Diurnal Group

14 February 2022

Share Price	**57p**
CP Fair Value	**241p**
Market Cap (£m)	96
Net Cash (£m)	34
Enterprise Value (£m)	62
Country	UK
Code	DNL
Index	FTSE AIM

Source: Calvine Partners Research

Driving the franchise

With the commercial rollout of Efmody and Alkindi, the platform to build Diurnal's commercial infrastructure in Europe is now in place. The US remains an important opportunity for Diurnal, with the potential to self-develop and self-commercialise Efmody if desired. In its favour, the US is a more homogeneous market and generally tractable when selling rare disease products through a small, highly targeted salesforce. There is also a distinct possibility that Efmody could achieve orphan drug status for both Congenital Adrenal Hyperplasia (CAH) and the broader Adrenal Insufficiency (AI) indication and the potential for premium pricing. The EMA and UK approval for Efmody should de-risk Efmody's US development. In addition, with an FDA Special Protocol Assessment (SPA) now in place for CAH and the prospect of AI approval in the longer term, Efmody has the potential to be a highly lucrative programme.

Broader endocrinology ambitions

Our focus, and that of the market, has generally been on the outlook for the cortisol replacement franchise at Diurnal. However, the company's ambitions are significantly broader and encompass other adrenal disorders as well as the treatment of male hypogonadism caused by low testosterone. DNL-300 (previously DITEST) offers some important benefits over existing testosterone replacement therapies (TRT), being the first native testosterone presentation with the intention of providing an effective oral therapy without the need for a high-fat meal and lower dihydrotestosterone. Diurnal has secured a branded generic (505(b)(2)) regulatory pathway in the key US market, which is usually associated with shorter, lower-cost clinical development and lower risk. TRT is a very large market opportunity, with DNL-300 likely representing the right treatment at the right time, given regulatory issues for the class.

Early signs of commercial progress

The recent trading update has provided encouraging signs for the adrenal franchise and Efmody in particular. The continued impact of the COVID-19 pandemic has impacted progress, but early indications are promising. We believe that the adolescent approval will be instrumental in gaining traction in CAH in Europe. The pandemic has also impacted the recruitment of patients into many clinical studies, but hopefully, this is easing. In this regard, there are important events on the near-term horizon, including starting the US (and Japan) Phase 3 study for Efmody in CAH (CONnECT), the pivotal study for Efmody in AI (CHAMPAIN) as well as the Phase 2 study for DNL-300 in male hypogonadism.

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Building a broad endocrinology platform

Efmody sales accelerating

Unsurprisingly, the near-term focus for management and the market has been on the early commercialisation of Diurnal's two cortisol replacement therapies, Efmody and Alkindi. With these two products approved, reimbursement for Efmody expanding, and additional launch geographies added, we look forward to CY H1 2022 providing more insight into the potential of Diurnal's adrenal franchise in Europe.

European ambitions realised

Europe represents a significant opportunity for the company as it seeks to deliver on its goal of sustainable profitability. Europe is the only market where Diurnal has committed to the self-commercialisation of Alkindi and Efmody. Self-commercialisation involves a degree of execution risk; however, this risk is mitigated as CAH is a rare disease requiring only a small, highly targeted salesforce detailing to specialist endocrinologists. If successful, Diurnal retains the full margin and the operating leverage that should follow from selling two products through a relatively fixed cost European infrastructure.

Europe will take time

Europe can be a challenging and disparate geography in which to launch a new product. Reimbursement generally takes about 12 months (often longer) as more countries are added. However, despite a lack of orphan drug status in Europe, pricing has been in line with other long-acting glucocorticoids (Plenadren). Also, the unexpected addition of a broader label to include adolescents should help secure earlier use of Efmody, particularly in the pre-pubescent patient population who are at greater risk of elevated androgens than adults. Indeed, younger CAH patients are easier to identify than adults, who may be lost to treatment given a desire to avoid the challenges of balancing high androgens with high glucocorticoids – until the threat of adrenal crisis becomes too much of an issue to ignore.

Not helped by ongoing restrictions

The challenges of launching a new product, albeit for a rare disease in Europe, have been compounded by the dislocation caused by the ongoing COVID-19 pandemic. When we last evaluated the launch environment for Efmody at the end of 2021, the success of vaccination suggested that 2022 would be a more benign period. However, the impact of Omicron has brought a challenging start to 2022.

Efmody the flagship CAH/AI therapy

Nevertheless, we remain of the view that the benefits associated with Efmody suggest it should be a desirable treatment option. In particular, the ability to mimic circadian delivery resulting in overnight androgen control at a physiological dose for cortisol replacement therapy, appears compelling. We have previously highlighted commentary from the EMA, which seems to confirm this view. These included 1. Improved hormonal balance, which could be maintained in the longer term, 2. The potential to use lower doses of corticosteroid in some patients, and 3."…. *the ability to offer*

clinical value by allowing dosing that resembles the daily rhythm of natural cortisol secretion."

