



## 2018 UPDATE AND 2019 OUTLOOK GIVEN AT THE CPHI CONFERENCE

- Estelle® Oral Contraception programme on track – US/CANADA Phase III arm due to complete in Q4 2018; partnering discussions ongoing including for US market
- Preparations for Phase III Donesta® trials moving ahead, including co-partnering discussions
- Further Marketing authorisations obtained for MyRing™
- Continuously improved IP portfolio
- Strengthened cash position

Liège, Belgium, 10 October 2018 – 20:30 CEST – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, provided an update on its key programmes at the CPHI world conference<sup>1</sup>.

### *Estelle® - Phase III in contraception*

Mithra believes that through the development of Estelle®, it is well positioned to offer a fifth-generation oral contraceptive pill which combines a unique safety profile with the quality of life benefits of established DRSP-based products. The Yaz® family of DRSP-based products are currently the best-selling contraceptive pills by value, with peak sales of EUR 1.2 billion, and are Mithra's benchmark for the commercialization of Estelle®.

On the business development front, Mithra has announced comprehensive licensing and supply agreements for a number of important pharmaceutical markets, including Europe, Japan, Canada, South Korea, Brazil and Russia. Recent positive Phase III clinical data has also increased interest among potential partners in other key markets in USA and Asia, including China, and South America.

The potential financial returns for Mithra from additional future agreements were demonstrated by the contract signed in September with Gedeon Richter to commercialize Estelle® in Europe and Russia. The terms of the agreement with Richter included an upfront payment totaling EUR 35 million and additional milestone payments of EUR 20 million depending on regulatory progress. Mithra is also entitled to receive additional sales-related milestones, guaranteed annual recurring revenues based on minimum annual quantities (MAQ), and tiered royalties ranging from high single-digit to substantial double-digits on net sales.<sup>2</sup>

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<sup>1</sup> Each year CPhI unites more than 100,000 pharmaceutical professionals through local and worldwide exhibitions, conferences and communities to network, identify business opportunities.

<sup>2</sup> Further information published in Mithra's press release: <https://investors.mithra.com/wp-content/uploads/2018/09/2018-09-12-details-GR-Estelle-en.pdf>

The agreements were followed by positive top-line results for the Phase III Estelle<sup>®</sup> study in Europe and Russia. The study successfully met its primary endpoint and achieved key secondary endpoints, including outstanding bleeding profile, cycle control, quality of life and safety and tolerability.

### *Donesta<sup>®</sup> - Phase II in menopause*

Mithra is also confident that Donesta<sup>®</sup> is well placed to become a new and safer treatment option for women in the menopause market, which is expected to be worth approx. USD 16 billion a year by 2025.<sup>3</sup>

A series of highly promising Phase IIb results have been presented this year for Donesta<sup>®</sup>, Mithra's next-generation hormone therapy (HT) product candidate with oral administration of Estetrol (E4). These data demonstrated a significant improvement in the frequency and severity of hot flushes, as well as in secondary menopausal symptoms such as VulvoVaginal Atrophy (VVA), while indicating a beneficial safety profile, including an encouraging cardiovascular safety profile and lower bone turnover versus placebo. This was again confirmed at the recent North American Menopause Society (NAMS) conference, where the Phase IIb results were presented to key KOLs in the field. Mithra is confident that if approved, Donesta<sup>®</sup> could offer a novel and differentiated therapy with an improved benefit/risk profile for women globally dealing with menopausal symptoms.

Preparations for a comprehensive Phase III trial of Donesta<sup>®</sup> are underway including good progress on the clinical trial protocols. Regulatory submission is expected in H2 2019. A number of discussions have been initiated with potential co-development partners for Donesta<sup>®</sup>.

### *Strengthening the pipeline through additional indications*

In addition to addressing major unmet need in the sizeable markets for oral contraception and menopause, Mithra believes that it can achieve considerable further value from the pursuit of additional indications for both Estelle<sup>®</sup> and Donesta<sup>®</sup>. A more detailed update will be provided in due course. To this end the Company is focused on extending the existing Estelle<sup>®</sup>, E4 and Donesta<sup>®</sup> intellectual property portfolio.

Based on the positive data from the hemostasis Phase II sub-study, Mithra applied for an additional patent claim for Estelle<sup>®</sup>. If granted, the patent would extend the existing E4 intellectual property estate, which comprises patents relating to the E4 synthesis process (until 2032) and E4 as a potential new emergency contraceptive option.

