Diurnal Group

26 March 2021

Back on track

Share Price	**88p**
CP Fair Value	**241p**
Market Cap (£m)	122
Net Cash (£m)	20
Enterprise Value (£m)	102
Country	UK
Code	DNL
Index	FTSE AIM

Source: Calvine Partners Research

The recommendation for Efmody (formerly Chronocort) approval by the EMA for the treatment of the inherited Orphan disorder congenital adrenal hyperplasia (CAH) in patients aged 12 and over should be transformational for Diurnal. With an endocrinology-based salesforce already in place in major European markets, Efmody should deliver significant scale and operating leverage. Additionally, we believe this removes a key uncertainty that has overshadowed the investment case for Diurnal and puts the company back on track with its initial ambitions to create an endocrinology franchise, starting with low cortisol disorders.

Pipeline potential

Following formal approval, we believe that Efmody offers the optimal cortisol replacement therapy, successfully delivering normal physiological levels and mimicking the body's circadian delivery. As a result, Efmody successfully reduces the overnight build-up of male sex hormones (androgens), which has blighted the lives of (particularly female) CAH sufferers. Importantly, in many patients, Efmody can do this using normal replacement glucocorticoid levels and allows patients to benefit from a better balance between hyperandrogenism and hypercortisolism. We believe this to be a major treatment advance for patients who have previously required supraphysiological levels of glucocorticoid to reduce high androgen levels.

Opening up the US and the larger AI indication

The approval of Efmody in Europe also provides access to the more significant adrenal insufficiency (AI) opportunity where patients also suffer from low cortisol levels. In Europe, the regulatory pathway appears straightforward, with Diurnal conducting a comparator study with Plenadren for optimal positioning. In the US, awareness of CAH has grown with increased drug development activity (the CRF-1 inhibitors). We look forward to the receipt of a Special Protocol Assessment by Diurnal as it seeks to confirm the US regulatory pathway for Efmody. Additionally, the bigger AI opportunity also looms large in the US as well as Europe. The US cortisol deficiency market represents a potentially lucrative opportunity for Diurnal, and one that we have previously suggested would be tractable to a small specialised sales force to capitalise effectively on this Orphan (CAH) opportunity. We have revisited our financial forecasts and valuation post the news and have increased the probability of the US CAH opportunity as well as the European and US AI indications. Further, we have reduced the discount rate in our DCF from 20% to a still conservative 15% which generates our fair value of 241p per share.

Dr Brian White
Partner
bw@calvinepartners.com

Andrew Keith
Partner
ak@calvinepartners.com

Diurnal well prepared for key launch

Pre-launch activities underway

At the recent results update, Diurnal provided additional detail on its preparedness for the approval of Efmody. Pre-launch activities in Europe have already begun with market access activities underway and launch stocks manufactured.

The approval of Efmody represents the culmination of Diurnal's ambitions to create a European adrenal franchise (we await the outcome of the UK's deliberations). Although Diurnal's child-friendly hydrocortisone preparation Alkindi is already marketed, market potential is modest particularly relative to Efmody. That said, one of the key objectives with Alkindi was to provide a commercial platform (in Europe and the US) ahead of the approval of Efmody.

Existing infrastructure and the small number of specialist centres should help expedite launch

Europe represents a relatively straightforward commercial opportunity for Diurnal, thanks not only to the existing infrastructure but also because there a limited number of key centres that treat CAH patients. Ultimately, the addition of Efmody should facilitate chronic treatment for patients suffering from low cortisol levels. Given the length of time that Alkindi has been in the main European markets, the salesforce should have gained a significant degree of familiarity with the endocrinology specialist physician community.

Consequently, Diurnal should be well placed to offer an appropriate treatment for those Alkindi patients (aged 12 and over) transitioning through puberty and those currently receiving less effective hydrocortisone preparation. In addition to benefiting patients and physicians, the addition of a high-value product like Efmody should deliver substantial operating leverage to Diurnal's European operations.

Important implications for rest of adrenal franchise aspirations

As Diurnal seeks to build on its adrenal franchise in Europe, a successful regulatory outcome for Efmody in CAH has important implications for the larger adrenal insufficiency indication. As a line extension, we anticipate clinical development should be relatively straightforward. The last remaining clinical hurdle comprises a comparator study versus an existing (outside the US) alternative modified-release hydrocortisone (Plenadren). The study which will start later in 2021 should allow the company to position Efmody optimally in the AI indication in Europe.

