Herantis Pharma

Sector: Biotech

Multimodal Potential

Redeye initiates coverage of Herantis Pharma, a biotech developing drug candidates in the difficult area of Parkinson's, an area with great potential to improve the standard of care. The case hinges on blockbuster potential in this expanding market, supported by experienced management, institutional ownership and a prospective licensing deal. While the share trades close to fair value, longer-term upside is compelling.

Significant Market with high unmet need

An alternative to current treatments of Parkinson's – a chronic neurodegenerative disease with a considerable impact on quality of life – is badly needed to reverse the disease's progression and prevent its high later-stage costs of care. In this rapidly growing market, we estimate Herantis' peak sales potential at more than USD 2.5bn.

Compelling Scientific Foundation

CDNF's multimodal mode of action differentiates it from the rest of the Parkinson's pipeline.This has attracted solid interest from the science community, including publication in leading journals, as well as early interest from specialist investors.

Credible Management and Ownership

Herantis' management and ownership help validate the case. While the business model is heavily reliant on partnering, the team has the deal experience and scientific expertise to handle this. Moreover, Herantis is backed by institutional investors – a strong signal for an early-stage company addressing a challenging indication.

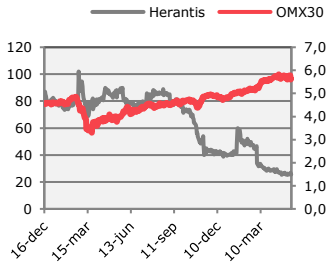
Long-term Play – But Near-Term Triggers Await

While our base case is close to the share's current levels, we see a compelling case as Herantis takes the important step back to clinic with its new, more convenient administration method. Positive pre-clinical data would de-risk the case and increase the value of CDNF, potentially in the near-term. Due to others' pipeline setbacks and emerging interest in Herantis' class of proteostasis-altering therapies, we see good potential for a substantial licensing deal (USD 475m in our base case) once the company presents efficacy data.

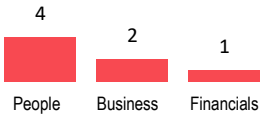
FAIR VALUE RANGE

BEAR	BASE	BULL
5	27,5	70

HRNTS VERSUS OMXS30



REDEYE RATING



KEY STATS

Ticker	HRNTS
Market	First North
Share Price (SEK)	25
Market Cap (Msek)	250
Free Float	55%

ANALYSTS

Fredrik Thor

Fredrik.thor@redeye.se

Anders Hedlund

Anders.hedlund@redeye.se

KEY FINANCIALS (mEUR)	2019	2020	2021	2022
Net sales	0	0	0	0
EBITDA	5,1	-6,3	-8,2	-7,7
EBIT	-6,1	-7,2	-9	-8,5

Investment Thesis

Rapid Growth as New Treatments Emerge

No disease-modifying drugs have yet been approved for Parkinson's disease. The current treatment regime, while initially effective in relieving symptoms, becomes less effective over time. Payers and doctors emphasize the need for a disease-modifying treatment that can stop and reverse this chronic neurodegenerative disease's progression, preventing the high costs and low quality of life associated with late-stage Parkinson's. While the Parkinson's market is relatively modest in size in view of the disease's economic burden (USD 4.5bn across the US, EU5, and Japan), we expect it to grow rapidly as new treatments emerge. We estimate the peak sales for Herantis alone at more than USD 2.5bn.

Compelling Science

We find the scientific foundation of Herantis' lead candidate CDNF compelling, despite its early stage. This is reinforced by the high interest from the science community, including several publications in leading journals such as Nature and early interest from significant investors. The case is based on the science of CDNF's multimodal mode of action, which differentiates it from other Parkinson's candidates. Furthermore, the candidate's broad mode of action makes it less dependent on a full understanding of the underlying pathological features. This adds to its attractions, given the current scientific knowledge gap and lack of established biomarkers.

Credible Management and Ownership

Herantis' management team and ownership are both solid factors that validate the investment case. The company's business model is heavily reliant on partnering at a relatively early stage, and we feel confident that this team, with experienced CEO Craig Cook at the helm since 2020, has the capacity to do so. We are also encouraged by ownership including Swedbank's health care fund, industrial partner Nanoform, and the Fourth National Swedish Pension Fund. For an early-stage, high-potential company such as Herantis, long-term focus is vital, and owners have been supportive so far - even after the company's recent pivot to new administration methods (a long-term positive) added short-term uncertainty.

Long-term Play – But Near-Term Triggers Await

While our base case is close to today's trading levels (10% upside), we see a compelling investment case over time as Herantis takes the important step back to clinic with its new and more convenient administration method. Positive pre-clinical data would de-risk the case and increase the value of CDNF further, in our view. There have been several recent setbacks in the Parkinson's pipeline, including candidates sponsored by Roche and Biogen, along with increased M&A activity in Herantis' class of proteostasis-altering therapies. With this in mind, we argue that CDNF will be in a good position to out-license once a new administration form has been validated in the clinical setting and efficacy has been shown.

Furthermore, Herantis' engineered derivative of CDNF, xCDNF, offers an attractive option for easier administration in Parkinson's - and potentially in other neurodegenerative diseases. This could lead to further upside once pre-clinical data has been evaluated.

Catalysts

Progress on New Administration Method - CDNF

Herantis changed direction after the phase I/IIa study was finalized in 2020, shifting away from intracranial infusion to other, less invasive methods. In January 2021, Herantis also announced a strategic partnership with Nanoform to develop a nose-to-brain administration method that can breach the blood-brain barrier. Herantis has several alternatives ongoing and is currently in the pre-clinical phase. A selection of method and data on sufficient active concentration that reaches the brain would de-risk the Herantis investment case and represent a positive trigger for the stock.

Time Horizon: 6 - 12 months

Initiation of clinical study CDNF

Herantis plan is currently to take CDNF into clinic with the new administration method in 2022/2023. Good regulatory guidance and a progress into clinic in 2022/early 2023 would be positive and indicate that the company is back on track progressing towards major inflection points.

Time Horizon: 12 - 24 months

Selection of lead candidate - xCDNF

Herantis' second Parkinson's asset, a derivative of CDNF, is a smaller peptide that allows for non-invasive penetration of the brain. While xCDNF has become more of a parallel track to CDNF in light of the change of administration method for that compound, the xCDNF project is exciting in Parkinson's and potentially also other neurodegenerative diseases, and its move to the pre-clinical stage and clinic would be positive.

Time Horizon: 6- 12 months

Counter Thesis

Tricky indication and development risks

There are currently no disease-altering treatment for Parkinson's disease and many promising candidates have failed at later development stages. Most biotech companies in the early stage do not make it to the market and Parkinson's drug development is rife with higher-than-average costs, risks and time to market.

Stalled progress into clinic

Herantis is a biotech company, which implies the typical development risks. Additionally, in fall 2020, Herantis decided to change administration method for CDNF, postponing the time to market. While we have a positive take on this decision, it does increase the development risks further given the uncertainty associated with these alternative administration methods.

Financing needs

Herantis has a strong ownership structure and recently finalized a private placement of some EUR 8 million. However, clinical development for Parkinson's is costly and Herantis' pivot to new administration methods prolongs its time to market. The company will need ongoing support from major owners and progress to clinic in the coming years.

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Management and Ownership

Herantis Pharma: Top owners, per 11th of May	Total amount of shares: 9 757 068	
Name	**Shares**	**% of capital**
Swedbank Robur Fonder	946435	9.7 %
Fjärde AP Fonden	607585	6.2 %
Inveni Life Sciences Fund I Ky	528134	5.4 %
Helsingin Yliopiston Rahastot	515483	5.3 %
Nanoform Finland Oyj	432432	4.4 %
Pensionsförsäkringsaktiebolaget Veritas	374948	3.8 %
Innovestor Kasvurahasto I Ky	328500	3.4 %
Joensuun kauppa ja kone Oy	301181	3,1 %
OP-Suomi Pienyhtiöt	275891	2.8 %
Sijoitusrahasto Säästöpankki Pienyhtiöt	260000	2.7 %
Total 10 top owners	4 557151	46,7%
Remaining owners	5 199 917	53,3%

We consider Herantis Pharma's ownership structure to be robust and an important validation of the investment case, thanks to several institutional owners in the top 10, including Swedbank Robur Healthcare, the Fourth Swedish National Pension Fund (AP4), and the company's industrial partner Nanoform. Due to significant interest from institutional owners, Herantis has managed to raise capital regularly in an efficient manner.

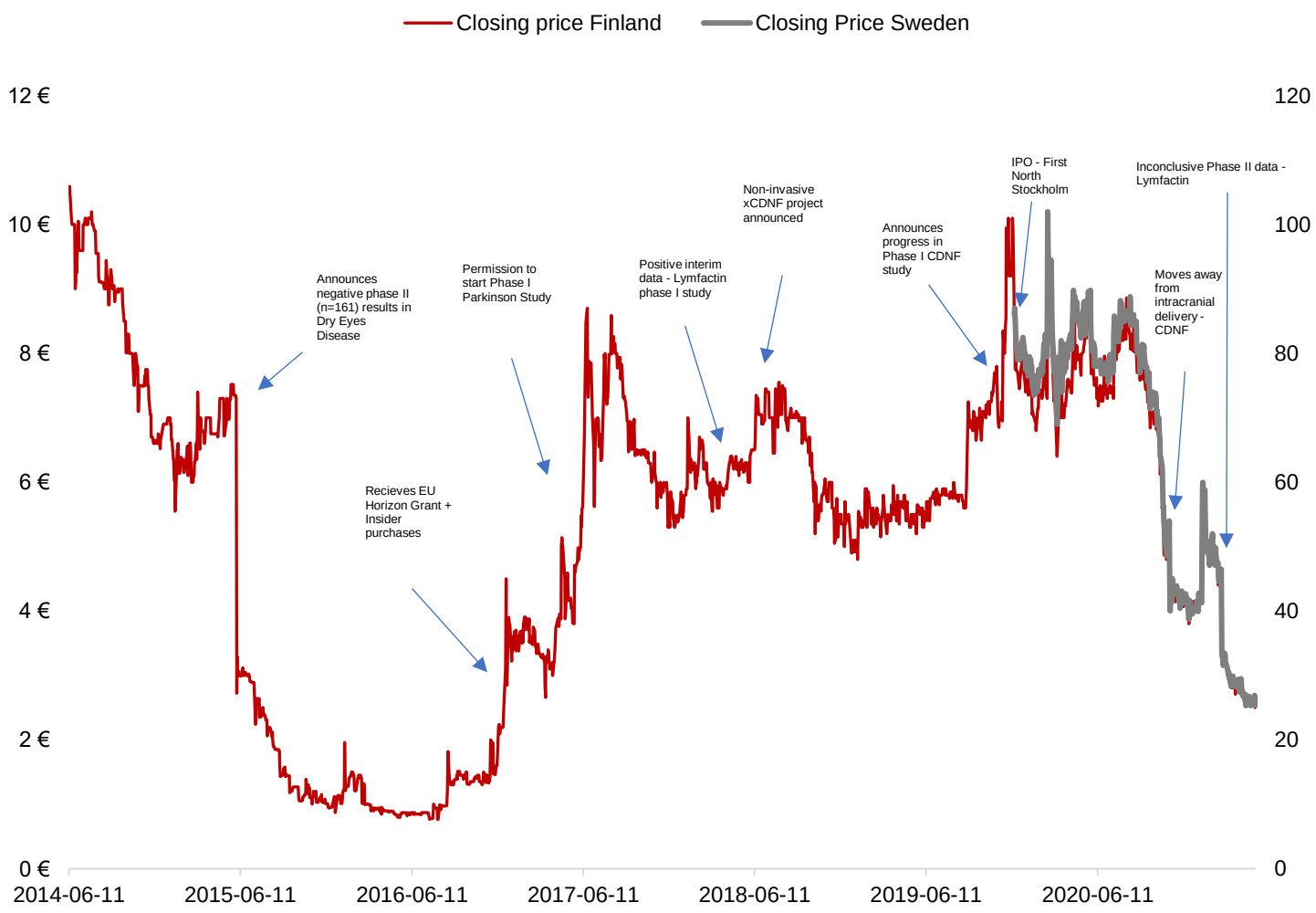
Management and Board

We highly value the experience of the management team, including CEO since 2020 Craig Cook. He has extensive experience from larger pharmaceutical companies as well as biotech companies, including deal experience from both sides. He is joined by an experienced team, including from a a scientific/medical, regulatory and financial perspective.