Well suited to the CAH patient

Given the clinical data, the unmet need, and EMA's supportive label, we anticipate strong support from CAH patient advocacy groups and endocrinologists treating the CAH patient. Indeed, the prospect of a more effective hydrocortisone preparation that better suits the needs of the CAH patient should lead to greater compliance. As we noted earlier, poor compliance has been a feature of high dose glucocorticoid use in CAH historically, leading to a higher risk of adrenal crisis. Importantly, the Phase 3 trial and the extension study confirmed a lower risk of adrenal crises in Efmody treated patients than standard GC therapy.

Recent trading update encouraging

The recent trading update has provided encouraging commentary on the commercial progress of Efmody in those geographies where it has been launched. Although Alkindi sales remain modest as expected, its availability allows Diurnal to treat children and adolescents with AI (including CAH). Together, Alkindi and Efmody allow Diurnal to provide a continuum of care throughout the CAH patient's life.

Existing infrastructure is a key asset

Notably, the existing infrastructure put in place to commercialise Alkindi is highly relevant to the commercialisation of Efmody. Diurnal's salesforce may be modest in size, but only a small number of key European endocrinology centres treat CAH patients. Therefore, the European sales infrastructure should be well prepared to expedite the awareness of Efmody to the relevant physicians.

Why is the market ignoring the larger AI indication?

Looking forward to the impact of Efmody

The addition of Efmody as the flagship cortisol replacement therapy is important and gives a halo effect to the overall franchise. Efmody brings rapidly increasing sales, delivers operating leverage, and provides a clear path to sustainable profitability.

…in AI as well as CAH

Importantly for the European franchise, the potential addition of the broader AI indication from 2024 promises to boost the overall market opportunity significantly. Although Efmody may be better suited to the unmet need of the CAH patient, effectively dealing with the risk of elevated androgen production overnight, it is well accepted that mimicking cortisol's circadian release in AI is also desirable. However, it's also fair to say that Plenadren - an existing sustained-release product - hasn't fared well compared to immediate release (IR) hydrocortisone, despite showing some limited benefit on weight loss, blood pressure and metabolic measures. Part of this may be due to the inability of Plenadren to mimic the typical early morning physiological increase in cortisol levels, suggesting that the more relevant comparator was prednisolone, which is often used in patients with compliance issues or who are intolerant of IR hydrocortisone. We also note that EMA suggested in its review that Plenadren could not be

Plenadren is not a good proxy

characterised as having a physiological pharmacokinetic profile. The refusal of the Scottish Medicines Consortium (SMC) to reimburse Plenadren provides meaningful insight into some of the challenges it faced post EMA approval. Indeed, the conclusion was that the data did not represent a "*…sufficiently robust clinical and economic analysis*". The review highlighted limitations, including a lack of blinding, short duration (12 weeks on treatment), and a risk of hypocortisolism later in the day. Ultimately the SMC believed that there was '*…a lack of robust data to support a claim of an improved metabolic profile and therefore of reduced cardiovascular risk*".

Diurnal's activities support optimal positioning

Finally, we suspect that Plenadren suffered from uneasy ownership (ViroPharma and then Shire through acquisition) prior to exclusivity expiring in November 2021. Given the lacklustre impact of Plenadren, Efmody must be positioned appropriately in this patient population. With this in mind, we look forward to the completion of the Phase 2 CHAMPAIN study comparing Efmody with Plenadren.

CHAMPAIN should deliver a superior label

A positive result from CHAMPAIN is important for various reasons. For Diurnal, AI is a more significant commercial opportunity than CAH. For patients, although there are no overnight androgens to worry about, circadian delivery is still beneficial, particularly if it leads to a reduction in glucocorticoid dose required to prevent adrenal crises. Even if successful, clearly there will be cost issues associated with treating patients with a higher-priced branded preparation like Efmody compared to generic IR hydrocortisone preparations and potentially a generic Plenadren. Consequently, we believe that this comparator study with Plenadren is important, with success delivering not only an approval in AI but also orphan drug status in Europe for the first time. Confirmation of orphan drug status in AI would help justify not only the premium pricing over generic hydrocortisone preparations, but would also remove any lingering doubt regarding Efmody's superior profile.

Efmody should be best in class

Inevitably all eyes are on the market introduction for Efmody in CAH, and perhaps the market is overlooking the more considerable AI opportunity awaiting the results of CHAMPAIN. Potentially the lacklustre performance of Plenadren in Europe in AI hasn't helped.