US adrenal opportunity a key focus now

US awareness of CAH rising

With Neurocrine and Spruce Biosciences developing the CRF1 inhibitors crinecerfont and tildacerfont respectively, awareness of the CAH patient and the need for new therapies, which could potentially transform treatment, has grown substantially.

Targeting CRF1 aims to lower the high androgen levels that results from the body's efforts to produce more cortisol precursors to address low/no cortisol. Presently, CAH patients use supraphysiological levels to reduce previously high androgen levels. Ultimately the treatment of CAH requires a fine balance between too

much androgen (hyperandrogenism) and too much cortisol (hypercortisolism). Simplistically, too much androgen is clearly much more of a problem for pre-pubescent females and less so for adult men.

Remains a challenging disorder for physicians

Further complicating matters is the heterogeneous nature of the disorder with significant inter and intra-patient variability depending on the nature of the mutation, with respect to the amount of cortisol produced and consequently, the need for tailored treatment approaches. In practise, patients can receive various different glucocorticoid preparations depending on the severity of the disorder.

The main opportunity for the CRF1 approach, as we see it, is for those patients who struggle to control their androgens with standard glucocorticoid therapy. We note for example that Spruce Biosciences is pursuing two patient populations (poorly and well-controlled), endeavouring to demonstrate that they can reduce the requirement for supraphysiological glucocorticoid treatment as well as reduce androgens generally.

We view Efmody and CRF-1 inhibitors as complementary

We view this as a complementary approach noting (from the recent JCEM publication) that many patients receiving Efmody are well controlled on adrenal replacement doses (during the extension study). Importantly, this reduction in glucocortocoid dose to adrenal replacement levels was associated with improvements in important patient outcomes including menstrual regularity as well as improved fertility (in both males and females).

We believe that Diurnal has already established the appeal of Efmody

Given the continued requirement for glucocorticoid replacement therapy, even if the CRF1 approach proves fruitful, we believe that the benefits of circadian delivery should result in Efmody becoming the preferred glucocorticoid treatment option in the CAH indication. This, coupled with the observation that control of overnight androgens can also be achieved with adrenal replacement doses, further re-enforces the appeal of using Efmody for treating physicians, we believe.

Undoubtedly, the intensifying competitive environment in the US has led to an increased awareness of CAH as an unmet medical need. CAH represents an Orphan indication with newborns identified through neonatal screening and while there is a risk of adult patients being lost to treatment, we suspect that this was more due to the undesirable effects of treatment with supraphysiological levels of glucocorticoid at a time (post-puberty) when high androgen levels are less of a concern.

Receipt of an SPA should help expedite US development

However, should Efmody successfully navigate the US regulatory system (confirmation of a Special Protocol Assessment would clearly be helpful), then its availability could address many of these patient concerns. Consequently, given the heightened awareness and the significant market potential, the US CAH market remains a potentially very lucrative opportunity and one that resource permitting should be tractable to a small endocrinology focussed sales force.

Risks

The principal risks associated with Diurnal are largely clinical and commercial in nature. Clinical trials of novel drugs can be associated with risk of failure and we note that the recent COVID-19 pandemic has resulted in delays to enrolment in clinical trials in general.

Diurnal has retained European rights to its adrenal disorder franchise, which brings commercialisation risks. We note that Diurnal has engaged the services of Ashfield, which has a successful track record in helping life science companies launch new products. Nevertheless, the pace of uptake is difficult to predict which could affect out forecasts although we recognise that market expectations for Alkindi are modest. Following Efmody launch in Europe our expectation is that Diurnal will benefit from the existing sales platform, with only incremental costs required to effect a successful launch.

Following Efmody commercialisation in Europe, we note that Diurnal is seeking to launch its products into what is largely a generic market environment. We have assumed a price for Efmody that is consistent with the European price of Plenadren – a once daily formulation of hydrocortisone which looks to be a reasonable proxy. We note that in this regard there is no equivalent product in the US. Should Diurnal choose to self develop Efmody in the US we look forward to the receipt of a Special Protocol Assessment to reduce the risk associated with this programme.

With Diurnal looking to partner several of its products in the US, including DITEST, there is an associated partnering risk.

As a development stage company, Diurnal is currently a loss making enterprise. Diurnal has successfully raised funds to continue with its development plans and aid the launch of Alkindi in Europe. Even with this near-term funding, our forecasts suggest that in order to progress its pipeline assets expeditiously, Diurnal may require additional funding.