Management Ownership			**Board of Directors**		
Name	**Shares**	**Options**	**Name**	**Shares**	**Options**
Craig Cook	0	479991	Timo Veromaa	8900	
Sigrid Booms	2400	40991	Frans Wuite	6280	
Henri Huttunen	78050	89777	James Philips	5706	
Antti Vuolanto	1100	92707	Aki Prihti	0	
Jutta Poutanen	100		Mats Thorén	0	
Tone Kvåle	4600	147000	Hilde Furberg	2000	
Magnus Sjögren	0	48785			

Source Euroclear; Holdings

Stock Performance (adjusted)



Source: Nasdaq OMX; Redeye Research

Herantis Pharma's stock price has had a volatile journey since the IPO in 2014, due to results from studies, prolonged clinical programs, and low liquidity. This journey has continued after the IPO on First North Stockholm – including the recent setback due to the inconclusive results in the Lymfactin phase II trial. We believe that the stock will stabilize and that positive new on progress for CDNF/xCDNF could turn the sentiment around.

Company Profile and Overview

Herantis Pharma Plc was founded in Helsinki, Finland, in 2008 by four neuroscientists from the University of Helsinki. The company was initially called Hermo Pharma Ltd. In 2014, it acquired Finnish drug development company Laurantis Pharma Ltd and changed its name to Herantis Pharma Plc. The company's headquarters are in Finland, it was publicly listed on Nasdaq First North Helsinki in 2014 and Stockholm in 2019, and it had 13 employees as of the end of 2020.

The company's lead asset is CDNF, a disease-modifying compound that targets Parkinson's disease. The compound has been tested in a phase Ib/IIa trial, where CDNF was administered directly to the brain of late-stage patients by surgical means. The compound is now currently being re-evaluated in the pre-clinical stage to allow for non-surgical administration routes to expand the target population. CDNF has a unique mode of action and acts through the maintenance and restoration of proteostasis, a process that can, if interrupted, in Parkinson's lead to neuronal cell death and the accumulation of protein aggregates – the two key pathological features of the disease.

Alongside CDNF, the company is also developing xCDNF, an engineered peptide based on active fragments of CDNF. This is administered via simple skin injection and is able to cross the blood-brain barrier non-invasively.

Finally, beyond its CNS assets, Herantis has a separate compound, Lymfactin VEGF-C, which addresses secondary lymphedema, a complication from breast cancer surgery that results in disrupted lymph drainage and is associated with swelling in the arms and legs. The compound was recently tested in a phase II trial, but results were inconclusive. Given this and the progress the company is making in CDNF and xCDNF, Herantis has decided to focus its in-house resources purely on CDNF and neurodegenerative diseases.

At present, there are no disease-modifying drugs approved for Parkinson's and the current treatment paradigm is based on Levodopa, a symptom-relief treatment with tapering efficacy over time. The demand for approved disease-modifying therapies is high, and while the market size is relatively modest compared to the incidence, due to generics and limited treatment options (USD 4.5bn in US, EU5 and Japan), the willingness to pay is high to reverse this chronic degenerative disorder. We expect the market to grow rapidly as new treatments emerge.

Herantis Pharma: Clinical Projects Under Development

	Project	Indication	Research	Pre-clinical	Phase I	Phase II	Phase III	NDA	Market
CNS	CDNF Intracranial CDNF Nasal & Subcutaneous xCDNF	Parkinson's Disease							
Lymphedema	Lymfactin	Secondary Lymphedema							

	Completed development phase
	Potential external development
	Ongoing phase

Source: Herantis Pharma; Redeye Research

Major Events and Financing Rounds – Herantis Pharma

Year	Event
2008	- Hermo Pharma founded by professors from University of Helsinki; focused on a CDNF portfolio
2010	- Received grant from Michael J Fox Foundation for CDNF Research
2014	- Acquired Laurantis Pharma. Herantis Pharma is established with the original CDNF assets plus new lymphedema assets - IPO on Nasdaq First North Finland; raised EUR 14.5m
2015	- Announced negative phase II (n=161) results in dry eye disease - Business Finland granted Herantis almost EUR 3m as an R&D loan for the development of CDNF
2016	- Started Lymfactin phase I trial - EUR 6m grant for CDNF development from EU Horizon 2020
2017	- Directed share issue of EUR 4.7m - Started CDNF clinical phase I-IIa trial
2018	- Started Lymfactin phase II trial - xCDNF program started
2019	- Directed share issue of EUR 5.8m - IPO on Nasdaq First North Stockholm and directed share issue of EUR 4.2m
2020	- Directed share issue of EUR 15m - Craig Cook appointed CEO and Tone Kvåle CFO - Positive outcome of CDNF phase I-IIa - Strategic shift away from invasive intracranial administration; changed clinical development plan
2021	- Strategic partnership with Nanoform on novel CDNF formulation method - Lymfactin phase II results announced - Strategic direction shifted fully to neurodegenerative diseases with CDNF and xCDNF

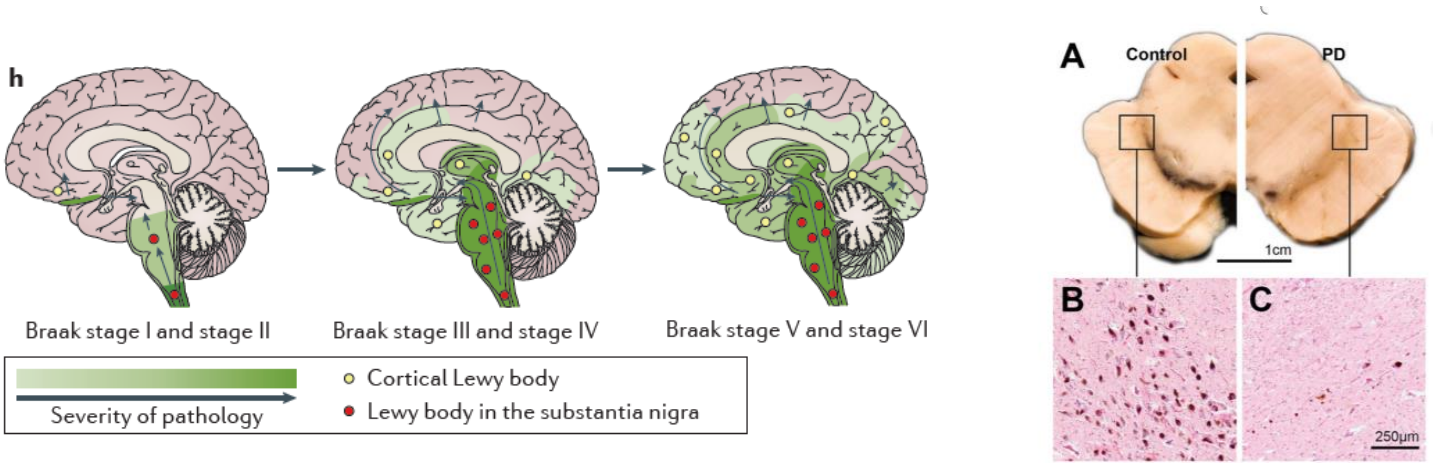
Parkinson's Disease – Overview

Parkinson's is a chronic degenerative disorder of the central nervous system (CNS) that has mainly been linked to movement deterioration and disorders. At more advanced stages of the disease, serious non-motor symptoms are also common, such as dementia, depression, and autonomic dysfunction. There is no cure or disease-altering treatment on the market and the devastating illness is associated with morbidity and worsened quality of life. Parkinson's is the second most common neurodegenerative disease after Alzheimer's and poses a significant cost to society. Parkinson's is typically split into two types: genetic and sporadic. Genetic Parkinson's accounts for roughly 5-10% of all reported cases. However, all forms of Parkinson's are believed to be a consequence of a complex interplay between environment and genetic predispositions.

Parkinson's is caused by the degeneration of dopamine-producing neurons in the brain, specifically in the substantia nigra region, and the accumulation of intracellular protein (alpha-synuclein). In early-stage patients, the loss of dopaminergic neurons is relatively concentrated but becomes more widespread at later stages, as shown in the diagram below to the left. The early loss of neurons suggests that the degeneration starts before motor symptoms are apparent. When dopamine neurotransmission is reduced due to the loss of dopamine-generating neurons, the muscles lose control and motor symptoms arise. Most of today's symptom-focused therapies target dopamine. The underlying mechanisms for the start of the degeneration and non-motor symptoms have not been fully established.

The aggregation of the alpha-synuclein protein in certain neurons is the other hallmark of sporadic Parkinson's; these are called Lewy bodies. These structures have been found to be increasingly complex and also constitute many other molecules. Lewy pathologies are known to occur in elderly people with other diseases, Alzheimer's being the most common diagnosis. As we will discuss later, many disease-modifying therapies for Parkinson's focus on a-synuclein accumulation.

A-Synuclein accumulation (left) and dopamine loss (right)

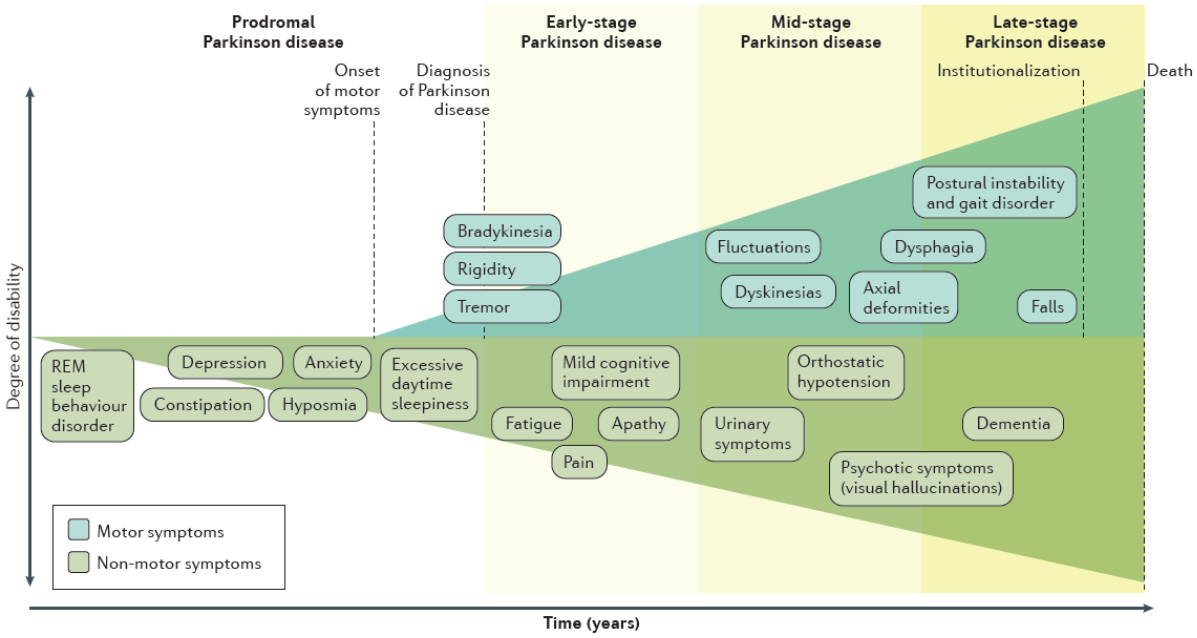


Source Poewe et al 2017; Obeso et al 2017

Diagnosis

Parkinson's is an underdiagnosed disease at present due to the lack of definite biomarkers and tests. It is mainly diagnosed through symptoms and by excluding other potential causes of them. However, there has been significant progress in research on new biomarkers, which could lead to earlier identification of Parkinson's in the future.

Symptoms and disease stages



Source Poewe et al 2017

As shown above, the symptoms of Parkinson's evolve over time. In the prodromal stage, symptoms have started to show but are typically non-motor symptoms and are insufficient to diagnose a patient with Parkinson's. The neurodegeneration starts even earlier in the pre-clinical stage of Parkinson's. A patient can be in the prodromal stage for several years or even decades. Patients are usually diagnosed when the first motor symptoms show, typically when they are in their late fifties. Both motor and non-motor symptoms progress over time, making Parkinson's a more severe and disabling disease, even with the current treatment regime, as we will describe further below.

A common way to follow the progression of Parkinson's is to use disease scales. The Hoehn and Yahr scale, from 1 to 5, is one of the most widely applied owing to its simplicity. 1-3 is defined as early stage and 4-5 as late-stage Parkinson's. The scale was created in 1967 and focuses on motor symptoms. The scientific understanding of symptoms has since progressed and scales that also measure non-motor symptoms, such as the Unified Parkinson's Disease Rating Scale (UPDRS), are now widely used, especially in clinical trials and research. The UPDRS scale consists of four parts and provides a comprehensive view of a patient's condition.