AI patients need improved treatment options

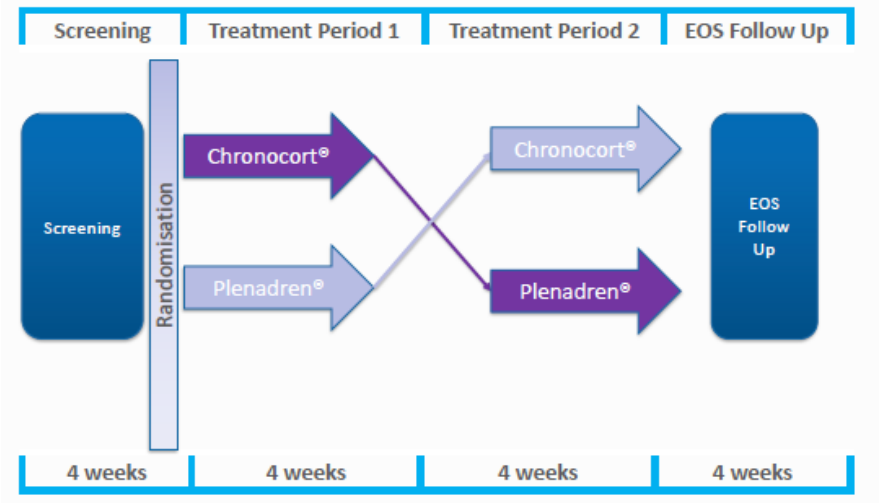
Nevertheless, we believe that Diurnal should be able to build a compelling case for Efmody in AI through CHAMPAIN. In many ways, AI represents a more straightforward proposition, delivering physiological doses of hydrocortisone to prevent adrenal crises, and is much more akin to a typical replacement therapy approach. Despite significant efforts to provide close to physiological dosing with existing glucocorticoid preparations, patients with AI still suffer from periods of hypo and hypercortisolism. Hypocortisolism runs the risk of adrenal crises, while hypercortisolism can result in fatigue, low libido, and cognitive issues. Moreover, there remains significant inter and intrapatient variability with no easy diagnostic means of ensuring that patients are adequately controlled.

Why do we think CHAMPAIN will be positive?

CHAMPAIN should deliver a differentiated label

The Phase 2 CHAMPAIN registration study assesses the ability of Efmody to deliver higher concentrations of cortisol versus Plenadren in the morning after 4 weeks of treatment in a crossover design. This is the primary endpoint. CHAMPAIN is also evaluating a broad range of secondary (and other) endpoints, including fatigue and quality of life measures, as well as looking at the response to therapy with respect to morning cortisol levels reaching a predefined level (>140 nmol/l). Although this is a Phase 2 study with limited numbers, we believe this to be a thorough analysis of the differences between Efmody and Plenadren and, if successful, should provide label claims which differentiate the two.

CHAMPAIN Study

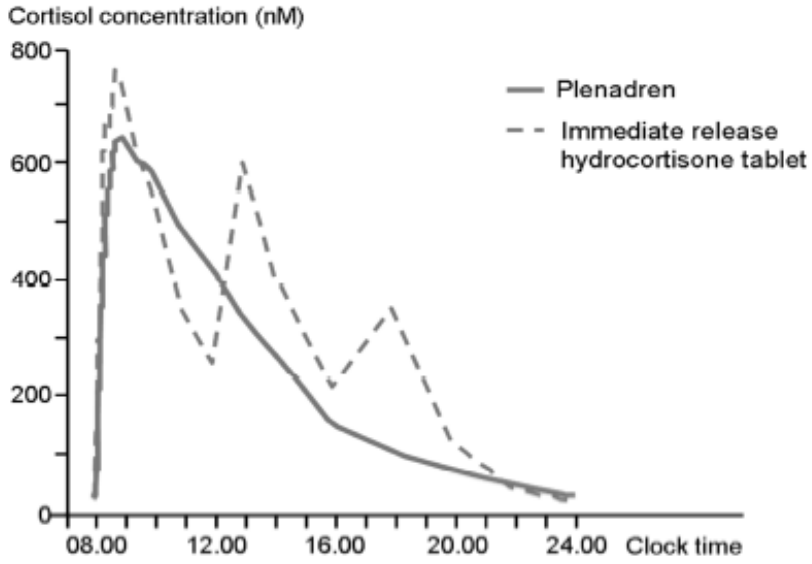


Source: Company presentation

Efmody delivery is very different to Plenadren

Efmody and Plenadren use different approaches to modify the release of hydrocortisone to mimic the physiological circadian release of cortisol. Plenadren, originally approved in Europe for AI in 2011, offers an immediate-release outer layer and an extended-release inner core from its once-daily dosing. Plenadren overall suffers from 80% of the bioavailability of IR hydrocortisone. It delivers a higher concentration of hydrocortisone during the first 4 hours after administration, but this rapidly tails off during the day and completely misses out on the early morning increase and peak on awakening. It is perhaps unsurprising that patients taking Plenadren suffered from hypocortisolism during the afternoon.

Despite the limitations associated with Plenadren resulting in the Scottish Medicines Consortium negative decision, we note that (unlike Efmody), Plenadren was awarded Orphan Drug status.



