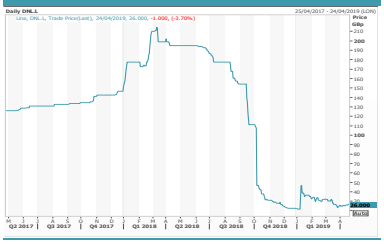
Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data	
EPIC/TKR	**DNL**
Price (p)	**27.0**
12m High (p)	196.0
12m Low (p)	21.0
Shares (m)	61.7
Mkt Cap (£m)	16.7
EV (£m)	9.8
Free Float*	20%
Market	AIM

**As defined by AIM Rule 26*

Description

Diurnal is a UK-based specialty pharma company targeting patient needs in chronic, potentially life threatening, endocrine (hormonal) diseases. Alkindi has received approval in Europe, with first sales started in May 2018; Chronocort has completed the largest and only Phase III trial globally in CAH.

Company information

CEO	Martin Whitaker
CFO	Richard Bungay
Chairman	Peter Allen
	+44 29 2068 2069
	www.diurnal.co.uk

Key shareholders

Directors	3.0%
IP Group	43.6%
Finance Wales	18.8%
Invesco	11.7%
Oceanwood Capital	7.1%
Polar Capital	4.3%

Diary

4Q'19	Alkindi US NDA submission
4Q'19	Chronocort EMA MAA

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DIURNAL GROUP

Clarity for Chronocort regulatory pathway

Diurnal (DNL) is a commercial-stage specialty pharmaceutical company focused on diseases of the endocrine system. Its two lead products are targeting rare conditions where medical need is currently unmet, with the aim of building a long-term 'Adrenal Franchise'. The first product, Alkindi®, is being launched in key EU markets, and this was expected to be followed by the adult version, Chronocort®. After unexpected Phase III results, positive feedback from the EMA has cleared the path for regulatory submission of Chronocort for adult CAH in Europe before the end of 2019, and allowed DNL to revise the primary endpoint in the protocol for the US Phase III trial.

- **Strategy:** DNL's goal is to create a valuable 'Adrenal Franchise' that can treat patients with chronic cortisol deficiency diseases from birth and for the rest of their lives. The long-term vision, once Alkindi and Chronocort are established in Europe and the US, is to expand the product offering to other endocrine conditions.

- **Interims:** The focus during 1H'19 has been to build-up the launch of Alkindi in Europe and establish commercial partners in other key territories. Sales during 1H'19 were in line with forecasts at £0.19m. Events around Chronocort caused some volatility in R&D spend, which left net cash of £6.9m at 31 December 2018.

- **EMA feedback:** Following a Scientific Advice meeting with EMA representatives to discuss the Phase III Chronocort results in CAH patients, the EMA has confirmed that the MAA for Chronocort can be submitted with no further trials needed; DNL expects to submit this in 4Q'19.

- **Risks:** Concerns about the US prospects for Chronocort have been allayed by the positive EMA outcome, which has allowed DNL to change the US Phase III protocol. However, it has added extra time into the US development process and delayed the point at which DNL is expected to become cashflow-positive.

- **Investment summary:** Alkindi, a cortisol replacement therapy designed for children under 18 years of age, is DNL's first product on the market. It is expected to be followed by Chronocort for adults – a larger market – which now has a clear pathway for regulatory approval in both Europe and the US. Despite this, the share price is still languishing well below valuations determined by peer group and DCF (225p) analyses, possibly due to the need for more capital later in 2019.

Financial summary and valuation

Year-end Jun (£m)	2016	2017	2018	2019E	2020E	2021E
Sales	0.00	0.00	0.07	1.14	2.14	5.56
SG&A	-1.99	-3.23	-6.21	-5.50	-7.12	-8.76
R&D	-3.89	-8.34	-10.02	-10.00	-10.85	-10.31
EBITDA	-5.87	-11.56	-16.16	-14.52	-16.03	-14.06
Underlying EBIT	-5.88	-11.56	-16.17	-14.53	-16.05	-14.07
Reported EBIT	-6.99	-12.08	-16.98	-15.38	-16.94	-15.01
Underlying PBT	-5.95	-11.64	-16.30	-14.45	-16.03	-14.12
Statutory PBT	-7.06	-12.16	-16.91	-15.30	-16.92	-15.06
Underlying EPS (p)	-12.48	-17.05	-25.68	-19.84	-21.97	-19.08
Statutory EPS (p)	-15.02	-18.04	-26.78	-21.23	-23.41	-20.59
Net (debt)/cash	26.88	16.37	17.28	4.23	-10.17	-23.64
Capital increases	24.52	0.05	13.40	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

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Interim results

Key features

Operational highlights

- **Alkindi:** Successful launch, as the specially-designed paediatric cortisol replacement therapy in Germany has been followed by the UK, with reimbursement negotiations ongoing across other European countries. In the US, DNL anticipates New Drug Application (NDA) submission in 4Q'19, with first sales in early 2021. In other territories, DNL continues to partner with key distributors.
- **Chronocort:** When all the data were analysed, despite missing the Phase III primary endpoint, the Scientific Advice from the EMA formally confirmed that Chronocort could be submitted for regulatory consideration without the need for further trials. This is an enormous relief for the company. Separately, the Phase III trial in the US can continue with a revised protocol. Consequently, DNL intends to submit its Market Authorisation Application (MAA) in Europe in 4Q'19, while the US trial will start around the end of 2019, subject to partnering or further funding.
- **Pipeline:** The oral testosterone replacement product has completed the Phase I/II proof-of-concept trial. Read-out is expected during 2Q'19. DNL anticipates engaging with a partner to run and fund the subsequent trial.

Commercial highlights

- **Sales infrastructure:** The EU commercial organisation and supply chain are in place in core territories with Ashfield Healthcare. Launches will follow the conclusion of pricing negotiations on a country-by-country basis.
- **Distribution:** Outside the core territories, DNL continues to expand commercial infrastructure, in countries that recognise the Alkindi EU regulatory dossier, by entering into local distribution agreements with specialist partners. This infrastructure will also be used for subsequent products.

Financial highlights

- **Sales:** Alkindi sales, mainly in Germany, were £0.19m in 1H'19 (nil in 1H'18). Strong growth has also been seen in the first two months of calendar 2019.
- **R&D:** Investment in 1H'19 was higher than forecast at -£7.62m (-£4.71m), due to preparatory work for the US Phase III Chronocort trial (currently on hold).
- **SG&A:** Underlying administration costs decreased 30% to -£1.85m (-£2.63m), lower than forecast, as expenditure was reined in to preserve the cash runway.
- **Net cash:** At 31 December 2018, net cash on the balance sheet was £6.9m, which was lower to our forecast due to higher R&D expenses.