Current Treatment Regime

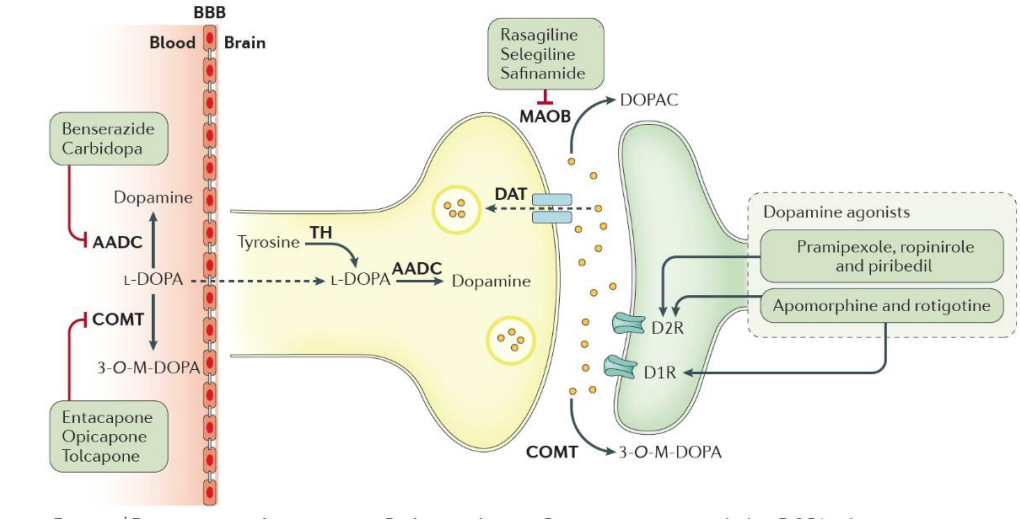
Levodopa

Today, the current treatment regime is based on symptom relief and has primarily been based on the same dopaminergic therapy paradigm since the 1970s, when the FDA approved Levodopa. Researchers discovered that Levodopa (or L-Dopa), a precursor amino acid of dopamine, can pass through the blood-brain barrier, unlike dopamine itself. Once in the central nervous system, it can convert into dopamine. The treatment rationale is to substitute the dopamine loss with systemic administration of Levodopa. The blood-brain barrier is a significant obstacle for most CNS therapies, prohibiting large molecules and most small-molecule drugs from entering the central nervous system.

While Levodopa remains a mainstay as a first-in-line drug and is the most potent treatment of motor symptoms, its use is also muddied by motor complications and tapering efficacy. Motor response fluctuations and on/off periods of symptom control are common, especially in the later stages of Parkinson's. The drug effect wears off before the next dose kicks in (the "on" period"). This is partly due to the short half-life of Levodopa but also because of the level of gastrointestinal absorption and blood-brain barrier transport, as only about 10% breaches the blood-brain barrier. Long-term use of Levodopa can also induce side effects, including involuntary movements (dyskinesia), leading some patients to postpone Levodopa treatment in the early stages.

Since the development of Levodopa, there have been advances in the scientific understanding of the regulation of nigrostriatal dopaminergic transmission, increasing the role and strategy of dopaminergic therapies.

Dopaminergic Therapy Modalities



Source: *Poewe et al 2017*

Levodopa is typically combined with Carbidopa, an AADC-inhibitor, to increase bioavailability and prevent dopamine metabolism outside of the central nervous system, leading to reduced side effects and lower required doses of Levodopa. Another addition is COMT-inhibitors such as Entacapone, which further enhance bioavailability and the half-life of Levodopa. This combination is currently the first-in-line for patients experiencing motor fluctuations (i.e. with on-off periods). Moreover, MAOB inhibitors are a class of enzymes used to reduce off time from Levodopa and as an alternative treatment in early-stage Parkinson's. In severe Parkinson's, a medical device can be inserted that delivers Levodopa by continuous intestinal administration (Duodopa intestinal gel from AbbVIe). Duodopa is one of the most lucrative drugs on the Parkinson's market and several studies have shown that it reduces motor fluctuations and dyskinesia versus oral Levodopa. However, Duodopa requires an invasive installation and is also expensive. Due to its efficacy, it is deemed cost-efficient amongst payers, and sales are expected to remain high.

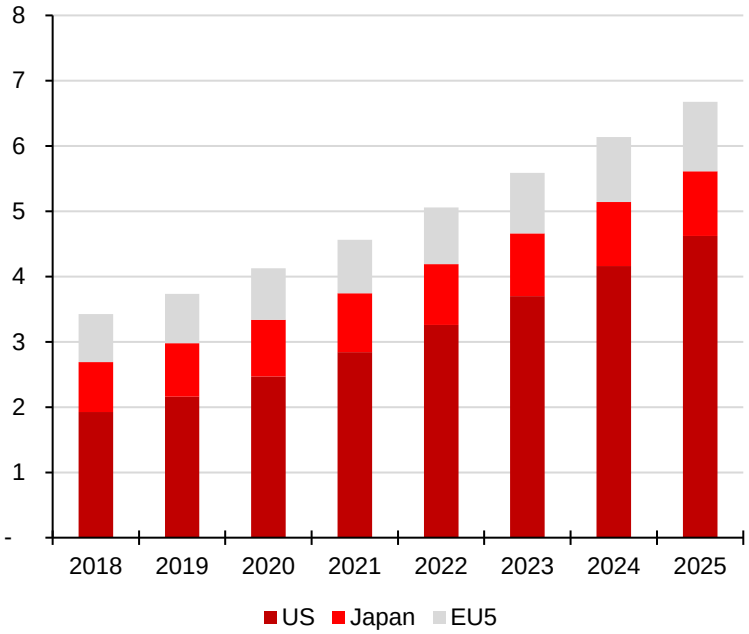
Finally, dopamine agonists are another class of drugs used to stimulate dopamine production. Unlike Levodopa, dopamine agonists do not convert to dopamine, but instead mimic its effects. While they have a longer half-life than Levodopa and a lower risk of leading to motor complications, their treatment effect is less and they may cause drowsiness and impulse dyscontrol.

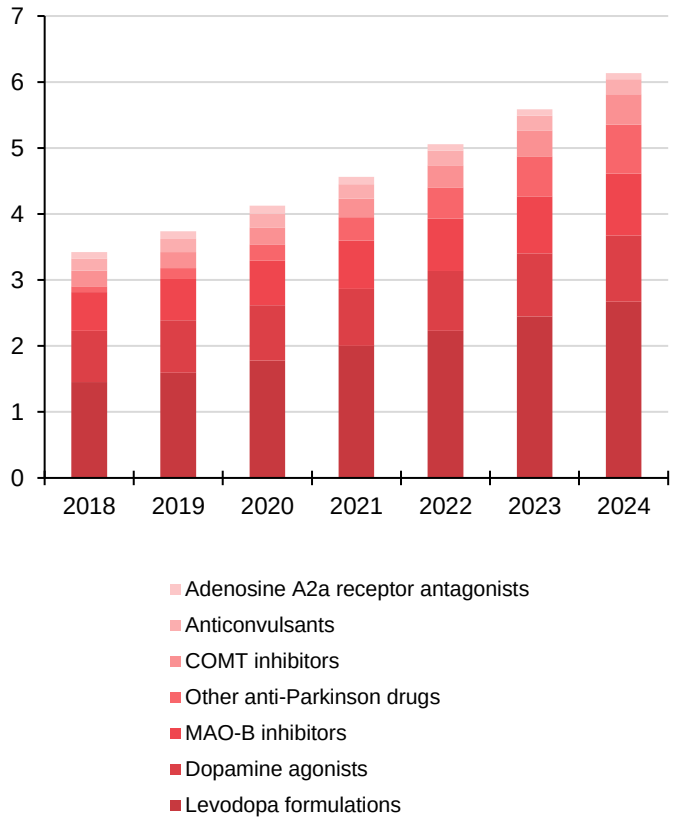
Deep Brain Stimulation

Deep brain stimulation (DBS) is a treatment option where electrodes are implanted in specific targets in the patient's brain. Due to the invasive nature of the procedure, it has mostly been reserved for patients in advanced stages of Parkinson's but has become more accepted for early-stage patients in recent years. DBS is a complicated procedure and requires a high level of multidisciplinary expertise. Adverse events are uncommon but include intracranial bleeding and, in the worst case, death (less than 1% of cases).

DBS was initially approved by the FDA for Parkinson's in 1997 and is today also used in other indications such as obsessive-compulsive disorder, epilepsy, and major depression disorder. The treatment effect of DBS correlates with the treatment response to Levodopa, meaning that the DBS is best used for patients who respond well to Levodopa but who have motor complication due to long-term use. Several studies have shown a significant increase in quality of life and reduced motor symptoms (up to 60-70%) with DBS.

Sales of PD Drugs Today (Bn $)





Source: Datamonitor; Redeye Research

The Parkinson's drug market in the EU5, Japan, and the US is worth roughly USD 4.5bn today and largely consists of mainstay drug classes and combination therapies. As we can see in the graph above to the right, Levodopa formulations are the highest-selling class, followed by dopamine agonists. Due to innovation and an aging population, growth is expected to remain high in the coming years and decades. The high rate of Parkinson's generics means the pharmaceutical cost per patient is relatively low today in comparison to other neurological diseases – although niche products, such as Duopa and Nuplazid, are costly treatments. However, the direct and indirect costs to society of Parkinson's patients is high; health economic studies have shown annual costs exceeding USD 20bn in the US alone. As innovative and disease-modifying drugs reach the market, we expect costs to increase in relation to the increased benefits.

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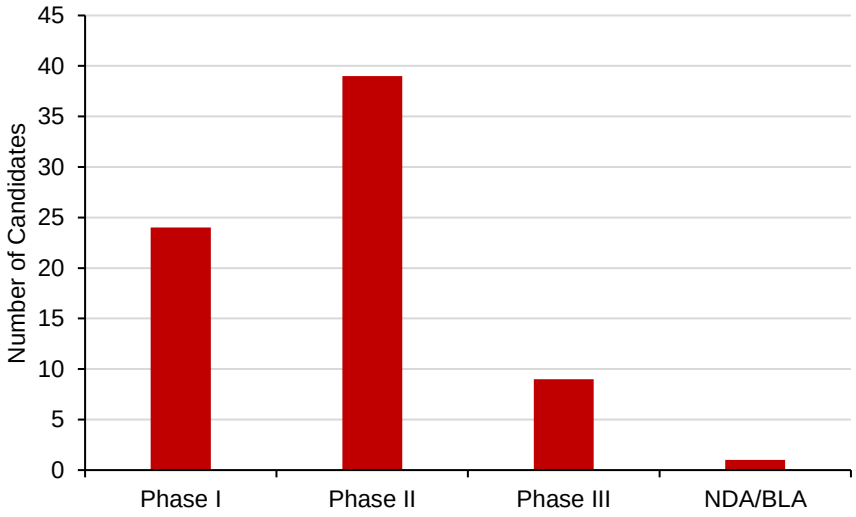
Unmet Need and the Pipeline of Parkinson's Therapies

While many of today's treatments are cost-efficient and clinically effective, there is an ongoing need for therapies that prevent disease progression, of which CDNF is one. Patients today still see accumulating symptoms over time and experience a reduced quality of life, including non-motor symptoms. Non-motor symptoms are under-reported and are not effectively targeted with today's treatment regime. According to Datamonitor, disease-modifying therapies are by far the most desired progress preferred amongst clinicians. Furthermore, payers' interest is high owing to the health economic benefits – late-stage Parkinson's in particular is associated with morbidity and a high economic burden to society.