Source: emc, Datapharm

Efmody profile much better suited to AI patient

Efmody, on the other hand, offers delayed release and sustained absorption of hydrocortisone. As we have seen in the clinic, it effectively controls overnight androgens, particularly relevant for the treatment of CAH. It is taken in a twice-daily toothbrush regimen with one-third of the total daily dose taken in the morning and the remainder taken at 11 pm just before bedtime. Unlike Plenadren, Efmody successfully provides physiological peak cortisol levels on awakening. Consequently, we believe there is a reasonable prospect of Efmody delivering a favourable comparison versus Plenadren with a primary endpoint measuring cortisol levels in the morning.

CHAMPAIN is now underway, and to that extent, we expect approval in FY 2024, although perhaps later in the current fiscal year (to end June) than we previously thought. Although this has resulted in a reduction in near term revenues, our peak sales expectations remain unchanged. The addition of the AI indication is important. It should significantly build awareness of the benefits of Efmody and also the breadth of Diurnal's adrenal (cortisol replacement) franchise.

US important to deliver global ambitions

The US is a key market

Europe can be a challenging market to self-commercialise new products given fragmented reimbursement and disparate healthcare delivery systems. On the other hand, the US remains the last bastion of (largely) free-market pricing, with orphan drugs in particular commanding premium pricing. As a reminder, Efmody (Chronocort in the US) currently has orphan designation for both adult CAH and AI in the US.

Diurnal may retain commercial rights in the US

Alkindi, however, is out-licensed to Eton Pharmaceuticals. Although such an option remains for Efmody, we would like to think that if possible, Diurnal should retain commercial rights, using Efmody to establish a US direct sales capability.

Delays have impacted US development of Efmody post the Phase 3 failure of the EMA study and the desire to have an agreed design with FDA resulting in securing a Special Protocol Assessment.

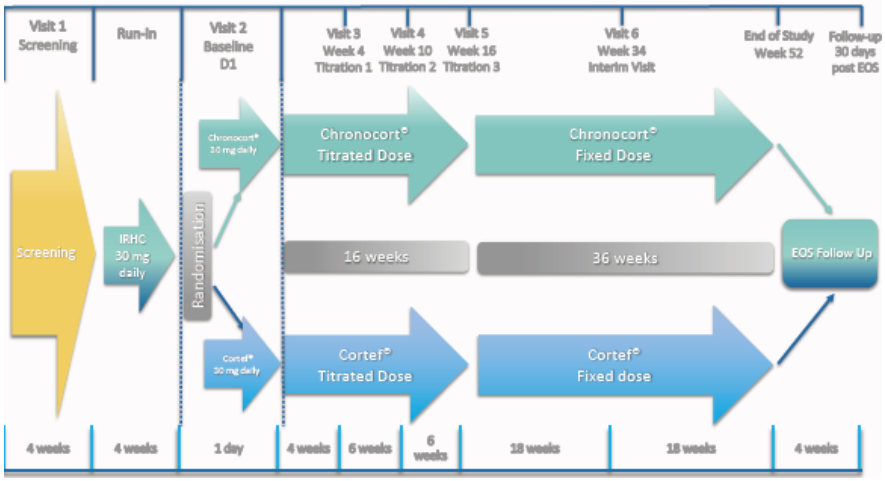
Phase 3 programme should deliver a differentiated label

Not only does the US benefit from a more homogeneous market, but we also suspect that awareness of CAH is likely greater thanks to the activities of those developing the CRF1 inhibitors crinecerfont and tildacerfont. Although this approach directly targets the elevated overnight androgen issue, replacement cortisol is still required.

CONnECT is a double-blind 52-week study with a biochemical responder analysis versus IR hydrocortisone in a non-inferiority design as the primary endpoint. Secondary endpoints should also provide important information comparing Efmody with IR hydrocortisone with respect to key measures, including steroid-sparing, fertility, body weight and quality of life. CONnECT is a comprehensive investigation of the benefits of Efmody with 28 secondary endpoints and 31 other outcome measures. Should the trial be successful, we expect that Efmody should be able to gain approval, orphan drug status, and a differentiated prescribing label.

CONnECT is also underway, and with 150 patients anticipated and 50 study centres globally planned, this is another significant undertaking for Diurnal. The primary completion date for CONnECT is expected to be towards the end of 2023, suggesting an H1 2024 filing and a 2025 commercial launch.

CONnECT - US Phase 3 CAH study



Source: Company presentation

DNL-300 potential is yet to be unlocked

Clear ambitions beyond cortisol

We suspect that Diurnal's ambitions to create a leading endocrinology franchise (ex-diabetes) have been constrained by resources and funding. Developing and commercialising Alkindi and Efmody has taken longer than anticipated, while the pandemic hasn't helped either with patient recruitment into clinical trials or patients meeting physicians for treatment.

