



12 May 2021

**Diurnal Group plc**  
("Diurnal" or the "Company")

**China licensing agreement with Citrine Medicine for Efmody®**

*Partnership extended with China-based rare disease therapeutics company*

*Total up-front payment and future milestones of up to \$29.75 million, with double-digit royalties on sales*

Diurnal Group plc (AIM: DNL), the specialty pharmaceutical company targeting patient needs in chronic endocrine (hormonal) diseases, announces it has extended its exclusive licence agreement with the specialty pharmaceutical company, Citrine Medicine, Inc. ("Citrine"), to include the registration, distribution and marketing of Efmody® (hydrocortisone modified-release hard capsules – development name Chronocort®) covering China, Hong Kong, Taiwan and Macau.

Under the terms of the licence agreement, Diurnal will receive a non-refundable upfront payment of \$1.0 million and will receive \$28.75 million in additional cash payments upon achievement of certain regulatory milestones and sales milestones based on annual sales thresholds. Diurnal will also receive tiered royalties on sales ranging from low to mid double-digits.

Citrine is a therapeutics platform company focused on the Greater China market that was co-founded by Vivo Capital, F-Prime Capital and Eight Roads Ventures. Citrine is focused on creating a therapeutic platform to deliver rare disease drugs to the Chinese market and to develop the first ever rare disease ecosystem in the country. The Company signed an original licensing agreement with Citrine in January 2021 for obtaining registration for Alkindi® (hydrocortisone granules in capsules for opening) as well as for all commercialisation activities in China.

Citrine will be responsible for obtaining registration for Efmody® as treatment of patients with the rare conditions congenital adrenal hyperplasia (CAH) and adrenal insufficiency (AI) in China and for all commercialisation activities, including pricing and reimbursement. Citrine will initially utilise product from Diurnal's European supply chain, with an option to establish its own supply chain in China in the future. It is estimated that CAH occurs in 1 in 6,084 births in China<sup>1</sup>. CAH is a group of genetic conditions that limit hormone production in the adrenal glands and was identified a rare disease by the Chinese health authorities in May 2018.

**Martin Whitaker, CEO of Diurnal, commented:**

*"We are pleased to expand our partnership with Citrine in China to include both of our lead cortisol deficiency products. We have been impressed by Citrine's local development, regulatory and commercialisation expertise for Alkindi® and look forward to this knowledge and experience being applied to Efmody®. Following the recent positive CHMP opinion received for Efmody® in Europe, this licensing agreement is in line with our strategy to optimise market access of our products outside of key European markets. If approved, Efmody® will provide a major breakthrough in China as the first licensed treatment for Chinese patients with CAH, that mimics the physiological circadian rhythm of cortisol, where there is a significant unmet patient need."*

**Melissa Bradford-Klug, President and Chief Business Officer of Citrine, commented:**

*"It is with much excitement that we extend our licensing agreement with Diurnal, which will ultimately enable us to serve the needs of Chinese patients of all ages suffering from CAH. The team at Diurnal are great partners and we look forward to continuing to work with them as we bring both Alkindi® and Efmody® through the regulatory approval process in China."*

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) 596/2014 (MAR).

<sup>1</sup> Zhong, K. et al. (2016) 'The status of neonatal screening in China, 2013', Journal of Medical Screening, 23(2), pp. 59–61. doi: 10.1177/0969141315597715.

For further information, please visit [www.diurnal.co.uk](http://www.diurnal.co.uk) or contact:

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## Notes to Editors

### About Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is an orphan condition caused by deficiency of adrenal enzymes, most commonly 21-hydroxylase. This enzyme is required to produce the adrenal steroid hormone, cortisol. The block in the cortisol production pathway causes the over-production of male steroid hormones (androgens), which are precursors to cortisol. The condition is congenital (inherited at birth) and affects both sexes. The cortisol deficiency and over-production of male sex hormones can lead to increased mortality, infertility and issues during sexual development including ambiguous genitalia, premature (precocious) sexual development and short stature. Sufferers, even if treated, remain at risk of death through an adrenal crisis.

Current therapy for CAH uses a variety of generic glucocorticoid (steroids including hydrocortisone, dexamethasone, prednisolone and prednisone in the US) with no standard treatment regimen. Approximately two-thirds of CAH patients are estimated to have poor disease control, leading to elevated androgen levels. The condition is estimated to affect a total of approximately 41,000 patients in Europe, with over 400,000 in the rest of the world.

### About Efmody<sup>®</sup> (hydrocortisone modified-release hard capsules)

Efmody<sup>®</sup> is a preparation of hydrocortisone that has been specifically designed to mimic the circadian rhythm of cortisol when given in a twice-a-day "toothbrush" regimen (administered last thing at night before sleep and first thing in the morning on waking) to control androgen excess and chronic fatigue in patients with diseases of cortisol deficiency. The first indication for Efmody<sup>®</sup> is Congenital Adrenal Hyperplasia (CAH) in adults and adolescents (children older than 12 years of age). Efmody<sup>®</sup> has been extensively studied in 239 human subjects including 138 CAH patients who have taken part in clinical trials in Europe and the US.

The positive opinion from the CHMP received in March 2021 is based on a Phase 3 study conducted in a total of 122 patients enrolled across 11 clinical sites, the largest ever interventional clinical trial completed in CAH. The Phase 3 data was supported by detailed analysis of data from an open-label safety extension study for patients completing treatment in the Phase 3 study, which is assessing the impact of treatment with Efmody<sup>®</sup> over an extended period, with a number of patients on this trial having been treated for over 54 months. Patient retention rates in this study have been high and patients on this trial have, to date, shown sustained benefit from extended Efmody<sup>®</sup> treatment.

### About Diurnal Group plc

Diurnal Group plc is a European, UK-headquartered, specialty pharmaceutical company dedicated to developing hormone therapeutics to aid lifelong treatment for rare and chronic endocrine conditions, including congenital adrenal hyperplasia, adrenal insufficiency, hypogonadism and hypothyroidism. Its



expertise and innovative research activities focus on circadian-based endocrinology to yield novel product candidates in the rare and chronic endocrine disease arena.

For further information about Diurnal, please visit [www.diurnal.co.uk](http://www.diurnal.co.uk)

#### **About Citrine Medicine**

Citrine Medicine is dedicated to improving the lives of patients with rare and intractable diseases by making diagnosis and essential treatments available and accessible to those who need them in China. Our mission is to build the first rare disease ecosystem in China and in doing so, enable people with rare diseases to live more normal lives. In addition to developing and marketing rare disease drugs, Citrine aims to establish a patient-centric platform which educates people on rare diseases, trains doctors on diagnosis and treatment, and helps doctors develop a full disease management protocol. Citrine's lead product candidate, Wakix<sup>®</sup> (pitolisant), is an investigational oral drug in development for the treatment of narcolepsy and obstructive sleep apnea in China. Citrine has initiated an Investigational New Drug (IND) submission for pitolisant in the treatment of narcolepsy and expects to complete the IND submission in the first quarter of 2021. Citrine also recently announced a strategic partnership that will allow the company exclusive rights to develop, register, and commercialize Alkindi<sup>®</sup> - the first clinically validated pediatric treatment for congenital adrenal hyperplasia – in the Greater China market. Citrine is headquartered in Shanghai and has other offices in Beijing, China and Cambridge, Mass.

For further information about Citrine Medicine, please visit [www.citrinemed.com](http://www.citrinemed.com)

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