MITHRA ANNOUNCES POSITIVE TOP-LINE RESULTS OF ESTELLE® PHASE III ORAL CONTRACEPTIVE STUDY IN EU/RUSSIA

- **Primary efficacy endpoint indicates excellent contraceptive efficacy, with a Pearl Index (PI) of 0.48 per 100 women, exceeding efficacy goals**
- **Key secondary endpoints achieved, including outstanding bleeding profile, cycle control, quality of life and safety and tolerability**
- **Estelle® Phase III stsudy in US/Canada on track to report top-line results in Q1 2019**
- **Data further support Estelle® as a novel, next-generation combined oral contraceptive for women**

Liège, Belgium, 8 August 2018, 07:30 CEST – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announced that its Phase III Estelle® study conducted in Europe and Russia successfully met its primary efficacy endpoint. Estelle® is Mithra's combined oral contraceptive (COC) candidate, composed of Estetrol (E4) 15 mg and drospirenone (DRSP) 3 mg.

The study assessed the efficacy, cycle control, general safety and acceptability of Estelle® in healthy women aged 18-50 years and involved subject participation for 12 months (13 cycles, 1 cycle = 28 days). Women with a Body Mass index (BMI) up to 35.0 kg/m² were allowed to participate.

The primary endpoint was contraceptive efficacy measured by the number of pregnancies per 100 women per 12 months of exposure (Pearl Index; PI) among the women aged 18-35 years old at study entry. Results showed a PI of 0.48 (confidence interval 0.15-1.11) during 13,688 cycles, with reported sexual activity and in the absence of other contraceptive methods. The PI corresponds to a 99.5% efficacy rate over one year of use, exceeding the efficacy goals of the study. A PI and its difference with the upper limit of the confidence interval below 1 is a regulatory requirement of the European Medicines Agency (EMA)[1].

Additionally safety, acceptability and general well-being of the subjects (measured by two validated questionnaires) were also analyzed. Results from the MDQ (menstrual distress questionnaire) and QOL (quality of life) questionnaire showed that Estelle® is well tolerated by women, while their overall quality of life is maintained.

Moreover, the safety profile did not demonstrate unexpected events. The global safety assessment will be communicated in detail once the Phase III US/Canada study has been completed.

Cycle control and bleeding profile, which are essential to women's compliance, showed an excellent regular bleeding pattern, comparable to that of Ethinyl-Estradilol (EE) containing oral contraceptives.

[1] EMEA/CPMP/EWP/519/98 Rev 1

The safety profile is supported by the unique Mode of Action (MOA) of E4, which is a Native Estrogen with Selective action in Tissues (NEST). It is present in the human fetus, where it is synthesized by the liver. Two earlier Phase II studies conducted by Mithra confirmed E4 has a minimal impact on liver cells including on the coagulation parameters[2] and the overall beneficial hemostatic profile. These coagulation parameters are considerably more increased by EE, present in most oral contraceptives, making Estelle® a promising new contraceptive solution for women with a unique benefit/risk profile.

Topline results from a parallel Phase III study of Estelle® in the US/Canada are on track to be announced in the first quarter of 2019.

Valerie Gordenne, CSO Mithra Women's Health, commented: *"The introduction of a new fetal estrogen with a unique MoA into the field of oral contraception provides an outstanding opportunity for women to use a well-tolerated and reliable contraceptive, with an improved benefit/risk profile. We are very encouraged by both the PI and the quality of life parameters, including the cycle control. Indeed, based on these results as well as our previously published Phase II results, we believe Estelle® offers a truly innovative, next-generation oral contraceptive option, and we are looking forward to the* results of our US/Canadian study."

François Fornieri, CEO Mithra Women's Health, commented: *"The top-line results from the first of two extensive international Phase III trials in our E4 Freedom program demonstrate that Estelle® has great potential as a novel, next-generation combined oral contraceptive for women. Estelle® has shown a strong contraceptive efficacy with a very low Pearl Index, even if compared to the most efficacious combined oral contraceptives currently commercialised. It was well tolerated and did not impact women's quality of life. These data further support our belief that Estelle®'s beneficial risk/benefit profile has the potential to offer real innovation and choice in contraception to women around the world. We look forward to presenting the full data from this trial at future scientific congresses as well as the top-line results of the US/Canada Phase III study in Q1 2019."*

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 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.

[2] Kluft C et al., Contraception 2017; 95(2):140-7 ; https://investors.mithra.com/wp-content/uploads/2018/03/2018-03-08-Hemostasis-ISGE-en-final.pdf

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.

******

For more information, please contact:

Investor Relations
François Fornieri, CEO
+32 4 349 28 22
investorrelations@mithra.com

Consilium Strategic Communication
Melissa Gardiner, Jonathan Birt, Olivia Manser
mithra@consilium-comms.com
+44 2 037 095 700

Scientific Contact
Prof. Jean-Michel Foidart
jmfoidart@mithra.com

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 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.