EDISON

Diurnal Group

Company update

Efmody launched in the EU and UK

Pharma & biotech

Efmody (also called Chronocort), an oral long-acting formulation of hydrocortisone, has been approved in the EU and UK to treat congenital adrenal hyperplasia (CAH) in individuals aged 12 years and older. The company has started the commercial launch of the product with a rollout in Germany, Austria and the UK at the beginning of September. CAH is an orphan disease caused by deficiency of adrenal enzymes, most commonly 21-hydroxylase. The total addressable EU market is worth $268m based on the price of Plenadren, a long-acting hydrocortisone.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
06/20	6.3	(5.1)	(4.1)	0.0	N/A	N/A
06/21	4.4	(11.1)	(6.6)	0.0	N/A	N/A
06/22e	7.9	(18.2)	(7.3)	0.0	N/A	N/A
06/23e	16.1	(13.2)	(5.1)	0.0	N/A	N/A

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

Diurnal marketing Efmody directly in Europe

Diurnal launched Efmody in the EU (specifically in Germany and Austria) and the UK for CAH. There are an estimated 41,000 patients in the EU/UK. The company is launching the product with its own salesforce and distributors.

SPA to de-risk the US Chronocort pivotal trial

In July, Diurnal reached a Special Protocol Assessment (SPA) agreement with the US FDA, which includes the trial design, endpoints and statistical analyses in the planned pivotal trial CONnECT (which can also be used for registration purposes in Japan). This randomised, double-blind, active-controlled Phase III trial will enrol 150 CAH patients 16 years and over. The treatment period is 12 months. There are an estimated 16,000 patients in the United States. The trial is expected to commence in Q4 CY21.

Alkindi up 18% in core commercial markets

Diurnal's total revenue for FY21 was £4.4m, with Alkindi sales of £2.3m, down slightly from FY20 due to a negative impact from Diurnal's Nordic partner. Proforma sales in the core markets of the UK, Germany, Italy and Austria were up 18% despite the negative impact of the COVID-19 pandemic.

Valuation: £251m or 149p per basic share

We have increased our total valuation to £251m from £230m mainly due to higher net cash and rolling forward our NPV. However, the valuation per share fell from 166p to 149p mainly due to a higher number of shares outstanding, primarily resulting from the £20.7m (gross) capital raise completed in May 2021. Net cash as of 30 June 2021 was £34.0m. Diurnal now has a clear cash runway to complete Efmody development in the United States and commercialise Efmody in the EU/UK.

29 September 2021

Price	**56.2p**
Market cap	**£95m**
	US$1.39/£
Net cash (£m) at 30 June 2021	34
Shares in issue	168.9m
Free float	68.1%
Code	DNL
Primary exchange	LSE
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(6.2)	(12.6)	(22.9)
Rel (local)	(4.2)	(12.6)	(36.8)
52-week high/low		89p	48p

Business description

Diurnal Group is a specialty pharma company developing new formulations of hormone-based products for the treatment of endocrine disorders. Its product Alkindi is marketed for paediatric (AI) in the US and EU. Efmody is approved for the treatment of CAH in the EU and UK.

Next events

Chronocort pivotal trial initiation	Q4 CY21

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Edison profile page

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Two approved products and a promising pipeline

Diurnal is an emerging endocrine company that has improved formulations of hydrocortisone in both Alkindi and Efmody with unique characteristics that can provide the patient with convenient dosing and improved efficacy. Its second product Efmody (an extended-release formulation of hydrocortisone) was recently approved in patients with CAH in the EU and UK, and subsequently launched in the UK and certain EU countries (namely Germany and Austria) in the first half of September. CAH is an orphan condition that is caused by enzyme deficiencies, most commonly 21-hydroxylase, which is an enzyme needed to produce the adrenal steroid hormone cortisol. Without cortisol, an over production of male hormones (androgens) occurs. This condition is inherited at birth and affects both males and females. Diurnal plans to begin a Phase III trial in the United States in Q4 CY21. Efmody has orphan disease designation for CAH in the United States, which provides seven years of market exclusivity.

The company's first launched product is Alkindi, a formulation of hydrocortisone intended to treat adrenal insufficiency (AI) in paediatric patients. Before its approval in the EU in 2018 and the United States in 2020, there were no hydrocortisone products provided in paediatric doses. Additional formulation improvements in the product include it being provided in a sprinkle format, which eases administration in children and has a taste masking layer. Eton Pharmaceuticals is the partner in the United States. Alkindi was approved by the FDA in September 2020 and marketing began in November 2020. Eton has not reported actual sales numbers yet.

