mithra
Women's Health

Investor Presentation

July 2023

Important Information

Important Notice

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Regulatory disclaimer:

- 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. After having successfully launched the first estetrol-based product in 2021, the contraceptive pill Estelle®, Mithra is now focusing on its second product Donesta®, the next-generation hormone therapy. Mithra also offers partners a complete spectrum of solutions from early drug development, clinical batches and commercial manufacturing of complex polymeric products (vaginal ring, implants) and complex liquid injectables and biologicals (vials, pre-filled syringes or cartridges) at its technological platform Mithra CDMO. Active in more than 100 countries around the world, is headquartered in Liège, Belgium.

General disclaimer:

- Mithra Pharmaceuticals is closely following the evolution of macroeconomic conditions, the geopolitical situation in Ukraine and the COVID-19 global health crisis and is in constant dialogue with its partners to assess the impact and adapt operations accordingly.
- Mithra Pharmaceuticals has put in place mitigation plans to minimise delays. The impact of increased demands on the healthcare systems, limitations on non-essential hospital visits and procedures, social-distancing and travel restrictions may result in further delays to execution of clinical studies and impact sales.
- Mithra Pharmaceuticals will continue to update the market as needed and whenever possible.

Note:

- Estelle® and Donesta® are registered trademarks of Mithra Pharmaceuticals or one of its affiliates.

Mithra

1

2 Innovative E4 platform

3 Complex Therapeutics

4 Mithra CDMO

5 Financial resources

mithra
Women's Health

Mithra at a glance

- **Global women's health company**
  - Liege, Belgium
  - Founded in 1999
  - Listed on Euronext Brussels in 2015: MITRA
- **Innovative Estetrol (E4) products**
  - Native estrogen
  - Safer benefit/risk profile compared to existing hormone-based solutions
    - Estelle, a new contraceptive
    - Donesta, potential treatment for menopausal symptoms & better aging
- **Innovative pipeline expansion**
- **CDMO & Complex Therapeutics**

Commercial development/ Performance in 2022

-59.6 million
EUR net loss

9.2 million
EUR Product sales of Estelle®

64.6 million
EUR milestones collected

1,000,000
Myring® vaginal rings produced in our CDMO

Dedicated to transforming women's health by offering new choices through innovative products

Positive
Top-line safety and efficacy results for Donesta Phase III (C302)

30
Countries in which our contraceptive pill Estelle® is commercialized (+ 19 in 2022)

36
Patents covering E4

Mithra as a company, as a stock

1999
Foundation

Since 2015
Listed on Euronext Brussels

38
R&D collaborators among 233 employees dedicated to innovation

56%
Women employees

How we drive our business to have a lower impact on environment and society (ESG)

-22%
Reduction in Greenhouse gas emission (target -55% by 2030)

100%
Successful inspections and customer audits

55%
Women in leadership positions (CEO N-2)

Fundamental Strength for Success

New pipeline next generation medicines for women's health

mithra Women's Health

Innovative Estetrol-based products with important commercial role in women's health

Revenue growth & strategic opportunities

- Estetrol; Myring®; Tibelia®; Zoreline®
- CDMO

Strong experienced management

Estelle® U.S. launch & sales ramping up

Donesta preparing for NDA filing

Strong Experienced Management

Chief Executive Officer
David Horn Solomon

Chief Scientific Officer
Graham Dixon

Chief Operating Officer
Xavier Paoli

Chief Commercial Officer
Jean Manuel Fontaine

Chief Financial Officer
Christophe Maréchal

ZEAL&
ZEALAND PHARMA
SILENCE THERAPEUTICS
COLUMBIA UNIVERSITY

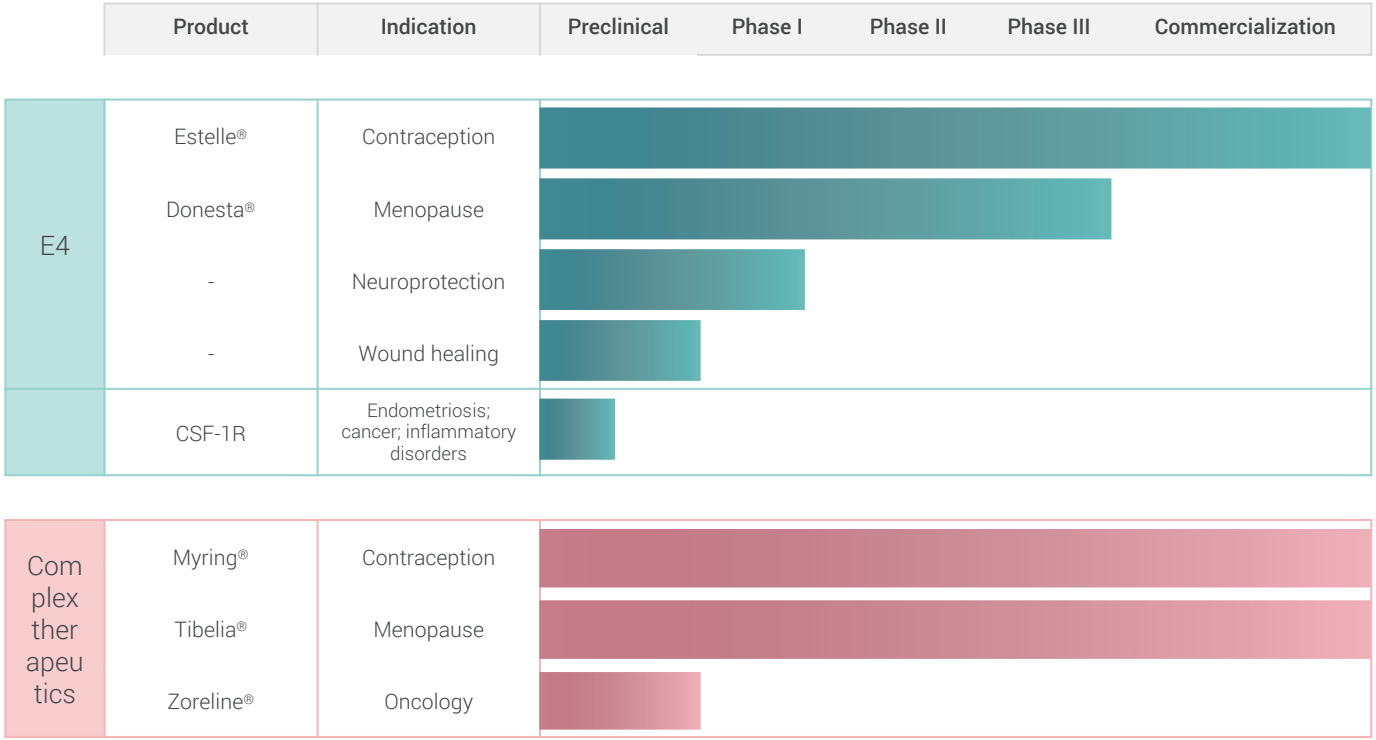
AstraZeneca
Galápagos
ZALUVIDA

ucb
GSK

Pfizer
Lundbeck
ucb

HAMON
SMBC

Diversified pipeline offering multiple near-term catalysts



An innovative Estetrol platform

1. Mithra
2. **2**
3. Complex Therapeutics
4. Mithra CDMO
5. Financial resources

Estetrol (E4)

