EDISON

Herantis Pharma

FY18 results

Progressing towards proof-of-concept data

Pharma & biotech

Top-line data from Phase I/II asset CDNF in Parkinson's disease (PD) is expected in H219; positive efficacy/safety data from this ongoing proof-of-concept clinical trial would serve as validation of the research efforts and additionally could crystallise value through partnering opportunities. Recently reported Phase II data from the MedGenesis-sponsored GDNF PD trial has read-across to Herantis's CDNF trial. The company is planning a directed share issue to a limited number of investors in addition to Herantis's directors. It is also preparing for a contemplated secondary listing on First North Stockholm. We value Herantis at €47.9m (€9.7/share).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/17	0.0	(2.2)	(0.5)	0.0	N/A	N/A
12/18	0.0	(4.2)	(0.8)	0.0	N/A	N/A
12/19e	0.0	(4.5)	(0.9)	0.0	N/A	N/A
12/20e	0.0	(4.2)	(0.9)	0.0	N/A	N/A

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

CDNF for Parkinson's disease readout expected H219

Herantis is developing CDNF, a neuroprotective factor that is believed to promote neurone survival and could potentially have an effect on motor and non-motor symptoms, in addition to potentially slowing down disease progression in PD. Top-line Phase I/II data is expected in H219. Herantis has in-licensed a next-generation, non-invasive CDNF, which has started early pre-clinical development. The Phase I/II CDNF trial is funded through an EU grant.

Steady progress in Lymfactin development in FY18

Lymfactin is a gene therapy to stimulate lymph vessel growth as a therapy for breast cancer-related associated (BCAL) secondary lymphedema. Herantis initiated the Phase II AdeLE (adenovirus gene therapy for the treatment of lymphedema) for BCAL in H118 and 12-month proof of concept safety and efficacy data are expected by end 2020. If the Phase II trial completes successfully then a Phase III programme in BCAL could initiate in 2021 either by Herantis or a potential development and commercialisation partner.

Financials: Cash runway into H219

R&D expenses increased to €2.1m (FY17: €1.4m) in FY18, reflecting the start of the Lymfactin Phase II in BCAL and preclinical work associated with in-licensed asset non-invasive CDNF. The FY18 net loss was €4.2m (FY17: €2.2m). Herantis's cash and cash equivalents of €2.2m suggest a cash runway into H119; we forecast additional illustrative financing of €2.5m in FY19. Herantis has announced a planned share issuance to cover its working capital requirements through to the end of 2020.

Valuation: rNPV suggests €47.9m or €9.7/share

Our valuation of €47.9m (or €9.7/share), vs €45.8m (€9.3/share) previously, includes net debt of €3.6m and is based on a risk-adjusted model for CDNF in PD (€4.3/share) and Lymfactin in BCAL (€6.2/share) with no contribution from CDNF for other neurodegenerative diseases.

6 March 2019

Price	**€5.40**
Market cap	**€27m**
Net debt (€m) as of 31 December 2018	3.6
Shares in issue	4.9m
Free float	68.4%
Code	HRTS
Primary exchange	NASDAQ OMX
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(8.5)	4.9	(10.0)
Rel (local)	(11.1)	(3.0)	(11.5)
52-week high/low		€7.5	€4.8

Business description

Herantis Pharma is a Finnish innovative biopharmaceutical company focusing on regenerative medicines for unmet needs. Key assets include CDNF for Parkinson's disease and Lymfactin for breast cancer associated lymphedema.

Next events

CDNF PD Phase I/II data	H219
Lymfactin Phase II data	End 2020

Analysts

Dr Susie Jana	+44 (0)20 3077 5700
Dr Daniel Wilkinson	+44 (0)20 3077 5734
Dr Sean Conroy	+44 (0)20 3681 2534

healthcare@edisongroup.com

Edison profile page

CDNF: Competitors publish clinical data on GDNF

Herantis is developing its innovative recombinant factor CDNF for the treatment of a range of neurodegenerative conditions. Neuro-trophic/protective factors (such as CDNF, MANF and GDNF) are endogenous secretory proteins that have been shown to have neuroprotective and neurorestorative effects, presenting the opportunity for their use in the treatment of Parkinson's disease (PD).