Pipeline (All Candidates)



Source: Datamonitor; Redeye Research

Treatment Modalities and Deals in Pipeline (Selection)

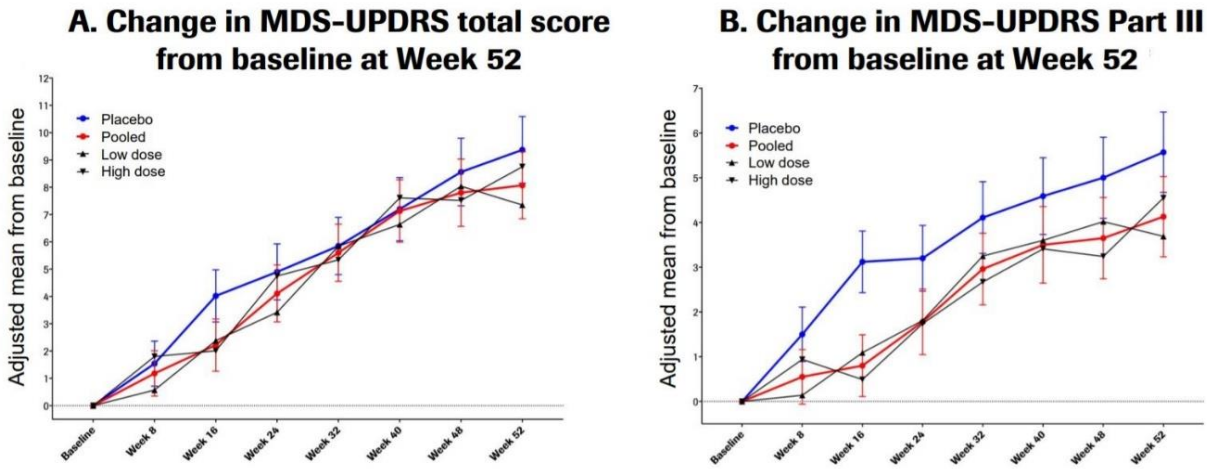
A-Synuclein targeted Therapies

Originator	Sponsor	Candidate	Phase	Upfront / Total (m USD)
Prothena	Roche	Prasinezumab	IIb	45 / 600
Neurimmune	Biogen	Cinpanemab	II (halted)	32.5 / 395
-	Affiris	Affitope PD01A	II	-
Genmab	Lundbeck	LU AF82422	I	10 / 50
Astra Zeneca	Takeda	MEDI1341	I	400+
AbbVie	BioArctic	ABBV0805	I	50 / 755
Protheostasis Therapeutics	Yumanity	YTX-7739	I	-
-	Promis Neuroscience	ProMis	Pre-Clinical	-
-	Denali Therapeutics	ATV: aSyn	Pre-Clinical	-

Source: Biomedtracker; company websites; Redeye Research

There are several different disease-modifying paradigms in the current Parkinson's pipeline. While no candidate is close to the market yet, we deem alpha-synuclein-focused therapies to be at the most advanced stage (clinically and financially). These therapies focus on a single component of proteostasis. Three approaches to inhibit alpha-synuclein toxicity have been proposed: Blocking spread through immunotherapy; blocking aggregation of alpha-synuclein; and promoting degradation of alpha-synuclein/reducing its production.

Prasinezumab, the passive immunotherapy candidate from Roche and Prothena, is the most advanced candidate among a-synuclein-targeted therapies and recently finalized its randomized placebo-controlled PASADENA phase II study, with mixed (at best) results. Roche entered into the collaboration with Prothena in 2013 in a deal consisting of an upfront payment of USD 45 million (and a total value of USD 600 million). As pictured in panel A below, Prasinezumab failed to show a statistically different treatment effect from placebo in the primary endpoint: UPDRS total score. However, as shown in panel B, there was an indication of efficacy in the part III sub score related specifically to motor symptoms. While Roche has decided to continue development thanks to these efficacy signals, a phase IIb study has been initiated. The new study will expand the study population and include patients with early Parkinson's who are on a stable Levodopa therapy. We consider the total data package mixed and believe confirmation in the upcoming trial will be needed for continued development into a pivotal study.



Source: Roche PASADENA Poster 2020

Other major pharmaceuticals within the segment are Biogen's Cinpanemab, Astra Zeneca and Takeda's MEDI1341, and Abbvie/Bioarctic's ABBV0805. Cinpanemab, also a passive immunotherapy, was discontinued in February this year as its phase II study did not meet primary or secondary endpoints. Biogen will focus on its other Parkinson's assets. Astra Zeneca/Takeda's candidate MEDI1341 is currently in phase I, due to be completed in July 2022.

In 2018, AbbVie exercised its option to license Bioarctic's portfolio of antibodies against a-synuclein for Parkinson's and other indications. At USD 50 million in initial milestone payment alone (and aggregated value upwards of USD 755 million), this is one of the most significant Parkinson’s deals of all time. Bioarctic's approach is to bind and eliminate misshapen and aggregated forms of a-synuclein (oligomers and protofibrils) using a monoclonal antibody.

From Herantis' perspective, Yumanity is an interesting peer, focusing on the process of proteostasis. Yumanity's compound inhibits SCD activity, a process that promotes a-synuclein neurotoxicity. The company has raised more than USD 100 million in funding and recently merged with another player in the proteostasis space: Proteostasis Therapeutics. Yumanity has also signed a research and licensing deal with Merck worth USD 500 million for two compounds addressing other neurodegenerative diseases.

Other Treatment Modalities (Selection)

Originator	Company	Candidate	Mechanism	Phase	Upfront / Total (m USD)
Prevail	Eli Lilly	PR001	GBA Mutation/Gene Therapy	I/II	Acquisition (1bn+)
Lysomal Therapeutics	BIAL	BIA 28-6156	GBA Mutation	II	Undisclosed / 130
-	Sanofi Genzyme	Venglustat	GBA Mutation	II (halted)	-
Amgen	MedGenesis	GDNF	NTF	II/III	Undisclosed
Oxford Biomedical	Axovant Sciences	AXI-Lenti-PD	Gene therapy	II	30 / 842
Denali Therapeutics	Biogen	DNL 151	LRRK2	I	560 / 1125
Voyager Therapeutics	AbbVie	AAV Portfolio	Gene Therapy	II/III	65 / 1540 [1]
Voyager Therapeutics	Neurocrine	AAV Portfolio	Gene Therapy	II	165 / 1700 [2]

Source: Biomedtracker; Company Websites: Redeye Research

Gene Therapy

While there are several interesting gene therapy projects, we see the most interesting assets as AAV-based therapies that featured in two recent deals. In December 2020, it was announced that Eli Lilly had acquired Prevail in a deal worth more than USD 1bn in total, indicating high interest and purchasing power among pharmaceutical companies for innovative assets. Prevail's focus is on Parkinson's with GBA1 mutations, the most common genetic risk factor: Approximately 10% of all patients diagnosed with Parkinson's carry the GBA1 gene. Several other candidates focus on the GBA1 mutation, including Lysomal/BIAL and Sanofi Genzyme (later halted in February this year). Another company within AAV-focused gene therapy is Voyager Therapeutics, which featured in several high-profile deals that were later terminated. While we note a high interest in the gene therapy segment, we do not see it as a fully competing modality to CDNF owing to its different targeting strategy and patient population.

Neurotrophic Factors

Neurotrophic factors have been considered as therapies for Parkinson's since the 1990s, when researchers discovered that GDNF (glial cell line-derived neurotrophic factors) could induce survival and sprouting of dopaminergic neurons in animal models. The pre-clinical work and initial phase I studies were promising, including long-lasting effects in humans, and interest in the Parkinson's community was high. Several clinical studies with GDNF have since been conducted, including a randomized placebo-controlled phase II study sponsored by Amgen. The study did not reach its primary goal, but hope was not fully abandoned as there were some methodological challenges specific to the study. Another study was initiated in 2010 by MedGenesis, now sponsored by the UK's National Health Service (NHS). The Bristol study did not reach its primary goal either but did show some indication of efficacy in F-dopa PET imaging. In 2014, Pfizer bought an option for the global rights but did

1 Later terminated
2 Also terminated

not exercise it. While plans for a phase III trials have been floated, the future of GDNF is uncertain.

Overall impressions: Pipeline and Deals

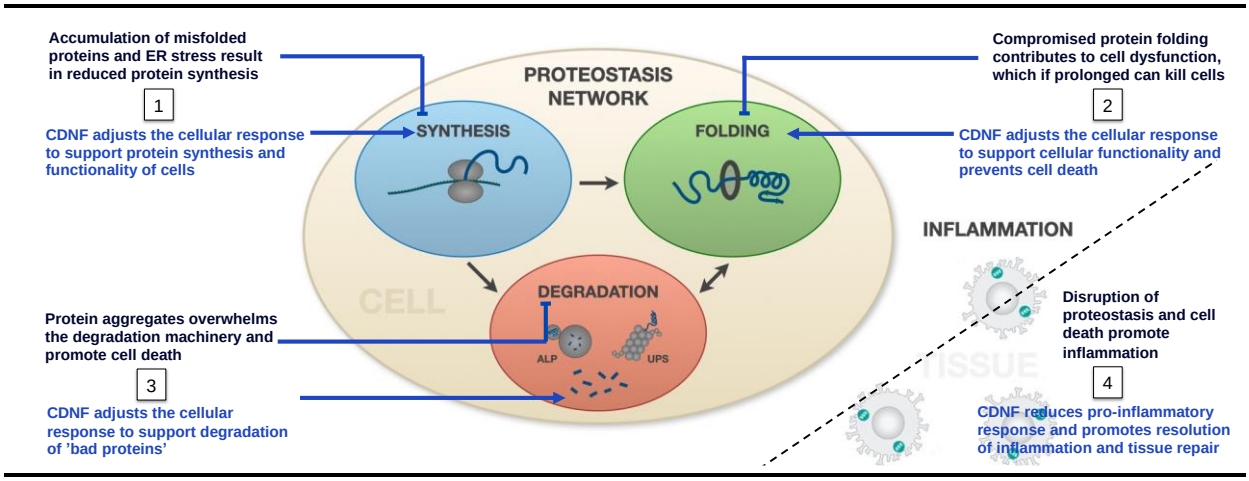
While the pipeline for Parkinson's is relatively crowded, most disease-modifying candidates are still far from the market and from demonstrating clear treatment effects. In our view, many of the proposed mechanisms are uncertain and progress in the upcoming trials, especially within the a-synuclein segment, will shed light on the pathology of a-synuclein and its role in Parkinson's. As we describe further below, Herantis' candidate has a unique mode of action and would also remain interesting even if a new disease-modifying candidates reach the market. We also note relatively high interest from pharmaceuticals and that innovative assets have been licensed in early stages, mostly based on pre-clinical data, including increased activity in the proteostasis space. Overall, we are encouraged by the progress and continued interest in the indication and believe that good data will merit significant interest from potential partners.

CDNF – Herantis Lead Canditate

Cerebral dopamine neurotrophic factor (CDNF) is a natural protein initially discovered by neuroscientists at the University of Helsinki. The protein has neurotrophic growth factor properties and was initially bundled with other factors, such as GDNF. However, further research showed that it has a very different structure and modes of action, as pictured below. CDNF is an unconventional neurotrophic factor and can protect cells in disease models – from apoptosis (cell death), for example – but has no effect when added to healthy cultured neurons. Furthermore, unlike GDNF, it has been shown to beneficially modulate alpha-synuclein toxicity and neuroinflammation, both important mechanisms in Parkinson's.

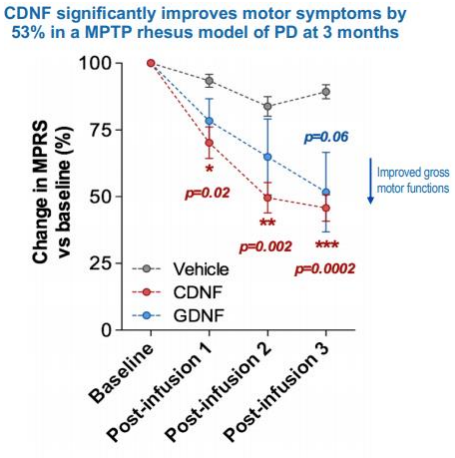
CDNF has multiple mechanisms but it is a survival-promoting treatment through the maintenance of proteostasis, which regulates proteins within cells to maintain their health. CDNF supports protein synthesis, folding, and functionality of cells, alleviates neuroinflammation, and promotes degradation of "bad proteins" – including the aggregation of pathological a-synuclein. One pathway is the unfolded protein response (UPR), which contributes to dopaminergic loss through a process called ER stress.

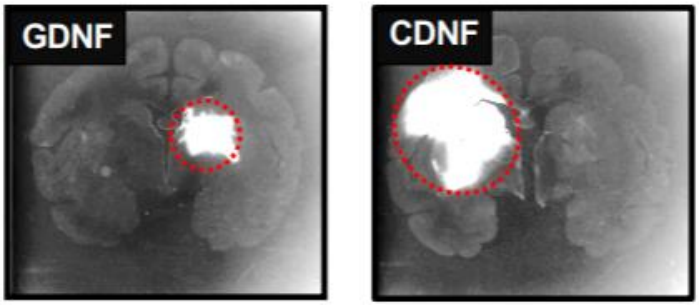
Proteostasis Network



Source: Herantis Pharma

Motor symptoms reduction (primates) (left) and comparison – brain tissue diffusion (right)





Source: Herantis Pharma Presentation 2020

In the chart above, we see a clear treatment effect of CDNF on motor symptoms in a rhesus model (primates), with a cumulative improvement of 53% after three months. The same study also found a significant treatment effect in terms of non-motor symptoms – a first for trophic factors. Above to the right, we see brain tissue diffusion of CDNF compared to GDNF, with a significantly higher volume of distribution of CDNF, further indicating its different mode of action.