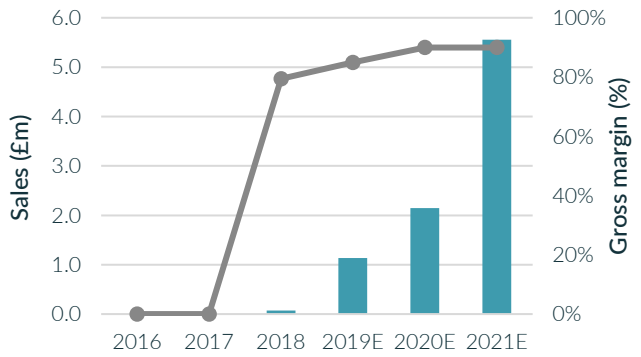
Diurnal interims 2018 – actual vs expectations

Half-year to end-Jun (£m)	1H'18 actual	1H'19 actual	Growth %	1H'19 forecast	Delta Δ
Sales	0.00	0.19	nm	0.20	-0.01
COGS	0.00	-0.03	nm	-0.03	0.00
Gross margin	-	82%	-	85%	+3.0ppts
R&D spend	-4.71	-7.62	+61%	-4.50	+3.12
Administration costs	-2.63	-1.85	-30%	-3.01	-1.16
Underlying EBIT	**-7.35**	**-9.31**	**+27%**	**-7.34**	**-2.03**
Net cash/(debt)	10.34	6.86	-	9.20	-2.30

nm = not meaningful

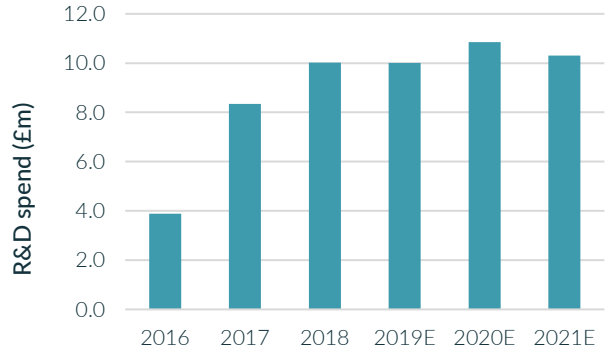
Source: Diurnal, Hardman & Co Life Sciences Research

Sales and gross margin



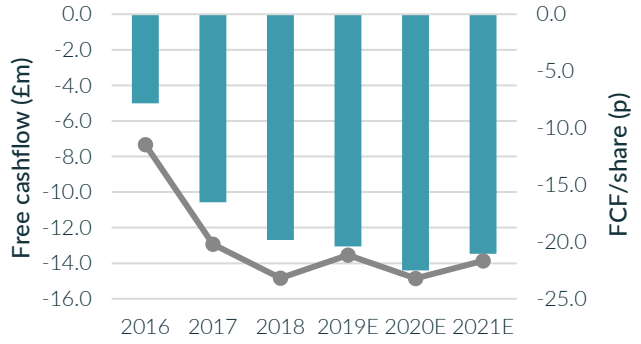
- Sales of Alkindi started in 2Q'18
- Gross margin expected to stabilise at 90% in near term
- First sales of Chronocort anticipated to start in 2021 in Europe

R&D investment



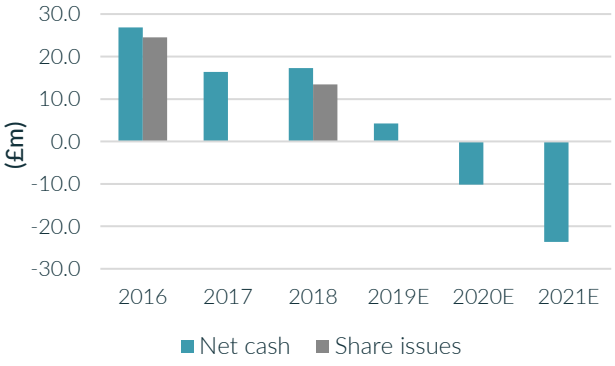
- US R&D on hold for a certain time awaiting EMA Scientific Advice feedback, which will now resume
- Preparatory works for US Phase III trial (£2.3m) accounted for 2018
- R&D costs expected to remain constant in following years due to long-term US Phase III in CAH anticipated to start by end-2019, followed by US study extension
- US Phase II in AI with Chronocort now anticipated to start around end 2019

Cashflow



- Cashflow driven by R&D investment and corporate overheads
- A European subsidiary has been established and a sales force of 14 has been recruited through Ashfield for commercial infrastructure
- Monthly average cashburn forecast at ca.£0.8m for remainder of fiscal 2019

Net cash and capital increases



- At 31 December 2018, net cash was £6.86m
- Placing of £9.89m net in 2018
- Conversion of outstanding convertible loan and accrued interest, total ca.£3.5m, in 2018
- DNL has enough cash until 4Q calendar 2019

Source: Company data, Hardman & Co Life Sciences Research

Operational update

Chronocort

Positive feedback from EMA

No further trials needed…

…paving the way for MAA submission in 4Q'19

In March 2019, DNL met with representatives of the EMA to discuss the way forward for Chronocort. Formal Scientific Advice following the meeting was positive, with the EMA confirming the clinical and regulatory pathway for Chronocort in Europe and that no further trials were required. Hence, DNL has confirmed its intention to submit a Marketing Authorisation Application (MAA) for Chronocort in Congenital Adrenal Hyperplasia (CAH) in Europe in 4Q'19, with approval likely in early 2021. This represents just a two-month delay compared with the original plan.

The dossier submitted on 7 December 2018 contained a comprehensive analysis of all the results from the DIUR-005 Phase III trial, together with the most up-to-date information from the extension study (DIUR-006). At the outset of the trial, there were a number of options available for the primary endpoint, and DNL elected to use the 'standard deviation score' (SDS). The EMA representatives understood the statistical issue with the Phase III data and, with evidence of better control of biomarkers and improved quality of life, agreed that SDS was not the optimal measure of the efficacy of Chronocort. Importantly, the feedback confirmed that no new data were needed for the purpose of regulatory submission.

