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Diurnal Group

Commercial and development progresses

Diurnal is a clinical stage specialty pharmaceutical company focused on diseases of the endocrine system. Its two lead candidates are targeted at rare diseases with unmet medical need, with the aim of building a long-term 'Adrenal Franchise'. Following successful completion of a Phase III trial, Infacort has been submitted to the European regulator for approval. Meanwhile, management is establishing the appropriate commercial infrastructure in preparation for launch in 2018. Trials with Chronocort for adults are continuing in Europe. Additional trials are required for approval of both products in the US, which are due to commence in 2H'17.

- **Strategy**: Diurnal's strategic goal is to create a valuable 'Adrenal Franchise' that can treat patients with chronic cortisol deficiency diseases from birth through to old age. Once Infacort and Chronocort are established in EU and the US, the long-term vision is to expand the product offering to other related conditions.

- **Interims:** Reported operating losses of -£5.7m (-£3.5m) largely reflect the increased investment in R&D. This fell through the cashflow statement leaving the company with net cash at the end of December of £22.3m, which was slightly better than forecast.

- **Commercialisation plans:** Ahead of regulatory approval by the EMA for Infacort, management had started to establish the relevant commercial infrastructure with the appointment of key global marketing support in Europe and Israel. Infacort will also be made available ahead of approval on a 'Named Patient' basis.

- **Risks:** There is a risk with all drugs in development that they might fail clinical trials or not be approved by the regulators. However, Diurnal is unusually low risk because its products are formulation variants of well-established drugs. Moreover, the PUMA dossier has been accepted for assessment by the EMA.

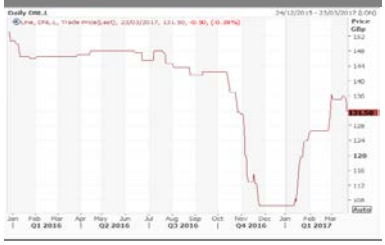
- **Investment summary:** Diurnal is focusing on diseases of the endocrine system. Infacort, a cortisol replacement therapy designed for children and babies, is the first product Diurnal will bring to the market. It will be followed by Chronocort for adults. The cortisol replacement market is for conditions that need life-long treatments, and has a potential value of $3.5bn.

Financial summary and valuation

Year end June (£m)	*2014	*2015	2016	2017E	2018E	2019E
Sales	0.00	0.00	0.00	0.00	1.04	3.43
SG&A	-0.38	-1.00	-1.99	-5.71	-7.43	-9.19
R&D	-1.21	-2.23	-3.89	-8.94	-9.03	-9.12
EBITDA	-0.93	-2.98	-5.87	-14.64	-15.52	-15.22
Underlying EBIT	-0.94	-2.99	-5.88	-14.65	-15.52	-15.22
Reported EBIT	-0.94	-2.99	-6.99	-15.16	-16.06	-15.79
Underlying PBT	-0.98	-3.02	-5.95	-14.76	-15.71	-15.51
Statutory PBT	-0.98	-3.02	-7.06	-15.27	-16.25	-16.08
Underlying EPS (p)	-3.72	-8.49	-12.48	-26.10	-27.91	-27.50
Statutory EPS (p)	-4.13	-8.72	-15.02	-27.09	-28.94	-28.59
Net (debt)/cash	-0.34	6.05	26.88	13.20	-1.32	-16.29
Capital increases	0.00	9.25	24.52	0.00	0.00	0.00

Source: Hardman & Co Life Sciences Research

Pharmaceuticals & Biotechnology



Source: Eikon Thomson Reuters

Market data

EPIC/TKR	DNL
Price (p)	129
12m High (p)	155
12m Low (p)	105
Shares (m)	52.2
Mkt Cap (£m)	67.4
EV (£m)	40.5
Free Float*	17%
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. Infacort has been submitted to the European regulator and Chronocort is in Phase III trials. Further development of the pipeline is on going

Company information

CEO	Martin Whitaker
CFO	Richard Bungay
Chairman	Peter Allen
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	www.diurnal.co.uk

