



Mithra holds today its Investor Day at Mithra CDMO

- Mithra's R&D and manufacturing center welcomes investors and analysts to give a strategic update of its pipeline and a tour of its facilities
- Extension of the Donesta[®] Clinical Program with three new studies carried out on estetrol's effect on symptoms significantly impacting postmenopausal women's quality of life: vulvovaginal atrophy, skin health and hair quality.
- Strategic repositioning of Donesta[®] product candidate as a comprehensive hormone therapy with an improved benefit / risk profile targeting, in addition to vasomotor symptoms (VMS), several major symptoms of menopause.
- Diversification of the R&D pipeline through rights' acquisition option relating to a development programs led by the Belgian company BCI Pharma on innovative kinase inhibitors notably indicated for the treatment of female cancers and endometriosis.
- Tyrosine kinases inhibitors represent the third fastest growing therapeutic class in 2020, with a 17% increase in revenues to USD 40.3 billion ¹.

Liege, Belgium, November 29, 2021 – 7:30 CET – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces the holding of its Investor Day today at its R&D and production center, the Mithra CDMO in Flémalle, Belgium.

As of 9:00 am CET, all presentations can be simultaneously followed by webcast on the Company's website or by clicking [here](#). A replay will also be available via this same link shortly after the end of the conference.

Consolidation of Donesta[®] product candidate

Donesta[®] is a next generation orally-administrated estetrol-based hormone therapy product candidate. Launched in late 2019, the phase III Clinical Program carried out on 2,300 postmenopausal women (40-65 years) aims to measure the treatment effects on vasomotor symptoms' frequency and severity with different doses of E4, especially for hot flashes. Many parameters such as the impact on breast density, endometrial safety, health-related quality of life and lipids, glucose metabolism and hemostasis parameters are also among the secondary objectives of these studies².

Convinced of the potential of E4 on other major estrogen deficiency symptoms affecting a majority of postmenopausal women, Mithra decided to broaden the scope of its Clinical Program by launching three additional studies:

¹ IQVIA FY 2020

² For more information about the E4 Comfort Phase III Program, please visit the website of Clinicaltrials.gov by clicking [here](#).

1. A Phase 3 study on the effect of E4 on **vulvovaginal atrophy** (vaginal dryness, pain during intercourse, urinary tract infections);
2. A Phase 2 study on the effect of E4 on **skin texture, quality and appearance**;
3. A Phase 2 study on the effect of E4 on **hair texture, quality and appearance**.

These three additional studies funded by Mithra for an amount of approximately EUR 20 million will be launched in 2022, depending on regulatory agencies' feedback.

Graham Dixon, CSO Mithra Women's Health, comments on this extension of the Donesta® Program:

"Following the publication of the WHI study in 2001, more than 65% of women decided to stop their hormonal treatment for fear of developing breast cancer or a cardiovascular disease. While this correlation was categorically denied by the scientific community as early as 2006, only 1 in 10 postmenopausal women in the world today choose to take hormonal treatment to relieve the many side effects impacting both their private and professional lives. We are convinced that thanks to its safety profile, Donesta® can offer a real complete alternative to significantly improve these women's quality of life and therefore be a game-changer."

The primary efficacy data of the Phase 3 Donesta® Program is expected by beginning of 2022. Depending on the evolution of the Covid-19 situation, study results and regulatory authorizations, Mithra believes it could achieve marketing authorization for Donesta® in H1 2024 for the United States/Canada and in H2 2024 for Europe. The global menopause market is currently worth nearly USD 10 billion, and is expected to reach around USD 17 billion by 2027³.

