold on Pfizer's tanezumab trials in June 2010 due to some patients experiencing a rapidly progressing, severe form of osteoarthritis leading to joint replacements. Despite this and bolstered by vast market, such as osteoarthritic pain (even an imperfect drug with a smaller market share could be lucrative), large pharma pushed for an FDA assessment. An FDA AdComm is planned for tanezumab on 24–25 March 2021 ahead of its potential approval for moderate-to-severe osteoarthritic pain. Similarly, long-term safety data for fasinumab are expected H121 that could define its path to approval.

Despite these challenges, the extensive efforts from large pharma to develop these anti-NGF targeting antibodies highlight the significant commercial need to develop effective, non-opioid based treatments. AlzeCure believes the addressable population for TrkA-NAM is c 250–300m patients and that with its downstream mechanism of action, TrkA-NAM could potentially offer safety improvement over these anti-NGF antibodies, by selectively attenuating NGF/TrkA signalling while sparing NGF/$p75^{NTR}$ signalling. AlzeCure's TrkA-NAM program is in an early preclinical development stage and successfully completed preclinical efficacy studies in December 2020. An oral candidate drug is expected to be **nominated during H221**.

Intellectual property

The compounds in the NeuroRestore platform all stem from a high throughput screening effort conducted by AlzeCure at the Karolinska Institute back in 2013. AlzeCure optimised and developed these, filing primary, composition of matter patents for compounds in December 2017, which should provide exclusivity and market protection out until at least December 2037. We note that given the length of time it takes to conduct late-stage CNS clinical trials, patent term extensions will likely be filed once market authorisations have been granted and these could extend patent protection by up to five years. We understand AlzeCure plans to file formulation patents for ACD 440 that could provide it with additional IP protection.

Sensitivities

AlzeCure is exposed to the drug development risks typically associated with pure play biotechs, namely clinical development delays or failures. Additional sensitivities exist around IP protection, regulatory risks, competitor successes, partnering setbacks and financing and commercial risks. Its focus on developing drugs for AD could be considered higher risk, but also higher reward in our opinion. Having projects that could have potential beyond AD does mitigate this risk to an extent.

While AlzeCure currently has a sufficient cash runaway to complete the ongoing clinical trials for ACD856 and ACD440, additional funding will be required to progress these as well as facilitating the progression of preclinical candidates. As the company has guided, assets will likely need to be partnered at some point as later-stage CNS studies can be costly due to large populations and study duration, hence the ability to successfully negotiate a deal is a key sensitivity, as well as the partner's willingness to progress these projects to commercialisation. We have assumed a deal in our valuation once meaningful Phase II proof-of-concept data are available, but we have limited visibility on the timing and terms.

Future drug pricing and market dynamics are invariably a key sensitivity, but can be hard to predict, especially if competitors are successful. Our current scenario for ACD856 assumes that a cognitive effect is seen that is superior to standard of care, which would warrant premium pricing paid to existing, generic AD drugs. If a disease-modifying effect will be obtained, market penetration and pricing should be higher. Conversely, if ACD856 has an efficacy that is only comparable to existing generic AD drugs, then it would invariably compete directly with these, although it could still be successful due to the vast market size.

Valuation

We value AlzeCure at SEK729m or SEK19.3 per share, based on a risk-adjusted net present value (rNPV) analysis, which includes an SEK112m in cash (no debt) at the end of FY20. A breakdown of our rNPV valuation, which uses a discount rate of 12.5%, is shown in Exhibit 8. We note that for NeuroRestore, we use a rather conservative success probability of 5%. In most other indications, the success probability for Phase I stage asset would be around 10%. Due to the lack of successful attempts to develop novel AD drugs so far, the success probability for these projects is significantly lower. However, lower success probability is built in the market's expectations, in our view. The attractive economics (large peak sales even if the drug provides only symptomatic relief) more than offset that, in our view.

Exhibit 8: Sum-of-the-parts AlzeCure valuation

Product	Indication	Launch	Peak sales* ($m)	NPV (SEKm)	Probability of success	rNPV (SEKm)	NPV/share (SEK)
NeuroRestore – ACD856	AD	2030	4,600	5,989.5	5.0%	481.9	12.8
Painless – ACD440	Neuropathic pain	2028	500	995.2	10.0%	134.4	3.6
Net cash, last reported				112.4	100.0%	112.4	3.0
Valuation				**7,097.1**		**728.7**	**19.3**

Source: Edison Investment Research. Note: WACC = 12.5%. *Peak sales are rounded to the nearest $100m.