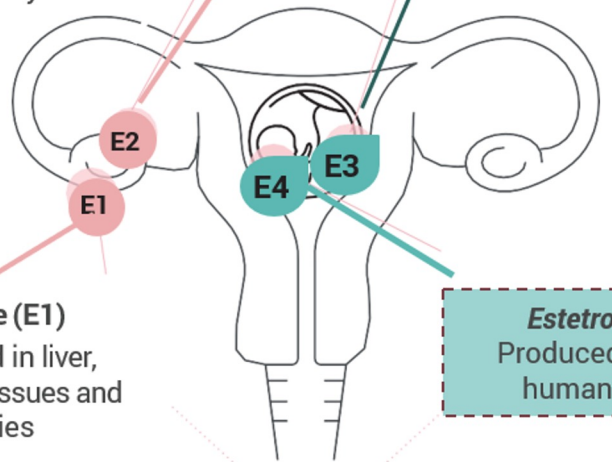
a new estrogen with an improved benefit/risk profile

E4: the early life native estrogen

Estrogens made **by** the body

Estradiol (E2)
Made in ovaries during reproductive years

Estriol (E3)
Produced by the foeto- placental unit



Estrone (E1)
Produced in liver, peripheral tissues and ovaries

Estetrol (E4)
Produced by the human fetus

Adult Estrogens

Fetal Estrogens

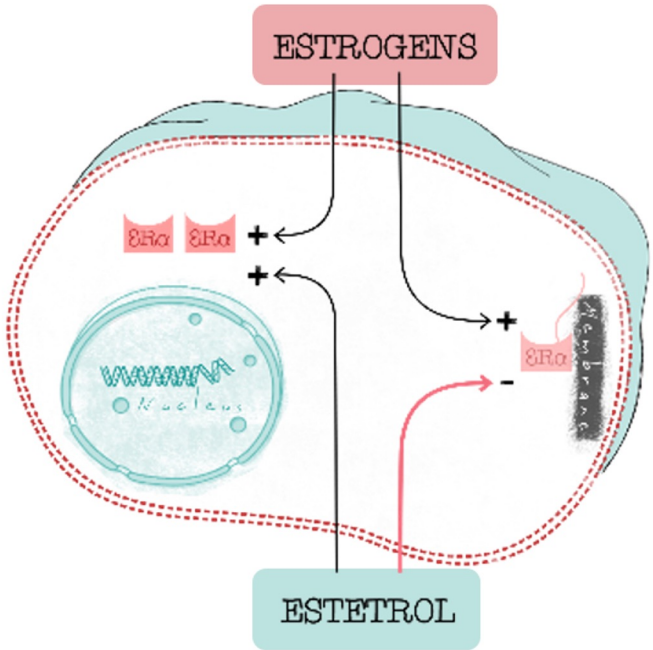
Estrogens made **outside** the body

Synthetic Estrogens *(e.g. Ethinyl Estradiol)*	Produced for medical use e.g. in birth control pills
Phytoestrogens	Found in plants, E1 e.g. in soybeans
Xenoestrogens	Endocrine disrupting agents coming from man-made products

Estetrol: unique mode of action compared to other estrogens

AGONIST on the nuclear ERα

- Activates the **nuclear estrogen receptor**[2-4]
- Important estrogenic activity on **the vagina, endometrium, bone and cardiovascular system** to provide beneficial effects[2-4]

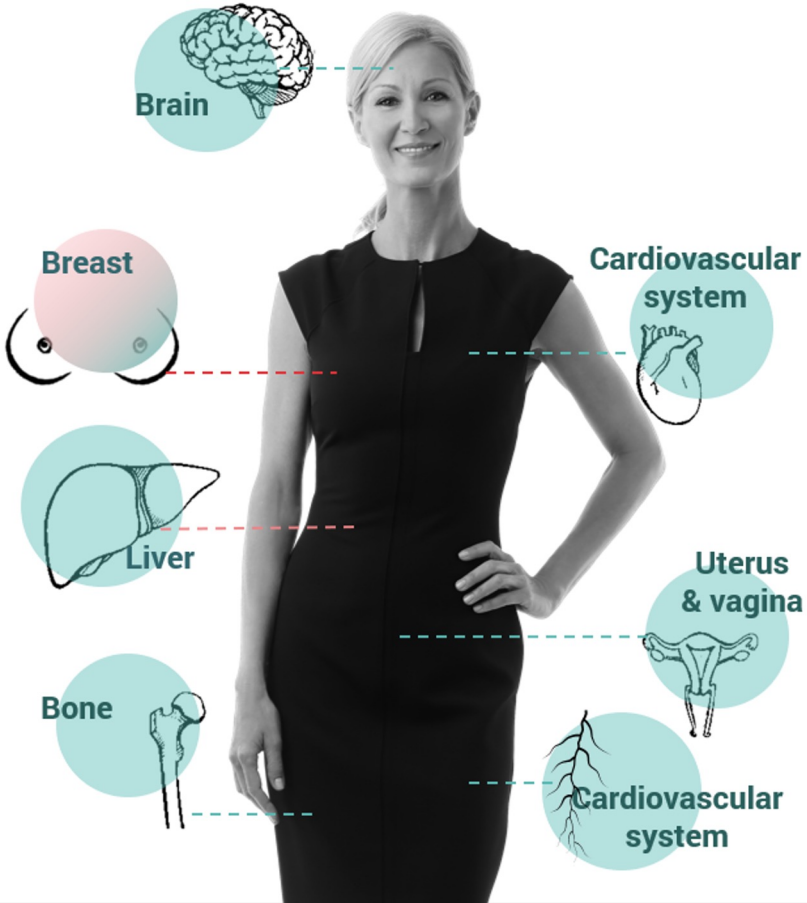


ANTAGONIST on the membrane ERα

- Blocks the **membrane estrogen receptor**[2-4]
- Neutral effect on the liver unlike other oestrogens[2-4]
- Low impact on breast tissue (normal and malignant)[5-8]

1. Abot A *et al. EMBO Mol Med* 2014.2.Foidart JM *et al.* InL Brinton RD et al (eds) 2019, Sex Steroids Effects on Brain, Heart and Vessels. ISGE Series.3.Arnal JF *et al. Physiol Rev* 2017. 4.Giretti MS *et al. Front Endocrinol*, 2014.5.Gerard C et al Endocrinol 2015. 6.Singer CF *et al. Carcinogenesis*, 2014. 7.Visser M *et al. Horm Mol Biol Clin Invest* 2012.

