Mithra Initiates Phase III Clinical Program for Donesta®

- **Recruitment of the first patient marking the launch of "E4 Comfort" Phase III Clinical Program for Donesta® in menopausal women with vasomotor symptoms**
- **Phase III program includes two pivotal studies aimed at enrolling a total of 2200 women aged from 40 to 65 years**

Liege, Belgium, 9 October 2019 – 7:30 CEST – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces the launch of the Donesta® Phase III clinical program called "E4 Comfort", with the recruitment of the first patient for the North American Phase III study with E4 monotherapy. Donesta® is a next generation orally-administered E4-based hormone therapy product candidate for the relief of vasomotor menopausal symptoms (VMS).

The E4 Comfort Phase III study will evaluate the efficacy and safety of Estetrol (15mg and 20 mg) for the treatment of moderate to severe VMS (i.e. hot flushes) in menopausal women. This clinical program includes two pivotal Phase III studies: the first one in North America (United States/Canada); the second one in 12 countries in Europe, Russia and South America. The recruitment of North American subjects has already begun; the first subject for the second study is anticipated in December 2019. The Phase III Program, entirely funded by Mithra, should be completed over a period of two years.

Presented at various international scientific conferences[1], results of a Phase IIb study for Donesta® showed that 15mg E4 significantly reduces the frequency and severity of hot flushes, as well as secondary menopausal symptoms such as vulvo-vaginal atrophy (VVA), while confirming a promising safety profile. These data also demonstrated an encouraging cardiovascular safety profile and lower bone turnover versus placebo[2]. The promising safety profile at both hemostatic and metabolic levels is consistent with the findings obtained during Clinical Program of Estelle® contraceptive.

Graham Dixon, CSO of Mithra Women's Health: *"The launch of the Phase III Clinical Program is a significant milestone in the development of Donesta®, highlighting the intensive work of our dedicated R&D team. Menopause symptoms affect a majority of women and can be quite disabling in everyday life. However, only less than 10% of women decide to treat their symptoms, mainly because of an important unmet need for novel hormone therapy treatments that offer an improved benefit/risk ratio, while addressing women's needs in terms of quality of life. Donesta® could offer women a real alternative, given its unique mode of action as a native estrogen."*

Depending on regulatory approvals, Mithra believes it could achieve marketing authorization for Donesta® in 2023. Ongoing patent applications would protect Donesta® intellectual property rights until 2039. Furthermore, Mithra remains focused on establishing the best commercial partnerships for

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1 World Congress on Menopause (June 2018), North American Menopause Society (October 2018) and European Menopause & Andropause Society Congress (May 2019).

2 As measured by a decrease in both the CTX-1 and osteocalcin markers with E4 use vs placebo. The effect is most pronounced for the 15 mg dose (near-significant for CTX-1 and significant at $p < 0.05$ for osteocalcin)

this promising product, as well as for PeriNesta®. Commercial licensing agreements in menopause and in perimenopause in the U.S. and in the main European markets will continue to be accelerated. The global menopause market currently stands at USD 12.6 billion and is expected to grow to approximately USD 16 billion by 2025[3].

About E4 Comfort Phase III Program

The Donesta® Phase III study program includes 2 studies which design is a worldwide randomized, multicenter, double-blind, placebo-controlled trial. The studies primary objective is to measure the effect of treatment with different E4 doses (15mg and 20 mg) compared to placebo on frequency and severity of moderate to severe VMS in menopausal women at 4 and 12 weeks. Secondary objectives include the evaluation of the effect of the treatment on a series of additional key efficacy and safety parameters.

The North American study (United States/Canada) is aimed at enrolling 1000 menopausal women between 40 and 65 years. The second pivotal study will be conducted in 12 countries (Europe, Russia, South America) with about 1200 menopausal women. For each pivotal study, women will be recruited at about 120 sites in the concerned areas.

For more information about the E4Comfort Phase III program, please visit http://www.clinicaltrials.gov (North American study online NCT04090957 - Europe/Russia/Latam study available in the coming weeks)

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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 contraception and menopause. Mithra's goal is to develop new and improved products that meet women's needs for better safety and convenience. Its three lead development candidates – a fifth generation oral contraceptive Estelle®, the first complete oral treatment for perimenopause PeriNesta™ and next-generation hormone therapy Donesta® - are built on Mithra's unique native estrogen platform, E4 (Estetrol). Mithra also develops and manufactures complex therapeutics and offers partners a complete spectrum of research, development and specialist manufacturing at its CDMO. Mithra was founded in 1999 as a spin-off from the University of Liège by 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

[3] Transparency Market Research 2017

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.