DNL-300 a large market

DNL-300 (previously DITEST) looks like an appealing proposition thanks to the sheer size of the market opportunity, which is approximately $5.0bn, according to Diurnal. Furthermore, the FDA has confirmed that development for DNL-300 should follow a branded generic 505(b)(2) pathway, which should streamline development.

Potential to be best in class

DNL-300 is a novel lipidic formulation of native testosterone. If approved, DNL-300 would be the only orally available testosterone replacement therapy (TRT) for the treatment of classical hypogonadism, which does not require patients to eat a high-fat meal.

DNL-300 Formulation

Ingredient	Grade	Quantity, % (w/w)	Quantity per capsule (mg)	Function
Testosterone	Ph. Eur.	5.43	40.0	Active ingredient
Sesame oil	Ph. Eur.	41.39	305.0	Carrier
Propylene glycol monolaurate	Ph. Eur.	31.62	233.0	Surfactant
Benzyl alcohol	Ph. Eur.	16.29	120.0	Solvent
Ethanol	Ph. Eur.	5.27	38.83	Solvent
Gelatin	Ph. Eur.	–	–	Capsule shell

Source: European Journal of Endocrinology

Non-oral therapies still dominate

To understand the relevance of DNL-300, it is important to appreciate the evolution of testosterone replacement therapy. Unfortunately, testosterone suffers from poor bioavailability, and for some time, the oral route of administration was deemed unviable. As a result, TRT has been dominated by topical formulations and injectable products. However, compliance rates with injectable and gel formulations remain poor, with switching between products commonplace. In addition, administration of injectable products can be painful, while topical formulations are associated with skin reactions and transference to women and children (hence a Black Box warning of virilisation).

No shortage of effort

Given the unmet need, efforts to manipulate testosterone have continued to attempt to find a suitable oral alternative. The endeavour has proven to be challenging given that testosterone is almost insoluble in water as well as fatty acid-based oils. Early efforts to formulate a suitable oral presentation resulted in the approval of modified testosterone preparations such as methyltestosterone (Android). However, although 17-alpha-alkyl testosterone-based products may have been effective at replacing

testosterone, they were associated with significant liver toxicity and, as a result, have not been widely used for the treatment of classical hypogonadism. Looking at the Android prescribing label, we note that cholestatic hepatitis and jaundice occur at a relatively low dose.

More worryingly, prolonged use of high doses has been associated with peliosis hepatitis and hepatic cancer.

Dissatisfaction with existing preparations high

Although oral testosterone has been available in Europe and Australia as testosterone undecanoate (branded as Andriol Testocaps and Aveed) for some time, it wasn't until the approval of Jatenzo that an oral formulation was available in the US. With the vast majority of prescriptions in the US still for non-oral TRTs, the opportunity for an effective oral treatment is significant, particularly given the apparent dissatisfaction that hypogonadal patients have for non-oral TRT. Indeed, it is clear that this dissatisfaction leads to considerable churn rates, with patients trying multiple different TRT preparations attempting to find one more suitable with fewer limitations.

Room for improvement

Although Jatenzo represents a significant improvement in convenience, it does have some limitations. Looking at the prescribing label, Jatenzo needs to be taken at the same time as meals (fasted administration not being a viable option), and we note that it can result in supraphysiological levels of dihydrotestosterone (DHT) while testosterone levels can be variable. Given the potential cardiovascular issues associated with the treatment of hypogonadal patients, the need for a high-fat diet is clearly less than optimal. Also, there may be a link between supraphysiological levels of DHT and heightened cardiovascular risk.

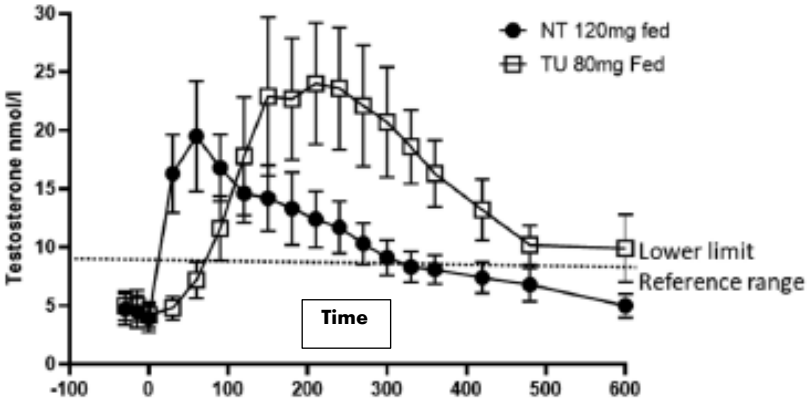
Jatenzo raising awareness

With the first oral TRT not associated with liver toxicity available in the US, Clarus has invested significant resources in raising awareness of Jatenzo. This included a 60-person salesforce in the US as well as a substantial investment in DTC advertising. Given that TRT looks to be promotionally sensitive, we look forward to Clarus raising awareness of the benefits associated with an oral alternative. Hopefully, once DNL-300 is available (if approved), the market for oral TRTs should be better established than it is today.