A favorable safety profile



- **Similar to other estrogens,** E4 has also a beneficial and positive impact on the cardiovascular system, brain, bone and endometrium

- **Unlike other estrogens**, E4 has a limited impact on the liver and breast

Breast: mixed activity on breast cell proliferation, migration and invasion[1], limited impact on breast at therapeutic dose

Liver:

- minimal impact on Sex Hormone Binding Globulin (SHBG) synthesis
- minimal impact on synthesis of coagulation factors (lower risk of VTE)
- limited lipid impact (including Triglycerides)

1. In presence of Estradiol (E2)

Visser et al. Climacteric 2008 | Mawet et al. Eur J Contracept Reprod Health Care 2015 | Gérard et al. J Endocrinol 2015 | Abot et al. EMBO Mol Med 2014 | Coelingh Bennink et al. Climacteric 2008 | Heegaard et al. Climacteric 2008 | Holinka et al. Biol Reprod. 1980 | Holinka et al. Climacteric 2008 | Pluchino et al. J Steroid Biochem Mol Biol 2014 | Tskitishvili et al. Exp Neurol 2014 | Guivarc'h et al. J Am Heart Assoc 2018 | Kluft et al. Contraception 2017 | Douxfils et al. Contraception 2020 | Klipping et al. Contraception 2021

Estetrol is an environmentally-friendly estrogen

EE (ethynyl estradiol)

- 97% of current marketed Combined Oral Contraceptives are based on EE
- Known as a major Endocrine Disrupting Chemical

vs

E4 (Estetrol)

Insignificant endocrine disruptor effects, whether in aquatic organisms or organisms living in the sediment

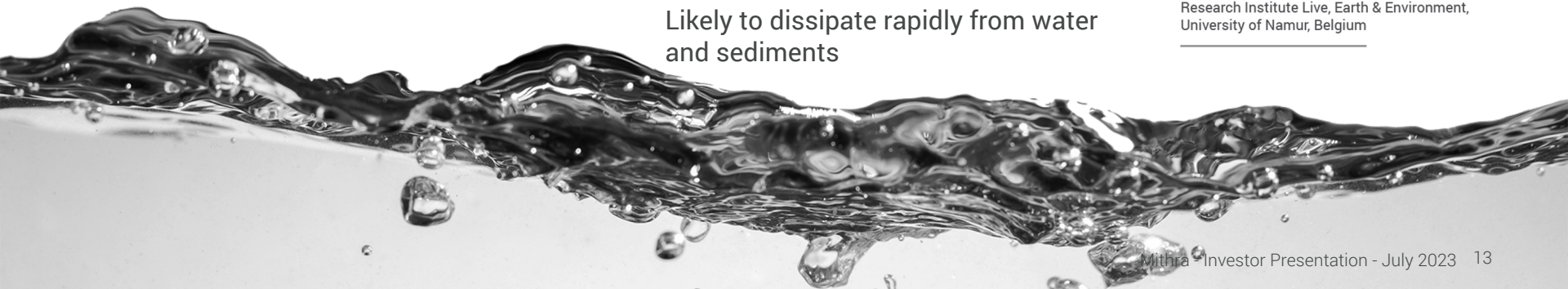
Amount of biologically active E4 released in the wastewaters after human use expected to be minimal

Does not accumulate in living organisms

Likely to dissipate rapidly from water and sediments

> **“All biotests carried out show without ambiguity that the endocrine disruptor effects of Estetrol are insignificant in comparison with those observed for natural or synthetic estrogens, whether in aquatic organisms or organisms living in the sediment.”**

Prof. Patrick Kestemont, President of the Research Institute Live, Earth & Environment, University of Namur, Belgium



Estelle®

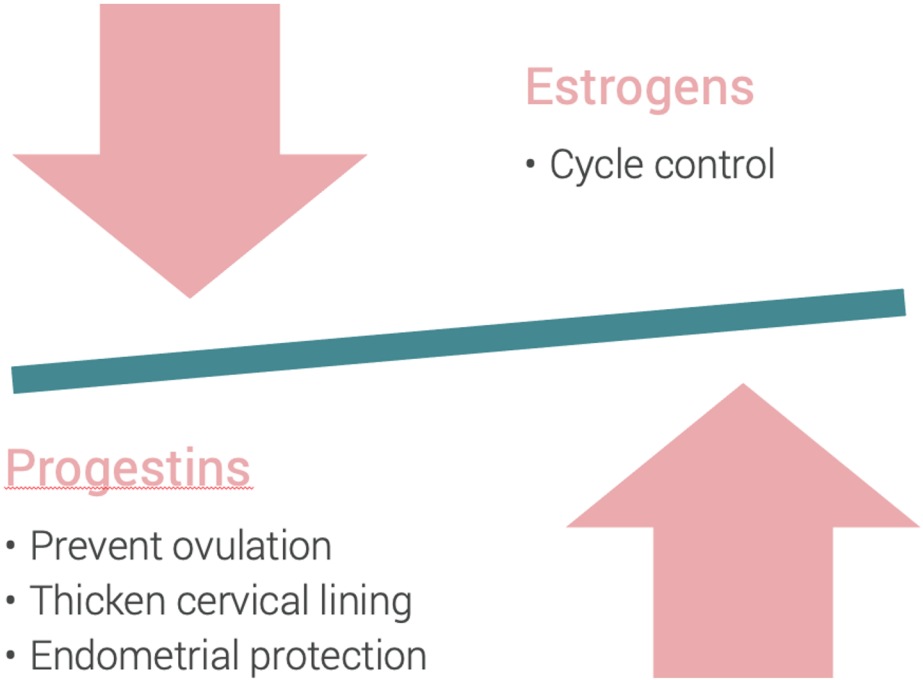
(15mg E4 / 3mg DRSP)

A New Era in Combined Oral Contraception (COC)

OBJECTIVE

Optimize women's physiological hormonal balance by combining the best progestin & estrogen according to their profile

The role of female sex hormones in COCs



Estelle® – addressing women's unmet need and improving women's contraceptive experience

Improving contraceptive experience

- Reliable contraceptive efficacy
- Excellent cycle control
- Proven superiority in comparison to Ethinylestradiol containing COCs
- Improved quality of life & high user satisfaction
  - Positive effect on skin
  - Low risk of drug-drug interaction

Addressing unmet needs

Favorable safety profile

- Favorable VTE risk profile with low impact on all markers of coagulation
- Minimal impact on breast tissue
- Minimal increase of triglycerides
- Minimal impact on glucose metabolism

Neutral impact on body weight
(including women with BMI 30-35 kg/m)

Source: K. Daniels et al., National Health Statistics report n° 62, 2013

Key partners for Estelle's commercialization

GEDEON RICHTER

Europe

Gedeon Richter Plc. is a major pharma. company which product portfolio covers many important therapeutic areas, including Women's Healthcare, Central Nervous System, and Cardiovascular areas