CDNF-based therapy is being evaluated by Herantis for its potential neuroprotective and neuro restorative properties in PD. CDNF is a recombinant factor, large molecule-based treatment that is unable to cross the blood brain barrier in its current formulation; it therefore needs to be administered into the exact region of the brain (the putamen) where it can target its effect. CDNF is dosed intracranially once a month (two- to three-hour infusion in the outpatient setting) using an implanted drug delivery device with portal access located behind the patient's ear. The novel drug delivery system (DDS) being used in the study has been developed by Renishaw, a global metrology company headquartered in the UK.

Recently published data (an original study and open-label extension study) from the MedGenesis-sponsored Phase II trial evaluating intermittent glial cell line-derived neurotrophic factor (GDNF) in PD has important read-across for CDNF despite the trial not reaching its primary efficacy endpoint. The original GDNF study enrolled 41 patients and utilised the same Renishaw DDS that Herantis is using to deliver CDNF. Initially six pilot-stage patients (randomised 2:1 to placebo) were enrolled before 35 additional patients (randomised 1:1 to placebo) were enrolled. Patients received 120ug of GDNF into the putamen every four weeks for 40 weeks. The primary endpoint was the change from baseline to week 40 in the OFF state (defined as motor fluctuations that result in the return of PD symptoms). The key results were as follows:

- Mean OFF state motor score decreased by 17.3% ±17.6% in the active arm compared to 11.8% ± 5.8% in the placebo group, demonstrating no statistically significant difference between treatments.
- PET (positron-emission tomography) imaging demonstrated the active arm generated a statistically significant increase in F-DOPA compared with the placebo. Additionally, delivery of GDNF produced a putamen-wide tissue engagement effect, overcoming prior delivery limitations.
- GDNF was well tolerated and no drug-related serious adverse events (AEs) were reported.
- Three serious AEs were recorded and considered to be related to the device, including two episodes of hypertrophic skin reaction and one occurrence of a possible localised port site infection that was treated with antibiotics. Education in the study population on device maintenance improved as the trial progressed and no intracranial infections occurred during the treatment period.
- Hypothesise for why the primary endpoint was not reached include failure of GDNF mechanism of action, low dosing, short study length, drug distribution in the putamen, recruiting patients too late in their disease progression, lag in effect, magnitude of placebo effect and sample size.

In the open-label follow-up, patients in both arms were treated with GDNF for a further 40 weeks. Patients who were treated for 80 weeks with GDNF demonstrated a reduction in mean OFF state motor score by 26.7% ±20.7% while patients on placebo for 40 weeks followed by GDNF for 40 weeks demonstrated a reduction in mean OFF state motor score by 27.6% ±23.6%.

While the failure of this trial to meet its primary endpoint is disappointing for the sector, Herantis's ongoing clinical trial with CDNF has some advantages. In pre-clinical models to date including a PD monkey model, CDNF has demonstrated superiority to GDNF (study). As dosing is believed to be a key sensitivity for neuro-trophic/protective factors, we take comfort from the fact that CDNF is being

dosed (in the clinical trial) at between approximately three- to 10-fold (300ug to 1200ug) the level GDNF was dosed at. However, we note as the compounds have different MoAs (mechanisms of action), bioavailability and distribution, any direct dosing comparisons should be taken lightly.

Next generation of CDNF in-licensed

Herantis's cerebral dopamine neuroprotective factor (CDNF) is unable to cross the blood brain barrier (BBB) in its current formulation and needs to be dosed intracranially; in the ongoing clinical study, this is achieved with a novel drug delivery system (DDS). Using such means to deliver CDNF is invasive to patients and carries risks, as demonstrated by the GNDF trial data. Herantis is actively looking to develop a non-invasive way of delivering CDNF.

In July 2018, Herantis in-licensed the global rights from the University of Helsinki for a second generation of CDNF. Publication of the patent covering this next generation of neuroprotective factors highlights the potential for these to be developed into a non-invasive treatment. These smaller proteins are based on recombinant CDNF and MANF (50–80 amino acid C-terminal fragments) and retain the same core pharmacological function, but are capable of crossing the BBB following systemic administration. Importantly, preclinical data (in rats) shows these fragments can be dosed systemically (subcutaneous injection) and have a neurorestorative effect in a motor function model of PD. Furthermore, additional preclinical studies indicate that this next generation of neuroprotective factors might have utility in the treatment of Huntington's disease and amyotrophic lateral sclerosis (ALS). These newly in-licensed molecules could become important for the longevity of the franchise.