Key shareholders

Directors	3.3%
IP Group	45.6%
Finance Wales	22.1%
Invesco	12.5%
Oceanwood Capital	6.7%
Sarum Investment	2.4%

Diary

Jun-17	FY-17
4Q-17	Infacort MA expected

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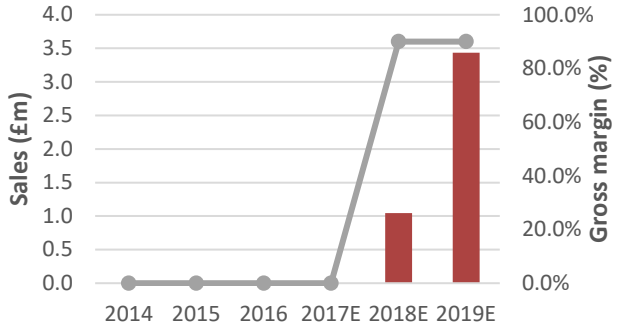
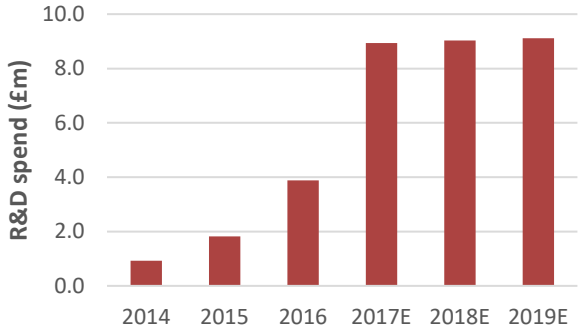
Sales & Gross margin



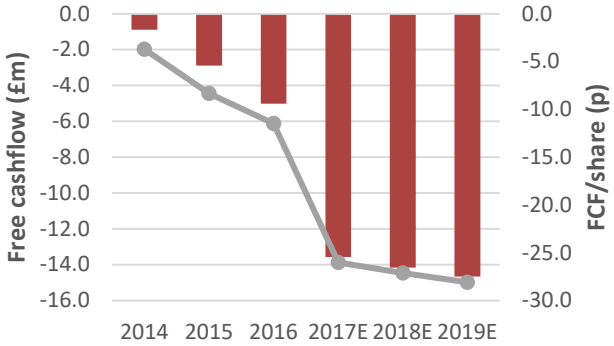
- First sales anticipated for Infacort in 2018
- Initial sales in Europe, and Israel thereafter

R&D investment



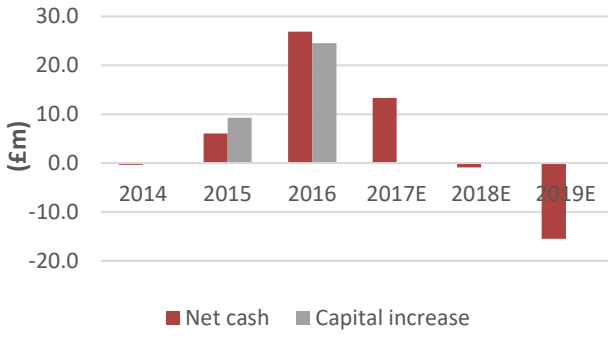
- Delay in recruitment for the Phase III with Chronocort impact R&D costs
- Modest investment for the oral testosterone proof-of-concept trial

Free cashflow



- The cashflow is driven by the R&D investment and corporate overhead
- Marketing activities in Europe ahead of regulatory approval for Infacort

Net cash/capital increases



- At 31st December 2016, net cash was £22.3m
- Cash will be impacted by the delay in recruiting for Phase III trial
- Further cash will be required for commercialisation of Infacort and Chronocort in Europe and the development programme for the US

Source: Company data; Hardman & Co Life Sciences Research

Interim results summary

The interim results for fiscal 2017 reinforced the goals set out at the time of Diurnal's IPO in December 2015. At that time, the company raised £30m (gross) funds to bring Infacort and Chronocort to commercialisation in Europe and start the relevant trials for the US. These results demonstrate that management is on-track to achieve these goals.

