# MITHRA ANNOUNCES LAST SUBJECT VISIT IN ESTELLE® PHASE III STUDY IN EU/RUSSIA AND COMPLETION OF ENDOMETRIAL SUBSTUDY

- **Estelle® Phase III studies remain on track to report top-line results in Q3 2018 from Europe/Russia and Q1 2019 from US/Canada**
- **Endometrial safety substudy expected to report results in Q3 2018**

**Liège, Belgium, 3 May 2018 – 7:30 AM** – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces that the last subject in the European/Russian Phase III Estelle® study has now completed her last study visit. Mithra also announces that the endometrial safety substudy has completed recruitment. Estelle® is Mithra's combined oral contraceptive (COC) candidate, composed of 15 mg Estetrol (E4) and 3 mg drospirenone (DRSP), and is currently being tested in two Phase III trials in Europe/Russia and in the US/Canada.

The Phase III European/Russian study of Estelle® has seen a lower than expected drop-out rate with over 1,200 women completing the minimum 13-cycles of treatment from the 1,577 women recruited. This could be indicative of the good user acceptability and well-being of study subjects taking Estelle®. In the US/Canadian study, 2,148 women were recruited, and the last subject visit is expected to take place in Q4 2018. As a reminder, the two pivotal studies have already fulfilled regulatory requirements for a minimum total of 20,000 cycles, of which 50% have to be from North America.

The endometrial safety substudy is part of the Phase III program in Europe/Russia and is a regulatory requirement to determine the endometrial safety profile of Estelle®. With recruitment now complete, the study is on track to report top line results in Q3 2018. In this study, endometrial biopsies have been obtained from 101 subjects at both the screening visit and the seventh study visit, with the paired biopsies analysed to assess the potential impact of Estelle® on the endometrium after at least 10 cycles of Estelle®.

**François Fornieri, CEO Mithra Women's Health:** *"The Phase III Estelle® program continues to make great progress and we are pleased to have achieved these two additional important milestones, with all study timings remaining on track. We continue to believe Estelle® is working as expected, with a strong contraceptive efficacy, and we hence hope to obtain a low Pearl Index (PI) in the European study. Moreover, the lower than expected drop-out rate provides yet another indication of the user acceptance of Estelle® and well-being of subjects using our novel COC product candidate. We look forward to reporting top-line results in Q3 2018 for Europe/Russia and in Q1 2019 for US/Canada. We continue to believe that Estelle® has the potential to become a true 'next generation' contraceptive, offering a beneficial risk/benefit profile to women worldwide."*

## About the *E4 Freedom* Estelle® Phase III program

The *E4 Freedom* Phase III program consists of two open-label, single arm studies. The European/Russian Phase III Estelle® study has enrolled 1,577 subjects aged 18-50 years of whom 1,350 subjects are aged 18-35 years. The study is taking place in 69 centers across Europe and Russia. The Phase III Estelle® study design in the US & Canada has enrolled 2,148 subjects aged 16-50 years of whom 1,940 subjects are aged 16-35 years. The study is taking place in approximately 77 centers

across the US and Canada. Estelle® is Mithra's combined oral contraceptive (COC) candidate composed of 15 mg Estetrol (E4) and 3 mg drospirenone (DRSP).

The objectives of both studies are to evaluate the contraceptive's efficacy, cycle control, and the general safety and acceptability of the 15 mg E4 (Estetrol) and 3 mg DRSP combination oral contraceptive pill in healthy women, and involves subject participation for a period of minimum 12 months (13 cycles, 1 cycle = 28 days).

The primary outcome is contraceptive efficacy measured by the number of pregnancies per 100 women per 12 months of exposure (Pearl Index; PI) in the primary population. In Europe/Russia this is in subjects aged 18-35 years old and in the US/Canada in subjects aged 16 to 35 years old.

Secondary outcomes include the method failure PI in the primary population as well as the PI within the overall study population. Also, cycle control and bleeding profile, safety and tolerability, and general wellbeing of the subjects (measured by two questionnaires) are analyzed. A pharmacokinetic (PK) substudy, in the US/Canada study, will assess the effect of various individual characteristics/covariates (such as race and BMI) on the PKs of 15 mg E4/3 mg DRSP.

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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 a 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 Mithra CDMO. Mithra was founded in 1999 as a spin-off of the University of Liège by Mr. François Fornieri and Prof. Dr. Jean-Michel Foidart and 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*

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