The company's third product candidate is DITEST, a novel oral formulation of testosterone for the treatment of hypogonadism. It is thought that two-thirds of patients have poor control on current treatments. Testosterone products are usually topically applied since oral formulations have been difficult to develop. DITEST has completed Phase I trials in the UK. The company intends to file an IND in H221 and initiate a multiple ascending dose (MAD) study shortly thereafter in the United States. Diurnal has secured an abbreviated 505(b)(2) route to a new drug application (NDA). This pathway is for products where the active pharmaceutical ingredient (in this case testosterone) has already been approved and allows the sponsor to use data from these previous applications in its clinical data package.

Exhibit 1: Diurnal's pipeline and addressable markets

Product	Drug	Indication	Status EU	Status US	Annual addressable market EU & US ($m)
Alkindi/Alkindi Sprinkle	Hydrocortisone	Paediatric AI	Approved 2018	Approved 2020	514
Chronocort/Efmody	Controlled release hydrocortisone	CAH	Approved 2021	Phase III ready	2,767
		AI	Pivotal study ready	Phase II	
DITEST	Testosterone	Hypogonadism	Phase I complete	Phase I complete	4,830
Not named	T3 modified release	Hypothyroidism	Preclinical	Preclinical	1,000
Not named	Oligonucleotide	Cushing's Disease	Preclinical	Preclinical	480

Source: Diurnal, Edison Investment Research

Plans for Efmody commercialisation

On 28 May, Diurnal received approval from the European Commission (EC) for Efmody, which treats adult and adolescent patients with CAH. The company is launching the product with its own salesforce and distributors.

In July 2021, Efmody received marketing approval in the UK for the treatment of CAH patients 12 years and older. The countries of England, Scotland and Wales are estimated to have approximately 5,000 CAH patients. After discussion with the UK Medicines and Healthcare Products Regulatory Agency (MHRA), Diurnal decided not to pursue orphan drug status for Efmody in the UK since it would probably delay the launch. This was consistent with the approach Diurnal took in the European Economic Area. Orphan drug designation would normally give 10 years of market exclusivity, but Diurnal believes its current patents will provide protection until at least 2033 in the UK.

In May, Diurnal expanded its existing partnership with China-based Citrine Medicine to also include Efmody. Diurnal received an upfront payment of $1.0m and would be entitled to receive $28.75m in additional cash payments when certain Efmody regulatory milestones and sales milestones based on annual sales thresholds are met. Citrine now has rights for Alkindi and Efmody in China, Hong Kong, Taiwan and Macau. Citrine plans to file an NDA with the National Medical Products Administration in H221 for Alkindi. It is estimated that CAH occurs in one in 6,084 births in China. In June, Diurnal received an additional $1.25m payment from Citrine as a result of the EC's approval of Efmody and certain milestones achieved by Citrine in China for Alkindi.

In June, Diurnal expanded its partnership with Er-Kim to market both Alkindi and Efmody in Romania and Bulgaria. The estimated combined market opportunity is over $13m. Diurnal signed the original agreement, which was for Turkey, in January.

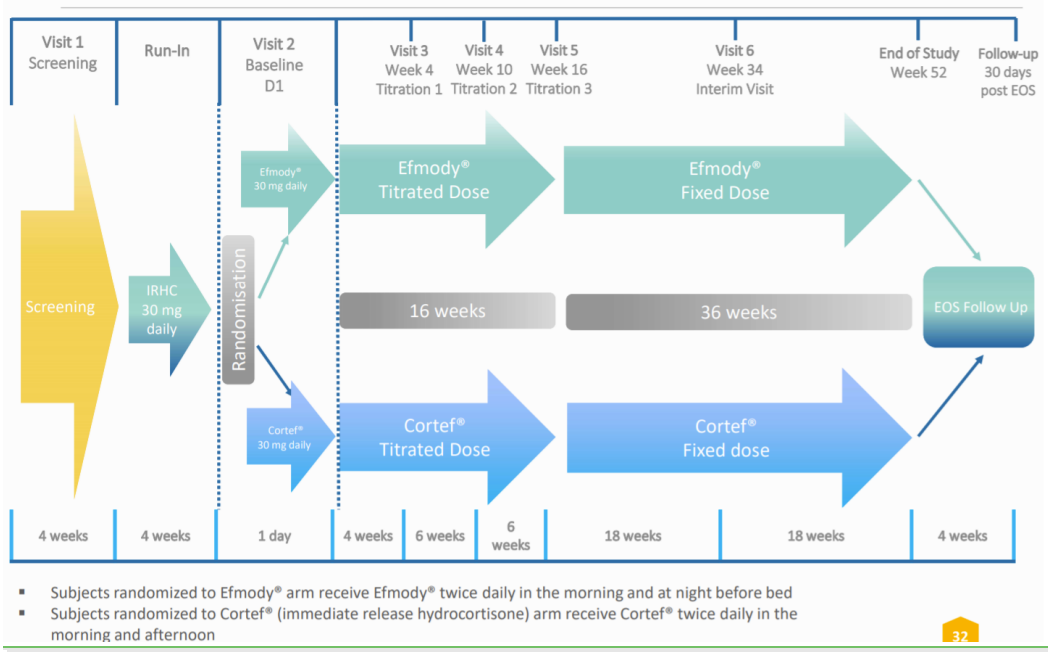
In January, Diurnal teamed up with Consilient Health to distribute Efmody in the Nordic region, which includes Sweden, Norway, Denmark, Finland and Iceland. This region has approximately 2,300 individuals with CAH and Diurnal estimates it to be worth €11.5m annually. In September 2020, Diurnal signed a deal with Consilient Health to market Alkindi and Efmody in the Benelux Union (the Netherlands, Belgium and Luxemburg).