Clinical data supportive

DNL-300 is a native testosterone that has been formulated for oral administration but designed to provide normal physiological levels of testosterone irrespective of the need for food. Potentially, DNL-300 should overcome some of the limitations associated with the current TRT profile of testosterone undecanoate. In a Phase 1 comparator pharmacokinetic study versus testosterone undecanoate, it was demonstrated that DNL-300 could return hypogonadal men to physiologically normal levels, irrespective of whether they are in the fed or fasted state. Importantly, DNL-300 was also associated with a 50% reduction in DHT levels compared to testosterone undecanoate. These are reassuring data confirming the expected clinical profile and differentiating DNL-300 from other oral presentations.

DNL-300 (NT) versus testosterone undecanoate (TU)



Source: European Journal of Endocrinology

Streamlined development on offer

DNL-300's streamlined 505(b)(2) pathway is associated with significantly lower costs and risks than traditional drug development. As a result, Diurnal has been able to progress DNL-300 using its own resources, although a partner will ultimately be required. Effectively, Diurnal (along with a commercial partner) can take advantage of data previously provided by other testosterone-based products as it seeks to provide a regulatory package that fulfils the Agency's requirement that DNL-300 is safe and efficacious.

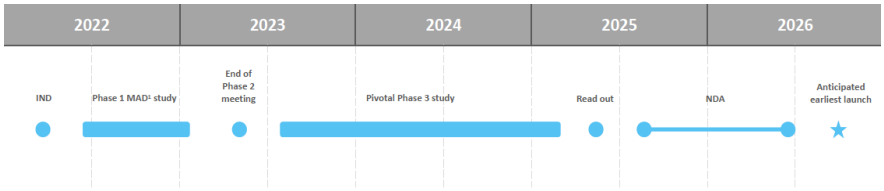
Unmet need is clear

TRT is a large market opportunity, with approximately 6% of US males affected by low testosterone levels (approx. 4-5 million men). There is a very clear need for oral products with fewer limitations than testosterone undecanoate that are more acceptable to patients than topical or injectable products.

DNL-300 likely needs a commercial partner

Indeed, given the challenges faced in diagnosis, concerns over abuse and the significantly higher prescribing of TRT in the US over Europe, we believe that a development partner with relevant expertise will be required to ensure optimal positioning and drive uptake in the relevant patient populations. Diurnal should be able to deliver a suitable commercial development partner, particularly given the well-defined low-risk regulatory pathway agreed with the FDA, as well as positive Phase 1 data. A Phase 1 multiple ascending dose study should commence in early 2022. As a result, we suspect that the earliest that Diurnal can achieve a satisfactory partnering agreement would be after a DNL-300 Type B (end of Phase 2) meeting with the FDA, probably in the 2023 timeframe. Diurnal's timing could be helped by the regulatory actions that have effectively limited the target population to patients with hypogonadism, specifically those with structural issues.

The DNL-300 clinical pathway



Source: Company presentation

Not yet included in our financial model

DNL-300 sits outside of our financial model and valuation, and much depends on the ability of Diurnal to attract the right commercial partner. However, the result of the forthcoming multiple ascending dose study should be helpful in further de-risking the pivotal study. There is little read-across from the ongoing Jatenzo launch in the key US market as these remain relatively early days, particularly as the launch phase has been directly impacted by restrictions associated with the COVID-19 pandemic.

At the same time, the roll out of Jatenzo does reflect some of the challenges faced in launching a new therapy in a market dominated by primarily topical and injectable generic TRTs despite their limitations. We also note that Clarus has previously guided towards ultimately achieving a low double-digit share of the US TRT market, with each point of share comprising $33m in sales. As highlighted previously, the regulatory pathway for Jatenzo (now approved) and Tlando (tentative approval) may have been chequered but much has been learnt from a regulatory perspective, which should reduce any concerns from potential DNL-300 partners.

Risks

The principal risks associated with Diurnal are primarily clinical and commercial. Clinical trials of novel drugs can be associated with risk of failure as well as delays, and we note that the ongoing COVID-19 pandemic has resulted in enrolment delays in clinical trials in general.

Diurnal has retained European rights to its adrenal disorder franchise, bringing commercialisation risks. The pace of uptake is difficult to predict, particularly given the ongoing COVID-19 dislocation, which could affect our forecasts, although we recognise that market expectations for Alkindi are modest. Following Efmody's launch in Europe, we expect that Diurnal will benefit from the existing sales platform, with only incremental costs required to support commercial launch.

Diurnal is seeking to launch its products into what is primarily a generic market environment. Accordingly, 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 there is no equivalent product in the US and have assumed that Efmody is priced at a premium. With Diurnal also now retaining US rights for now, we look forward to the company securing a price which reflects Efmody's orphan designation.