Dr. Carolyn Myers, BioEnsemble Ltd., added: *"Our quantitative market research program surveying over 1000 prescribers and women confirms a large unmet medical need in the menopause market resulting from misperceptions about the use of current HT. The research also highlights the significant opportunity for a novel, safe hormone that will treat menopausal symptoms beyond VMS. Research findings confirmed that Donesta®'s profile is attractive to current users of HT from which we believe Donesta® can take a large share, and Donesta® can make inroads amongst the 54% of women who currently do not seek medical treatment because of their safety concerns of current HT. In addition to Donesta® being safe, when approved with the additional indications, it will provide women with a single product option to treat many of their symptoms long term."*

Diversification of asset-based pipeline through a partnership with BCI Pharma

Considering its advanced asset-based pipeline, which has seen two major commercial launches over the past two years (the first estetrol-based product Estelle® oral contraceptive and Myring® vaginal ring), Mithra is strengthening its leadership position in women's health by acquiring a new innovative development axis in a fast-growing market: inhibitors of tyrosine kinases, notably indicated in the treatment of cancer and endometriosis.

Mithra acquires the rights relating to two development programs led by the Belgian company BCI Pharma on innovative inhibitors of CSF1R kinase. These CSF1R inhibitors are part of a new innovative class of immune-modulatory drugs with established clinical tolerability⁴ and proven efficacy⁵. They act on the CSF1 receptor which is involved in many inflammatory processes and is over expressed in many

³ Market Research Future, 2020; IQVIA 2019

⁴ Cannarile et al. Journal for ImmunoTherapy of Cancer (2017) 5:53

⁵ Monsestime et al. Drugs in R&D (2020) 20:189–195

pathologies, in particular cancers, neurological disorders and autoimmune diseases. The innovative class of tyrosine kinases inhibitors represents the third fastest growing therapeutic class in 2020, with a 17% increase in revenues to USD 40.3 billion.

Under the terms of the contract, Mithra has an option to acquire patents covering CSF1R inhibitor series with upfront payment of EUR 2.25 million on execution of option, following the first results conducted by BCI Pharma. Mithra will fund the preclinical and clinical development with a focus on female cancers and endometriosis, while potentially targeting other orphan indications, such as metastatic breast cancer (TNBC). Currently in the preclinical stage, BCI Pharma should initiate clinical development in 2023, with marketing authorizations expected for 2031.

Dominique Surleraux, CEO at BCI Pharma said: *"We are very excited to initiate this strategic partnership with Mithra. This collaboration represents the successful execution of our overarching corporate strategy to deliver new therapy from our disruptive technology which delivers novel, potent and selective kinase inhibitors. We look forward to advancing candidates to the clinic and ultimately achieving the company's vision to bring new treatment options to patients with difficult-to-treat cancer, endometriosis and others."*

Leon Van Rompay, CEO Mithra Women's Health, commented: *"We are very pleased to collaborate with BCI Pharma on this innovative development opportunity in a fast-growing market that will allow us to diversify our pipeline in women's health and beyond. Selective kinase inhibitors play a crucial role in many diseases and we look forward to seeing the first results of BCI's studies on their effect on female cancers and endometriosis."*

Didier Malherbe, BCI Pharma Board Chairman, added: *"I'm really happy about the partnership between the two Walloon biotech companies. This demonstrates the capability of Belgium biotech to create value in a very dynamic health research environment."*

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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. 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

Donesta[®], Estelle[®] and MyRing[®] are registered trademarks of Mithra Pharmaceuticals or its affiliates.

About BCI Pharma

BCI Pharma is a biotech company with extensive expertise in medicinal chemistry, with a special focus on an innovative chemical library. The company designs and validates innovative kinase inhibitor libraries (Bikin 1-3).

Its kinase platform is based on a new chemotype with excellent physical and chemical properties which enable BCI to run research projects on inflammation, neuroinflammation, pain, cancer and metabolic diseases. BCI also provides screening technology in the discovery of selective, potent kinase inhibitors. BCI identify a preclinical candidate BCI-1446 as a new way to treat peripheral neuropathic pain and psoriasis. Right now BCI has 3 running projects and has advanced partnerships discussions with giant pharma and biotech. So far, the company has received around €2 million public/private investment and research grants from the Walloon Region to support its research projects. BCI is based at two sites: Liège (Belgium, biology) and Montpellier (France, medicinal chemistry). It has ten employees.

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.

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