US CONnECT Efmody trial to begin in calendar Q421

The SPA agreement with the FDA was announced in July 2021. The SPA determines that the trial design adequately meets objectives that would support a US regulatory filing. The pivotal study is called 'A randomised, double-blind, active-controlled, Phase 3 study of Chronocort compared with immediate-release hydrocortisone replacement therapy in participants aged 16-years and over with CAH (CONnECT)'. Study start-up activities have already begun, since the study is planned to start in the fourth quarter of calendar 2021. The trial design is pictured below. It will enrol up to 150 patients with CAH, who will be treated for 52 weeks.

The study design is a bit complex. There is four weeks of screening followed by a four-week run-in period in which patients switch to immediate release hydrocortisone (IRHC) 30mg daily prior to beginning the double-blind, placebo-controlled, 12-month treatment. The proposed primary endpoint is biochemical responder non-inferiority of Efmody twice-daily versus twice daily immediate release hydrocortisone after 52 weeks of randomised treatment. The company has estimated that the trial could be completed in 2023, with an NDA filing in 2024. We have similar timelines in our model. We will monitor the CONnECT trial as it proceeds to see if enrolment is in line with our estimates.

Exhibit 2: US pivotal trial schema



Source: Diurnal

Diurnal also plans to conduct a head-to-head Phase II study in Europe comparing Efmody to Plenadren to seek to demonstrate superiority in order to potentially get a line extension to AI in adults. Plenadren is a modified release hydrocortisone; however, it does not mimic the circadian rhythm and is not approved for CAH. Plenadren is approved in Europe for AI in patients over 18 years old. The trial is expected to commence in Q4 CY21.

Valuation

We have increased our total valuation to £251m from £230m mainly due to higher net cash and rolling forward our NPV. However, the valuation per share fell from 166p to 149p mainly due to a higher number of shares outstanding following a £20.7m (gross) offering that was completed in May.

Exhibit 3: Diurnal valuation

Product	Indication	Geography	Clinical stage	Prob. of success	Launch year	Peak sales ($m)	rNPV (£m)
Alkindi	Paediatric AI	Europe	Approved	100%	2018	16	7.63
		US	Approved	100%	2020	10	4.93
Chronocort	Adult CAH	Europe	Approved	100%	2021	63	93.52
		US	Phase III	50%	2024	84	31.02
	Adult AI	Europe	Pivotal study	50%	2023	131	47.04
		US	Phase II	30%	2026	150	21.38
Ditest	Hypogonadism	US	Phase II	25%	2025	70	11.38
Total							216.89
Net cash and deposits (as of 30 June 2021) (£m)							34.04
Total firm value (£m)							250.93
Total basic shares (m)							168.90
Value per basic share (p)							149
Dilutive options (m)							4.83
Total diluted shares (m)							173.73
Value per diluted share (p)							145

Source: Edison Investment Research

Exhibit 4 highlights milestones that we believe will drive the valuation of Diurnal over the rest of CY21. We believe the most significant is the execution of the Efmody launch in the in the EU and the initiation of the Efmody CONnECT trial in the United States.

Exhibit 4: Diurnal 2021 milestones

Outlook	
Approval of Efmody in European Economic Area	Done
Conclude Efmody SPA in US	Done
First commercial launch of Efmody in Europe	Done
Submission of DITEST IND in US	
Begin Efmody/Plenadren comparative trial	
Start DITEST multiple ascending dose study in the US	
Start Efmody Phase III study in the US	

Source: Diurnal, Edison Investment Research

Financials

Diurnal recently reported FY21 results, which featured revenues of £4.4m, down from £6.3m in FY20 primarily due to a fall in licensing income from £3.9m in FY20 to £2.1m in FY21. The licensing figure for FY20 included a $5m upfront payment from Eton Pharmaceuticals. The company's operating loss increased to £11.6m from £5.4m due to the fall in revenues, increased investment in clinical development and Efmody launch preparations.