Financial Model and Summary

Revisited our risk-adjusted revenue forecasts

The approval of Efmody in Europe has allowed us to revisit our risk-adjusted revenue forecasts for the adrenal franchise. Previously our forecasts carried a 75% probability of approval for the CAH indication in Europe which we have now moved to 100%. Sticking with Europe, we have also adjusted our probability of success for Efmody in the AI indication moving it from 50% to 75%. This may seem churlish given the straightforward regulatory pathway, but we also recognise the lingering risk in any clinical development pathway and look forward to the results of the comparator study with Plenadren.

US prospects for Efmody should become clearer shortly

The US potentially offers a large and lucrative market opportunity for Diurnal, not just for its adrenal franchise but also for its overall endocrinology ambitions. While Alkindi has been licensed to Eton Pharmaceuticals (a highly appropriate partner), Efmody offers a different proposition initially in the adult CAH population. Diurnal is awaiting the receipt of a Special Protocol Assessment which should deliver a confirmed clinical trial protocol. Consequently, if a positive result is delivered, there should be a high probability of approval.

Without seeing details of the Phase 3 trial design, it is difficult to judge how relevant a positive European approval is to the potential US study outcome, but we have previously commented but with the learnings of the failed European Phase 3 trial, we would expect Diurnal to be in a much better position to devise a clinical trial protocol which best delivers the benefits associated with Efmody in the CAH population. As a result, we have moved our probability of approval from 50% to 75%.

Retention of US Efmody development would result in Diurnal receiving full margin

The AI indication in the US will require a separate clinical programme and we note that Diurnal is suggesting a Phase II study beginning in 2022. Should Diurnal choose to retain commercial rights to Efmody in the US market, the company would retain the full margin and deliver further operating leverage to the US CAH business. We have employed the same 75% probability (from 50%) as the CAH indication.

Looking forward to significant operational leverage in Europe post Efmody launch

One of the most important aspects of the European Efmody approval is the potential to capitalise on the existing endocrinology sales platform now well established in several major European markets. Given it usually takes 12 months+ to gain reimbursement throughout Europe, the platform should be well prepared for an expeditious launch post approval. Targeting the appropriate endocrinologists in Europe should be a straightforward proposition with the existing platform, and so we look forward to significant operating leverage as the rollout progresses.

With the European adrenal franchise now secured, Diurnal can look forward to focussing on progressing its geographic and pipeline ambitions. We have already highlighted the company's previous US aspirations, recognising the importance of the US pharma market as the last bastion of (mainly) free pricing.

Still potential upside should DITEST progress further

The net effect of these changes has been to increase our revenue expectations for the adrenal franchise at Diurnal. However, we have still to include any contribution from the testosterone replacement therapy DITEST suggesting further upside should data prove positive.

Increase in fair value to 241p

At the same time, we have revisited our thoughts on fair value and believe that the European approval merits a reduction in the discount rate from 20% that we employed previously to a still conservative 15% which provides a fair value of 241p (from 99p previously).

Diurnal Valuation Matrix (£ per share)

	Terminal Growth Rate				
Discount rate	**1%**	**2%**	**3%**	**4%**	**5%**
10.0%	3.20	3.56	4.03	4.65	5.51
12.5%	2.53	2.75	3.02	3.35	3.76
15.0%	2.08	2.23	2.41	2.61	2.86
17.5%	1.76	1.87	1.99	2.14	2.30
20.0%	1.52	1.60	1.70	1.80	1.92
22.5%	1.33	1.40	1.47	1.55	1.64
25.0%	1.18	1.23	1.29	1.36	1.43
27.5%	1.06	1.10	1.15	1.20	1.26
30.0%	0.96	0.99	1.03	1.08	1.13