With Diurnal looking to partner several of its products in the US, including DNL-300, there is an associated partnering risk.

As a development stage company, Diurnal is currently a loss-making enterprise. However, the company has successfully raised funds to continue with its pipeline development ambitions and support the launch of Alkindi and Efmody in Europe.

Financial Model and Summary

Encouraging trading update

The recent trading update from Diurnal has helped reset expectations, with a strong performance from Alkindi and the prospect of accelerating sales from Efmody. It must be very frustrating for management that the recent R&D day did not take place as scheduled. It would have been particularly helpful for the market to hear feedback on Efmody's early launch experience, which underpins confidence in accelerating sales.

Pandemic restrictions unhelpful generally

Nevertheless, looking at our expectations, there can be little doubt that the ongoing pandemic has made the launch phase for Efmody more difficult, despite the pre-existing commercial infrastructure. While we still expect Efmody to be available in AI by 2024, we suspect that this will be later in the year than we previously expected. Hopefully, the recent relaxation in restrictions will be helpful as Efmody's launch phase and international roll out continue as well as aiding recruitment into CHAMPAIN and CONnECT.

European label important

While the use of hydrocortisone as a treatment for adrenal insufficiency is not new, developing a therapy that replicates the circadian release, delivering physiologically relevant levels, has been a long-held goal of the pharmaceutical industry. This is particularly true for the treatment of CAH patients. These patients have the double whammy of low cortisol and a build-up of male androgen levels and take supraphysiological doses of glucocorticoid as a result. Consequently, many (adult patients in particular) can be lost to therapy. Efmody's potential to control overnight androgens at a lower hydrocortisone dose is key to its success in the patient population. We suspect that the inclusion of adolescents in the European label will prove to be more important than many currently recognise.

Indication expansion and additional geographies driving growth

Based on this observation, we have high hopes for Efmody, which appears to mimic physiological release better than any other oral treatment. This feature is key to Efmody's commercial success in CAH. It is also behind our confidence in the ability of CHAMPAIN to deliver a positive result in the broader AI disorder. The US (and Japan) CAH study is primed to go, with the benefit of an agreed protocol (under an SPA), driving our overall Efmody forecasts.

We suspect that the R&D day would have shone additional light on the potential for DNL-300 in hypogonadal men. This is a significant opportunity, and we look forward to the oral TRT market developing ahead of DNL-300's availability.

These are exciting times for Diurnal. It now has two licensed products in Europe, which should serve the continuum of adrenal insufficiency, particularly for CAH patients. Plans for the US are now in place, and we look forward to Efmody delivering on its promise in CAH as well as the broader AI indication. The company has the wherewithal to progress DNL-300, and the pipeline behind is beginning to emerge, highlighting management's ambition to create a broad endocrinology franchise.

Diurnal Group Income Statement (£m)

Year to June	2019A	2020A	2021A	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Sales	**1.04**	**6.31**	**4.37**	**7.54**	**19.03**	**56.69**	**101.14**	**148.14**	**221.98**	**374.62**	**506.32**	**578.79**
COGS	(0.22)	(0.67)	(0.78)	(1.88)	(3.81)	(11.34)	(20.23)	(29.63)	(44.40)	(74.92)	(101.26)	(115.76)
Gross profit	**0.82**	**5.65**	**3.59**	**5.65**	**15.22**	**45.35**	**80.91**	**118.51**	**177.59**	**299.69**	**405.06**	**463.03**
gross margin	78.5%	89.4%	82.2%	75.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
SG&A	(6.66)	(7.04)	(8.29)	(9.20)	(9.89)	(10.20)	(14.16)	(16.30)	(19.98)	(33.72)	(60.76)	(81.03)
R&D	(8.69)	(4.63)	(6.92)	(16.59)	(18.64)	(21.54)	(23.26)	(25.18)	(28.86)	(41.21)	(50.63)	(57.88)
Other operating income	0.00	0.63	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Operating profit	**(14.53)**	**(5.39)**	**(11.60)**	**(20.13)**	**(13.32)**	**13.61**	**43.49**	**77.03**	**128.75**	**224.77**	**293.67**	**324.12**
Finance income	0.13	0.11	0.06	0.34	0.20	0.11	0.21	0.52	1.10	2.04	3.65	5.75
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)**	**(11.54)**	**(19.79)**	**(13.12)**	**13.71**	**43.69**	**77.55**	**129.85**	**226.82**	**297.32**	**329.87**
Tax	2.11	1.21	1.49	1.49	3.28	(3.43)	(10.92)	(19.39)	(32.46)	(56.70)	(74.33)	(82.47)
Net income	**(12.29)**	**(4.07)**	**(10.05)**	**(18.30)**	**(9.84)**	**10.28**	**32.77**	**58.16**	**97.39**	**170.11**	**222.99**	**247.40**
EPS Basic (p)	-19.70	-4.30	-7.33	-10.90	-5.86	6.12	19.51	34.63	57.99	101.30	132.79	147.32
EPS Diluted (p)	**-19.70**	**-4.30**	**-7.33**	**-10.90**	**-5.86**	**6.12**	**19.51**	**34.63**	**57.99**	**101.30**	**132.79**	**147.32**