Net cash as of 30 June 2021 was £34.0m. The company completed an offering in May in which Diurnal issued 29.6m shares at a price of 70p and raised approximately £20.7m (gross). The funds will be used to fund the Efmody pivotal trials in the United States through to registration for the CAH indication. In addition, some of the funds may be used to support the earlier stage pipeline. In July an additional 973,682 shares at a price of 5p were issued to management, which brings the total shares outstanding to 168.9m.

The company now has a clear cash runway to commercialise Efmody in the EU/UK and conduct the CONnECT trial in the United States, and it expects the cash on hand to last to profitability in 2024.

We still forecast a raise of £25m (modelled as illustrative debt) in FY22 prior to our forecast of profitability in 2024. The size of the offering is hard to predict due to possible licensing and/or partnerships. We think the raise will be necessary to advance the pipeline.

Exhibit 5: Financial summary

£'k	2020	2021	2022e	2023e
Year end 30 June	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Sales	2390	2267	7802	15856
Royalties & Milestones	3923	2104	137	208
Revenue	6,313	4,371	7,939	16,064
Cost of Sales	(668)	(779)	(720)	(951)
Gross Profit	5,645	3,592	7,219	15,113
EBITDA	(5,151)	(11,125)	(18,225)	(13,172)
Normalised operating profit	(5,176)	(11,149)	(18,249)	(13,196)
Amortisation of acquired intangibles	0	0	0	0
Exceptionals	627	15	0	0
Share-based payments	(843)	(466)	(466)	(466)
Reported operating profit	(5,392)	(11,600)	(18,715)	(13,662)
Net Interest	114	62	62	62
Joint ventures & associates (post tax)	0	0	0	0
Exceptionals	0	0	0	0
Profit Before Tax (norm)	(5,062)	(11,087)	(18,187)	(13,134)
Profit Before Tax (reported)	(5,278)	(11,538)	(18,653)	(13,600)
Reported tax	1,206	1,489	3,497	2,549
Profit After Tax (norm)	(3,905)	(9,009)	(14,777)	(10,672)
Profit After Tax (reported)	(4,072)	(10,049)	(15,156)	(11,050)
Minority interests	0	0	0	0
Discontinued operations	0	0	0	0
Net income (normalised)	(3,905)	(9,009)	(14,776)	(10,671)
Net income (reported)	(4,072)	(10,049)	(15,156)	(11,050)
Basic average number of shares outstanding (m)	95	137	203	209
EPS - basic normalised (p)	(4.1)	(6.6)	(7.3)	(5.1)
EPS - diluted normalised (p)	(4.1)	(6.6)	(7.3)	(5.1)
EPS - basic reported (p)	(4.3)	(7.3)	(7.5)	(5.3)
Dividend (p)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	1,770	240	240	240
Intangible Assets	79	92	92	92
Tangible Assets	23	148	148	148
Investments & other	1,668	0	0	0
Current Assets	19,206	41,550	51,998	41,919
Stocks	1,241	1,625	1,801	2,377
Debtors	1,337	3,433	1,958	3,961
Cash & cash equivalents	15,434	34,037	45,785	33,126
Other	1,194	2,455	2,455	2,455
Current Liabilities	(2,555)	(4,163)	(4,301)	(4,806)
Creditors	(2,555)	(4,163)	(4,301)	(4,806)
Tax and social security	0	0	0	0
Short term borrowings	0	0	0	0
Other	0	0	0	0
Long Term Liabilities	(36)	(63)	(25,063)	(25,063)
Long term borrowings	0	0	(25,000)	(25,000)
Other long term liabilities	(36)	(63)	(63)	(63)
Net Assets	18,385	37,564	22,874	12,290
Minority interests	0	0	0	0
Shareholders' equity	18,385	37,564	22,874	12,290
CASH FLOW				
Op Cash Flow before WC and tax	(5,151)	(11,125)	(18,225)	(13,172)
Working capital	(380)	(845)	1,438	(2,074)
Exceptional & other	(1,398)	109	0	0
Tax	2,120	1,199	3,497	2,549
Net operating cash flow	(4,809)	(10,662)	(13,290)	(12,696)
Capex	(45)	(163)	(24)	(24)
Acquisitions/disposals	0	0	0	0
Net interest	114	62	62	62
Equity financing	10,670	28,762	0	0
Dividends	0	0	0	0
Other	0	713	0	0
Net Cash Flow	5,930	18,712	(13,252)	(12,658)
Opening net debt/(cash)	(9,147)	(15,434)	(34,037)	(20,785)
FX	357	(109)	0	0
Other non-cash movements	0	0	0	0
Closing net debt/(cash)	(15,434)	(34,037)	(20,785)	(8,126)

Source: company reports, Edison Investment Research

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