With its widely acknowledged steroid chemistry expertise, Richter is a significant player in the Women's healthcare field worldwide

mayne pharma

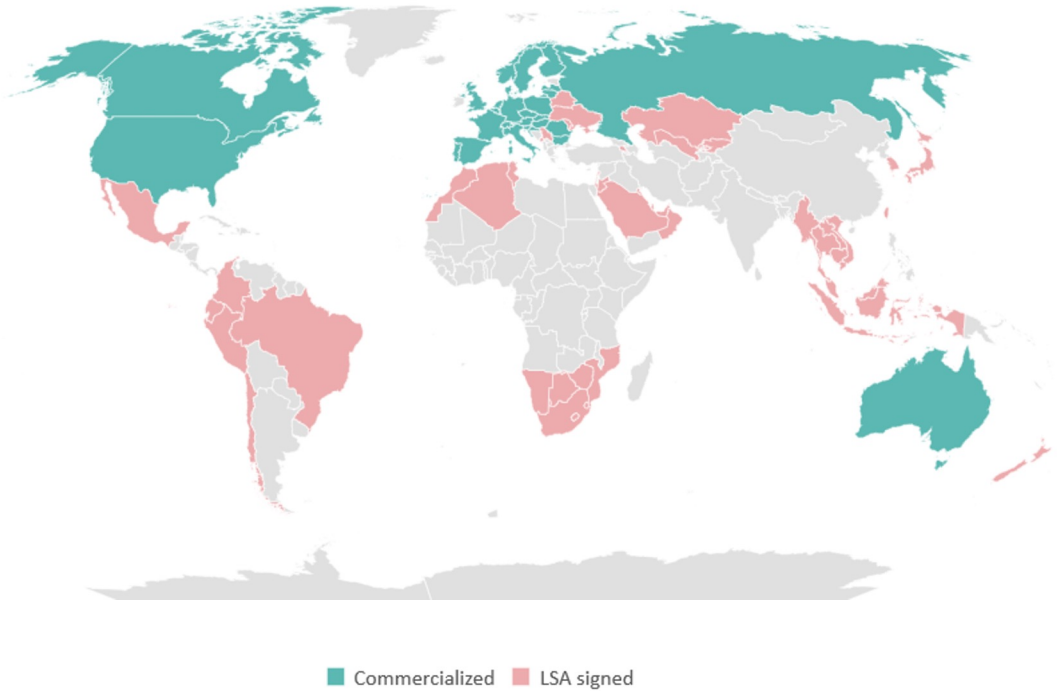
U.S. and Australia

Mayne Pharma is an ASX-listed specialty pharma. company focused on commercializing novel and generic pharmaceuticals, offering patients better, safe and more accessible medicines

It has a 40-year track record of innovation and success in developing new oral drug delivery systems

Mithra holds 4.96% of the outstanding shares

Estelle® – Commercialization progress worldwide

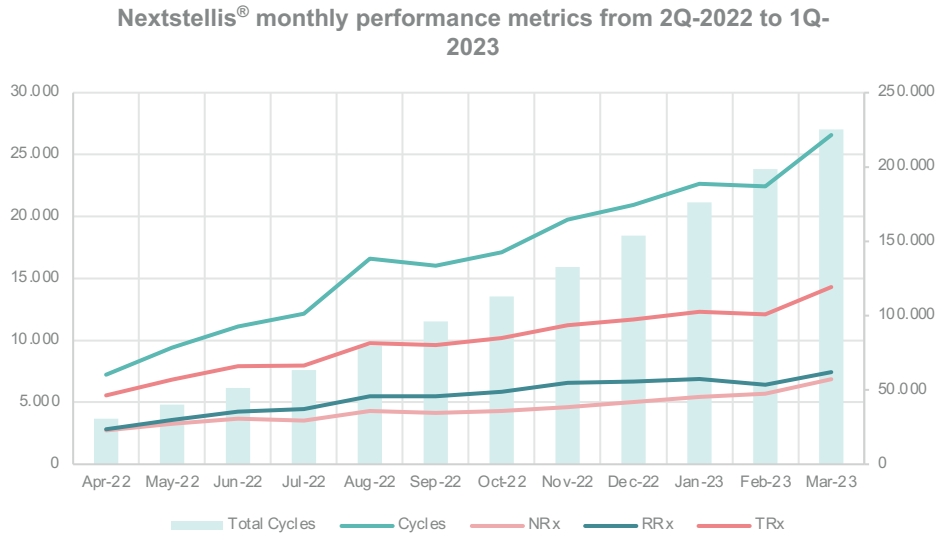


Commercialization started in 2021

In 2023 – First launches in:

- Latin America
- Asia
- Middle East
- Ex CIS countries

Estelle® in the US – NEXTSTELLIS® highlights



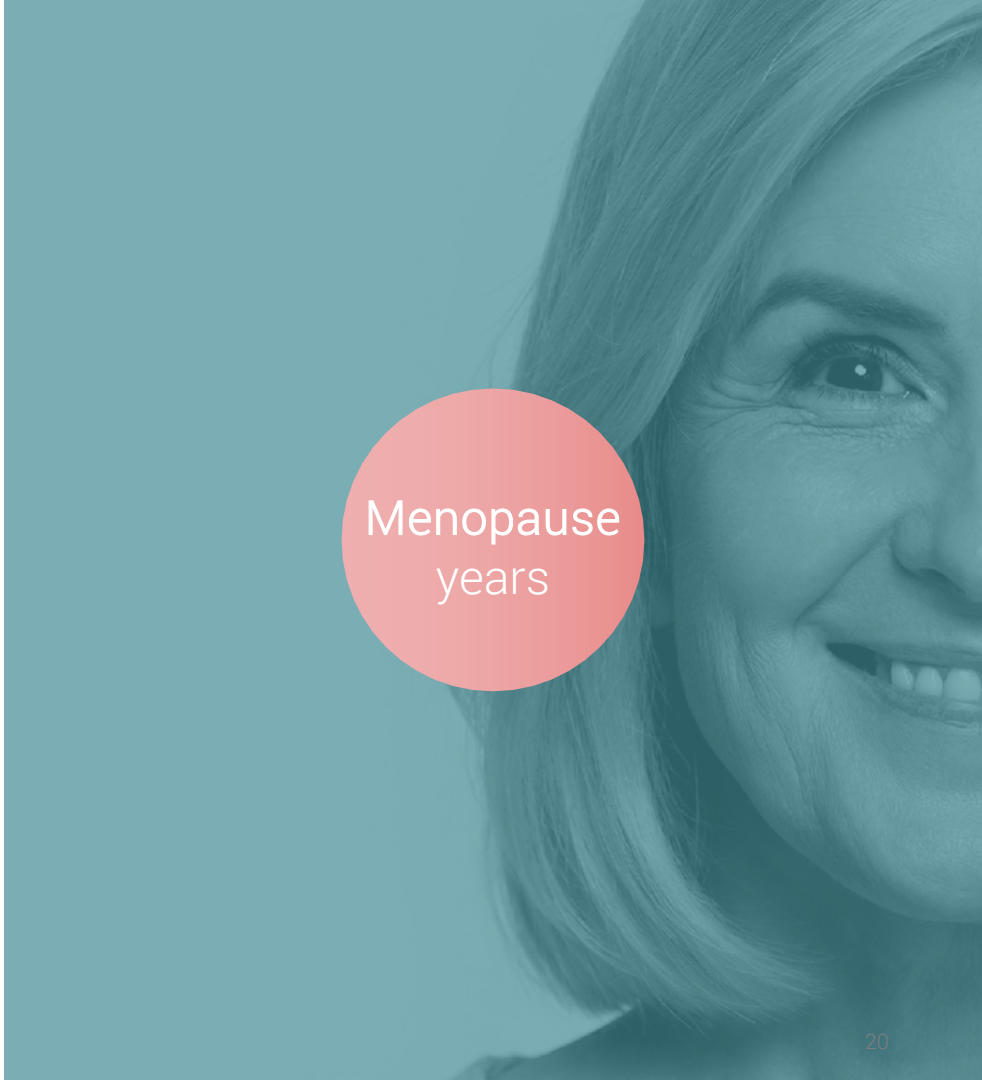
Nextstellis® growth is accelerating thanks to new commercial strategy implemented by Mayne in December 2022