EMA feedback will allow DNL to re-define primary endpoint for Phase III US trial

This feedback will also help to define the primary endpoint and confirm the protocol for the Phase III trial in CAH patients in the US. Separately, the use of Chronocort in Adrenal Insufficiency (AI), a different orphan condition that represents a larger market potential, with patients taking the same glucocorticoid medications as CAH and where there is still a high unmet medical need, can be explored in a different trial. A US Phase II trial is expected to start around the end of 2019, subject to partnering or further funding.

Chronocort in CAH patients

European Phase III trial

The Phase III trial [DIUR-005, NCT02716818] enrolled a total of 122 patients across 11 specialist centres (10 Europe and one in the US) and seven countries. It represents the largest-ever interventional study carried out in CAH patients. On entry, androgens from each patient were measured every two hours over a 24-hour period, and then patients were randomised to either receive Chronocort or continue on standard-of-care for a period of six months.

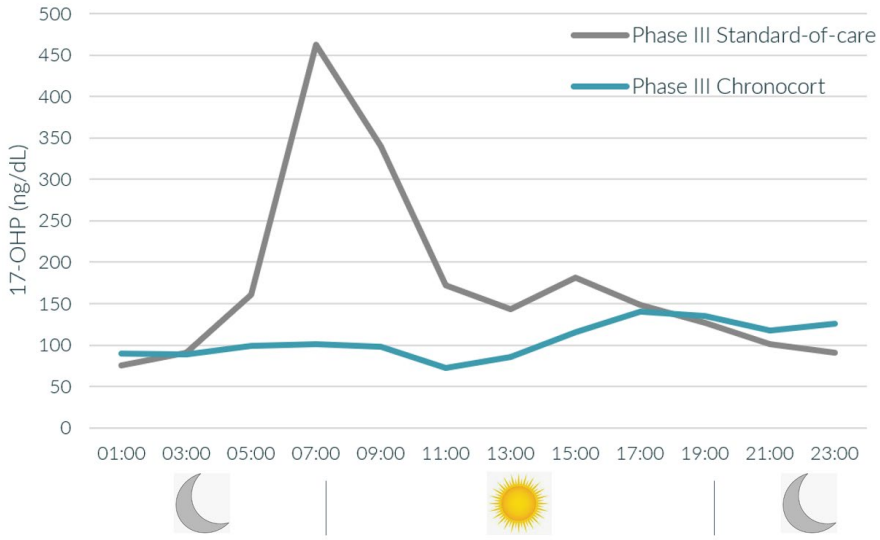
The primary objective of this trial was to demonstrate that Chronocort was superior to standard therapy; however, this endpoint was not met (the Phase III headline data were detailed in our recent note, published on 16 January 2019, Chronocort – seeking regulatory advice).This came as a surprise, because the data from the Phase II study showed a compelling effect in controlling androgens when compared with standard-of-care using the SDS statistical measure.

Chronocort was efficacious…

…but not 'superior' to standard-of-care

After six months' treatment, the blood levels of 17-OHP in patients were recorded. In patients receiving Chronocort, the biomarker level was within the normal range, and all were well-controlled, indicating that Chronocort was efficacious. However, this was also the case in many patients receiving standard treatment. Therefore, the primary objective of demonstrating 'superiority over standard-of-care' was not met. This was contrary to the Phase II trial where patients receiving standard-of-care were not well controlled.

Phase III results: Chronocort vs standard-of-care – 17-OHP level



Note: values in the graph are approximate
Source: Diurnal, adapted by Hardman & Co Life Sciences Research

Despite not meeting its primary endpoint, Chronocort bears several significant advantages compared with standard-of-care

On the other hand, the full analysis of the data also highlights several crucial advantages that Chronocort reveals compared with standard-of-care, as shown below:

- Chronocort achieved androgen control in both 17-OHP and another androgen marker androstenedione (A4) at a lower dose (30mg) compared with the standard treatments (35mg).
- Crucially, Chronocort achieved the desired level of 17-OHP in the critical early-morning period – a level that is usually too low in patients with standard-of-care (increased cortisol levels address morning fatigue).
- No adrenal crisis with Chronocort (an event requiring hospitalisation for several days) vs three events with the standard-of-care.
- Significantly lower overall 17-OHP levels over the 24-hour-period, as measured by the area under the curve (see graph above).
- Less variable biomarker levels on Chronocort.
- Chronocort was well tolerated and provided the natural overnight cortisol release, unlike standard therapy.
- Fewer 'sick days' in patients receiving Chronocort (during sickness, the cortisol level naturally increases): 26 days vs 36 days with standard-of care.
- Additional unexpected benefits with Chronocort, such as less fatigue and return of menstrual cycles in female patients.

Extension study

Data from the Phase III safety extension study with Chronocort helped discussions with the EMA

Following completion of the Phase III study, DNL has been conducting an open-label, safety extension study [DIUR-006, NCT03062280] for patients wishing to continue on Chronocort or electing to switch from their current glucocorticoid therapy (standard-of-care) to Chronocort. To date, a total of 91 patients have been enrolled. The main aspect of the trial is to assess the long-term safety and tolerability of Chronocort, with the study expected to run until regulatory approval of Chronocort. DNL has indicated that there has been a low drop-out of the extension study (less than 10%).

In an interim analysis (March 2018), DNL stated that three patients had been on Chronocort for more than 24 months and seven for 18 months, and they were all still continuing the treatment. This analysis indicated additional benefits of Chronocort, such as:

- 17-OHP and A4 androgen control maintained over the 24-month period;
- further steroid dose reduction over the period;
- weight and body-mass index (BMI) maintained during the period; and
- metabolic parameters unchanged.

DNL will continue to assess interim data from the long-term Chronocort study, which will provide additional information to determine whether the effect can be maintained and whether there will be additional clinical benefits.

US Phase III trial in CAH

Change to 'non-inferiority' clinical endpoint for Phase III trial in US

The outcome of the EMA Scientific Advice meeting has its importance in guiding amendments to the protocol for the US Phase III trial, and means that DNL can now resume all the regulatory and preparatory works. It is expected that DNL will communicate further with the FDA to seek advice about improving the protocol and/or endpoints for this trial. The protocol will be altered with a different statistical measure of efficacy and a non-inferiority outcome of Chronocort vs. standard-of-care. The US phase III study is now expected to start around end-2019, and DNL has indicated that it is considering partnering with a suitable specialist pharma company to run and help fund the trial. However, it does still have the option to run the trial by itself, although this would require additional capital.

