Mithra receives guidance from the FDA for the DONESTA® NDA marketing authorization filing in the United States

- DONESTA® for the treatment of vasomotor symptoms of menopause, is expected to target the entire accessible US market of nearly 63 million women between the ages of 45 and 65, pending FDA approval
- Following FDA advice, preparation of filing is proceeding with a filing date now planned in Q4 2024
- FDA marketing authorization, contingent upon successful completion of the approval process, now expected in Q4 2025
- Agreement for US commercialization partner for DONESTA® now expected during 2024
- Mithra to seek DONESTA® approval in US and Europe concurrently for the treatment of vasomotor symptoms of menopause; target submission date for EMA filing also expected in Q4 2024
- Patent coverage in the US for DONESTA® as a treatment for vasomotor symptoms associated with menopause is expected until 2039

Liege, Belgium, 30 November 2023 – 7:00 CET – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces that the US Food and Drug Administration (FDA) has provided feedback regarding its new drug application (NDA) marketing authorization filing in the United States. This follows an agreement in principle with the FDA for Mithra to conduct additional endometrial data analyses. As a result, the formal NDA submission is now planned for Q4 2024 to allow for the time required to perform these additional analyses pursuant to FDA guidance.

Pending regulatory approval, DONESTA® is expected to target a US market of nearly 63 million women between the ages of 45 and 65 years-old and experiencing vasomotor symptoms of menopause (VMS). Due to the variation observed by Mithra in the endometrial biopsy diagnoses — which could have resulted in a limited addressable market for DONESTA®— the company has decided to conduct additional endometrial data analyses from its phase 3 program for the DONESTA® menopause candidate-medication. The delay will enable complementary data to be submitted and evaluated for both FDA and the European Medicines Agency (EMA) submissions within the same time frame. Mithra is actively continuing the process of collecting and providing all required data to the FDA for submission.

Mithra continues to actively seek a commercialization partner for the US market and has already received positive interest from several potential candidates. Mithra will continue to progress discussions with potential partners in parallel to the NDA submission process. Mithra recently announced licensing agreements in other regions (*e.g.,* Canada and Europe). Mithra aims to establish an agreement for DONESTA® US commercialization during 2024. Mithra has engaged with Stifel as its financial advisor to oversee the process of establishing a commercialization partner for DONESTA®.

"We strongly believe that DONESTA® will be a game-changer for the treatment of the symptoms of menopause and Women's Health in the United States, Europe and other parts of the world," said David H. Solomon, CEO of Mithra. "As with any new medication, obtaining clearance requires the necessary diligence and learning, and we have actively requested additional data analyses to ensure we prioritize an accurate assessment of the DONESTA® benefit-to-risk profile. DONESTA® has the potential to offer differentiated efficacy, safety and convenience to millions of women who are underserved and often suffer in silence from the symptoms of menopause. DONESTA® clinical results to date suggest it may be one of the biggest advances in menopausal hormone therapy in the past decades. DONESTA® and the potential benefits it will offer to women in the US is demonstrated by our recent commercialization deals in other regions throughout the world. Furthermore, we are excited that the FDA will review the DONESTA® file for the total applicable population in the US. With patent protection expected until 2039 in the US, we are excited about the long exclusivity period for DONESTA® in the treatment of the symptoms of menopause. We believe it is in our shareholders' interest to take additional time to sign a US deal under conditions where the full value of DONESTA® will be captured; the delay affords us additional time to run our process and find the best partner," said Mr. Solomon. "For this reason, we have updated our guidance while we focus on re-starting the review of the data and ensure the integrity of the regulatory process."

Graham Dixon, Chief Scientific Officer of Mithra added, "The FDA's feedback is very valuable to facilitate the regulatory review process. These additional data will be submitted to the EMA in the same timeframe. This will allow Mithra to request marketing approvals to both the FDA and the EMA, concurrently. Estetrol's action on the uterine lining is well understood and expected. These additional data inform our research on other promising applications of E4 in women's health. In fact, this effect can potentially be used as a treatment to enhance fertility for women who are undergoing IVF, for example. We have begun research to explore an estetrol-based solution for this market."

DONESTA® is Mithra's next generation orally administrated estrogen; an estetrol-based hormone therapy product candidate offering a potential long-term solution for treating various symptoms of menopause. Estetrol (E4) is the first native estrogen, present in developing human fetuses and is manufactured from a plant-based source.

E4 acts differently from classical estrogens. Its selective activation of nuclear estrogen receptors and its unique metabolism result in a low impact on haemostasis and breast tissue with an expected improvement in the benefit-to-risk profile. In early 2022, Mithra announced positive top-line efficacy results of the DONESTA® phase 3 program, which demonstrated a meaningful reduction in VMS from baseline and compared to placebo with all co-primary efficacy endpoints statistically met. Data also showed improved quality of life and reduction of genito-urinary symptoms of menopause, as secondary efficacy endpoints.

For more information, please contact:

Mithra Pharmaceuticals SA
Alex Sokolowski, PhD
Head of Investor Relations
investorrelations@mithra.com
+32 (0)4 349 28 22

Frédérique Depraetere
Communication Director
info@mithra.com
+32 (0)4 349 28 22

About Mithra

Mithra Pharmaceuticals SA (Euronext: MITRA) is a Belgian biopharmaceutical 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®, Mithra is now focusing on its second product DONESTA®, the next-generation hormone therapy. Mithra also offers partners a complete spectrum of solutions from early drug development, clinical batches and commercial manufacturing of complex polymeric products (vaginal ring, implants) and complex liquid injectables and biologicals (vials, pre-filled syringes or cartridges) at its technological platform Mithra CDMO. Active in more than 100 countries around the world, is headquartered in Liège, Belgium. 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.