- Nextstellis® has continued to achieve **solid growth during 1H-2023** to date driven by access improvements (Co-Pay) and new targeting strategy implemented by Mayne in December 2022
- **> 225,000 cycles** dispensed since launch in June 2021
  > 71,600 cycles dispensed in 3 months since January 2023
  * update from March 2023
  >7,000 weekly cycles from now
- Growth 1Q-2023 vs 4Q-2022 of **NRx +30% and TRx +18%**
  RRx expected to improve following patient retargeting initiative in December 2022
- Experienced **WH sales team of 100** (up from 86) able to reach target customers
- **Direct-to-Consumer (DTC) campaign** launched in July 2022 with **GoodRx and TV campaign** launched in February 2023
- Potential upside from Affordable Care Act (ACA) when fully enforced

Donesta®

(E4 only)

A new era in
Hormone Therapy (HT)



Hormone Therapy (HT)

- Treatment recommended to address **long-term biological changes**, including common symptoms of menopause, that result from declining levels of the natural hormones (estrogen and progesterone) during and after menopause.
- HT also helps **to balance estrogen and progesterone** in women around the time of menopause.
- **Collapsing** of HT's use worldwide after the announcement of the first results of the **Women's Health Initiative (WHI) in 2002,** which indicated that HT could have more detrimental than beneficial effects.
- Ph2 POC trials to launch in 2023 in skin quality, hair quality and FSAD

Donesta® – Potential to target symptoms beyond VMS

Clinical Phase	Primary Endpoint	Secondary Endpoint
Phase 3	E4 effect on reducing Vaso-Motor Symptom frequency / severity, H & NH* women	Effect on lipids, glucose metabolism, hemostasis parameters, breast density endometrial safety, health-related quality of life, treatment satisfaction and vulvar and vulvo-vaginal atrophy
Phase 2	E4 effect on various aspects of Female Sexual and Urogenital Functions	Effect of E4 on quality of life
Phase 2	Effect of E4 on skin health, quality and appearance	Effect of E4 on quality of life and various skin-related endpoints
Phase 2	Effect of E4 on hair texture, quality and appearance	Effect of E4 on quality of life and various hair-related endpoints

Hysterectomized and non-hysterectomized

Donesta® – Partnership with Gedeon Richter

Seeking for the highest long-term added value for Mithra and Gedeon Richter
Strengthening our long-term partnership

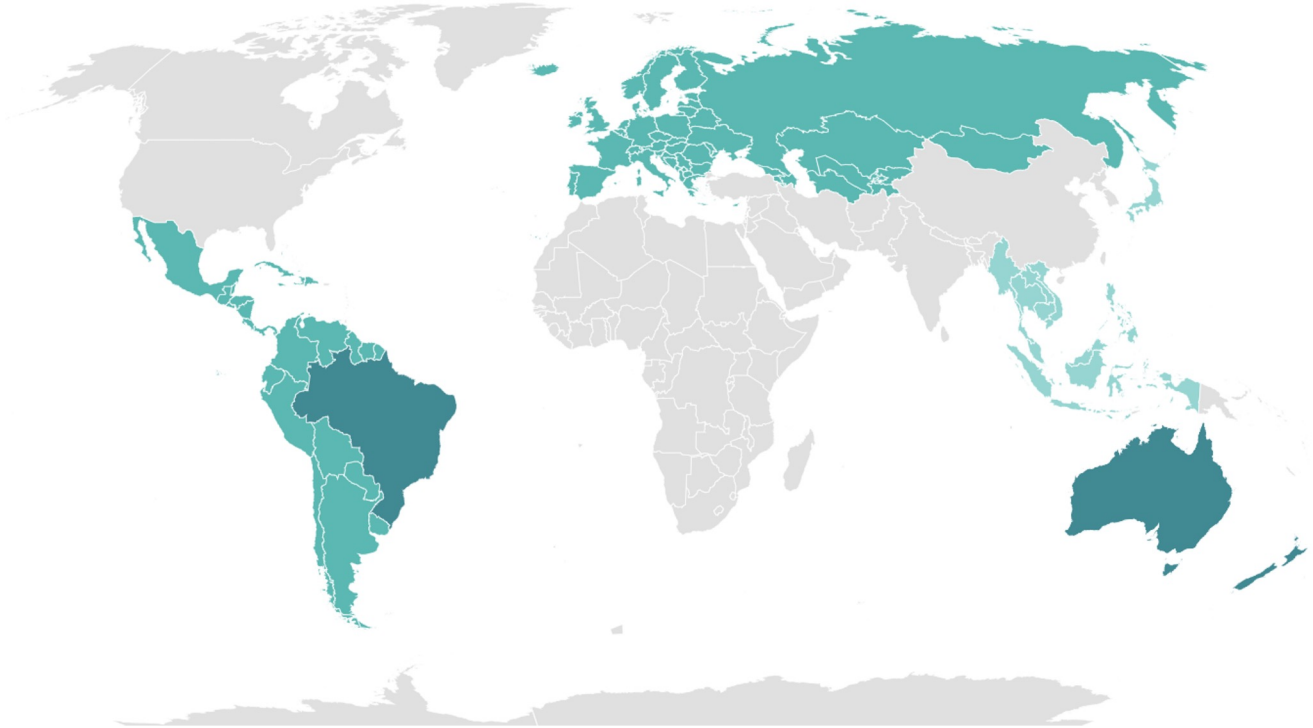
Upfront & milestone payment structure

- Upfront payment 55m EUR
- Regulatory milestones 15m EUR
- Double-digit royalties tiered on net sales