Operational highlights

- **Infacort:** Following successful completion of the Phase III registration trial in Europe, Infacort was submitted to the EMA for market authorisation and validated on schedule in December 2016, with first sales expected in 1Q 2018
- **Chronocort:** Enrolment into the European Phase III Chronocort trial for CAH has surpassed 50%, albeit the rate of recruitment was slower than anticipated. The rate has picked up following the addition of more centres, but launch is now expected in 2019 (from 2018)
- **US trials:** Following constructive discussions with the FDA, Diurnal expects to start the Phase III programmes for both Infacort and Chronocort on schedule later in once full trial protocols have been accepted by the regulator following submission in mid-year
- **Native oral testosterone:** A new trial has commenced, with first patient dosed, in the target patient population males suffering from hypogonadism

Commercial highlights

- Appointment of Ashfield, part of UDG group (UDG.L), a leading global organisation for sales support and medical infrastructure, for commercialisation of Infacort in Europe
- Appointment of Sharp Packaging Service, also part of UDG group (UDG.L), for its expertise in managing the supply chain
- Partnership with Clinigen (CLIN.L) to make both Infacort and Chronocort available to patients with no other treatment options via a 'Named Patient Access' programme in Europe ahead of formal commercial approval

Financial highlights

- **R&D:** Investment in 1H'17 was slightly lower than forecast at -£3.96m (-£1.82m), reflecting the Phase III trial programme and regulatory costs
- **SG&A:** Addition of key personnel was reflected in SG&A costs of -£1.39m (-£1.55m), the comparator having exceptional costs ahead of the company's IPO
- **Net cash:** At 31st December 2016, net cash on the balance sheet was £0.35m better than expected at £22.25m
- **CFO:** Appointment of Richard Bungay in January 2017

Diurnal interims 2017 – actual vs expectations

Half-year to end Oct (£m)	1H'16 actual	1H'17 actual	growth %	1H'17 forecast	Delta
R&D spend	-1.82	-3.96	+120%	-4.20	+0.24
Administration	-1.55	-1.39	-10%	-1.50	+0.11
Underlying EBIT	**-3.38**	**-5.34**	**+58%**	**-5.70**	**+0.35**
Net cash/(debt)	30.03	22.25		21.90	+0.35

Figures may not add up exactly due to rounding
Source: Diurnal; Hardman & Co Life Sciences Research

Development overview

Progress summary

In the year since IPO, when Diurnal raised £30m gross funds to progress its two lead candidates, Chronocort and Infacort, through to European commercialisation, management has hit all of its key milestones:

Use of proceeds

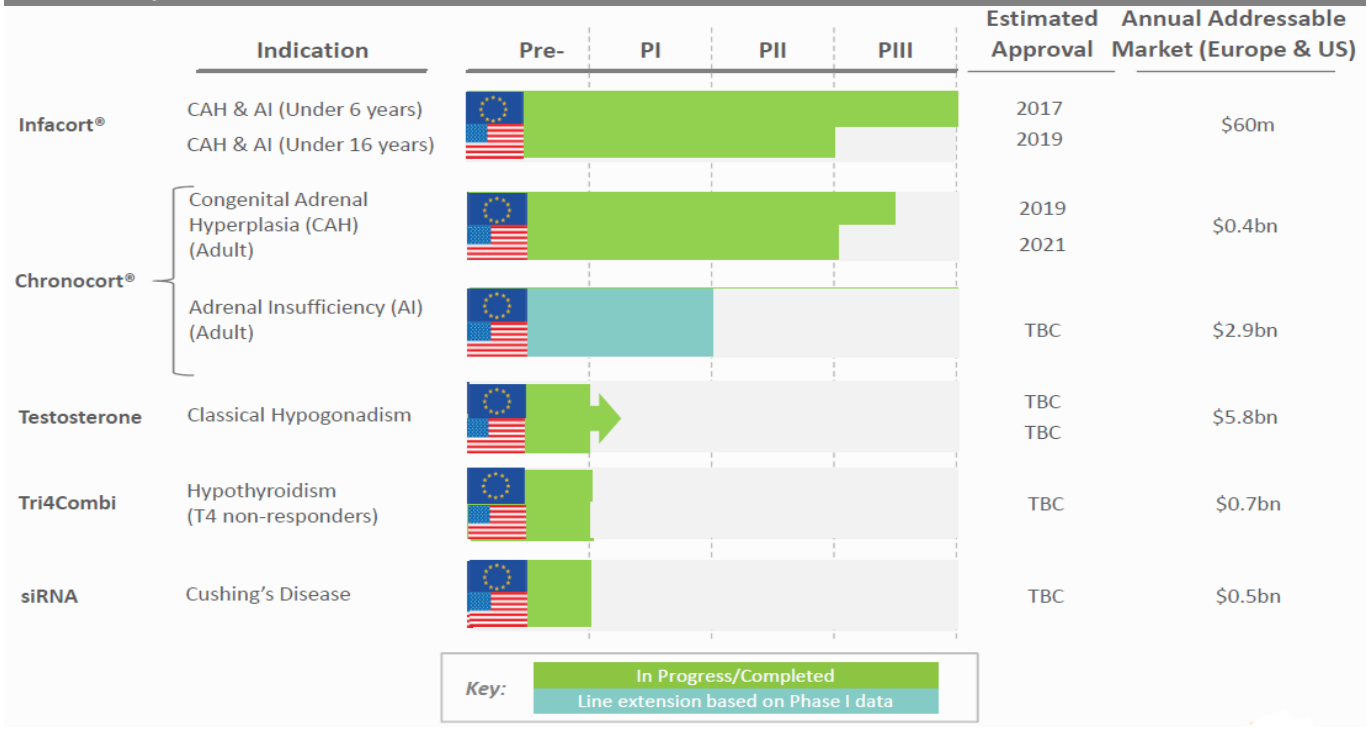
Product	Status	Date
Infacort	► Complete Phase III European registration trial	✓ Completed
	► Submission of PUMA file to EMA	✓ Completed
	► Obtain market authorisation from EMA	Exp.4Q 2017
	► Generate first sales	Exp. 1Q 2018
	► Complete development in the US	Exp. 2Q 2018
Chronocort	► Complete Phase III European registration trial	Exp. 1H 2018
	► Commence development in the US	Exp. 2H 2017
Commercial capability	► Agreements established	✓ In progress

Source: Company reports; Hardman & Co Life Sciences Research

Pipeline

Diurnal has five products in its pipeline, with three in clinical development and two under pre-clinical evaluation. A new biologic reagent has entered the research pipeline for the treatment of Cushing's disease.

Diurnal – Pipeline



Source: Diurnal

Chronocort – Europe

Patients are being recruited into a Phase III registration trial for congenital adrenal hyperplasia (CAH), and to date, over 50% of the 110 patient target have been enrolled. However, the rate of recruitment has been slower than originally anticipated by the CRO due to the intense nature of the trial (four two-day visits over six months) leading to slower scheduling of patients than anticipated. The addition of a further centres into the programme (total: 11 centres in six countries) recently has accelerated the rate of enrolment. However, this has added approximately six months into the overall timetable and recruitment is now expected to be completed during 2H 2017, with the last patient finishing the trial protocol at the end of 1H 2018. The first read out of results should take place about three months thereafter. These changes will increase the trial cost and push back market approval in into 2019 (previously 2018), with first sales now expected in 1H 2020. In addition, Diurnal is undertaking a follow-on study to provide safety data to support the registration and commercialisation programmes.