Our valuation only includes the two clinical-stage assets, ACD856 for AD and ACD440 for neuropathic pain. We currently do not value any other potential indications or projects in the preclinical stages, but will reconsider them if AlzeCure will progress with them. We note that although the projects in the Alzstatin program are still in preclinical stage, they could move into the clinic within the next 24 months. This is a drug candidate for AD with potentially disease-modifying properties, so a major indication. Using the model, we developed for NeuroRestore and tweaking the assumption, we calculate that such a drug could reach c $15bn in peak sales (details below).

NeuroRestore

Target population and geography

In our model we use the US and the top 14 wealthy European countries (top five, Benelux, Scandinavia, Switzerland and Austria). One of the key questions is which setting is the best for a symptomatic drug across the severity spectrum of AD. Minimal cognitive impairment (MCI) and the early-stage AD settings are a natural target for Alzstatin, as the disease-modifying approach in AD is increasingly moving towards earlier stages. Treating moderate to severe patients with disease modifying therapy can be too late. It is rational to assume that symptomatic treatment would likely be accepted in later stages.

But as we discussed, ACD856 could potentially show disease-modifying activity, so it could be used in different stages of AD. Even if it shows a symptomatic-only effect, it could still be useful in early-stage AD, and even in MCI stage, if the drug is safe. For all these reasons we use the mild AD patient population as the target population, as this setting will likely overlap in future development paths for ACD856 and Alzstatin. According to different sources:

- In 2019, there were approximately 5.8 million AD patients in the US (Alzheimer's Association) and 7.1 million in the top 14 Western European countries (Alzheimer Europe).
- Mild AD diagnostic rates were 30% in the US and 21–32% in top five European countries (based on GlobalData's primary research); we use the mid-point of 25% in Europe.
- Treatment rates of mild AD patients were 72% in the US and 46–66% in the top five European countries (GlobalData); we use the mid-point of 55% in Europe.

This translates into the target populations we use in our model: 1.2 million in the US and 980 thousand in European countries, approximately 2.2 million mild AD patients in total treated.

Overall, we view current market size estimates and even existing treatment paradigms in different countries as not limiting the potential of novel effective AD drugs, as they would likely disrupt the status quo and expand the treated population.

Other assumptions

We assume a price of US$6,000 per patient per year in the US (a premium to branded generics currently) and a 50% discount in Europe. We assume market penetration of 30% with peak sales of US$4.6bn achieved in seven years after launch in 2030. We assume that AlzeCure will out-license ACD856 during the Phase II stage in 2024 and that until then the company will invest c $17m in development. After the out-licensing we assume that the partner will take over the development (although various other arrangements, such as co-development, are possible). We assume Phase III start in 2026 and launch in 2030. Licensing deals that we view as comparable are listed in Exhibit 9. We use the average values: an upfront payment of US$55m and total milestone payments of US$550m spread across the R&D (one-third of the total amount) and commercial phases (two-thirds of the total amount). We assume AlzeCure will receive a tiered royalty rate of 14–18%.

Exhibit 9: Relevant licensing deals in AD and pain

Date	Licensor	Licensee	Product	Stage	Upfront (US$m)	Deal value (excl upfront) (US$m)
Alzheimer's disease						
26 March 2013	Otsuka Holdings	Lundbeck	5-HT6 (serotonin) antagonist	Phase II	150	675
23 December 2014	Roivant Sciences/Axovant Sciences	GlaxoSmithKline	5-HT6 (serotonin) antagonist	Phase II	5	155
5 September 2011	Roche	Evotec	Monoamine oxidase B inhibitor	Phase II	10	820
Pain management						
9 September 2019	Flexion	Xenon	NaV1.7 Inhibitor	Phase I	3	125
28 May 2019	Centrexion Therapeutics	Eli Lilly	SSTR4 agonist	Phase I	47.5	950

Source: EvaluatePharma

Painless

Top-down approach used

Due to the highly fragmented pain relief market and the fact that ACD440 is still in the early stages of clinical development, we believe a bottom-up approach of estimating peak sales is not feasible at the moment. The topical pain relief market has been dominated by generic NSAIDs, primarily the brand Voltaren (diclofenac, Novartis), which had sales of $360m in 2020 (EvaluatePharma), although it has reached $1bn+ in the past. It is not a direct comparison as it is perceived as a branded generic available OTC and used for many forms of pain, such as trauma. The most comparable drug in terms of setting, namely, neuropathic pain, would be Lyrica (pregabalin, Pfizer), which is one of the standard of care drugs. Lyrica sales in neuropathic pain plateaued at c $3bn before patent expiry in 2019. However, it is an oral formulation, so not a direct benchmark drug as well, in our view. Keeping in mind this range, we use what could be considered a conservative assumption of $500m in peak sales assumed to be reached in seven years after the launch in 2028.