Source: Calvine Partners Research

Diurnal Group Cash Flow Statement

Diurnal Cash Flow (£m) Year to June	2019A	2020A	2021E	2022E	2023E	2024E	2025E
Net income	(12.29)	(4.07)	(18.12)	(16.54)	(0.07)	40.67	71.08
Licensing income received as non-cash		(1.04)					
Fair value adjustment to investments		(0.63)					
Dep/Amort/Impair	0.02	0.03	0.01	0.01	0.01	0.02	0.04
Share- based payment	0.83	0.84	0.84	0.84	0.84	0.84	0.84
Net Fx gain	(0.01)	(0.36)					
Financial income	(0.13)	(0.11)	(0.15)	(0.07)	0.09	0.10	(0.31)
Financial expense	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tax	(2.11)	(1.21)	0.00	0.00	(0.02)	13.56	23.69
(Increase) in receivables	1.36	0.12	0.04	(0.18)	(0.29)	(0.78)	(0.70)
Increase in payables	(3.14)	0.07	0.07	0.17	0.19	0.62	0.56
(Increase) in inventories	(0.55)	(0.57)	0.05	(0.85)	(0.94)	(0.58)	0.56
Interest paid	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Tax paid/ received	2.28	2.12	0.00	0.00	0.02	(13.56)	(23.69)
CFO	(13.74)	(4.81)	(17.27)	(16.62)	(0.17)	40.89	72.06
PP&E	(0.03)	(0.01)	(0.01)	(0.01)	(0.08)	(0.10)	(0.17)
R&D capitalised	(0.04)	(0.04)					
Investments	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Interest received	0.13	0.11	0.15	0.07	(0.09)	(0.10)	0.31
CFI	0.07	0.07	0.15	0.07	(0.17)	(0.19)	0.14
Net proceeds from issuance of share capital	5.53	10.67	9.30	0.00	0.00	0.00	0.00
Repayment of borrowings	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Net proceeds from new borrowings	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
CFF	5.53	10.67	9.30	0.00	0.00	0.00	0.00
Increase in cash	(8.15)	5.93	(7.82)	(16.55)	(0.34)	40.69	72.20
Cash brought forward	**17.28**	**9.14**	**15.07**	**7.25**	**(11.65)**	**(13.21)**	**10.41**
Fx		0.36					
Cash EOP	**9.14**	**15.07**	**7.25**	**(11.65)**	**(13.21)**	**10.41**	**46.56**

Source: Calvine Partners Research

Diurnal Group Income Statement

Diurnal Income Statement (£m) Year to June	2019A	2020A	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Sales	**1.04**	**6.31**	**2.48**	**20.01**	**48.54**	**126.32**	**196.79**	**357.74**	**429.31**	**484.33**	**568.07**	**608.27**
COGS	(0.22)	(0.67)	(0.74)	(5.00)	(9.71)	(25.26)	(39.36)	(71.55)	(85.86)	(96.87)	(113.61)	(121.65)
Gross profit	**0.82**	**5.65**	**1.74**	**15.01**	**38.83**	**101.06**	**157.44**	**286.19**	**343.45**	**387.47**	**454.45**	**486.62**
gross margin	78.5%	89.4%	70.0%	75.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
SG&A	(6.66)	(7.04)	(9.80)	(10.01)	(14.56)	(18.95)	(33.46)	(57.24)	(68.69)	(72.65)	(85.21)	(91.24)
R&D	(8.69)	(4.63)	(10.21)	(21.61)	(24.27)	(27.79)	(29.52)	(35.77)	(42.93)	(48.43)	(56.81)	(60.83)
Other operating income	0.00	0.63	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Operating profit	**(14.53)**	**(5.39)**	**(18.27)**	**(16.61)**	**0.00**	**54.32**	**94.46**	**193.18**	**231.83**	**266.38**	**312.44**	**334.55**
Finance income	0.13	0.11	0.15	0.07	(0.09)	(0.10)	0.31	1.03	2.48	4.25	6.28	8.66
Finance expense	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PBT	**(14.40)**	**(5.28)**	**(18.12)**	**(16.54)**	**(0.09)**	**54.22**	**94.77**	**194.21**	**234.31**	**270.63**	**318.72**	**343.21**
Tax	2.11	1.21	0.00	0.00	0.02	(13.56)	(23.69)	(48.55)	(58.58)	(67.66)	(79.68)	(85.80)
Net income	**(12.29)**	**(4.07)**	**(18.12)**	**(16.54)**	**(0.07)**	**40.67**	**71.08**	**145.66**	**175.73**	**202.97**	**239.04**	**257.41**
EPS Basic (p)	-19.70	-4.30	-13.94	-11.96	-0.05	29.40	51.39	105.30	127.04	146.73	172.81	186.09
EPS Diluted (p)	**-19.70**	**-4.30**	**-13.94**	**-11.96**	**-0.05**	**29.40**	**51.39**	**105.30**	**127.04**	**146.73**	**172.81**	**186.09**

