Mithra Receives Orphan Drug Designation from FDA for E4 in Neonatal Encephalopathy Treatment

- **The US Food and Drug Administration granted E4 an ODD for the treatment of life-threatening hypoxic ischemic encephalopathy (HIE)**
- **This new designation expands E4's broad potential in therapeutic areas beyond the leading indications in women's health**
- **Mithra continues its preclinical studies in HIE, a severe pediatric syndrome that affects 30,000 newborns each year in Europe and the United States**

Liege, Belgium, 2 April 2019 – 7 :30 CET – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health today announces that it has received Orphan Drug Designation (ODD) from the Food and Drug Administration (FDA) for the use of E4 in Neonatal Encephalopathy (NE). In addition to its three late-stage E4-based product candidates for contraception, perimenopause and menopause, Mithra is developing E4's potential in other therapeutic areas, particularly in neuroprotection for the treatment of hypoxic ischemic encephalopathy (HIE), a life-threatening form of neonatal asphyxia.

A subset of NE which accounts for 50-80% of cases, EHI affects approximately 30,000 newborns each year in the European Union and the U.S.[1] This syndrome is a consequence of the reduction in the supply of blood or oxygen to the baby's brain before, during or shortly after birth. Nearly one in four infants affected will die prior to discharge from the neonatal intensive care unit. Among surviving infants, severe neurological impairment and long-term disability are observed, with 46% affected at 18-22 months follow-up[2]. Currently, HIE is treated with therapeutic hypothermia, or 'cooling', in order to reduce brain damage, but this treatment has limited efficacy and comes at a high cost[3,4]. Given its significant mortality and morbidity in the newborn and the lack of available therapeutic alternatives, the development of a new E4-based treatment could meet a serious unmet medical need.

The FDA has granted Orphan Drug designation for E4 in the treatment of HIE based on promising preclinical results, in particular in pathophysiology, general well-being and motor functions. Mithra had already obtained this Orphan Drug designation from the European Medicines Agency (EMA) in June 2017 and the non-clinical program is moving forward. This program has been previously funded and Mithra will seek partners for the clinical development.

François Fornieri, CEO of Mithra Women's Health, commented: *"The Orphan Drug Designation for E4 in Neonatal Encephalopathy underlines the potential of our unique natural E4 estrogen platform in areas beyond Women's Health, including neuroprotection. Hypoxic Ischemic encephalopathy affects*

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[1] Kurinczuk et al. *Early Hum Dev* 2010; 86: 329-338, 2010.

[2] Shankaran et al. *Early Hum. Dev.* 1991; 25(2):135–148.

[3] Cotten & Shakarn. *Expert Rev Obstet Gynecol*. 2010; 1;5(2):227-239.

[4] Regier et al. *Value Health*. 2010; 13(6):695–702.

30,000 infants each year in Europe and the United States and still has a limited supply of treatments, both in terms of efficacy and access. The first promising results of our preclinical studies and this dual designation as an orphan drug, encourage us to pursue our development of an alternative treatment for this life-threatening pediatric syndrome."

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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, manufactures and markets 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 Mr. 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 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.