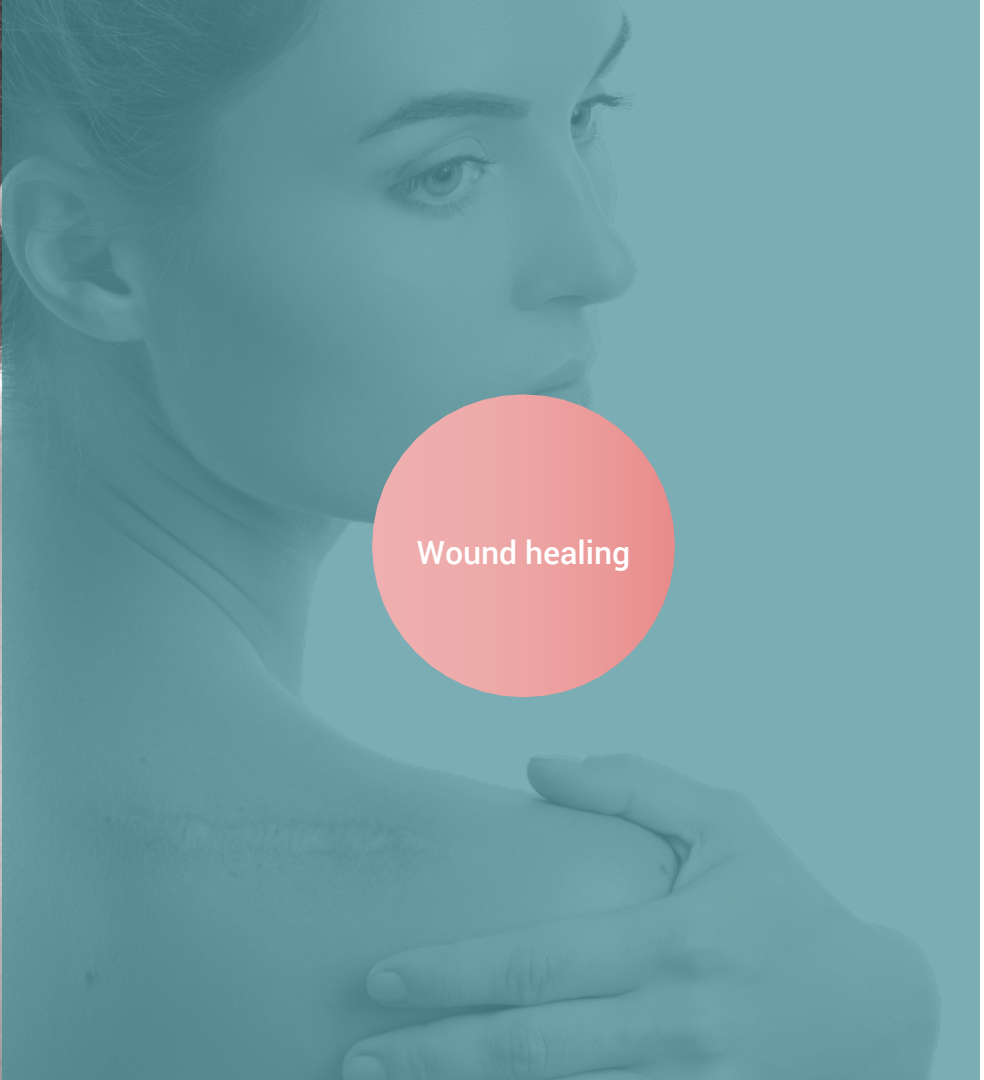
Territories covered

- Exclusivity: Europe, Russia, CIS countries, Central & Latin America
- Semi-Exclusivity: Brazil, Australia, New Zealand

Donesta® – Territories already covered



GR Exclusivity*
GR Semi-exclusivity*
FUJI Pharma Exclusivity



E4 potential beyond women's health

Neuroprotection:
Neonatal Hypoxic-Ischemic Encephalopathy (NHIE)

- **Brain damage** (encephalopathy) caused by oxygen deprivation (hypoxia) and limited blood flow (ischemia) in newborns (> 36 weeks) and entailing high mortality among <5 year old children and chronic neurological disability
- **Orphan Drug Designation** designation in EMA and in the U.S.

E4 has shown **neuroprotective activity** in non clinical models

Clinical study launched in Q2 2022 on healthy adults to characterize the novel E4 formulation for i**ntravenous formulation**

Next step
Launch of **clinical trial** on the neonatal population anticipated in H2 2023

Wound healing

- **Development of E4-based product for topical application** enabling faster and more effective healing
- **Potential for therapeutic use in both the acute and chronic wound settings**
- **No EMA-approved drugs** for advanced wound healing

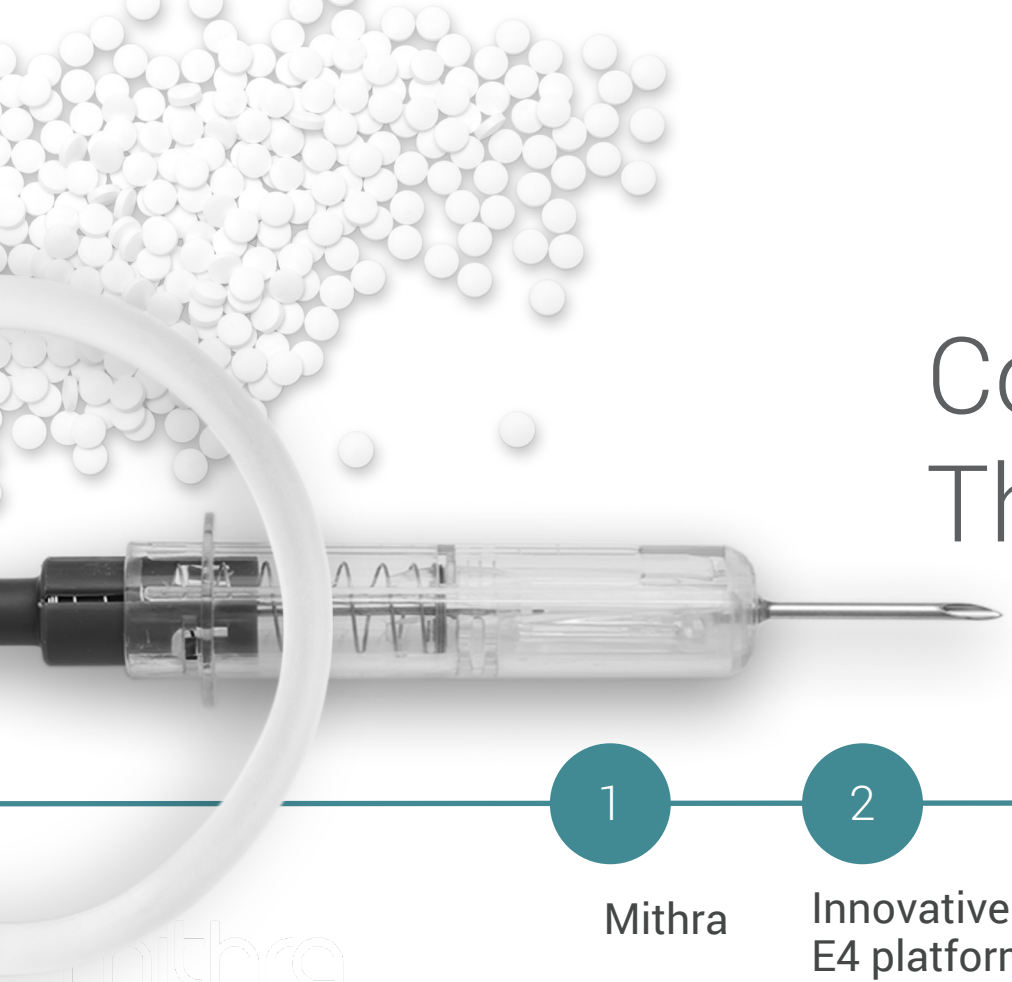
E4 has been shown to **promote wound healing** in non clinical models