Source: Calvine Partners Research

Diurnal Group Cash Flow (£m)

Year to June	2019A	2020A	2021A	2022E	2023E	2024E
Net income	(12.29)	(4.07)	(10.05)	(18.30)	(9.84)	10.28
Licensing income received as non-cash		(1.04)				
Fair value adjustment to investments		(0.63)	(0.02)			
Dep/Amort/Impair	0.02	0.03	0.02	0.05	0.05	0.16
Share- based payment	0.83	0.84	0.47	0.84	0.84	0.84
Net Fx gain	(0.01)	(0.36)	0.11			
Financial income	(0.13)	(0.11)	(0.06)	(0.34)	(0.20)	(0.11)
Financial expense	0.00	0.00	0.00	0.00	0.00	0.00
Tax	(2.11)	(1.21)	(1.49)	0.00	(3.28)	3.43
(Increase) in receivables	1.36	0.12	(2.10)	1.55	(0.02)	(0.93)
Increase in payables	(3.14)	0.07	1.64	1.34	0.62	0.28
(Increase) in inventories	(0.55)	(0.57)	(0.38)	0.49	(0.01)	0.01
Interest paid	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Tax paid/ received	2.28	2.12	1.20	0.00	3.28	(3.43)
CFO	(13.74)	(4.81)	(10.66)	(14.37)	(8.55)	10.54
PP&E	(0.03)	(0.01)	(0.14)	(0.05)	(0.62)	(0.75)
R&D capitalised	(0.04)	(0.04)	(0.03)			
Investments	**0.00**	**0.00**	**0.71**	**0.00**	**0.00**	**0.00**
Interest received	0.13	0.11	0.06	0.34	0.20	0.11
CFI	0.07	0.07	0.61	0.29	(0.43)	(0.64)
Net proceeds from issuance of share capital	5.53	10.67	28.76	0.00	0.00	0.00
Repayment of borrowings	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**
CFF	5.53	10.67	28.76	0.00	0.00	0.00
Increase in cash	(8.15)	5.93	18.71	(14.09)	(8.98)	9.90
Cash brought forward	**17.28**	**9.14**	**15.07**	**34.04**	**19.95**	**10.97**
Fx		0.36				
Cash EOP	**9.14**	**15.07**	**34.04**	**19.95**	**10.97**	**20.87**

Source: Calvine Partners Research

Diurnal Group Balance Sheet (£m)

Year to June	2019A	2020A	2021A	2022E	2023E	2024E
Intangible assets	0.05	0.08	0.09	0.09	0.10	0.10
PP&E	0.03	0.02	0.15	0.15	0.72	1.30
Inv held at fair value through P&L		1.67	0.00	0.00		
Non-current assets	0.08	1.77	0.24	0.24	0.82	1.40
Trade and other receivables	3.56	2.53	3.43	1.88	1.90	2.83
Inventory	0.67	1.24	1.63	1.13	1.14	1.13
Inv held at fair value through P&L			1.49	0.00	0.00	0.00
Financial assets	0.00	0.00	0.97			
Cash & Cash equivalents	9.15	15.43	34.04	19.95	10.97	20.87
Current assets	13.38	19.21	41.55	22.97	14.01	24.84
Total Assets	**13.46**	**20.98**	**41.79**	**23.21**	**14.83**	**26.24**
Loans and borrowings	0.00	0.00	0.00	0.00	0.00	0.00
Trade and other payables	(2.50)	(2.56)	(4.16)	(4.00)	(2.21)	(1.93)
Current liabilities	(2.50)	(2.56)	(4.16)	(4.00)	(2.21)	(1.93)
Loans and borrowings	0.00	0.00	0.00	0.00	0.00	0.00
Trade and other payables	(0.02)	(0.04)	(0.06)			
Non-current liabilities	(0.02)	(0.04)	(0.06)	0.00	0.00	0.00
Total Liabilities	**(2.52)**	**(2.59)**	**(4.23)**	**(4.00)**	**(2.21)**	**(1.93)**
Share capital	4.23	6.08	8.40	8.40	8.40	8.40
Share premium	42.15	50.97	77.41	77.41	77.41	77.41
Consolidation reserve	(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
Retained earnings	(32.49)	(35.72)	(45.30)	(63.11)	(72.45)	(61.66)
Total equity	**10.94**	**18.39**	**37.56**	**19.76**	**10.42**	**21.21**

Source: Calvine Partners Research

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