Mithra Announces Improved Consolidated Topline Results from Donesta® Phase 3 Studies and Launch of Recruitment for the Extension of European Study

- **Consolidated analysis of Phase 3 top line data showed even more positive results than initially announced, with all four co-primary endpoints met**
- **Donesta® safety profile confirmed by independent Data Safety Monitoring Board (DSMB), which recommended to continue the Phase III Clinical Program**
- **Launch of the recruitment of the additional 300 menopausal women thanks to a successful mitigation plan**

Liege, Belgium, 14 April 2022 – 7:30 CEST – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health today announces consolidated positive topline results of Phase 3 Donesta® Program. Donesta® is Mithra's next generation orally-administrated estetrol (E4)-based hormone therapy product candidate offering a potential long-term solution for treating different symptoms of menopause, simultaneously or sequentially, caused by estrogen loss.

All four co-primary endpoints met

On 14 January 2022, Mithra announced the first efficacy data of Donesta® Phase 3 Program, which demonstrated a meaningful reduction in vasomotor symptoms (VSM) from baseline and compared to placebo[1]. After further in-depth analysis of all the research data consolidated by the Contract Research Organization in charge of the management of the Donesta® studies, Mithra is particularly pleased to announce that the efficacy results are even better than previously announced. This consolidated analysis showed that all co-primary efficacy endpoints[2] were statistically (all $p<0.05$) met in both studies. Even in the C302 study, the result for the severity criteria reached statistical significance at week 4, and not at week 5 as initially reported.

Launch of Recruitment for Extension European Study

Mithra also announces today the initiation of the recruitment of 300 additional menopausal non-hysterectomised women for its Donesta® European Study (C301), following the decision of the independent Data and Safety Monitoring Board (DSMB).

The experts of the DSMB completed the first 2022 quartely safety assessment of the Phase 3 Clinical Program of Donesta® and recommended to continue the studies, allowing Mithra to launch the recruitment for the extension of the European study[3]. Thanks to the implementation of our mitigation plan activated immediately after the beginning of the geopolitical crisis in Eastern Europe, all the

[1] Mithra's press release 14/01/2022

[2] The co-primary efficacy endpoints are the mean change from baseline in the frequency and severity of moderate to severe VMS at week 4 and week 12 compared to placebo.

[3] Mithra's press release 21/09/2021

Russian sites originally selected for participating in the study were replaced by other sites to ensure a direct start of recruitment. The recruitment of these 300 women should be completed within the next 6 months. Barring any unforeseen event, Mithra confirms its ambition to achieve marketing authorization for Donesta® in H1 2024 for the United States and in H2 2024 for Europe.

The Donesta® Phase III Clinical Program is still ongoing with patients completing a treatment duration for 52 weeks. The primary safety data are anticipated at the end 2022 for the North American study (C302) and for end H2 2023 for the European study (C301).

Leon Van Rompay, CEO Mithra Women's Health, commented: *"These excellent efficacy results demonstrates that Donesta® should offer the most complete profile of symptom relief compared to any of the existing or pipeline therapies for menopause symptom treatment. By the end of the year we will be able to demonstrate again the unique safety profile of E4, building further on the fantastic potential of this molecule. From the very beginning of the geopolitical crisis, our teams have immediately activated a mitigation plan allowing us to launch the recruitment of the additional European study right after the DSMB's green light. Despite the current economical and geopolitical context, we don't expect any delay for the obtention of the marketing authorizations, which demonstrates that Mithra's teams remain fully focused on our achievements and strongly committed to converting the potential of our products into success."*

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About E4 Comfort Phase 3 Program

*Donesta® phase III Clinical Program "E4 Comfort" carried out on 2,300 postmenopausal women (40-65 years) includes 2 pivotal studies: one in America (*NCT04090957*-C302); and a second spread over 14 countries in Europe, Russia and America (*NCT04209543 *-C301). Both studies are worldwide randomized, multicenter, double-blind, placebo-controlled trials.*

Each studies is composed of an efficacy and a safety part. The efficacy part in each studies is designed to evaluate the frequency and severity of vasomotor symptoms (VMS) in both hysterectomized and non-hysterectomized postmenopausal participants after treatment with two doses of E4 (15 mg or 20 mg) or placebo for 12 consecutive weeks. For endometrial protection, all non-hysterectomized subjects will receive treatment with 200 mg progesterone (P4) once daily for 14 consecutive days, after completion of the E4/placebo treatment.

The safety part of the C302 study is designed to evaluate the general safety and secondary endpoints (health-related quality of life, treatment satisfaction, hemostasis, lipid and glucose metabolism, breast density and endometrial safety) in hysterectomized and non-hysterectomize women after treatment with E4 20 mg for one year. The safety part of the C301 study is designed to evaluate the endometrial safety of E4 20 mg in combination with continuous administration of 100 mg P4 in non-hysterectomized women for one year.

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®, Mithra is now focusing on its second product Donesta®, 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. 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.