Financials: Cash injection needed to fund beyond 2019

Herantis reported an FY18 net loss of €4.2m (€2.2m in FY17). R&D expenses increased to €2.1m (FY17: €1.4m), reflecting the advancement of the R&D pipeline including the start of the Lymfactin Phase II in BCAL and preclinical work associated with in-licensed asset non-invasive CDNF. We note the majority of funding for the Phase I/II CDNF trial is through an EU grant. Cash burn amounted to €3.7m in FY18 (FY17: €2.6m). In the near term, Herantis will continue to be cash consumptive and operate as a non-revenue generating biotech. Cash and cash equivalents at 31 December 2018 were reported at €2.2m and debt at €5.9m (Business Finland loans). We forecast an FY19 net loss of €4.5m and model a raise of €2.5m (as illustrative debt) in 2019 to fund Herantis. We note management is planning a directed share issue to a limited number of investors and the company's directors, additionally, it is preparing for a contemplated secondary listing on the First North Stockholm marketplace. Herantis has previously been granted R&D loans from Business Finland, of which €1.1m remains to be drawn down; in H118 the company drew down €0.3m. Additionally, the Phase I-II study (TreatER) of CDNF in PD is essentially funded by a grant (Horizon 2020) of €6.0m.

Valuation: €47.9m or €9.7/share

We value Herantis at €47.9m or €9.7/share based on a risk-adjusted NPV analysis, which includes €3.6m net debt at the end of December 2018 and risk-adjusted contributions for CDNF in PD and Lymfactin in BCAL. We have rolled forward our model and updated for net cash but left our operating assumptions unchanged. The breakdown of our NPV valuation, which uses a 12.5% discount rate, is shown in Exhibit 1. As detailed in our Herantis initiation note, we have applied a top-down analysis of the PD and BCAL markets, which form the basis of our sales projections.

Exhibit 1: Valuation breakdown

Product	Indication	Phase	Probability of success	rNPV (€m)	Per share (€)
CDNF	Parkinson's disease	I/II	5%	20.9	4.3
Lymfactin	BCAL	II	10%	30.6	6.2
Net debt at 31 December 2018				(3.6)	(0.7)
Valuation				**47.9**	**9.7**