In our view, the pre-clinical package for CDNF is promising and the treatment potential is consistent in several animal models and outcome measures. Herantis' research on CDNF has also been published in the prestigious journal Nature, indicating a high interest among the scientific community. Pre-clinical research support that CDNF[3]:

1. Reduces a-synuclein accumulation
2. Restores dopaminergic function
3. Prevents degeneration of dopaminergic neurons
4. Improves motor and non-motor symptoms

CDNF's broad treatment effect is interesting, in our view, and well-positioned in a Parkinson's pipeline that mainly consists of mechanism-specific treatments. Targeting specific mechanisms of Parkinson's may require better understanding of the disease's pathology, including the causal chain of events and variability between patients. For example, some mechanisms may be more relevant to modulate in some patients than others (such as alpha-synuclein aggregation). By comparison, CDNF's broader treatment effect makes it less dependent on the ability to understand the pathology at the patient level.

3 For example, see Lindholm, Päivi, et al. "Novel neurotrophic factor CDNF protects and rescues midbrain dopamine neurons in vivo." *Na*ture 448.7149 (2007): 73-77, and Huttunen HJ and Saarma M. CDNF Protein Therapy in Parkinson's Disease. Cell Transplant. Apr 4, 2019.

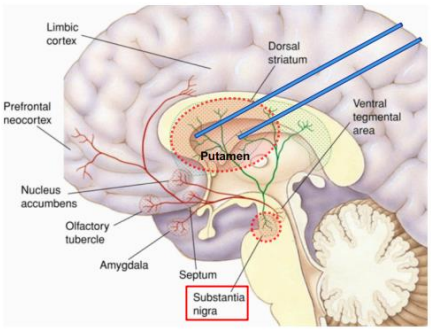
The Phase I Trial – "TreatER"

Herantis finalized its phase I study in Parkinson's in 2020 with overall positive results on safety and tolerability. This was the first clinical study using CDNF and was partly funded by the EU Horizon 2020 project, with clinical trial sites in Finland and Sweden. The study used an advanced intracranial drug delivery method developed by Renishaw Neuro Solutions, which delivered CDNF directly to the targeted anatomical area of the brain, the putamen, thus bypassing the blood-brain barrier. The study (n=17) comprised two parts: An initial part where patients were randomized into either placebo or two active CDNF arms, followed by an extended part where all patients received CDNF.

Safety:

There were a few serious adverse events (SAE) in the study, all related to surgery, the administration method, or the device. None were related directly to CDNF. While sharpened routines eliminated further adverse events, this highlighted the risk that the administration method could pose further regulatory and commercial hurdles. Moreover, due to the Renishaw system's invasive nature, only patients with moderately advanced Parkinson's (i.e. with few to no surviving dopamine neurons left to rescue) could be enrolled in these clinical trials. Consequently, this was a typical first-in-human trial to study safety, rather than efficacy. To be able to show efficacy and a disease-modifying effect with neurorestorative treatments, patients with earlier-stage Parkinson's would have been required (i.e. those who still have viable dopaminergic neurons in their brains that can respond to treatment).

Administration – Renishaw system

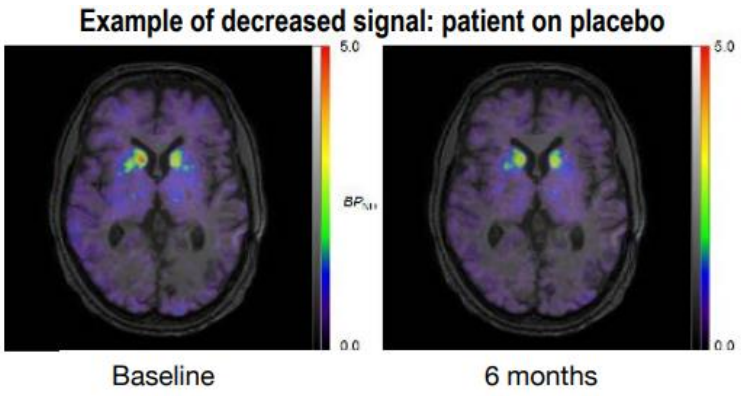


Source: Herantis Pharma Presentation 2020

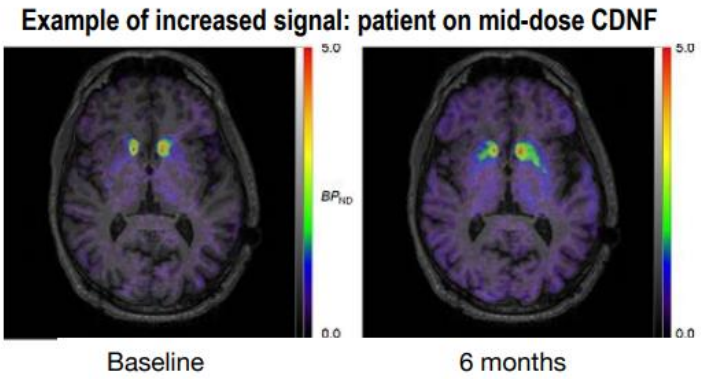
Despite the challenging patient population and the study being neither designed nor powered to show efficacy, there were some initial signs of effects: In the dopamine transporter PET imaging below, we see an example of increased signals in a patient with an active dose of CDNF compared to a patient on placebo. The high increase in activity in some patients indicates a biological response to CDNF. Furthermore, biomarker data in cerebrospinal fluid appears to change in the treatment group – and the positive change correlates with motor score improvement and imaging results. We find it positive that the different indicators point in the direction of a clinical effect and that learnings from these indicators can be applied in further studies. However, due to heterogeneous responses and few patients, no real conclusions about effect can be drawn at this stage.

DAT-PET Scanning (Panels A & B) – Linking of biomarker, motor score and imaging Panel (C)

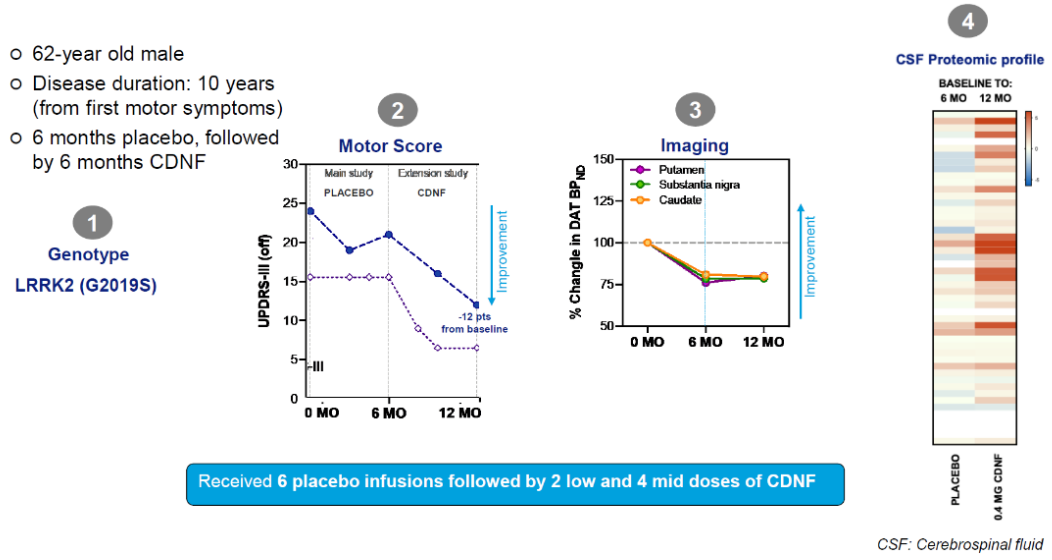
A



B



C



CSF: Cerebrospinal fluid

Source: Herantis Pharma Presentation 2020; 2021

Shift away from Intracranial Delivery – Status and Routes Forward

Due to the clinical risks and commercial limitations with the Renishaw intracranial delivery system, and as such administration proved suitable only for patients with advanced stage Parkinson's, Herantis announced in an R&D update as of November 2020 that it has commenced evaluation and development of alternative administration methods and is looking to move away from intracranial delivery. Alongside its phase I study, Herantis has investigated intranasal (nose-to-brain) and subcutaneous (under-skin) administration.

The route that allows for nose-to-brain blood-brain-barrier penetration is the olfactory epithelium, a tissue inside the nasal cavity that has been explored in recent years for BBB penetration. This is a developing area, however, and challenges remain. Research from Herantis so far indicates that pharmacologically active levels of CDNF are achievable via these methods. The company is advised that a theoretical active target concentration of up to 10% breaching with the olfactory epithelium may be possible – a high number. We believe that a lower number would also suffice.

The company has also initiated a collaboration with Nanoform to pack the protein in nanoparticles through Nanoform's biological nanoparticle platform. While relatively new for biologics, this technology allows for increased tissue compatibility and could potentially bolster the likelihood of reaching a therapeutic concentration of CDNF. Nanoform will perform two non-binding formulation studies during 2021. The current timetable is for Herantis to finalize the pre-clinical work using the new administration methods, evaluate the alternatives, and initiate regulatory discussion during 2022, and then proceed to clinic.

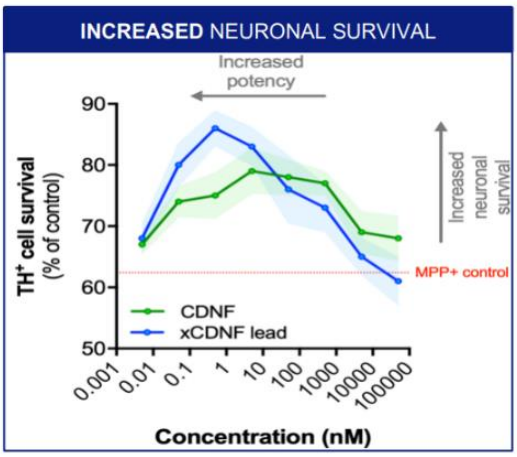
While the shift to alternative administration methods introduces new challenges, we are positive about this change and believe it will be beneficial in the long run. We are especially encouraged that patients with early Parkinson's will be easier to target and study in upcoming trials, as it will then be possible to show clinical effect at an early stage when CDNF is most effective. This will, in our view, increase the likelihood of a potential partnership at an earlier stage compared with the previous setup. Furthermore, easier administration may also have positive benefits for the timetable, such as quicker and cheaper studies.

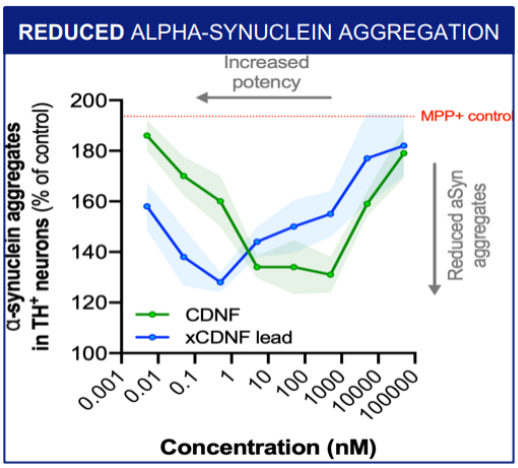
xCDNF

Alongside this, Herantis has been developing a smaller CDNF derivative called xCDNF. This synthetic compound has been engineered to pass through the blood-brain barrier while maintaining the neuroprotective and proteostasis-altering activity of CDNF. The goal of xCDNF is to allow an easier administration route via subcutaneous injection, increasing the market potential and target population compared with the previous invasive administration method of CDNF. As CDNF is moving towards easier administration routes, the difference in terms of market potential and convenience becomes smaller. While the blood-brain barrier is less of a challenge for xCDNF, the risks here are in maintaining the same properties and effect as CDNF in humans as well. Data generated to date, as shown below, suggests that the engineering of xCDNF has been successful in terms of properties and the ability to breach the blood-brain barrier.