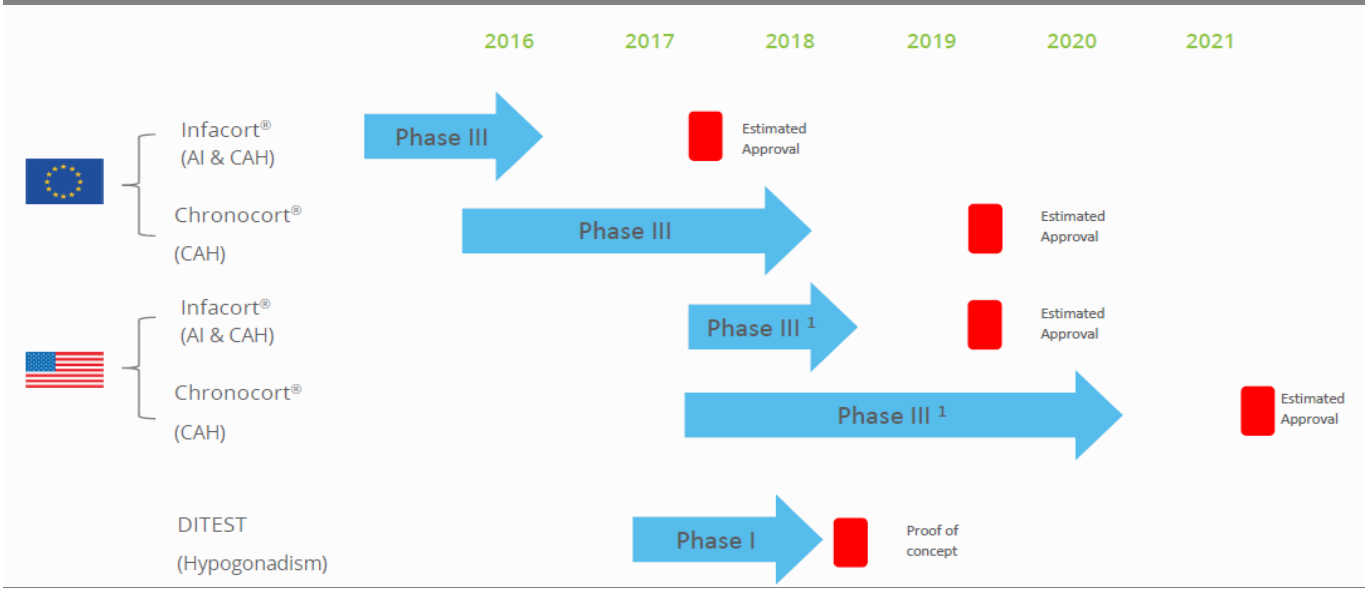
Progress in the US

Diurnal has been in active discussions with the FDA during the last six months to ascertain the requirements for the registration of both Infacort and Chronocort in the US. Due to the differences in the trial design for both products, the FDA will require one additional US efficacy trial for each product. Designs of both trials have already been proposed and full protocols will be submitted around mid-year, allowing the trials to commence in parallel in later in 2017. In addition to the results from these trials, the FDA is expected to take the data from the European trials into consideration.

Native oral testosterone

Diurnal has started a Phase I proof-of-concept trial in Europe with DITEST, a testosterone replacement therapy for hypogonadism. The first patient was enrolled in November 2016. The study will evaluate the absorption of testosterone compared to the standard of care in 24 adult men with primary and secondary hypogonadism. Safety and tolerability will also be assessed and first data are expected in 2H 2017.

Diurnal – Development timetable



[1] *Subject to confirmation from the FDA*

Source: Diurnal

Commercialisation of Infacort

Using a virtual business model, Diurnal outsources most of its activities. Therefore, it is important for management to have everything in place ready for the EMA approval of Infacort, so that sales can take place relative shortly thereafter.

Establishing European supply chain and commercial infrastructure

Diurnal retains the full value of Infacort through direct commercialisation with relevant partners:

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

Both Ashfield and Sharp are part of the UDG Healthcare group (UDG.L), a global provider of outsourced commercialisation services to the pharmaceutical industry.

While the initial focus will be on Infacort, this infrastructure will also be deployed at the appropriate time for Chronocort. In addition, with this in place, Diurnal become a more attractive partner for companies with drugs in the endocrine field looking to out-licence for commercialisation in Europe.

Patient access programme

In March 2016, Diurnal has announced a partnership with IDIS Managed Access, a division of Clinigen (CLIN.L) to launch Infacort and Chronocort via a Patient Access programme in Europe, ahead of marketing authorisation. Clinigen is a global leader in providing unlicensed products to patients on a Named Patient basis. The programme will enable physicians to have access to Infacort and Chronocort in situations where there are no other treatment options for cortisol replacement.