Following the receipt of orphan drug designation from the European Medicines Agency (EMA) for E4 for neuroprotective treatment of life threatening Hypoxic Ischemic Encephalopathy in newborn babies, Mithra is consolidating its proof of concept prior to clinical development with support from regional grants. In addition, **Mithra is also exploring the further potential of E4 in a range of new indications based on its IP portfolio which comprises 29 patent families** including, among others, E4 synthesis pathway, headache, and breast cancer. Moreover, Mithra is continuously expanding its IP portfolio to further strengthen and extend the E4 intellectual property estate.

### *Strong cash position to execute strategy and maximize portfolio potential*

Mithra continues to have a strong cash position, with the capacity to maximize the potential of its lead products and pipeline. At the end of June 2018, the Company had a cash position of EUR 85.8 million, supported by an oversubscribed fundraising announced in May 2018 which raised EUR 77.5 million. Since then, Mithra received EUR 20 million for the divestment of the BeLux generic portfolio and will

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<sup>3</sup> Transparency Market Research (2017); IMS link (Q2 2016); Datamonitor (2014).

get shortly the upfront payment totaling EUR 35 million for the license and supply agreement signed with Gedeon Richter, which in aggregate is much more than the cash burn over the period. As such, **these strategic transactions are improving significantly the 30<sup>th</sup> June cash position.**

In addition, Mithra is continuing the roll out of promising products including MyRing™, the hormonal contraceptive vaginal ring, which is on track for launch in the US in 2019. As such Mithra recently obtained further marketing authorisations in Czech Republic and Poland. Moreover, international partnering discussions across the portfolio are expected to continue in order to boost revenues and underscore the Group's financial strength in the short- and medium term.

**François Fornieri, CEO of Mithra Women's Health commented:** *"Mithra is excellently placed to bring two products with blockbuster potential to the market in the near to medium-term, based on our innovative E4 platform.*

*The promise of Estelle® as a new generation oral contraceptive offering clear benefits to women has already been underlined by top-line results from the extensive Europe/Russia Phase III study. We now look forward to results from the parallel US/Canada study, which will be completed in due course.*

*Prospects for our second blockbuster candidate Donesta® for hormone therapy have been buoyed by a series of encouraging data from the Phase IIb trial, showing a statistically significant reduction in the frequency of hot flushes. This was again confirmed at the recent NAMS conference. We look forward to updating the market on partnering discussions for Estelle® globally, including the attractive US market, and Donesta® in due course.*

*In addition to maximizing the value of Estelle® in contraception and Donesta® in menopause, we are focused on creating greater value through additional indications. With differentiated lead products in large markets of unmet need, a strong financial position, the roll out of promising approved products including MyRing™, and the potential for further lucrative partnerships, we believe we are uniquely positioned for continued growth."*

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#### **About Mithra**

Mithra (Euronext: MITRA) is dedicated to providing innovation and choice in women's health, with a particular focus on fertility, contraception and menopause. Mithra's goal is to develop new and improved products that meet women's needs for better safety and convenience. Its two lead development candidates - a fifth generation oral contraceptive, Estelle®, and a next generation hormone therapy, Donesta®- are built on Mithra's unique natural estrogen platform, E4 (Estetrol). Mithra also develops, manufactures and markets complex therapeutics and offers partners a complete spectrum of research, development and specialist manufacturing at its Mithra CDMO. Mithra was founded in 1999 as a spin-off of the University of Liège by Mr. François Fornieri and Prof. Dr. Jean-Michel Foidart and is headquartered in Liège, Belgium. Further information can be found at: [www.mithra.com](http://www.mithra.com)

**Important information**

*The contents of this announcement include statements that are, or may be deemed to be, "forward-looking statements". These forward-looking statements can be identified by the use of forward-looking terminology, including the words "believes", "estimates," "anticipates", "expects", "intends", "may", "will", "plans", "continue", "ongoing", "potential", "predict", "project", "target", "seek" or "should", and include statements the Company makes concerning the intended results of its strategy. By their nature, forward-looking statements involve risks and uncertainties and readers are cautioned that any such forward-looking statements are not guarantees of future performance. The Company's actual results may differ materially from those predicted by the forward-looking statements. The Company undertakes no obligation to publicly update or revise forward-looking statements, except as may be required by law.*

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