The projects will continue to run in tandem as separate projects. Given the interplay between the CDNF and xCDNF programs, management expects the clinical development to be accelerated compared with CDNF thanks to increased knowledge as the CDNF project develops. According to Herantis, xCDNF is planned to progress to clinic in late 2023/24. We believe that xCDNF remains an interesting asset and one of several strategies for Herantis to successfully reach a therapeutic level of CDNF past the blood-brain barrier. xCDNF's properties are also attractive for other neurodegenerative diseases.

xCDNF compared to CDNF – Neuronal survival and effect on Alpha-Synuclein





Source: Herantis Presentation 2020

Event	Timing
CDNF – Complete formulation and pre-clinical administration routes	H2 2021
xCDNF - selection of lead candidate	H1 2021
xCDNF – start of pre-clinical phase	H2 2021

Source: Herantis Pharma

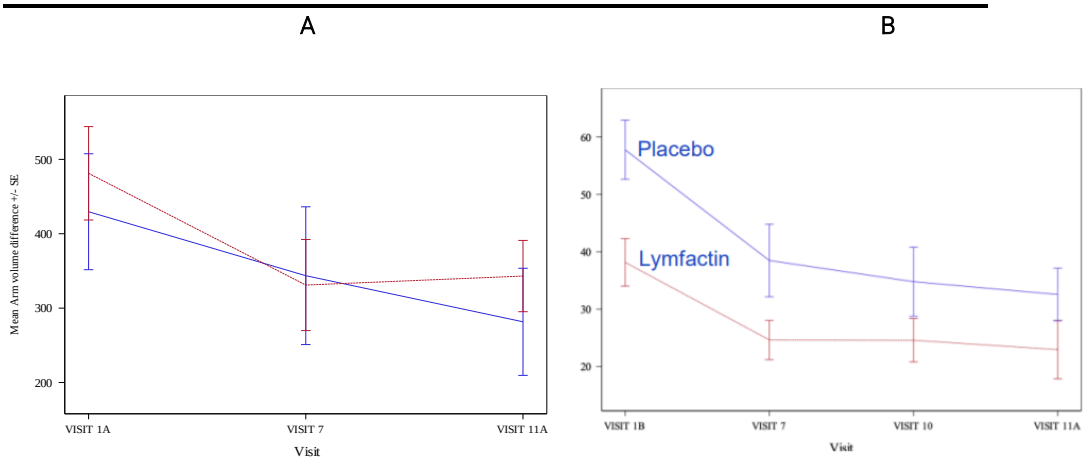
Lymfactin – Treatment for Secondary Lymphedema

Herantis Pharma's second asset is Lymfactin – a disease-modifying candidate for secondary lymphedema. Herantis' current clinical development is for the use of Lymfactin for breast cancer related to secondary lymphedema (BCRL). The company announced inconclusive top-line data from its phase II efficacy study this March, and it will now focus its internal capacity on CDNF and could potentially out-license Lymfactin.

Secondary lymphedema is a condition caused by damage to or dysfunction of the lymphatic system, leading to the accumulation of interstitial fluids. This process causes swelling of the affected region (mainly the arms and legs) and, by extension, chronic inflammatory processes. A common cause of BCRL is complications in relation to axillary lymph node dissection (ALND) – removing lymph nodes from the armpit to prevent the spread of breast cancer. Radiotherapy can also affect the lymph system and lead to lymphedema.

The phase II trial was randomized and placebo-controlled (n=39) and compared Lymfactin on top of lymph node transfer surgery to surgery alone in the placebo group. In other words, the goal was to show an improvement on the standard of care today. The primary outcome measures were arm volume reduction and a quality-of-life index filled out by the patient (Lymphedema Quality of Life Inventory).

Arm volume reduction (panel A) and QOL (panel B)



Source: Herantis Pharma

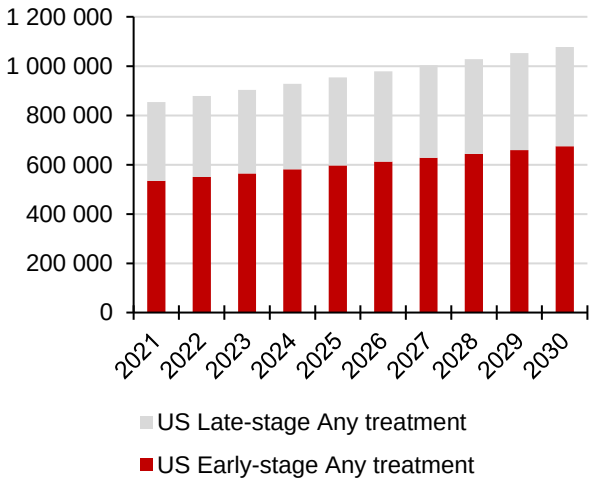
As evident above (especially panel B), there were differences at baseline in the placebo and treatment arm. This makes it challenging to isolate the effect of Lymfactin, as the groups also had different characteristics from the beginning. Furthermore, the treatment effect in the two primary endpoints was variable and no clear average difference could be established. There were some positive signs in secondary and exploratory endpoints, such as tissue water content and physician score, but as the primary endpoints could not be evaluated, their importance is less certain.

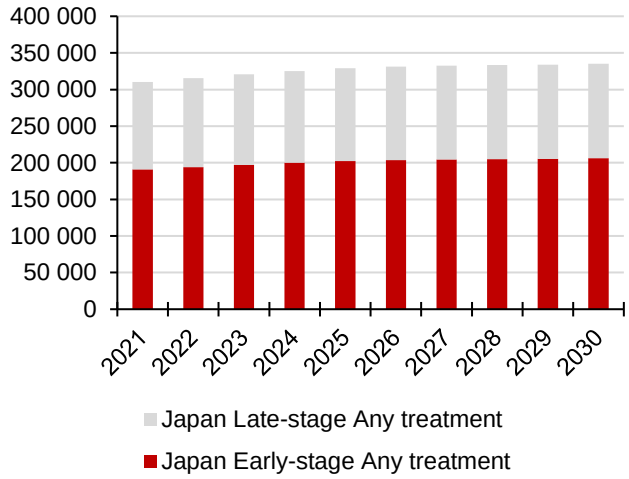
The trial was the first of its kind, and according to Herantis, in retrospect, not optimally designed. Furthermore, having significant baseline differences between the placebo arm and treatment arm was probably the result of a combination of chance in the recruitment of patients and the study design. While a new study with a better design could still show a clinical effect, this would be time-consuming and expensive. We endorse Herantis' shift to focusing fully on CDNF and neurodegenerative diseases, whether this means Lymfactin is outlicensed or discontinued in the end.

Epidemiology and Market Size – Parkinson's Disease

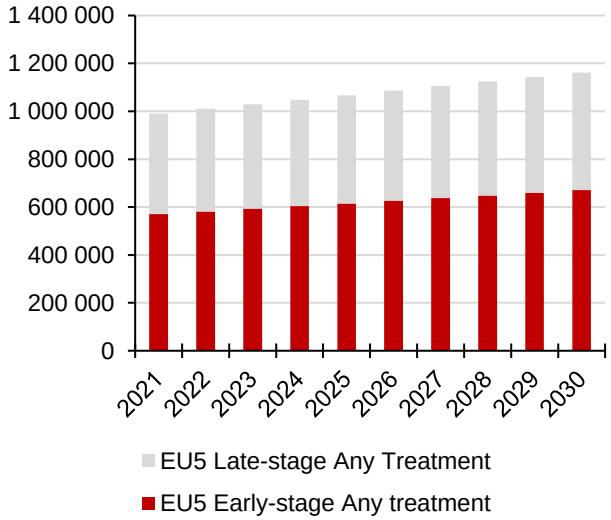
Parkinson's disease is the second most common neurodegenerative disease and affects 0.1-0.2% of the world population. Parkinson's is positively correlated with age and roughly 1% of the population aged over 60 get the disease. In total, roughly 2 million in EU5, the US, and Japan have Parkinson's and receive some form of treatment. 1.3 million of these patients are in the early stages, defined as 1-3 on the Hoehn-Yahr scale, which we define as the primary market for CDNF in its new administration form. The prevalence of Parkinson's is expected to grow in the upcoming decades, mostly due to an aging population.

Prevalence of treated patients US (left) and Japan (right)

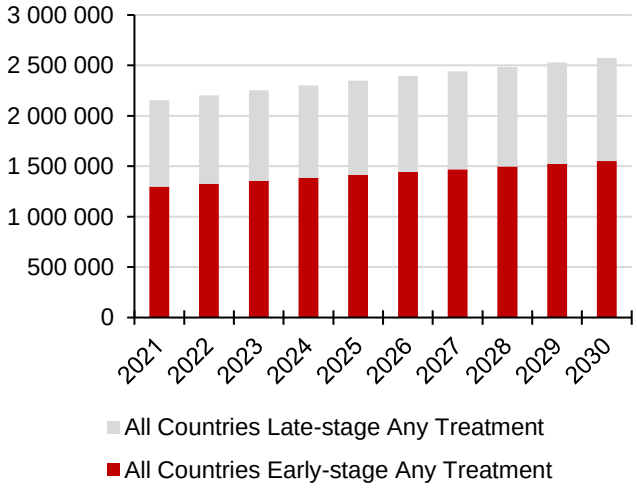




Prevalence EU5



Prevalence Total



Source: Datamonitor; Redeye Research

Financials and Valuation

Probability of Success (PoS) – CDNF

	Pre-clinical	Ph I - Ph II	Ph II - Ph III	Ph III - NDA	NDA - Approval	LoA
Parkinson's Disease*	-	57%	31%	68%	94%	12%
Our assessment**	75%	70%	27,5%	68%	94%	9%

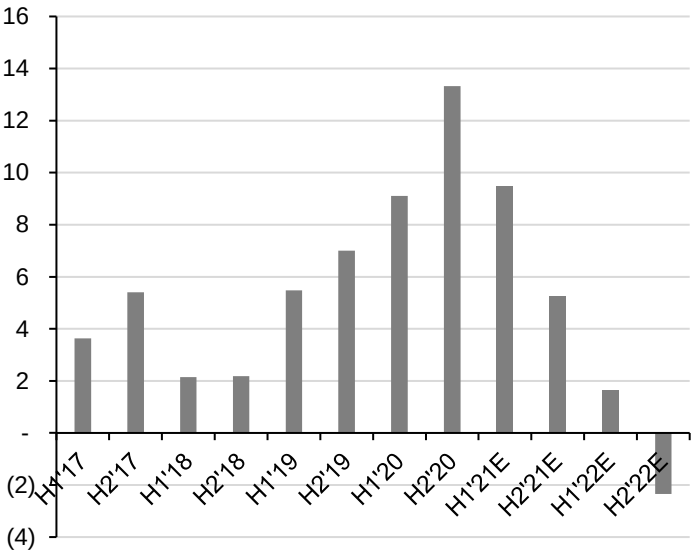
Source: Informa 2020, Redeye Research***

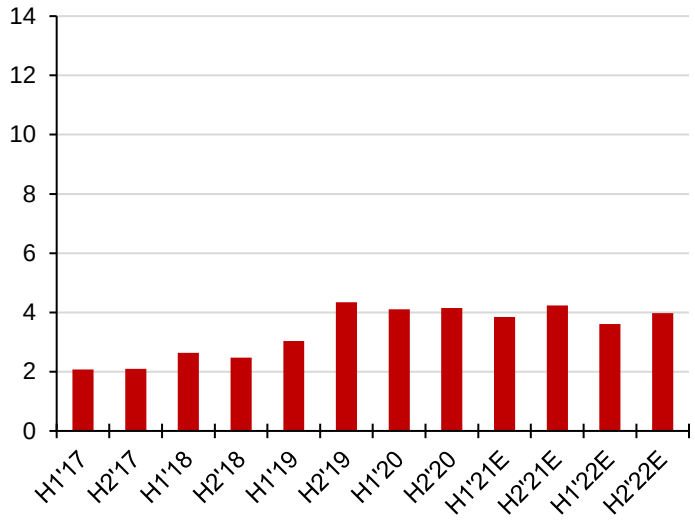
There are high risks involved in early-stage biotech companies, and the variability between projects is high. In our assessment of CDNF's probability of success, we have looked at success rates in the neurology area and specifically for Parkinson's. We found roughly a 12% chance of a Parkinson's asset in phase I reaching the market and 8% for the neurology field in general. While Parkinson's projects are slightly more likely to succeed, no disease-modifying treatments have been approved and we believe there is more uncertainty on average in such projects – especially in the phase II study focusing on efficacy.

As we reviewed in an earlier section though, CNDF has successfully finalized a phase I study using an intracranial delivery system and Herantis has, in our view, a strong pre-clinical package. In the short term, we see the key risk for the company as successfully deciding on an alternative administration method – specifically, to get a therapeutic concentration of CDNF to breach the blood-brain-barrier. The company has several approaches, and indications so far are positive, but the blood-brain barrier is a key obstacle for many novel CNS drugs and a potential issue is a prolonged time to clinic. We land at a likelihood of approval for CNDF of 9%, where we set the probability of success of going to clinic in late 2022/early 2023 at 75%, with a slightly higher probability of success in the phase I trial thanks to good safety data from the earlier phase I/IIa trial.