We assume that AlzeCure will out-license during the Phase II stage in 2023 and that until then the company will invest c $10m in development. We assume Phase III start in 2025 and launch in 2028. Licensing deals that we view as comparable are listed in Exhibit 9. We include an upfront payment of US$5m and total milestone payments of US$120m spread across the R&D (one-third of the total amount) and commercial phases (two-thirds of the total amount). We assume AlzeCure will receive a tiered royalty rate of 14–18%.

Estimating the peak sales of a disease-modifying AD drug

Alzstatin projects are still in the preclinical development, which is the main reason we do not include them in our valuation. However, Alzecure has chosen the drug candidate and currently is conducting in vivo toxicology studies, so it could move into the clinic sometime in 2022/2023. Given the large indication (potentially disease-modifying effect in AD), we have used our model to estimate potential peak sales for a disease-modifying AD drug.

We use the same mild AD patient population and most of other assumptions as for NeuroRestore. All timelines are delayed by two years. The two variables that are most likely to differ, in our view, are the penetration rate and the pricing. We have doubled the penetration rate for a successful disease modifying drug to 50% from 30% and also the price tag to $12k from $6k in the US (50% discount in Europe). Keeping other assumptions the same (timelines, R&D costs, licensing deal probability, etc), we calculate potential peak sales of a DMT could reach c $15bn. As a sense check, EvaluatePharma collects consensus forecasts with a time horizon until 2026. For aducanumab the current estimate is $4.2bn, however it is still in an exponential growth stage at that time. We believe it is widely expected that a truly disease modifying AD drug would reach $10bn+.

Financials

AlzeCure reports no income and in FY20 it reported SEK71.6m in operating loss, of which most (SEK62.4m, of which SEK495k is amortisation and depreciation) was booked as R&D expense. In FY19 the operating loss was SEK50.9m indicating that spending increased due to more R&D activities. We expect the spending to increase somewhat further in 2021 as both clinical trials are in full swing and forecast SEK82.0m in operating loss.

In our valuation model we assume out-licensing deals for ACD856 in 2024 and for ACD440 in 2023. The assumed deal terms are described above, however, we don not include the upfront payments in our financial forecasts, as these are still risk-adjusted.

AlzeCure had cash of SEK112m at the end of FY20, which according to our model should provide funding into 2022. We assume am illustrative long-term liability of SEK 57m in 2022 (as per our research principles in lieu of equity funding). Notably, its existing budget is sufficient to reach the readouts from both clinical trials, as well as other potential catalysts from the preclinical R&D pipeline:

- ACD440 Phase Ib data is expected sometime in mid-2021, during summer;
- ACD856 Phase I SAD data in mid-2021;
- ACD856 Phase I MAD data in H221;
- Filing for Phase IIa ACD440 study is H221; and trial start 2022
- Potential announcements from the preclinical studies with Alzstatin platform and TrkA-NAM for pain.