Much of the cash investment already made will be useful when the study re-starts

The US regulator has requested a head-to-head Phase III trial, whereby CAH patients are enrolled in a randomised fashion to receive either a single type of medication (immediate-release hydrocortisone twice-daily) or Chronocort twice-daily. Patients will be treated for up to 12 months, and a long-term follow-up programme will also be proposed for assessing the long-term safety of Chronocort. Despite the trial being paused, DNL has already spent £2.3m to date in preparation work and site identification for the study, much of which will come in useful when the study re-starts. Meanwhile, cost-saving measures have been implemented successfully in order to extend the cash runway.

Chronocort in AI patients

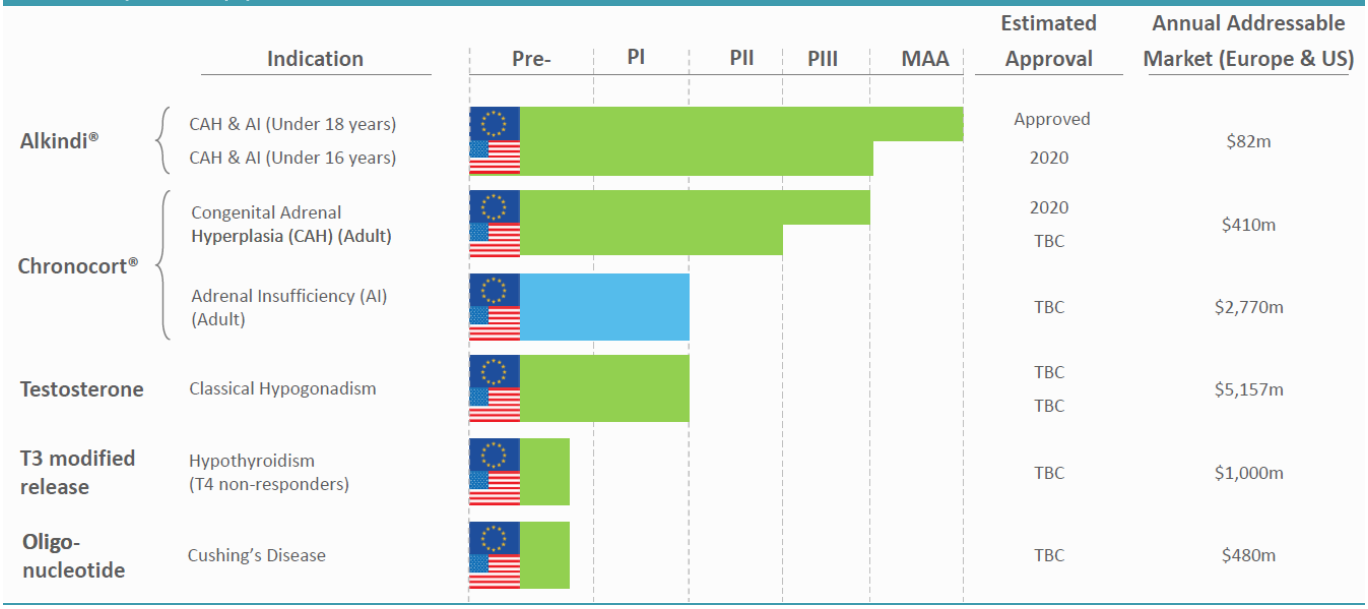
DNL intends to start a Phase II trial in order to address the large AI market. This trial is expected to be conducted at some of the same sites as the Phase III CAH trial, and DNL will investigate different options to finance it, such as grant funding, partnering or further capital. As such, the trial is anticipated to start around the end of 2019.

Product pipeline

Five programmes: three products in clinical and two in pre-clinical development

While much of the attention and resources have been focused on its two leading products, DNL has been extending its R&D pipeline by advancing products through pre-clinical development and into Phase I. Notably, DNL has completed a Phase I/II proof-of-concept study with DITEST (oral native testosterone) for hypogonadism, with headlines expected in 1H'19. Overall, DNL is progressing five additional programmes, with three products in clinical development, and two under pre-clinical evaluation.

Diurnal – product pipeline



Source: Diurnal, Interim results presentation 28 March 2019

Established supply chain and commercial infrastructure

Together with its partner Ashfield, DNL has put in place a commercial infrastructure, with the aim of retaining the full value of Alkindi through direct commercialisation in core European markets. The company has been working closely with a number of relevant partners and created a solid commercial infrastructure:

- **Manufacturing:** Already established (since 2012) with the experienced and specialist GMP supplier, Glatt Pharmaceutical Services GmbH, to produce solid pharmaceutical dosage formulations based on multi-particulate systems.
- **Packaging:** Agreement with Delpharm for its expertise in supply chain management.
- **Sales & marketing:** Appointment of Ashfield Healthcare for sales and medical infrastructure support to establish a network of medical liaison staff in key European territories.

Through Ashfield, DNL has the possibility of establishing a flexible EU commercial organisation that can be modified rapidly if the need arises. While this infrastructure has been established for the commercialisation of Alkindi and Chronocort, it should be recognised that DNL has become a more attractive partner for companies with endocrine drugs which they are looking to out-license for commercialisation in Europe.

Commercialisation agreements

Commercialisation agreements with specialist local distributors in key territories

In order to mitigate any potential effect of Brexit, DNL has established a wholly-owned subsidiary Diurnal Europe B.V. in the Netherlands. In other territories, DNL will expand its commercial activity through the use of local distributors with knowledge of either endocrine or niche markets, who will be responsible for dealing with the local regulatory authorities.

Israel

In March 2016, Diurnal signed a marketing and distribution agreement with Medison, to make Alkindi available in Israel. The deal will also cover Chronocort when it becomes available. The Ministry of Health in Israel has confirmed receipt of the Alkindi submission and that it has been validated. Market authorisation is expected to take a year, and first sales are therefore expected during 2020.

Medison provides a vast spectrum of integrated services, including registration, reimbursement, nursing, distribution and marketing, for companies looking to enter the Israeli healthcare market, and, more specifically, the niche indications. With around 1,000 patients affected, the market opportunity is estimated at $6.3m.

Australia and New Zealand

DNL has licensed (February 2018) exclusive rights to sell Alkindi and Chronocort in Australia and New Zealand to Emerge Health, a specialist hospital pharma company. Around 1,750 patients are affected by Paediatric AI and CAH, giving an estimated market worth $10.2m. DNL expects Emerge Health to submit Alkindi for market approval during 2019 in Australia, and the dossier will be based on the European approval, together with published trial data.