Although no decisions have been made on Infacort pricing, our forecasts assume that Diurnal will use Plenadren, a once daily formulation of hydrocortisone from Shire (SHP.L) as a benchmark ($7,000 p.a.). Because Diurnal is allowed to cover manufacturing and distribution costs, the Named Patient price is likely to be at a premium.

Distribution agreement in Israel

In March 2016, Diurnal also expanded its commercial activity with the marketing and distribution agreement with Medison, to make Infacort available in Israel. The deal will also cover Chronocort when it becomes available. The market authorisation submission in Israel will be based on the EMA approval package. 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.

Israel is considered to be a substantial market for Diurnal products given the higher proportion of the population affected by CAH and with an estimated population of 1,000 paediatric patients affected by adrenal insufficiency AI and congenital adrenal hyperplasia CAH, providing potential sales of up to $7m per annum.

Financial summary

- **SG&A** – In the run up to launch of Infacort in Europe, investment is being made in marketing infrastructure, primarily through a small sales force
- **R&D** – The delay in recruitment for the Chronocort Phase III trial has a modest impact on the timing and size of R&D cost
- **Net cash** – At 31st December 2016, Diurnal had a net cash of £22.25m on its balance sheet
- Based on our forecasts, the Company has sufficient cash to take Infacort to the market

Financial overview

Year end June (£m)	*2014	*2015	2016	2017E	2018E	2019E
Profit & Loss						
Sales	0.00	0.00	0.00	0.00	1.04	3.43
COGS	0.00	0.00	0.00	0.00	-0.10	-0.34
SG&A	-0.38	-1.00	-1.99	-5.71	-7.43	-9.19
R&D	-1.21	-2.23	-3.89	-8.94	-9.03	-9.12
Underlying EBIT	-0.94	-2.99	-5.88	-14.65	-15.52	-15.22
Share based costs	0.00	0.00	-0.49	-0.51	-0.54	-0.57
Exceptional items	0.00	0.00	-0.62	0.00	0.00	0.00
Statutory EBIT	**-0.94**	**-2.99**	**-6.99**	**-15.16**	**-16.06**	**-15.79**
U/L pre-tax profit	-0.98	-3.02	-5.95	-14.76	-15.71	-15.51
Tax liability/credit	0.00	0.00	0.49	1.13	1.14	1.15
Weighted average (m)	**23.76**	**34.61**	**43.75**	**52.21**	**52.21**	**52.21**
Underlying basic EPS (p)	-3.72	-8.49	-12.48	-26.10	-27.91	-27.50
Balance sheet						
Share capital	0.00	0.00	0.00	0.00	0.00	0.00
Reserves	-0.76	-9.31	23.32	9.18	-5.93	-20.86
Loans/Debt	0.02	0.02	0.00	0.00	0.00	0.00
less: Cash	0.72	6.07	30.11	16.70	2.46	-12.21
Invested capital	**0.02**	**-0.01**	**-0.94**	**-1.41**	**-2.00**	**-1.95**
Cashflow						
Trading profit	-0.94	-2.99	-5.88	-14.65	-15.52	-15.22
Working capital	-0.04	0.02	0.95	0.61	0.14	-0.60
Company op cashflow	**-0.98**	**-2.96**	**-5.55**	**-14.03**	**-15.38**	**-15.82**
Capital expenditure	0.00	-0.01	0.00	0.00	0.00	0.00
Free cashflow	**-0.88**	**-2.88**	**-5.02**	**-13.41**	**-14.24**	**-14.67**
Share issues	0.00	9.25	24.52	0.00	0.00	0.00
Change in net debt	**-0.88**	**6.37**	**20.83**	**-13.67**	**-14.52**	**-14.98**
Opening net cash	0.49	-0.34	6.05	26.88	13.20	-1.32
Closing net cash	**-0.34**	**6.05**	**26.88**	**13.20**	**-1.32**	**-16.29**

**Year to July*

Source: Hardman & Co Life Sciences Research

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