Unique molecular mode of action of E4 compared to other estrogens, improving both **wound closure** and **dampens local inflammation**

Next steps

Finalization of E4 new formulation & preparation of a 1st punch biopsy study in humans

Launch of clinical program expected in H2 2023



Complex Therapeutics

1. Mithra
2. Innovative E4 platform
3.
4. Mithra CDMO
5. Financial resources

Leveraging know-how of complex therapeutics

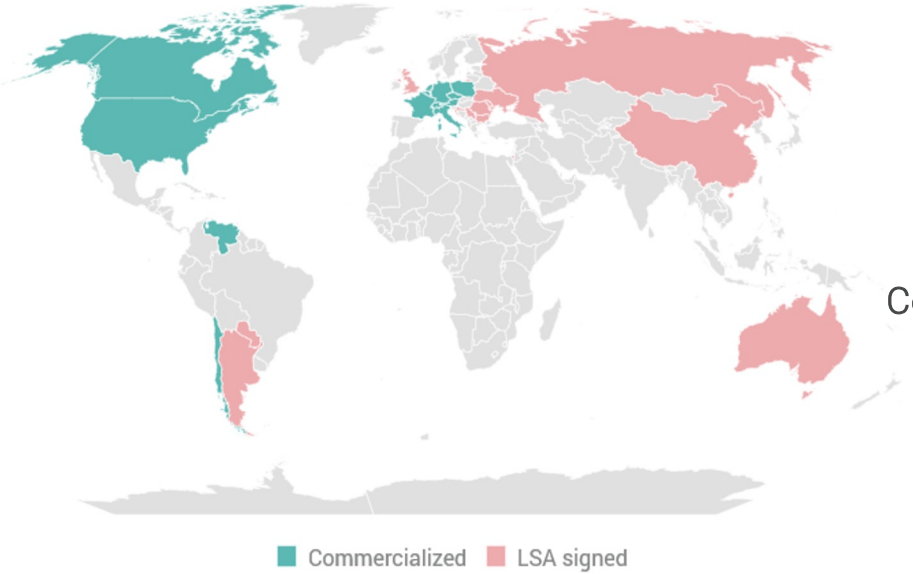
- Expertise in developing complex and innovative **polymer products**
- Targeting safer, long-lasting delivery and controlled release of established approaches to **contraception, menopause and hormone-dependent cancers**
- Manufactured in-house at **Mithra CDMO**

Advancing our complex therapeutics business

Products	Description	Indication	Opportunity	Status
Myring® 	**Contraceptive vaginal ring** (based on etonogestrel/ EE/polymers)	**Contraception**	**Circa $580m*** Original product: NuvaRing® from Merck	**Commercialized**
Zoreline® 	**Biodegradable SQ implant** (goserelin)	**Prostate & breast cancer and benign gynecological indications**	**Circa $963m**** Original product: Zoladex® from AstraZeneca	**New formulations assessed** via animal PK/PD comparative study for 1 month and 3 months implant
Tibelia® 	**Therapeutic solution for HT composed of tibolone** (synthetic steroid)	**Menopause**	**Circa $117m**** Original product: Livial® from Merck	**Commercialized**

** According to IQVIA, sales are for the 12 months ended June 2022*
*** Source: IQVIA quantitative market research, Q2 2022*

Myring® - commercialization overview & focus on US



US contraceptive vaginal ring market

Nuvaring® and generics sales are valued at c. **USD 580 million**[1] for c.5,500,000 rings

Commercial Myring launch started in January 2023 with EUR 1.6 million milestone collected by Mithra

Manufacturing at Mithra CDMO facility

1 According to IQVIA, sales are for the 12 months ended June 2022

Mithra CDMO

1 Mithra

2 Innovative E4 platform

3 Complex Therapeutics

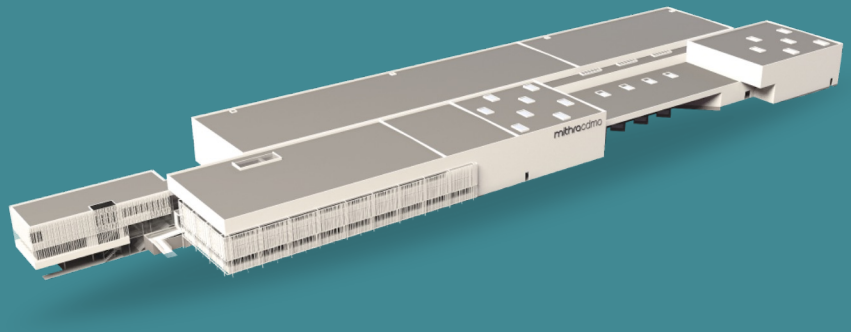
4

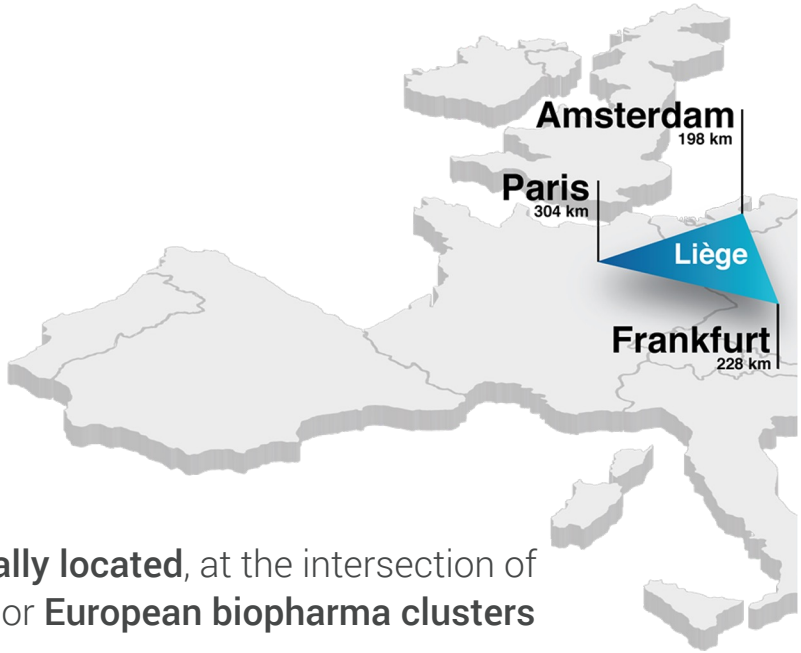
5 Financial resources

An integrated R&D and manufacturing platform

Specialized pharmaceutical ecosystem, to take products from POC to market

- 15,000 m² state-of-the art facilities
- Dedicated R&D and production areas
- Ability to handle high potent and complex developments
- Pilot, clinical & commercial batches
- GMP Standards compliance





