



MITHRA STRENGTHENS E4 PATENT POSITION IN AUSTRALIAN MARKET

- **Patents granted for Estetrol (E4) synthesis protect manufacturing process until 2032**
- **Certificate of grant covers E4's use alone as an emergency contraceptive**

Liège, Belgium, 6 July 2017 – Mithra (Euronext Brussels: MITRA), a company specialized in Women's Health, today announces that the Australian Patent Office, IP Australia, has granted patents covering the synthesis process of Estetrol (E4).¹ IP Australia has also accepted a patent application for a patent covering E4 alone as an emergency contraceptive.² E4, a naturally occurring estrogen, is currently being studied in the *E4 Freedom* Phase III study program in contraception (Estelle®, 15 mg E4/3 mg drospirenone) and in the *E4 Relief* Phase II trial for menopause (Donesta®, dose-finding study with E4 alone).

The synthesis patents, which run until 2032, is an essential IP layer to extend existing patent families and protect the production know-how of Mithra's E4-based product candidates. The synthesis process, which optimizes and reduces the costs of manufacturing E4, was developed in exclusive partnership with PCAS (France), a leading manufacturer of complex molecules. The patent follows similar patents granted in territories including Europe, Eurasia and Hong Kong.

The additional emergency contraception patent, when granted, will specifically cover E4 as a potential new emergency contraception option where E4 is used alone. This new method differs from currently approved emergency contraceptives which include progestin-only pills and combined estrogen-progestin pills. E4's potentially improved safety profile when compared to currently marketed estrogens, could provide an attractive alternative to emergency contraceptive options available to women today.^{3,4} E4's use as an emergency contraception is supported by its specific and unique mode of action wherein E4 activates the nuclear estrogen receptor but blocks the membrane

¹ Patent references: 2012320423, 2012264601, 2012264602

² Patent reference: 2012293593. The patent has been accepted, and should be granted in the near future.

³ See e.g. Kluft et al. 2016; Gerard et al. 2015; Visser et al. 2012

⁴ A similar patent allowance was obtained from the United States Patent and Trademark Office (USPTO) in January 2017 (U.S. Application Serial Number 14/238,310)

estrogen receptor. Research suggests that inhibition of the membrane estrogen receptor plays a key role in suppressing ovulation.⁵

François Fornieri, CEO of Mithra, commented: *“We are pleased with the IP progress made in Australia, both with regard to the synthesis of E4 as well as for E4’s development in emergency oral contraceptive applications. Given its unique mode of action, E4 has the potential to revolutionize the contraceptive and menopause market, offering a potentially improved safety profile compared to the current generation of estrogens, and we consider Australia an important additional market for these indications.”*

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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 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 CDMO.

⁵ Adlanmerini et al. 2014. *PNAS* 111 (2): E283-E290

Mithra was founded in 1999 as a spin-off from the University of Liège by Mr. François Fornieri and Prof. Dr. Jean-Michel Foidart. Mithra is headquartered in Liège, Belgium. Further information can be found at: 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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