Nordic regions

Concomitant with the interim results, DNL announced that it had out-licensed the exclusive right to market and sell Alkindi in the Nordic regions – covering Sweden, Norway, Denmark, Finland and Iceland – to Anthrop Pharmaceuticals AB. With an estimated of 490 paediatric patients in this region, the market is significant and estimated at $3.1m. Anthrop is a specialist pharmaceutical company based in Sweden with expertise in selling niche products to the hospital sector, including paediatric treatments.

Japan

DNL is in search of a local partner in Japan where first patents for Alkindi and Chronocort have been granted by the Japanese Patent Office. Japan has substantial market potential with around 6,700 patients with CAH and 58,000 with AI, giving an estimated market worth $415m.

Marketing and distribution agreements

Country	Partner	Marketing and distribution agreement	First sales	Patents granted	Addressable market[2]
Israel[1]	Medison Pharma	Yes	2020	Yes	$6.3m
Australia & New Zealand	Emerge Health	Yes	2020	Yes	$10.2m
Nordic regions	Anthrop Pharma	Yes	2019	Yes	$3.1m
US	TBA	TBA	2021	Yes	$132m (plus indication expansion
Japan	TBA	TBA	TBC	Yes	$415m

[1]Including the Palestinian Authority; [2]DNL estimates based on price of $6,369 per patient p.a.
Source: Diurnal, interim results presentation 28 March 2019

Alkindi

European market authorisation

Alkindi is the first licensed paediatric treatment for both AI and CAH

It is almost a year since the EMA approved Alkindi for AI and CAH. This drug is being targeted at new-borns and children up to 18 years of age with cortisol deficiency, although the initial focus will be on children up to six years of age.

First direct sales

Alkindi sales rolled-out across Europe, starting in Germany in 2Q'18, followed by the UK, and with further countries coming up

Despite being a centralised EU authorisation, there is a staged roll-out of Alkindi, influenced by the timetable for agreeing pricing with the relevant authorities in each country. This is normal practice for drugs approved in the EU. Following approval in Germany, Alkindi has been approved in the UK, and pricing has been agreed in Austria and Sweden. The roll-out in other countries has been slower than expected due to external factors, such as slow discussions with the country regulators, Brexit, and also the implementation of new regulatory rules (Falsified Medicines Directive), which requires a unique bar code for each package.

Alkindi packaging – four doses (0.5mg to 5mg)

Source: Diurnal, Interim results presentation 28 March 2019

Sales of Alkindi during the six-month period ended 31 December 2018 were £0.19m, derived mostly from Germany. However, the company indicated that the take-up was improving following its UK launch, as evidenced by a similar sales level in just the first two months of 2019.

In addition, DNL has received a positive Scottish Medicines Consortium pricing & reimbursement decision, allowing the roll-out of sales of Alkindi in Scotland.

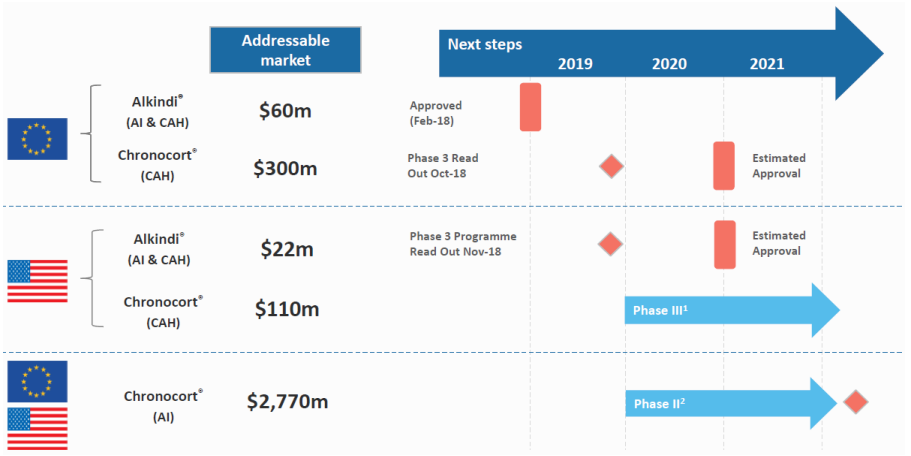
US update

FDA submission for Alkindi before the end of 2019

Meanwhile, development is progressing well in the US, with DNL building up the regulatory programme. As part of the registration package, the European dossier will be used, as well as two additional studies, both successfully completed, as detailed below.

- A food matrix study and bioavailability studies have been completed successfully and met the primary endpoint in healthy volunteers, which confirmed the pharmacokinetics of Alkindi together with safety and tolerability.
- A meeting took place with the FDA in February 2019 to confirm the regulatory path for Alkindi in the US, and determined that no further studies were needed for Alkindi. DNL anticipates submission of its NDA in the US by the end of 2019, for an estimated approval around the end of 2020. DNL is in discussions with a number of potential licensing partners for the US market, in readiness for first sales in 2021. It is likely that the same licensing partner would also be used for Chronocort.

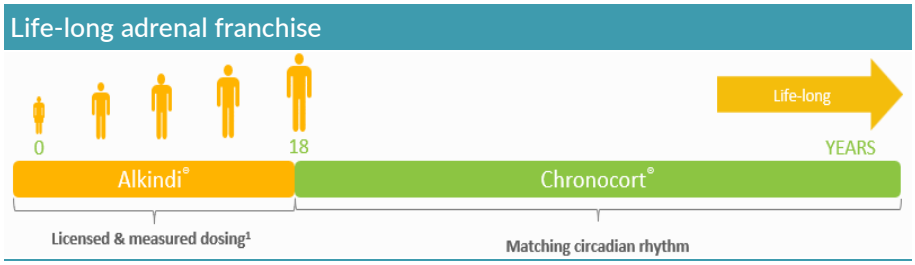
Diurnal – development timetable



[1] Subject to confirmation from the FDA
[2] Subject to NIH Grant, further funding or partnering
Source: Diurnal, Interim results presentation 28 March 2019

The adrenal franchise

With Alkindi and Chronocort, the aim is to create a long-life "adrenal franchise", where patients will start with Alkindi and then move on to Chronocort for the rest of their lives.



Source: Diurnal

Building a pipeline in endocrinology

Building the endocrine pipeline

DNL's vision is "to become a world-leading endocrinology speciality pharma company". It aims to maximise its commercial infrastructure in the niche field of endocrinology, which is dominated by small biotech. As well as developing internal products, management is considering all available options – product acquisition, in-licensing, and partnership opportunities – in order to maximise this opportunity.