Source: Calvine Partners Research

CALVINE

Diurnal Group Balance Sheet

Diurnal Balance Sheet (£m)							
Year to June	**2019A**	**2020A**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**
Intangible assets	0.05	0.08	0.01	0.01	0.01	0.01	0.01
PP&E	0.03	0.02	0.02	0.02	0.10	0.17	0.31
Inv held at fair value through P&L		1.67	1.67	1.67			
Non-current assets	0.08	1.77	1.69	1.69	0.10	0.18	0.32
Trade and other receivables	3.56	2.53	0.02	0.20	0.49	1.26	1.97
Inventory	0.67	1.24	0.15	1.00	1.94	2.53	1.97
Financial assets	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cash & Cash equivalents	9.15	15.43	7.25	(9.31)	(9.65)	31.05	103.25
Current assets	13.38	19.21	7.42	(8.10)	(7.22)	34.84	107.19
Total Assets	**13.46**	**20.98**	**9.11**	**(6.41)**	**(7.12)**	**35.02**	**107.50**
Loans and borrowings	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Trade and other payables	(2.50)	(2.56)	0.03	0.20	0.39	1.01	1.57
Current liabilities	(2.50)	(2.56)	0.03	0.20	0.39	1.01	1.57
Loans and borrowings	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Trade and other payables	(0.02)	(0.04)	(0.05)				
Non-current liabilities	(0.02)	(0.04)	(0.05)	0.00	0.00	0.00	0.00
Total Liabilities	**(2.52)**	**(2.59)**	**(0.02)**	**0.20**	**0.39**	**1.01**	**1.57**
Share capital	4.23	6.08	6.08	6.08	6.08	6.08	6.08
Share premium	42.15	50.97	59.47	59.47	59.47	59.47	59.47
Consolidation reserve	(2.94)	(2.94)	(2.94)	(2.94)	(2.94)	(2.94)	(2.94)
Other reserve	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Retained earnings	(32.49)	(35.72)	(53.34)	(69.38)	(68.95)	(27.78)	43.79
Total equity	**10.94**	**18.39**	**9.26**	**(6.78)**	**(6.35)**	**34.82**	**106.40**

Source: Calvine Partners Research

Disclosures

Calvine Partners LLP is an appointed representative of Midmar Capital LLP, which is authorised and regulated by the Financial Conduct Authority in respect of UK investment advisory or arranging activities.

This publication has been commissioned and paid for by Diurnal Group and as defined by the FCA is non-independent research. This report is considered to be a marketing communication under FCA Rules, and it has not been prepared under the laws and requirements established to promote the independence of investment research and it is not subject to any prohibition on dealing ahead of the dissemination of investment research. This information is widely available to the public.

This report in the United Kingdom is directed at investment professionals, certified high net worth individuals, high net worth entities, self-certified sophisticated investors, eligible counterparties as defined by Financial Services and Markets Act 2000 (Financial Promotion) Order 2000. The report may also be distributed and made available to persons to whom Calvine Partners is lawfully permitted. This publication is not intended for use by any individual or entity in any jurisdiction or country where that use would breach law or regulations, or which would subject Calvine Partners or its affiliates to any registration requirement within such jurisdiction or country.

Calvine Partners may provide, or seek to provide, services to other companies mentioned in this report. Partners, employees, or related parties thereof may hold positions in the companies mentioned in the report subject to Calvine Partners' personal account dealing rules.

Calvine Partners has only used publicly available information believed to be reliable at the time of this publication and made best efforts to ensure that the facts and opinions stated are fair, accurate, timely and complete at the publication date. However, Calvine Partners provides no guarantee concerning the accuracy or completeness of the report or the information or opinions within. This publication is not intended to be an investment recommendation, personal or otherwise, and it is not intended to be advice and should not be treated in any way as such. Any valuation estimates, such as those derived from a discounted cash flow, price multiple, or peer group comparison, do not represent estimates or forecasts of a future company share price. In no circumstances should the report be relied on or acted upon by non-qualified individuals. Personal or otherwise, it is not intended to be advice and should not be relied on in any way as such.

Forward-looking statements, information, estimates and assumptions contained in this report are not yet known, and uncertainties may cause the actual results, performance or achievements to be significantly different from expectations.

This report does not constitute an offer, invitation or inducement to engage in a purchase or sale of any securities in the companies mention. The information provided is for educational purposes only and this publication should not be relied upon when making any investment decision or entering any commercial contract. Past performance of any security mentioned is not a reliable indicator of future results and readers should seek appropriate, independent advice before acting on any of the information contained herein. This report should not be considered as investment advice, and Calvine Partners will not be liable for any losses, costs or damages arising from the use of this report. The information provided in this report should not be considered in any circumstances as personalised advice.

Calvine Partners LLP, its affiliates, officers or employees, do not accept any liability or responsibility with regard to the information in this publication. None of the information or opinions in this publication has been independently verified. Information and opinions are subject to change after the publication of this report, possibly rendering them inaccurate and/or incomplete.