



## Mithra announces positive preclinical data demonstrating Estetrol's efficacy in wound healing

- Positive results from preclinical studies demonstrating that Estetrol promotes wound healing, supporting its use in clinic
- Robust mechanism of action data show that Estetrol improves wound closure and dampens local inflammation, supported by a unique gene signature, compared to other estrogens
- Development of a novel Estetrol formulation for topical application is ongoing, with potential benefit in both acute and chronic wound settings

**Liege, Belgium, 12 October 2022 – 7:30 CET** – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces positive results from preclinical studies demonstrating the efficacy of Estetrol in wound healing. Estetrol (E4) is a naturally occurring estrogen produced by the human fetus during pregnancy, which can be synthesized from plant source. Beyond Women's health, Mithra is also exploring Estetrol's potential in other areas of application, in particular in pediatric neuroprotection and wound healing.

Preclinical data from two different studies conducted by the Hull York Medical School in collaboration with Mithra, show that Estetrol is able to promote wound healing, strengthening the case for its therapeutic use in wound care. In a first study, Estetrol was shown to promote healing of injured human cells, both primary fibroblasts (components of the deeper layers of the skin) and keratinocytes (cells found in the outer layer of the skin). These two cell types play a crucial role in wound healing.

This healing promoting potential of Estetrol treatment was also confirmed in an in vivo study using a model of delayed healing<sup>1</sup>. Significantly improved healing was observed after topical treatment with an Estetrol-based formulation, associated with a 100% increase in re-epithelialisation and a dampening of local inflammation. Global gene expression analysis highlighted a unique molecular mode of action of Estetrol in wound healing compared to Estradiol (E2), strengthening the case for its therapeutic use in wound care.

**Professor Matt Hardman, Director of Research, Hull York Medical School (UK), commented:** *"We have known for several decades that estradiol (E2) can have beneficial effects on both the skin and wounds, yet E2 has never made it to the clinic. These new findings of healing promotion with Estetrol (E4) administration are hugely encouraging. What is particularly exciting is that E4 appears to act on multiple aspects of healing at the same time. There is a high probability that these positive effects will translate into patients, offering a potential new treatment for problem wounds that could be both effective and safe."*

**Graham Dixon, Chief Scientific Officer Mithra Women's Health, commented:** *"Scar formation after a wound is a major medical problem that can have devastating consequences for patients, with severe physiological and psychological effects. Today, there are no reliable treatments to prevent scarring. Previous studies<sup>2</sup> have shown that early gestation human fetal skin wounds repair more rapidly*

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<sup>1</sup> Wound model in which healing is delayed due to bacterial infection. Delay of healing is associated to reduced re-epithelialisation and heightened inflammatory response.

<sup>2</sup> "Scarless Fetal Wound Healing: A Basic Science Review", <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4229131/>

*and in the absence of scar formation, in contrast to adult wounds. Significant differences exist among gene expression profiles of fetal and postnatal wounds. Since Estetrol is one of the few fetal specific hormones, it could play an important regulatory role in wound healing without scarring. Its minimal skin penetration would prevent systemic exposure while its neutrality on coagulation would offer considerable added safety in comparison to other estrogens."*

**Professor Keith Harding, Head of the Wound Healing Research Unit, School of Medicine, Cardiff University, commented:** *"The results presented are extremely encouraging for the use of Estetrol in treatment of wounds. There is potential in both the acute and chronic wound settings. In my opinion the data fully supports confirmation of this potential in the clinic".*

This significant milestone paves the way to the next phases of development. Mithra will finalize the development of its novel formulation of Estetrol for topical application in order to produce a first clinical batch. Depending on the results, the clinical program is expected to be launched in the second half of 2023 with a punch biopsy study aimed to explore the safety and efficacy of Mithra's E4 topical lead formulation.

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### For more information, please contact:

**Benoît Mathieu (IRO)** : +32 473 35 80 18 – [investorrelations@mithra.com](mailto:investorrelations@mithra.com)

**Maud Vanderthommen (Press)** : +32 473 58 61 04 – [press@mithra.com](mailto:press@mithra.com)

### About Mithra

*Mithra (Euronext: MITRA) is a Belgian biotech company dedicated to transforming Women's Health by offering new choices through innovation, with a particular focus on contraception and menopause. Mithra's goal is to develop products offering better efficacy, safety and convenience, meeting women's needs throughout their life span. Mithra explores the potential of the unique native estrogen estetrol in a wide range of applications in women health and beyond. After having successfully launched the first estetrol-based product in 2021, the contraceptive pill Estelle<sup>®</sup>, Mithra is now focusing on its second product Donesta<sup>®</sup>, the next-generation hormone therapy. Mithra also develops and manufactures complex therapeutics in the areas of contraception, menopause and hormone-dependent cancers. It offers partners a complete spectrum of research, development and specialist manufacturing at its technological platform Mithra CDMO. Active in more than 100 countries around the world, Mithra has an approximate headcount of 300 staff members and is headquartered in Liège, Belgium.*

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*Estelle<sup>®</sup> and Donesta<sup>®</sup> are a registered trademark of Mithra Pharmaceuticals or one of its affiliates.*

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