Also, during the period, DNL has been investigating opportunities for alternative capital for the early-stage programmes, such as grant funding. DNL has applied for various grants, and it has already received positive feedback due to the unmet needs that the company is aiming to address.

In the meantime, DNL is evaluating products for additional endocrine conditions

European Phase I/II in hypogonadism completed

The Phase I/II proof-of-concept trial with DITEST, a new oral formulation of native testosterone for the treatment of male hypogonadism, is now completed. The study was designed to evaluate the pharmacokinetic data in 12 patients with primary and secondary hypogonadism. The study consisted of two parts:

- the first part of the trial was about safety and tolerability of DITEST in 12 patients; and
- the second part involved a higher dose of DITEST in both fasted and fed states.

Final trial results are expected to be communicated during 2Q'19 and, depending on positive outcomes, DNL will have discussions with potential partners about taking the product forward.

Hypothyroidism

Early development of a modified-release T3 (triiodothyronine) product continues to progress. It is believed that up to 20% of the hypothyroidism population does not respond to pro-hormone T4 therapy, which is the current standard-of-care. DNL sees a considerable opportunity for this innovative product.

Potential treatment for Cushing's disease

DNL is reviewing its options with an oligonucleotide silencing RNA (siRNA) acting on the pituitary gland for a potential treatment for Cushing's disease, a condition characterised by an excess of cortisone secretion. *In vitro* studies, assessing the stability of the molecule in different formulations, have shown that the molecule is robust and efficacious. DNL owns the Orphan Drug Designation for this molecule in Europe.

Conclusion

Alkindi continues to be rolled out across Europe as local pricing negotiations reach a conclusion. Meanwhile, with positive feedback from the EMA, DNL can now resume all the regulatory work in preparation for Chronocort's MAA in Europe, expected in 4Q'19. In addition, preparatory work can recommence for the US Phase III trial in adult CAH, which had been paused temporarily, with enrolment expected to start in early 2020.

The slight delays caused by the Chronocort trial outcome, together with the current share price, have put pressure on the balance sheet, although careful cost control has extended the cash runway modestly. In addition, DNL has the option to out-license/partner products for certain territories, including the US.

Financial forecasts

Profit & Loss

- **Sales:** For the first six-month period, Alkindi sales were £0.19m, a figure already exceeded during the first two months of 2019, with sales at £0.2m. The 2019E sales figures will depend on two factors, both of which are difficult to predict: the timing of reimbursement in remaining European countries and the cycle of patients returning for clinic appointments (typically three- to six-month cycle).
- **COGS:** Despite being in the early launch phase, gross margins for Alkindi in 1H'19 were 82%. This is expected to stabilise at around 90% in the near term.
- **SG&A:** Spend in fiscal 2018 was characterised by the investment in European infrastructure in readiness for the launch of Alkindi. Investment in fiscal 2019 will be more modest, coupled with some tightening of the general corporate overheads. In 1H'19, the underlying spend was reduced by 30%.
- **R&D:** The outcome of the Phase III study with Chronocort prompted a pause in R&D investment. Now that the clinical and regulatory pathway has been positively confirmed following the EMA Scientific Advice, investment will resume for the Phase III trial in CAH patients and the Phase II trial in AI patients, although precise timing of this spend is difficult to predict.

Profit & Loss account						
Year-end June (£m)	2016	2017	2018	2019E	2020E	2021E
Sales	0.00	0.00	0.07	1.14	2.14	5.56
COGS	0.00	0.00	-0.02	-0.17	-0.22	-0.56
SG&A	-1.99	-3.23	-6.21	-5.50	-7.12	-8.76
R&D	-3.89	-8.34	-10.02	-10.00	-10.85	-10.31
EBITDA	-5.87	-11.56	-16.16	-14.52	-16.03	-14.06
Depreciation	-0.01	-0.01	-0.01	-0.01	-0.01	-0.01
Licensing/royalties	0.00	0.01	0.00	0.00	0.00	0.00
Underlying EBIT	**-5.88**	**-11.56**	**-16.17**	**-14.53**	**-16.05**	**-14.07**
Share-based costs	-0.49	-0.52	-0.81	-0.85	-0.89	-0.94
Exceptional items	-0.62	0.00	0.00	0.00	0.00	0.00
Statutory EBIT	-6.99	-12.08	-16.98	-15.38	-16.94	-15.01
Net interest	-0.07	-0.09	-0.13	0.09	0.02	-0.05
Underlying PBT	**-5.95**	**-11.64**	**-16.30**	**-14.45**	**-16.03**	**-14.12**
Reported PBT	-7.06	-12.16	-16.91	-15.30	-16.92	-15.06
Tax liability/credit	0.49	2.73	2.28	2.28	2.47	2.35
Tax rate	-7%	-22%	-13%	-15%	-15%	-16%
Underlying net income	**-5.46**	**-8.91**	**-14.02**	**-12.17**	**-13.56**	**-11.77**
Statutory net income	-6.57	-9.43	-14.62	-13.02	-14.45	-12.71
Ordinary 5p shares:						
Period-end (m)	52.21	52.32	61.34	61.71	61.71	61.71
Weighted average (m)	43.75	52.24	54.60	61.34	61.71	61.71
Fully-diluted (m)	43.75	56.66	59.42	65.80	65.80	66.18
Underlying basic EPS (p)	**-12.5**	**-17.1**	**-25.7**	**-19.8**	**-22.0**	**-19.1**
Statutory basic EPS (p)	-15.0	-18.0	-26.8	-21.2	-23.4	-20.6
Underlying fully-dil. EPS (p)	-12.5	-15.7	-23.6	-18.5	-20.5	-17.8
Statutory fully-dil. EPS (p)	-15.0	-16.6	-24.6	-19.8	-21.8	-19.2
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0

Source: Hardman & Co Life Sciences Research

Balance sheet

- **Net cash/(debt):** At 31 December 2018, DNL had gross cash of £6.9m, and no debt. Based on current forecasts, DNL is expected to have sufficient cash through to the end of calendar 2019. DNL is contemplating the option of finding a partner to run the US Phase III trial in CAH and the global Phase II in AI, which could have a positive impact on its cash position in the event of a deal.
- **Inventory:** Stock levels of Alkindi have been increased in preparation for upcoming country launches.
- **Convertible debt:** At the same time as the Placing in April 2018, IP Group converted its outstanding convertible loan and accrued interest (total ca.£3.5m) into shares. Since our model monitors changes in net debt, this is accounted for as part of the capital increase to reflect the movement from debt into shares.

Balance sheet						
@31 June (£m)	2016	2017	2018	2019E	2020E	2021E
Shareholders' funds	25.93	17.08	16.88	3.86	-10.59	-23.29
Cumulated goodwill	0.00	0.00	0.00	0.00	0.00	0.00
Total equity	25.93	17.08	16.88	3.86	-10.59	-23.29
Share capital	2.61	2.62	3.07	3.07	3.07	3.07
Reserves	23.32	14.46	13.81	0.80	-13.65	-26.36
Provisions/liabilities	0.00	0.00	0.00	0.00	0.00	0.00
Deferred tax	0.00	0.00	0.00	0.00	0.00	0.00
Long-term debt	3.24	3.51	0.00	0.00	0.00	0.00
Short-term loans	0.00	0.00	0.00	0.00	0.00	0.00
less: Cash	16.11	8.88	17.28	4.23	-10.17	-23.64
less: Deposits	14.00	11.00	0.00	0.00	0.00	0.00
Invested capital	**-0.94**	**0.71**	**-0.40**	**-0.37**	**-0.41**	**0.34**
Fixed assets	0.00	0.02	0.03	0.05	0.08	0.12
Intangible assets	0.01	0.00	0.02	0.02	0.02	0.02
Inventories	0.00	0.00	0.12	0.30	0.57	1.47
Trade debtors	*0.00*	*0.00*	*0.08*	*0.14*	*0.36*	*0.93*
Other debtors	*0.53*	*4.03*	*5.02*	*4.77*	*4.53*	*4.30*
Tax credit/liability	*0.00*	*0.00*	*0.00*	*2.28*	*2.37*	*2.41*
Trade creditors	*0.00*	*-1.72*	*-3.32*	*-3.82*	*-4.02*	*-4.22*
Other creditors	*-1.48*	*-1.62*	*-2.35*	*-4.10*	*-4.32*	*-4.68*
Debtors less creditors	-0.95	0.68	-0.57	-0.73	-1.07	-1.26
Invested capital	**-0.94**	**0.71**	**-0.40**	**-0.37**	**-0.41**	**0.34**
Net cash/(debt)	**26.88**	**16.37**	**17.28**	**4.23**	**-10.17**	**-23.64**

Source: Hardman & Co Life Sciences Research

Cashflow

- **Working capital:** Because of the long shelf-life and relatively low volumes, there is no significant increase in working capital requirements.
- **Placing:** £10.5m (gross)/£9.9m (net) new capital was raised in the Placing in April 2018.
- **Capital increase:** Based on our forecasts, in order to support the commercialisation of products and the clinical trial programme, the company will need to raise more capital during 2019. In addition, DNL is seeking a suitable partner to run its trials with Chronocort, which would have a consequence on the amount of money that needs to be raised.

Cashflow						
Year-end June (£m)	2016	2017	2018	2019E	2020E	2021E
Underlying EBIT	-5.88	-11.56	-16.17	-14.53	-16.05	-14.07
Depreciation	0.01	0.01	0.01	0.01	0.01	0.01
Inventories	0.00	0.00	-0.12	-0.18	-0.27	-0.90
Working capital	0.95	1.09	0.66	-0.74	-0.68	-1.67
Other	-0.62	-0.27	0.00	0.00	0.00	0.00
Company op. cashflow	**-5.55**	**-10.74**	**-15.50**	**-15.26**	**-16.72**	**-15.72**
Net interest	0.04	0.19	0.11	0.00	0.02	-0.05
Tax paid/received	0.49	0.00	2.74	2.28	2.37	2.41
Operational cashflow	**-5.02**	**-10.55**	**-12.66**	**-12.98**	**-14.32**	**-13.37**
Capital expenditure	0.00	-0.02	-0.02	-0.04	-0.05	-0.05
Free cashflow	**-5.02**	**-10.57**	**-12.69**	**-13.05**	**-14.40**	**-13.46**
Dividends	0.00	0.00	0.00	0.00	0.00	0.00
Acquisitions	0.00	0.00	0.00	0.00	0.00	0.00
Disposals	0.00	0.00	0.00	0.00	0.00	0.00
Cashflow after investments	**-5.02**	**-10.57**	**-12.69**	**-13.05**	**-14.40**	**-13.46**
Share repurchases	0.00	0.00	0.00	0.00	0.00	0.00
Share issues	24.52	0.05	13.40	0.00	0.00	0.00
Change in net debt	**20.83**	**-10.51**	**0.91**	**-13.05**	**-14.40**	**-13.46**
Hardman FCF/share (p)	-11.5	-20.2	-23.2	-21.2	-23.2	-21.7
Opening net cash	6.05	26.88	16.37	17.28	4.23	-10.17
Closing net cash	**26.88**	**16.37**	**17.28**	**4.23**	**-10.17**	**-23.64**

Source: Hardman & Co Life Sciences Research

Valuation

Comparative valuation

There are many specialty pharmaceutical companies with diverse product ranges that are reflected in their market capitalisations. For our comparative valuation analysis, a group of quoted specialty pharma companies working in the field of endocrinology – but not working in diabetes/insulin – have been selected, to provide a guide about the relative valuation of Diurnal. This gives an indication of the valuation uplift potential for DNL as it makes further progress in the US.

- **Ascendis:** Trials with TransCon formulation technology to extend the release properties of growth hormone for use in hypoparathyroidism.
- **Corcept:** High valuation is likely due to the fact that it has a product on the market generating sales. Korlym (mifepristone) was launched in 2012 for patients suffering from Cushing's syndrome associated with hyperglycaemia and had sales of $251m in 2018. Corcept is seeking to expand its use into prostate, ovarian and breast cancers, alcohol dependence, and anxiety and stress disorders.
- **Millendo Therapeutics:** The company went public in December 2018, following its merger with OvaScience and focused on novel endocrine diseases. It is currently advancing the development of nevanimibe, a selective inhibitor of acyl-CoA:cholesterol acyltransferase 1 (ACAT1), for the treatment of CAH, as well as endogenous Cushing's syndrome. Nevanimibe completed a Phase II proof-of-concept clinical study in 10 patients with classic CAH, in addition to corticosteroids, to assess its efficacy. Nine patients completed the trial, and one discontinued due to a serious adverse event (enteritis). A Phase IIb study has been initiated, enrolling 20 to 24 CAH patients, with results expected in 1H'20.
- **Viking:** Developing therapeutics for patients suffering from metabolic and endocrine disorders – lead product VK5211 is in Phase II clinical trials.

Comparative valuation

Company	Ascendis	Corcept.	Diurnal	Millendo	Viking
Ticker	ASND	CORT	DNL	MLND	VKTX
Local currency	$	$	£/p	$	$
Share price	107.8	12.0	27.0	15.8	8.8
Shares in issue (m)	42.1	114.7	61.7	13.4	72.0
Market cap. (lc, m)	4,542.2	1,376.7	16.7	211.1	634.9
Market cap. (£m)	3,491.3	1,058.2	16.7	162.2	488.0
Cash (lc, m)	312.6	206.8	6.9	73.3	301.5
Debt (lc, m)	0.0	0.0	0.0	-0.6	0.0
EV (lc, m)	4,229.6	1,169.9	9.8	138.3	333.4
EV (£m)	3,251.1	899.2	9.8	106.3	256.3
Relative EV (x)	**331.8**	**91.8**	**-**	**10.9**	**26.2**
2019E sales (£m)	0.0	251.2	1.1	0.0	0.0
EV/sales (x)	-	4.7	8.6	-	-

lc = local currency
Share prices and currencies taken at close of business on 18 April 2019
Source: Hardman & Co Life Sciences Research

As seen many times before with UK small-cap pharma/biotech companies, US peers trade at much higher valuations and tend to be very well capitalised, allowing these companies to realise their full potential. However, such analysis does provide an indication of upside potential when DNL's products become further de-risked.

Discounted cashflow

The best approach to valuing biopharmaceutical companies is to prepare detailed discounted cashflow (DCF) analyses of key products through to patent expiry, and then to risk-adjust the NPV based upon industry standards for the probability of the product reaching the market.

A tried and tested DCF model…

On the basis that Diurnal's strategy is, predominantly, to be a fully-integrated specialist pharmaceutical company, with its own sales force in key territories, a DCF has been prepared based on the following key assumptions:

…which is based on clearly stated assumptions…

- Alkindi will develop market shares in the EU and US of 20% five years from first launch.
- Chronocort will develop market shares in the EU and US of 20%-25% five years from first launch for both CAH and AI.
- Sales and cashflow forecasts are for the duration of the marketing exclusivity period in each territory, after which generic versions could emerge, eliminating any terminal value – this approach may be considered conservative.
- WACC is at the cost of equity, which is estimated to be 10%.
- The risk adjustment – the probability of the product reaching the market – for Alkindi is 100% in Europe and 80% in the US; for Chronocort, it is 80% for Europe and 40% for the US. The weighted average risk adjustment is 56%.
- No account has been taken of potential future products, e.g. sex hormones.

…and adjusted for the probability of products reaching the market based on industry standards

Diurnal – DCF valuation summary

WACC	NPV (£m)	Risk-adj. NPV (£m)	Risk-adj. NPV per share (p)
8%	310	174	282
9%	277	155	252
10%	**248**	**139**	**225**
11%	222	124	201
12%	198	111	180

Source: Hardman & Co Life Sciences Research

The risk-adjusted NPV of Diurnal is £139m, or 225p per share…

Based on our clearly stated assumptions, the net present value of the cashflows that could be generated from DNL's first two products alone equates to £248m. Risk-adjustment to take account of their different stages of development in different territories reduces this to £139m, or 225p per share.

Conclusion

…suggesting that there is plenty of upside potential for shareholders

Whichever valuation method is used, there appears to be significant upside potential for the stock. However, the current share price remains dogged by the unexpected outcome of the Phase III trial in Europe with Chronocort, despite the fact that the EMA has seen the data, and paved the way for a regulatory submission later this year. The share price also reflects the fact that the company will require more capital in 2019 in the absence of any significant licensing deals. DNL's US competitors, shown in the competitive analysis above, are cash-rich and looking for complementary endocrine products. Therefore, failure of the UK market to recognise the full potential value could see the emergence of a predator.

Company matters

Registration

Incorporated in the UK with company registration number: 05237326.

UK Headquarters:

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Cardiff Medicentre
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Cardiff, CF14 4UJ
UK

+44 29 2068 2069

www.diurnal.co.uk

Board of Directors

Board of Directors

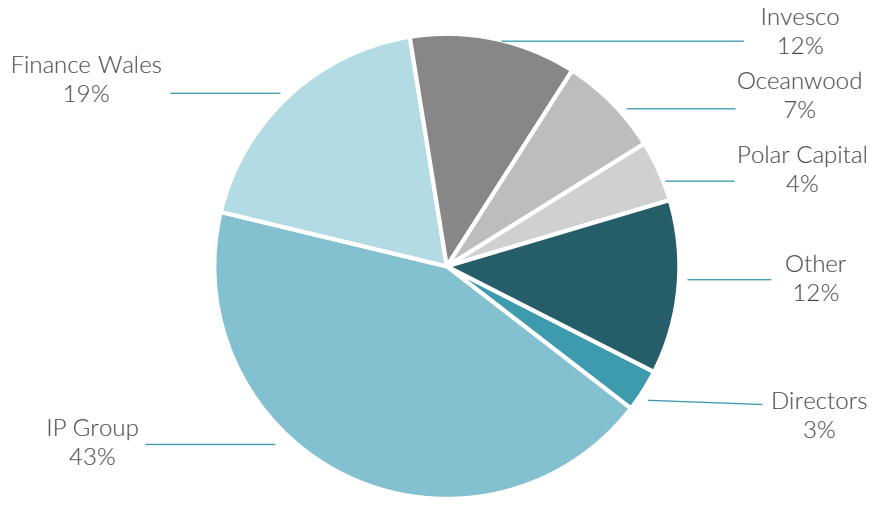
Position	Name	Remuneration	Audit
Chairman	Peter Allen	M	M
Chief Executive Officer	Martin Whitaker		
Chief Financial Officer	Richard Bungay		
Chief Scientific Officer	Richard Ross		
Non-executive director	John Goddard	M	C
Non-executive director	Alan Raymond	C	
Non-executive director	Sam Williams	M	M

M = member, C = chair
Source: Company reports

Share capital

On 17 April 2019, there were 61,710,858 Ordinary shares of 5p in issue.

Shareholders



Source: Hardman & Co Life Sciences Research

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