Financials

Cash Position (left) and Operating Expenses (right) in EUR million





As we can see in the graph to the right, operating expenses have increased in the last few years, mostly due to R&D costs – Herantis had two clinical studies (phase Ib/2a & phase II) ongoing at the same time. As Herantis will outlicense/discontinue Lymfactin and is currently in the pre-clinical phase with CDNF, we expect costs to be further concentrated to CDNF – although we project some costs associated with the follow-up period in the Lymfactin trial. We expect operating expenses on par with 2020 in 2021 due to many ongoing activities for CDNF and xCDNF: The Selection of lead candidate for xCDNF, pre-clinical work and choice of administration method for CDNF, and CMC (chemical, manufacturing and controls) for the establishment of the new compound. Herantis has had a relatively stable cash position in recent years due to a strong interest from institutional investors and grants from for example as EU Horizon. Depending on activities, we estimate a cash runway well into 2022 for Herantis given today's cash burn.

Pricing:

As there are currently no disease-modifying treatments for Parkinson's and most pipeline candidates are several years from the market, pricing is difficult. We believe that CDNF will target early-stage Parkinson's patients with the new administration method, as the candidate is believed to have a stronger effect when there are still plenty of dopamine neurons left. Furthermore, from a health economics point of view, disease-modifying treatments are more attractive early on as preventing late-stage Parkinson's before it occurs is especially beneficial. We look at relevant late-stage treatments today (Duopa and deep brain stimulation) with high benefits and cost, plus newer treatments focusing on specific symptoms, such as Nuplazid. We arrive at a range of USD 20,000 to 50,000 in the US. While none of these drugs are disease-modifying, they address patients at the critical stage where the willingness to pay is high. We set our price for CDNF in the US in the mid-range of our reference drugs and at a 50% discount in the EU5 and Japan.

	Pricing per Year (in USD)
US	35000
EU5	17500
Japan	17500

Deal Assumptions

Originator	Sponsor	Candidate	Phase during Licensing	Upfront	Total (m USD)
Prothena	Roche	Prasinezumab	Pre-clinical	45	600
Neurimmune	Biogen	Cinpanemab	Pre-clinical	32.5	395
BioArctic	Abbvie	ABBV0805	Pre-clinical	50	755
Astra Zeneca	Takeda	MEDI1341	Pre-clinical	400	400+
Average	-	-	-	45	540
Herantis Pharma	**-**	**CDNF**	**After Phase IIb**	**45**	**475**

Herantis' strategy is to out-license the candidate at an early stage. Having analyzed the pipeline and historical deals in the space, we find that licensing deals for a-synuclein-targeting are the most relevant reference deals, given that they are disease-altering and relatively close in terms of mechanism and addressable population. We conclude that most high-profile deals take place early, mostly at the pre-clinical stage, but that these deals include a portfolio of compounds and are relatively few in comparison to the number of compounds in the pipeline.

In our base case, we land at a licensing deal size slightly below average from this selection of high-quality licensing deals and believe that Herantis will outlicense CNDF and xCDNF after demonstrating a significant treatment effect. Today, we estimate that this will be after a phase II CDNF trial using the new administration method. While our assumptions are relatively conservative, we see good optionality for further upside if Herantis closes a deal at an early stage. This would be especially likely if Herantis were able in its upcoming phase I CDNF trial to replicate the efficacy signs from the previous phase I trial and to harness further insights using a more biomarker-driven approach – for example, an inductive study approach.

Our Sales assumptions

- Market launch in 2031
- Market penetration of 10% in the US and EU5/Japan
- Net pricing of USD 35000 and USD 17500 in the US and EU5/Japan, respectively
- Royalty rate of 15% in all markets
- Deal size of USD 475 million

With these assumptions, we arrive at global peak sales of USD +2.5 billion in Parkinsons.

Sales model CDNF – US (in million USD)

		2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
US	**2021**										
Prevalence Diagnosed Parkinson	854 555	1 099 804	1 120 809	1 141 154	1 160 998	1 180 507	1 196 644	1 211 832	1 250 159	1 272 850	1 272 850
% receiving treatment	90%	92%	92%	92%	92%	93%	93%	93%	93%	93%	93%
No. receiving treatment (~90%)	811 827	1 009 800	1 031 144	1 051 960	1 072 394	1 092 595	1 109 746	1 126 078	1 164 016	1 187 514	1 189 889
Target Population: Early Stage Parkinson	63%	63%	63%	63%	63%	63%	63%	63%	63%	63%	63%
Adressable patients	508 204	632 135	645 496	658 527	671 319	683 965	694 701	704 925	728 674	743 384	744 871
Launch curve		0,10	0,40	0,62	0,80	0,90	0,95	1,00	1,00	1,00	1,00
Penetration		1%	4%	6%	8%	9%	9,5%	10,0%	10,0%	10,0%	10,0%
Patients treated for the year		6 321	25 820	40 829	53 706	61 557	65 997	70 492	72 867	74 338	74 487
Total patients treated to date		6 321	32 141	72 970	126 675	188 232	254 229	324 721	397 589	471 927	546 414
Penetration, patients		1%	4%	6%	8%	9%	10%	10%	10%	10%	10%
Compliance rate	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
List price	35000	37 142	37 885	38 643	39 416	40 204	41 008	41 828	42 665	43 518	44 388
Gross to net %	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Pricing CDNF		31 571	32 202	32 846	33 503	34 173	34 857	35 554	36 265	36 990	37 730
Sales $mm		**140**	**582**	**939**	**1260**	**1473**	**1610**	**1754**	**1850**	**1925**	**1967**
growth			317%	61%	34%	17%	9%	9%	5%	4%	2%

Source: Redeye Research

Sales Model CDNF – EU5 (in million USD)

		2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
EU	**2021**										
Prevalence Parkinson	783 347	934 464	950 791	966 894	983 216	1 000 284	1 017 317	1 033 768	1 033 768	1 033 768	1 033 768
% receiving treatment	85%	87%	87%	87%	87%	87%	88%	88%	88%	88%	88%
No. receiving treatment (~90%)	744 179	810 324	826 131	841 803	857 725	874 360	891 027	907 247	909 062	910 880	912 702
Target Population: Early Stage Parkinson	59%	59%	59%	59%	59%	59%	59%	59%	59%	59%	59%
Adressable patients	439 066	478 091	487 417	496 664	506 058	515 873	525 706	535 276	536 347	537 419	538 494
Launch curve		0,10	0,40	0,62	0,80	0,90	0,95	1,00	1,00	1,00	1,00
Penetration		1%	4%	6%	8%	9%	10%	10%	10%	10%	10%
Patients treated for the year		4 781	19 497	30 793	40 485	46 429	49 942	53 528	53 635	53 742	53 849
Total patients treated to date		4 781	24 278	55 071	95 555	141 984	191 926	245 454	299 088	352 830	406 680
Penetration, patients		1%	4%	6%	8%	9%	10%	10%	10%	10%	10%
Compliance rate	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%
List price	17500										
Gross to net %	15%	18 571	18 943	19 321	19 708	20 102	20 504	20 914	21 332	21 759	22 194
Pricing CDNF		15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
		15 785	16 101	16 423	16 752	17 087	17 428	17 777	18 133	18 495	18 865
Sales $mm		**49**	**204**	**329**	**441**	**516**	**566**	**619**	**632**	**646**	**660**
growth			316%	61%	34%	17%	10%	9%	2%	2%	2%

Source: Redeye Research

Sales Model CDNF – Japan (in million USD)

		2031	2032	2033	2034	2035	2036	2037	2038	2039	2040
Japan	**2021**										
Prevalence Parkinson	187 744	202 942	203 136	203 380	203 729	204 249	204 385	204 544	204 544	204 544	204 544
% receiving treatment	85%	87%	87%	87%	87%	87%	88%	88%	88%	88%	88%
No. receiving treatment (~90%)	159 582	175 982	176 502	177 068	177 726	178 536	179 012	179 510	179 869	180 229	180 589
Target Population: Early Stage Parkinson	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%	62%
Adressable patients	98 941	109 109	109 431	109 782	110 190	110 692	110 988	111 296	111 519	111 742	111 965
Launch curve		0,10	0,40	0,62	0,80	0,90	0,95	1,00	1,00	1,00	1,00
Penetration		1%	4%	6%	8%	9%	10%	10%	10%	10%	10%
Patients treated for the year		1 091	4 377	6 806	8 815	9 962	10 544	11 130	11 152	11 174	11 197
Total patients treated to date		1 091	5 468	12 275	21 090	31 052	41 596	52 726	63 878	75 052	86 248
Penetration, patients		1%	4%	6%	8%	9%	10%	10%	10%	10%	10%
Compliance rate	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%	65%
List price	17500	18 571	18 943	19 321	19 708	20 102	20 504	20 914	21 332	21 759	22 194
Gross to net %	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Pricing CDNF	17500	15 785	16 101	16 423	16 752	17 087	17 428	17 777	18 133	18 495	18 865
Sales $mm		**11**	**46**	**73**	**96**	**111**	**119**	**129**	**131**	**134**	**137**
growth			309%	59%	32%	15%	8%	8%	2%	2%	2%

Source: Redeye Research

Our Valuation

Herantis has a total of three assets (CDNF, xCDNF, and Lymfactin). As xCDNF is still in the research stage, and further away from clinic, we do not present detailed estimates for this yet, but we do include a technology value to reflect its potential. We also do not include a licensing deal for Lymfactin at this stage, given the inconclusive data and its low priority on Herantis' side. However, we do see both of these projects as options for further upside, and we will most likely dig deeper into the potential of xCDNF in our base case once the project gets closer to clinic.

For CDNF, we assume peak sales of 10% in the US, EU5 and Japan following positive results in a pivotal study terms of motor- and non-motor symptoms, and we assume a six-year launch curve before reaching peak market penetration in 2036. We base this assumption on a study by Robey & David, 2017, which found the historical averages for prescription drugs to reach peak sales in year six on the market. Our estimate for sales erosion is based on assumed patent expiry in 2040. Our model uses a weighted average cost of capital (WACC) of 13%, based on Redeye's company quality rating. From this, we derive a fair value of some SEK 270 million, leading to a base case of SEK 27,5.

Summary: Valuation

Project	Indication	Stage	Launch	Peak sales (EURm)	Probability	Value, r-adj (EURm)	Value, r-adj per share (EUR)	Value, r-adj per share (SEK)
CDNF	Parkinsons Disease	Pre-clinical	2031	2 295	9%	21	2,2	22
				Technology Value xCDNF		3,5	0,4	4
				Net cash, end Q4		5	0,6	6
				Shared costs		-5	-0,5	-5
				Equity Value		**26**		
				Shares outstanding		9,8		
				Base case			**2,7**	**27,5**

Sensitivity Check

To reflect the uncertainties in our base case, we show in this section how our valuation is changed by the WACC, Likelihood of Approval and CDNF pricing. As we can see, the valuation is highly impacted by the Likelihood of Approval – a value that could change rapidly following how the pre-clinical work proceed. This further indicates potential and risks in the case, also in the short term.

WACC/LoA (left) and pricing (right)

LoA CDNF \ WACC	14%	13%	12%	11%
12%	32	37	42	50
9%	22	**27,5**	31	34
7%	17	19	22	25
5%	12	14	16	18

US pricing in Dollar (EU5/Japan half)	Base Case (SEK)
50 000	39
35 000	27,5
25 000	19
20 000	15

To provide a dynamic view of our valuation of Herantis, we also model a pessimistic scenario (Bear Case) and an optimistic scenario (Bull Case). These are based on possible outcomes of CDNF over the next two-three years (see below).