Exhibit 10: Financial summary

Year end 31 December	SEK'000s	2018	2019	2020	2021e	2022e
		IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Total revenues		0	0	0	0	0
Cost of sales		0	0	0	0	0
Gross profit		0	0	0	0	0
SG&A (expenses)		(2,558)	(6,035)	(9,375)	(9,609)	(9,850)
R&D costs		(36,828)	(44,499)	(61,861)	(71,861)	(75,454)
Other income/(expense)		3,597	(84)	152	0	(254)
Exceptionals and adjustments		0	0	0	0	0
Reported EBITDA		(35,789)	(50,618)	(71,084)	(81,470)	(85,558)
Depreciation and amortisation		(104)	(290)	(495)	(544)	(580)
Reported Operating Profit/(loss)		(35,893)	(50,908)	(71,579)	(82,015)	(86,137)
Finance income/(expense)		(92)	50	213	68	0
Other income/(expense)		0	0	0	0	0
Exceptionals and adjustments		0	0	0	0	0
Reported PBT		(35,985)	(50,858)	(71,366)	(81,947)	(86,137)
Income tax expense		0	0	0	0	0
Reported net income		(35,985)	(50,858)	(71,366)	(81,947)	(86,137)
Basic average number of shares, m		22.8	37.8	37.8	37.8	37.8
Basic EPS (SEK)		(1.58)	(1.35)	(1.89)	(2.17)	(2.28)
Diluted EPS (SEK)		(1.58)	(1.35)	(1.89)	(2.17)	(2.28)
BALANCE SHEET						
Property, plant and equipment		597	1,768	1,944	2,071	2,162
Intangible assets		17	17	17	17	17
Other non-current assets		7	7	7	7	7
Total non-current assets		621	1,792	1,968	2,095	2,186
Cash and equivalents		234,549	182,499	112,434	30,356	1,000
Trade and other receivables		8	16	8	12	10
Other current assets		2,604	2,448	3,417	3,417	3,417
Total current assets		237,161	184,963	115,859	33,785	4,427
Non-current loans and borrowings*		0	0	0	0	56,870
Total non-current liabilities		0	0	0	0	56,870
Trade and other payables		3,646	2,997	3,966	3,966	3,966
Other current liabilities		967	1,751	3,106	3,106	3,106
Total current liabilities		4,613	4,748	7,072	7,072	7,072
Equity attributable to company		233,169	182,007	110,755	28,808	(57,329)
CASH FLOW						
Operating Profit/(loss)		(35,893)	(50,908)	(71,579)	(82,015)	(86,137)
Depreciation and amortisation		104	290	495	544	580
Other adjustments		0	0	0	0	0
Movements in working capital		(392)	283	1,363	(4)	2
Interest paid / received		(93)	50	213	68	0
Income taxes paid		0	0	0	0	0
Cash from operations (CFO)		(36,274)	(50,285)	(69,508)	(81,407)	(85,556)
Capex		(459)	(1,461)	(671)	(671)	(671)
Acquisitions & disposals net		0	0	0	0	0
Other investing activities		0	0	0	0	0
Cash used in investing activities (CFIA)		(459)	(1,461)	(671)	(671)	(671)
Net proceeds from issue of shares		217,330	(381)	0	0	0
Movements in debt		0	0	0	0	56,870
Other financing activities		0	77	114	0	0
Cash from financing activities (CFF)		217,330	(304)	114	0	56,870
Increase/(decrease) in cash and equivalents		180,597	(52,050)	(70,065)	(82,078)	(29,356)
Cash and equivalents at beginning of period		53,952	234,549	182,499	112,434	30,356
Cash and equivalents at end of period		234,549	182,499	112,434	30,356	1,000
Net (debt) cash		234,549	182,499	112,434	30,356	(55,870)

Source: AlzeCure Pharma accounts, Edison Investment Research. Note: *Long-term debt used instead of equity issue.

Contact details	Revenue by geography
AlzeCure Pharma AB Hälsovägen 7 SE-141 57 Huddinge Sweden +46 (0)70 786 94 43 www.alzecurepharma.se	N/A

Management team

Chief executive officer: Martin Jönsson	Chief scientific officer: Johan Sandin
Martin Jönsson joined AlzeCure Pharma as CEO in January 2020 and has more than 20 years' experience in the global pharmaceutical industry, previously working for Roche and Ferring in senior positions in several different areas. He has worked with business development, sales, marketing, alliance management and medical affairs. Martin holds an MSc in business from the University of Lund and has studied at the University of Freiburg, Germany, and the University of Ottawa, Canada.	Johan Sandin is a co-founder of AlzeCure Pharma and was CEO from 2017 until the appointment of Martin Jönsson. Since then he has held the position of chief scientific officer. Johan is a behavioural pharmacologist in neurology with significant academic and industrial experience. He has 17 years of experience in drug discovery, including 10 years at AstraZeneca where he held several scientific, project and leadership roles with responsibility for in vitro biology, in vivo biology and biochemical biomarkers within the CNS field. Johan holds a PhD in neuroscience from Karolinska Institute, Sweden.
Chief financial officer: Birgitta Lundvik	
Birgitta Lundvik has been CFO of AlzeCure Pharma since 2017. She has more than 25 years of experience from software development, life science and real estate companies and has been CEO at Hansoft Technologies, Favro and Nonna Holding. She has taken part in several M&A projects and has a broad experience of venture capital companies. Birgitta holds an MSc in business from Uppsala University and an eMBA in finance from Stockholm Business School, Sweden.	

Principal shareholders	(%)
BWG Invest Sàrl (William Gunnarsson)	11.6
FV Group AB	5.3
Nordnet Pension Insurance	4.8
AlzeCure Discovery AB	4.5
Sjuenda Holding AB	4.2
SEB-Stifelsen	3.7
Futur Pension	2.8

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