Ideally located, at the intersection of major **European biopharma clusters**

Strategy for the CDMO is to leverage our unique expertise in polymers (long-acting, implants, vaginal rings) and injectables for high value-added commercial projects and products

Financial resources

1. Mithra
2. Innovative E4 platform
3. Complex Therapeutics
4. Mithra CDMO
5.

Financial resources: overview

Facility	LDA Capital	Highbridge/ Whitebox	Goldman Sachs[1]
Total amount (EUR)	75 million	100 million	100 million
Available (EUR)	52.8 million	12.5 million	80 million
Maturity date	April 2025	August 2025	February 2024

1) Contract terminated

Cash runway update

- Cash and cash equivalents of EUR 26 million as at 30 April 2023
- Cash inflows since 30 April 2023 of EUR 25 million
    - Highbridge and Whitebox subscription for EUR 2.5 million of new shares in May 2023
    - Drawdown of Tranche C1 of Highbridge/Whitebox loan facility in June 2023 in the amount of EUR 12.5 million
    - Sale of 4,221,815 Mayne Pharma shares in June 2023 at a price of AUD 3.86 for proceeds of approximately AUD 16.3 million (approximately EUR 10 million)
- R&D expenses of EUR 60 million for full year 2023
- Based on the foregoing, cash runway extended to September 2023
- Mithra needs additional working capital to address its operating and capital expenditures, and therefore intends to implement one or more of cash runway extension and balance sheet repair measures or elements, some of which have already been initiated (see below)

Cash runway extension and balance sheet repair measures

- Management expects entering into another Donesta® license and supply agreement(s) for the United States in 2023, which should generate upfront payments, supply revenues and royalties
- Access tranche C2 of Highbridge/Whitebox loan facility in the amount of EUR 12.5 million, which may be drawn subject to certain conditions
    - If, at any time, the outstanding amount under the Highbridge/Whitebox loans is less than EUR 20 million (e.g., as a result of conversion of loans into shares of Mithra) and Mithra does not meet the conditions to draw Tranche C2, it will nevertheless be permitted to draw additional loans up to an amount of EUR 20 million
- Management may consider selling or out-licensing assets depending on its financial needs
- Management announced its intention to affect a full refinancing of Company's debt obligations
- Company still has access to the LDA facility for an amount of EUR 53 million
- Management may delay or put on hold R&D projects (with the exception of Donesta® (C301 & C302), Myring® and Estelle® PASS R&D projects) depending on its financial situation
- Management could activate a further cost reduction plan, consisting in shifting some R&D projects expenses out of the women's health E4 pipeline and halting any capital expenditures and non-critical operating expenses at the CDMO facility
- In relation to R&D activities outside of the women's health E4 pipeline, management intends to pursue its negotiations on the funding of its projects based on financings against royalties and/or co-development strategies, in order to create value in the short term based on proof of concepts or early clinical results

Next steps

Donesta

- NDA filing with FDA
- Additional Phase 2 studies to support differentiation for treatment of menopause symptoms
  - Hair
  - Skin
  - Sexual desire

Estetrol

- New indications in women's health
  - IVF implantation – exploratory clinical studies on endometrial thickening
- New pharmacoecenomic Phase 2 and Phase 4 studies to establish safety of E4 (Estelle/Donesta) in breast cancer & blood clotting

Zoreline

- 1-month & 3-month formulation studies

Contact us

investorrelations@mithra.com

mithra
Women's Health

Rue St-Georges 5/7 - 4000 Liège
Tel : +32 (0)4 349 28 22
https://www.mithra.com/en/investors/

Donesta® - Phase 3 (E4 Comfort)

2 multicenter, randomized, double-blind, placebo-controlled trials in post-menopausal women

C302 [1]		
Study part	VMS Efficacy	Safety
Target population	Post-menopausal H and NH* 40-65 years	Post-menopausal H and NH* 40-65 years
Trial Size	600 subjects	400 subjects
Dosing	15 / 20 mg E4**	20 mg E4
Duration	12 weeks (efficacy) + 40 weeks safety	52 weeks

C301 [2]		
Study part	VMS Efficacy	Safety
Target population	Post-menopausal H and NH* 40-65 years	Post-menopausal NH [4] 40-65 years
Trial Size	600 subjects	600 subjects
Dosing	15 / 20 mg E4**	20 mg E4 + 100 mg P4
Duration	12 weeks	52 weeks

Primary endpoint:

Efficacy **-** to measure the effect of treatment with 15mg and 20mg of E4 compared to placebo on the frequency and severity of VMS at weeks 4 and 12 (C301 & C302)

Safety **-** to evaluate the general safety of treatment with E4 (C302) and the endometrial protection when combined with P4 (C301)

Secondary Endpoints:

Effect of treatment on additional key efficacy and safety parameters (lipid, glucose metabolism, hemostasis, bone turnover, endometrial safety, breast density, health-related quality of life and treatment satisfaction)

[1] US, Canada [2] EU, Russia, Latam (+US, Canada) *H: Hysterectomized & NH: Non-Hysterectomized ** vs. placebo

Phase 3 trials: top line efficacy results

- Donesta® demonstrates a **statistically significant** and **meaningful reduction** in the frequency and severity of moderate to severe VMS from baseline and compared to placebo
- **All co-primary endpoints were met** statistically in both studies (all $p < 0.05$).
- Both **frequency and severity** of hot flushes showed a **continued decrease** week after week until week 12 (end of efficacy study) where:
  - VMS frequency declined by up to 80% compared to baseline with Donesta®.
  - VMS severity was reduced by up to 56% compared to baseline with Donesta®.
- **Positive impact of Donesta® on the quality of life** based on secondary endpoints evaluated at 3 months in the C301 study (hot flushes, mood swings, anxiety, sleep, joint pain, skin & hair quality, libido,…). For C302 study, results for secondary endpoints at 3 months and 12 months are expected in Q1 2023.