Bear Case	Base Case	Bull Case
5 SEK	27,5 SEK	70 SEK
The pre-clinical development of CDNF is prolonged and CDNF goes back into clinic in 2024 with mixed data on blood-brain-barrier penetration.		Herantis presents convincing pre-clinical data of therapeutic concentrations of CDNF in the brain using nose-to-brain administration and goes back into clinic in 2022. The company outlicenses CDNF/xCDNF and the partner takes the development costs for all clinical phases.
LoA: 5%		LoA 13%
CDNF launched 2032		CDNF launched 2030
USD 45 / 475 Licensing Deal in 2028 (risk adjusted)		USD 45 / 500 Licensing Deal in 2022 (not risk-adjusted)

Balance Sheet (in EUR million)

Balance Sheet	2018	2019	2020	2021E	2022E
Current Assets					
Cash & Equivalents	1	6	12	4	(3)
Debtors	0	0	0	0	0
Securities	1	1	1	-	-
Total Current Assets	**2**	**7**	**14**	**4**	**(3)**
Non-Current Assets					
Property, Plant & Equipment, Net	-	-	-	-	-
Goodwill	-	-	-	-	-
Development Expenses	5	4	3	3	3
Intangible Rights	-	-	-	-	-
Total Non-Current Assets	**5**	**4**	**3**	**3**	**3**
Total Assets	**7**	**11**	**16**	**7**	**(0)**
Current Liabilities					
Short-Term Debt	1	0	1	1	1
Short-term Trade Creditors	0	2	1	1	1
Total Current Liabilities	**1**	**2**	**3**	**2**	**2**
Non-Current Liabilities					
Long-Term Debt	6	7	6	6	6
Total Non-current Liabilities	**6**	**7**	**6**	**6**	**6**
Shareholder's Equity	(0)	2	8	(1)	(8)
Total Liabilities & Equity	**7**	**11**	**16**	**7**	**(0)**
Net Debt	6	1	(5)	3	10

Board of Directors		
Name		**Experience**
Timo Veromaa	Chairman of the Board	Timo Veromaa MD, PhD, MBA, has been a Herantis board member since 2012 and chairman since April 2020. He is also the former executive chairman of Domainex Ltd and was the CEO and President of Biotie Therapies Corp., from 2005 until its acquisition by Acorda Therapeutics in 2016. He is also the Chairman of Finnish BioBanks FINBB from 2017, Professor of Practice in Drug Development at the University of Turku, Finland and he was Chairman of Finnish Bioindustries FIB 2012-2018. During the beginning of his career, he was Medical Director of Schering Ltd. in Finland, Senior Scientist and Project Director of Collagen Corp. and a Postdoctoral Fellow at Stanford University. Timo Veromaa has a PhD in immunology from the University of Turku and Special Competence in Pharmaceutical Medicine from the Finnish Medical Association.
Frans Wuite	Deputy Chairman of the Board	Frans Wuite MD, MBA has been a Herantis Board member since 2014 and vice chairman since April 2020. Frans Wuite was CEO of Acesion Pharma ApS until 2020. Prior to this, he was CEO and President of Oncos Therapeutics Oy, COO of Warren Pharmaceuticals Inc, Co-founder and Board Director of Araim Pharmaceuticals Inc, and member of Amgen's European management team, where he was in charge of establishing the anaemia franchise. Before Amgen, he was President of Pharmacia-Leiras BV, a joint venture for marketing products with novel dose delivery technologies for women's healthcare in Europe.
Jim Philips	Member of the Board	Jim (James) Phillips MD, MBA has been a board member of Herantis since 2014. He is currently CEO of PAION AG a commercial stage pharmaceutical company. Jim Phillips previous roles included CEO of Imevax GmbH, CEO for Midatech Pharma PLC, President of EUSA Pharma Europe (prior to its sale in 2012 to Jazz Pharma), and CEO & founder in Talisker Pharma (acquired by EUSA in 2006). Prior to that he worked at Johnson & Johnson and Novartis as a senior executive in pharmaceutical development & commercialisation.
Aki Prihti	Member of the Board	Aki Prihti has been a Herantis Board member since 2014. Currently he is CEO of Aplagon Oy and CFO and board member of Medtentia International Ltd Oy. He was previously the chairman of Laurantis Pharma Ltd from 2010–2014. Aki Prihti is one of the founding partners of the venture fund management company Inveni Capital and currently serves as a board member in Onbone Oy and Aranda Pharma Oy. Prior to transitioning to life science venture capital, he worked in the corporate finance arm of Salomon Brothers in London.
Hilde Furberg	Member of the Board	Hilde Furberg was elected to the Herantis Pharma board in 2021. Hilde Furberg has worked in companies such as Genzyme and Baxter, she was most recently SVP and General Manger / European Head of Rare Diseases at Sanofi Genzyme. Since 2005, Hilde has also worked as non-executive director and Board member of Probi, Pronova, Clavis, Bergenbio and Algeta. She holds a Master of Science from the University of Oslo.
Mats Thorén	Member of the Board	Mats Thorén, has been a Herantis Board member since 2020. Currently CEO of Vixco Capital. He was one of the founding partners of Catella Healthcare, an investment firm in the Healthcare business. Mats Thorén has been a first-ranked equity research analyst in Sweden with SEB and the Head of Swedish Healthcare with SHB Markets Corporate Finance.

Management

Name	Title	Experience
Craig Cook	CEO	Craig is the CEO at Herantis since 2020 and a medical doctor with an MBA from LBS. He has a long experience from the pharmaceutical and biotech sector, including senior positions at Eli Lilly, Johnson & Johnson, Novartis and EMD Serono. Furthermore, he has experience from the entrepreneur side of the industry and was previously the CEO of Midatech Pharma.
Tone Kvåle	Chief Financial officer	Tone is the CFO since 2020 and has a 20 year+ experience from the biotech and life science industry. She was before Herantis CFO at publicly listed company's such as Nordic Nanovector & NorDiag. She has also had senior positions at Thermo Fischer (then Invitrogen) and been involved in M&A, licensing deals and raised financing in several rounds. She serves as a director of the board of Bonesupport and has a diploma in finance/administration from The Arctic University of Norway.
Antti Vuolanto	Chief Operating Officer	Antti joined Herantis in February 2018 as COO. Previously he served as COO at Valo Therapeutics, as Executive Vice President at Targovax ASA, and COO and co-founder at Oncos Therapeutics Ltd that merged with Targovax in 2015. He has also held senior management positions at other biotech companies. Has a PhD in Technology at Aalto University, Finland, in 2004 in bioprocess engineering.
Henri Huttunen	Chief Scientific Officer	Henri co-founded Herantis in 2008 and served as the company's CEO for the first two years. He has previously held research positions at the University of Helsinki, Orion Pharma, and Massachusetts General Hospital, Harvard Medical School (USA). Dr. Huttunen has a PhD in biochemistry from the University of Helsinki and 25 years of experience in neuroscience research. While he was an adjunct professor, Dr. Huttunen lead an academic research group focusing on molecular mechanisms of neurodegenerative diseases at the Neuroscience Center, University of Helsinki.
Magnus Sjögren	Chief Medical Officer	Magnus works full time as CMO at Herantis since 2021, but has previously been a consultant CMO since 2017. He is a has a background as a Psychiatrist with 25 years+ of experience in clinical psychiatry. He is also Associate Professor at Gothenburg University since 2002 and a Lecturer at Copenhagen University since 2015, and the author of more than 135 scientific publications. Dr. Sjögren has held several senior executive and scientific positions: Chief Medical Officer at DiaGenic ASA; Vice President at UCB Pharma in Belgium and UK; Global Head of Translational Medicine in Schering-Plough; Senior Clinical Research Director in Organon NV and AstraZeneca.
Jutta Poutanen	Head of Quality	Jutta has served as Chief Pharmaceutical Officer at Laurantis Pharma Ltd. and subsequently Herantis Pharma Plc. since August 2010 until April 2021, whereafter she was promoted to Head of Quality. Prior to the merger that formed Laurantis Pharma, Ms. Poutanen was Development Manager, Product Development of BioCis Pharma Ltd since August 2008. In her earlier career she has among others worked as Senior Research Scientist at Orion Pharma. She has over 20 years of working experience in pharmaceutical industry in formulation, product and process development and she holds a MSc in pharmacy from University of Helsinki.
Jani Koskinen	Head of CMC	Jani joined Herantis Pharma Plc. in December 2014. He works as a Head of CMC taking care of tasks related to manufacturing and process development. Before joining Herantis Mr. Koskinen worked for Biotie Therapies, University of Helsinki and Fit Biotech having over 15 years of experience in manufacturing and process development of biopharmaceuticals. He holds a MSc in bioprocess engineering from the Helsinki University of Technology (Aalto-university).
Sigrid Booms	Head of Regulatory Affairs and Compliance	Sigrid has been with Herantis since 2011 and is the Head of Regulatory Affairs & Compliance since 2020. Mrs. Booms has more than 25 years of experience in global development of pharmaceuticals for human use, with previous positions in regulatory affairs at Orion Pharma and at a global clinical CRO as Director, Regulatory Affairs. During her career, she was involved in several drug development projects in the CNS therapeutic area and is currently the study director for the CDNF (protein) clinical development in Parkinson's disease. Over the years she has become a specialist in regulatory aspects for nonclinical and early phase clinical development. Mrs. Booms holds a Licentiate in pharmacy from the University of Utrecht in the Netherlands.

Summary Redeye Rating

The rating consists of three valuation keys, each constituting an overall assessment of several factors that are rated on a scale of 0 to 1 points. The maximum score for a valuation key is 5 points.

Rating changes in the report

People: 4

Herantis' management and ownership help validate the case. While the business model is heavily reliant on partnering at a relatively early stage, the team has the deal experience and scientific expertise to handle this. Moreover, Herantis is backed by institutional investors – a strong signal for an early-stage company addressing a challenging indication.

Business: 2

We believe that CDNF will have large potential given the high need for disease-modifying treatment options for Parkinson's, but it is still early stage and the company will not be profitable for a number of years.

Financials: 1

Herantis Pharma is a pre-revenue company with negative cashflows with many years until reaching the market. On a positive note, Herantis has a strong record of raising funds – positive given the upcoming needs.

Redeye Rating and Background Definitions

Company Quality

Company Quality is based on a set of quality checks across three categories; PEOPLE, BUSINESS, FINANCE. These are the building blocks that enable a company to deliver sustained operational outperformance and attractive long-term earnings growth.

Each category is grouped into multiple sub-categories assessed by five checks. These are based on widely accepted and tested investment criteria and used by demonstrably successful investors and investment firms. Each sub-category may also include a complementary check that provides additional information to assist with investment decision-making.

If a check is successful, it is assigned a score of one point; the total successful checks are added to give a score for each sub-category. The overall score for a category is the average of all sub-category scores, based on a scale that ranges from 0 to 5 rounded up to the nearest whole number. The overall score for each category is then used to generate the size of the bar in the Company Quality graphic.

People

At the end of the day, people drive profits. Not numbers. Understanding the motivations of people behind a business is a significant part of understanding the long-term drive of the company. It all comes down to doing business with people you trust, or at least avoiding dealing with people of questionable character.

The People rating is based on quantitative scores in seven categories:

- Passion, Execution, Capital Allocation, Communication, Compensation, Ownership, and Board.

Business

If you don't understand the competitive environment and don't have a clear sense of how the business will engage customers, create value and consistently deliver that value at a profit, you won't succeed as an investor. Knowing the business model inside out will provide you some level of certainty and reduce the risk when you buy a stock.

The Business rating is based on quantitative scores grouped into five sub-categories:

- Business Scalability, Market Structure, Value Proposition, Economic Moat, and Operational Risks.

Financials

Investing is part art, part science. Financial ratios make up most of the science. Ratios are used to evaluate the financial soundness of a business. Also, these ratios are key factors that will impact a company's financial performance and valuation. However, you only need a few to determine whether a company is financially strong or weak.

The Financial rating is based on quantitative scores that are grouped into five separate categories:

- Earnings Power, Profit Margin, Growth Rate, Financial Health, and Earnings Quality.

Redeye Equity Research team

Management

Björn Fahlén
bjorn.fahlen@redeye.se

Tomas Otterbeck
Tomas.otterbeck@redeye.se

Technology Team

Jonas Amnesten
jonas.amnesten@redeye.se

Douglas Forsling
Douglas.forsling@redeye.se

Danesh Zare
Danesh.zare@redeye.se

Niklas Sävås
Niklas.savas@redeye.se

Fredrik Nilsson
fredrik.nilsson@redeye.se

Tomas Otterbeck
tomas.otterbeck@redeye.se

Mattias Ehrenborg
Mattis.ehrenborg@redeye.se

Viktor Westman
viktor.westman@redeye.se

Forbes Goldman
forbes.goldman@redeye.se

Mark Siöstedt
mark.siostedt@redeye.se

Henrik Alveskog

Henrik.alveskog@redeye.se

Editorial

Mark Siöstedt
mark.siostedt@redeye.se

Joel Karlsson
Joel.karlsson@redeye.se

Life Science Team

Gergana Almquist
gergana.almquist@redeye.se

Oscar Bergman
oscar.bergman@redeye.se

Anders Hedlund
anders.hedlund@redeye.se

Niklas Elmhammer
niklas.elmhammer@redeye.se

Mats Hyttinge
mats.hyttinge@redeye.se

Johan Unnerus
Johan.unnerus@redeye.se

Christian Binder
Christian.binder@redeye.se

Filip Einarsson
filip.einarsson@redeye.se

Fredrik Thor
fredrik.thor@redeye.se

Kevin Sule
Kevin.sule@redeye.se

Disclaimer

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Redeye Rating (2021-05-18)

Rating	People	Business	Financials
5p	26	17	4
3p - 4p	124	102	40
0p - 2p	5	36	111
Total	155	155	155

Duplication and distribution

CONFLICT OF INTERESTS

Fredrik Thor. owns shares in the company No
Anders Hedlund owns shares in the company : No
Redeye performs/have performed services for the Company and receives/have received compensation from the Company in connection with this.