Source: Edison Investment Research

Exhibit 2: Financial summary

Accounts: IFRS; year end: 31 December; €m	2016	2017	2018	2019e	2020e
INCOME STATEMENT					
Total revenues	25	0	0	0	0
Cost of sales	0	0	0	0	0
Reported gross profit	25	0	0	0	0
SG&A (expenses)	(942)	(1,024)	(1,244)	(1,256)	(1,269)
R&D costs	(27)	0	0	(2,160)	(2,182)
Other (includes exceptionals)	(2,273)	(1,703)	(2,424)	232	235
Depreciation	(1,203)	(1,218)	(1,202)	(1,213)	(910)
Adjusted EBIT	(4,420)	(3,945)	(4,871)	(4,397)	(4,126)
Reported EBIT	(4,420)	(3,945)	(4,871)	(4,397)	(4,126)
Finance income/ (expense)	(4)	1,780	691	(60)	(101)
Other income (expense) (includes exceptionals)	0	0	0	0	0
Adjusted PBT	(4,425)	(2,165)	(4,180)	(4,457)	(4,227)
Reported PBT	(4,425)	(2,165)	(4,180)	(4,457)	(4,227)
Income tax expense	0	0	0	0	0
Adjusted net income	(4,425)	(2,165)	(4,180)	(4,457)	(4,227)
Reported net income	(4,425)	(2,165)	(4,180)	(4,457)	(4,227)
Earnings per share					
Basic EPS (€)	(1.1)	(0.5)	(0.8)	(0.9)	(0.9)
Diluted EPS (€)	(1.1)	(0.5)	(0.8)	(0.9)	(0.9)
Adjusted basic EPS (€)	(1.1)	(0.5)	(0.8)	(0.9)	(0.9)
Adjusted diluted EPS (€)	(1.1)	(0.5)	(0.8)	(0.9)	(0.9)
Average number of shares - basic (m)	4.1	4.2	4.9	4.9	0.0
Average number of shares - diluted (m)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Property, plant and equipment	9	7	5	4	3
Goodwill	0	0	0	0	0
Intangible assets	6,590	5,663	4,735	3,524	2,616
Other non-current assets	712	392	118	117	116
Total non-current assets	7,311	6,061	4,857	3,644	2,734
Cash and equivalents	2,829	5,402	2,186	1,442	624
Inventories	0	0	0	0	0
Trade and other receivables	65	109	105	105	105
Other current assets	0	0	0	0	0
Assets classified for sale	0	0	0	0	0
Total current assets	2,895	5,511	2,290	1,546	729
Non-current loans and borrowings	8,018	6,022	5,878	8,378	10,878
Trade and other payables	0	0	0	0	0
Other non-current liabilities	0	0	0	0	0
Total non-current liabilities	8,018	6,022	5,878	8,378	10,878
Trade and other payables	186	278	200	200	200
Current loans and borrowings	103	547	507	507	507
Other current liabilities	324	634	651	651	651
Liabilities of assets held for sale	0	0	0	0	0
Total current liabilities	613	1,460	1,358	1,358	1,358
Equity attributable to company	1,575	4,090	(89)	(4,546)	(8,774)
Non-controlling interest	0	0	0	0	0
CASH FLOW STATEMENT					
Profit before tax	(4,425)	(2,165)	(4,180)	(4,457)	(4,227)
Depreciation of tangible assets	1,203	1,218	1,202	1,213	910
Amortisation of intangible assets	0	0	0	0	0
Share based payments	(0)	(2,021)	(3)	0	0
Other adjustments	5	240	(688)	60	101
Movements in working capital	166	372	(79)	0	0
Net cash from operating activities (pre-tax)	(3,052)	(2,355)	(3,747)	(3,184)	(3,216)
Interest paid / received	16	(244)	15	(60)	(101)
Income taxes paid	0	0	0	0	0
Cash from operations (CFO)	(3,036)	(2,599)	(3,732)	(3,244)	(3,317)
Capex (includes acquisitions)	(10)	0	0	0	0
Other investing activities	(61)	(0)	7	0	0
Cash used in investing activities (CFIA)	(71)	(0)	7	0	0
Net proceeds from issue of shares	0	4,680	0	0	0
Movements in debt	0	0	509	2,500	2,500
Other financing activities	396	492	0	0	0
Cash from financing activities (CFF)	396	5,172	509	2,500	2,500
Currency translation differences and other	0	0	0	0	0
Increase/(decrease) in cash and equivalents	(2,711)	2,573	(3,216)	(744)	(817)
Cash and equivalents at beginning of period	5,541	2,829	5,402	2,186	1,442
Cash and equivalents at end of period	2,829	5,402	2,186	1,442	624
Net (debt) cash	(5,291)	(1,168)	(4,200)	(7,444)	(10,761)
Movement in net (debt) cash over period	N/A	4,123	(3,033)	(3,244)	(3,317)

Source: Herantis Pharma accounts, Edison Investment Research

General disclaimer and copyright

This report has been commissioned by Herantis Pharma and prepared and issued by Edison, in consideration of a fee payable by Herantis Pharma. Edison Investment Research standard fees are £49,500 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the Edison analyst at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Myonlineadvisers Pty Ltd who holds an Australian Financial Services Licence (Number: 427484). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

Neither this document and associated email (together, the "Communication") constitutes or form part of any offer for sale or subscription of, or solicitation of any offer to buy or subscribe for, any securities, nor shall it or any part of it form the basis of, or be relied on in connection with, any contract or commitment whatsoever. Any decision to purchase shares in the Company in the proposed placing should be made solely on the basis of the information to be contained in the admission document to be published in connection therewith.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document (nor will such persons be able to purchase shares in the placing).

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

The Investment Research is a publication distributed in the United States by Edison Investment Research, Inc. Edison Investment Research, Inc. is registered as an investment adviser with the Securities and Exchange Commission. Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a) (11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia