



mithra
Women's Health

Expert Tips Days

29 September 2018

Michaël Dillen
CLO
VP Corporate Development

Management team – Co-founders



François Fornieri
Chief Executive Officer
Co-founder

- Over 30 years in the Pharma industry
- Founder & CEO of Uteron Pharma (sold to Watson/Actavis)
- Master in Chemical Engineering



Jean-Michel Foidart
Scientific Committee & Board member
Co-Founder

- Former CSO of Uteron Pharma & Actavis Belgium
- Former Head of the Gynecology and Obstetrics Department of the University of Liège
- MD & PhD in Cell Biology & Biochemistry

Expert in Women's Health

re-energizing the \$22bn Contraceptive and \$8.6bn Menopause market*

Estetrol (E4)

mithra^{cdmo}

Complex
Therapeutics

1. Highly **innovative** new approaches based on **E4**, a **native estrogen** with **improved benefit/risk profile**
2. **Complex Therapeutics**: leveraging polymer science & formulation expertise to develop complex generics
3. **Powered by Mithra CDMO** (Contract Development & Manufacturing Organization)

*Based on Datamonitor 2014; Transparency Market Research 2017..

Advanced pipeline offering multiple mid-to near-term catalysts

	Product	Indication	Ph1	Ph2	Ph3		Next milestone
E4*	Estelle®	Contraception	[Blue bar]				PhIII results US/Canada Q1 2019
	Donesta®	Menopause	[Teal bar]				Phase III submission H2 2019

*Preclinical: Neuroprotection (ODD in neonatal encephalopathy)

			PK/PD	BioEq	Filing	Market Approval	Next milestone
Complex Therapeutics	Myring™	Contraception	[Purple bar]		[Orange bar]		MA's EU Q3 2018; MA US H1 2019
	Zoreline®	Cancer	[Purple bar]				Q4 2018: PK results
	Tibelia®*	Menopause	[Light purple bar]		[Light orange bar]		2018: Additional launches



E4 (Estetrol)

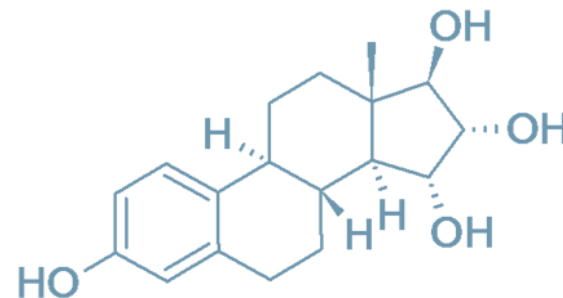
Answer from nature with unique potential

E4: **native estrogen** produced by **human fetus** around week 9

Fetal plasma levels 12x higher than those of mother

E4's broad potential for use in Women's Health validated in **multiple peer-reviewed academic journals**¹⁻⁸

E4-based programs protected by **29 patent families**, including synthesis pathway until 2032

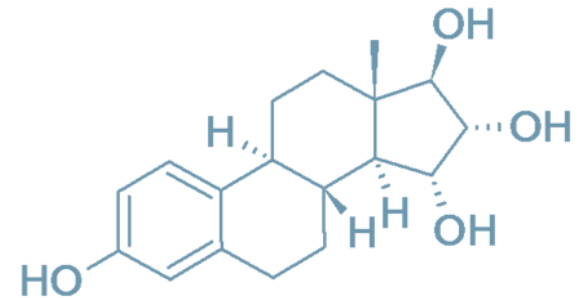


- ¹ Klufft C et al., *Contraception* 2016.; ² Gerard C et al., *Oncotarget* 2015;6(19):17621-36.; ³ Visser M et al., *Horm Mol Biol Clin Invest.* 2012;9:95-103.; ⁴ Visser M et al., *Climacteric* 2008; 11 Suppl 1:64-8.; ⁵ Mawet M et al., *Eur. J. Contracept. Reprod. Healthcare* 2015:1-13.; ⁶ Apter D. et al., *Contraception* 2016;94(4):366-73; ⁷ Abot et al., *EMBO* 2014: 6 (10); ⁸ Apter et al., *Eur. J. Contracept. Reprod. Healthcare* 2017:22(4)

Unmet clinical need potentially addressed by E4

- + Favorable **VTE** risk profile^{1,#}
- + Favorable **drug-drug interaction** profile⁴
- + Minimal increase of **triglycerides**^{5, †}
- + Lower **breast pain**⁶ and lower **carcinogenic** potential in the presence of E2^{2,3,7}
- + Good **user acceptability**, body weight control, excellent cycle control, improved spotting and general well-being^{6,8}

Excellent safety and efficacy results for Estelle® (15 mg E4/3mg DRSP) & Donesta® (E4 alone)



¹ Klufft C et al., *Contraception* 2016.; ² Gerard C et al., *Oncotarget* 2015;6(19):17621-36.; ³ Visser M et al., *Horm Mol Biol Clin Invest.* 2012;9:95-103.; ⁴ Visser M et al., *Climacteric* 2008; 11 Suppl 1:64-8.; ⁵ Mawet M et al., *Eur. J. Contracept. Reprod. Healthcare* 2015:1-13.; ⁶ Apter D. et al., *Contraception* 2016;94(4):366-73; ⁷ Abot et al., *EMBO* 2014: 6 (10); ⁸ Apter et al., *Eur. J. Contracept. Reprod. Healthcare* 2017:22(4)

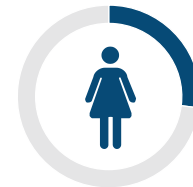
Estelle® for Contraception, a \$22bn blockbuster market¹

Regulators are encouraging new approaches through non-reimbursement, market withdrawal and warnings for existing products

Generation pill	Better user acceptability	Improved safety profile
1st & 2nd generation	✗	✓
3rd & 4th generation (e.g. Yaz family: peak sales €1.2bn; EE + DRSP) ¹	✓	✗
Potential 5th generation (E4 + DRSP)	✓ mithra Women's Health	✓ mithra Women's Health



24%
use alternative
methods¹



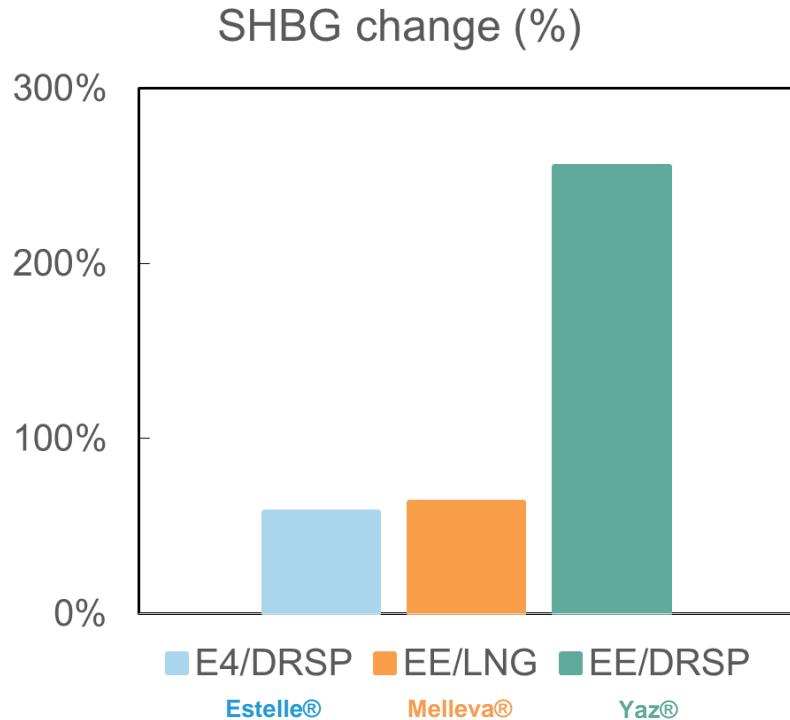
27%
use no
contraceptive
at all²



30%
of US women not
taking pill mainly due
to safety or
convenience⁴

- ¹ Transparency market research 2017. \$22bn is total hormonal contraceptive market. The oral contraceptive market stands at \$9.6bn.
- ² IMS Health Data
- ³ In the 8 biggest markets: US, France, Germany, UK, Spain, Italy, Belgium & Netherlands. United Nations, Department of Economic and Social Affairs, World Bank
- ⁴ K. Daniels et al., National Health Statistics report n° 62, 2013

Estelle® Phase II substudy: Reduced VTE risk profile



Change of SHBG (Sex-hormone binding globulin) plasma levels as marker of VTE risk¹

Cycle 6 – Baseline (Mean change)

- Limited impact on SHBG levels for Estelle® (E4/DRSP)
- In line with EE/LNG (Melleva®), the 'safest' 2nd generation pill
- Much lower than 4th generation benchmark EE/DRSP (Yaz®)

Estelle Phase III Europe/Russia: Positive Top-line results¹

- Efficacy rate > 99,5 %
- Key secondary endpoints achieved:
 - Outstanding cycle control with an excellent regular bleeding pattern
 - Quality of life maintained
 - Well tolerated with no unexpected safety events²
- Estelle® Phase III study in US/Canada on track to report top-line results in Q1 2019

Ref: 1) Press Release, 8/08/18 : [Mithra Announces Positive Top-Line Results of Estelle® Phase III Oral Contraceptive Study in EU/Russia](#)

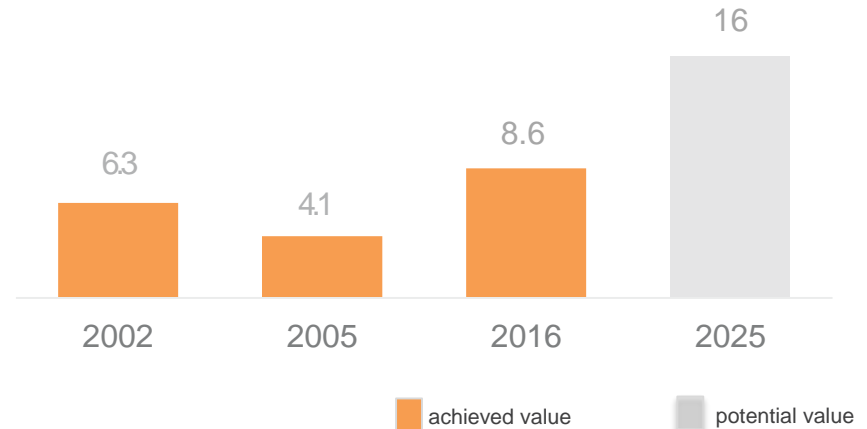
2) The global safety assessment will be communicated in detail once the Phase III US/Canada study has been completed



Donesta[®] for Menopause, \$8.6bn blockbuster market¹

- 78%¹ of menopausal women suffer VMS (hot flushes) - only 7.8% receive HT²
- Increased safety issues: VTE, stroke, breast cancer risks
- No new estrogen-based products for more than 10 years, but renewed interest & developments (hormonal & non-hormonal)
- \$16bn billion potential HT Market in 2025 – VMS potential with safer alternative

Menopause market (in \$bn)^{3,4}



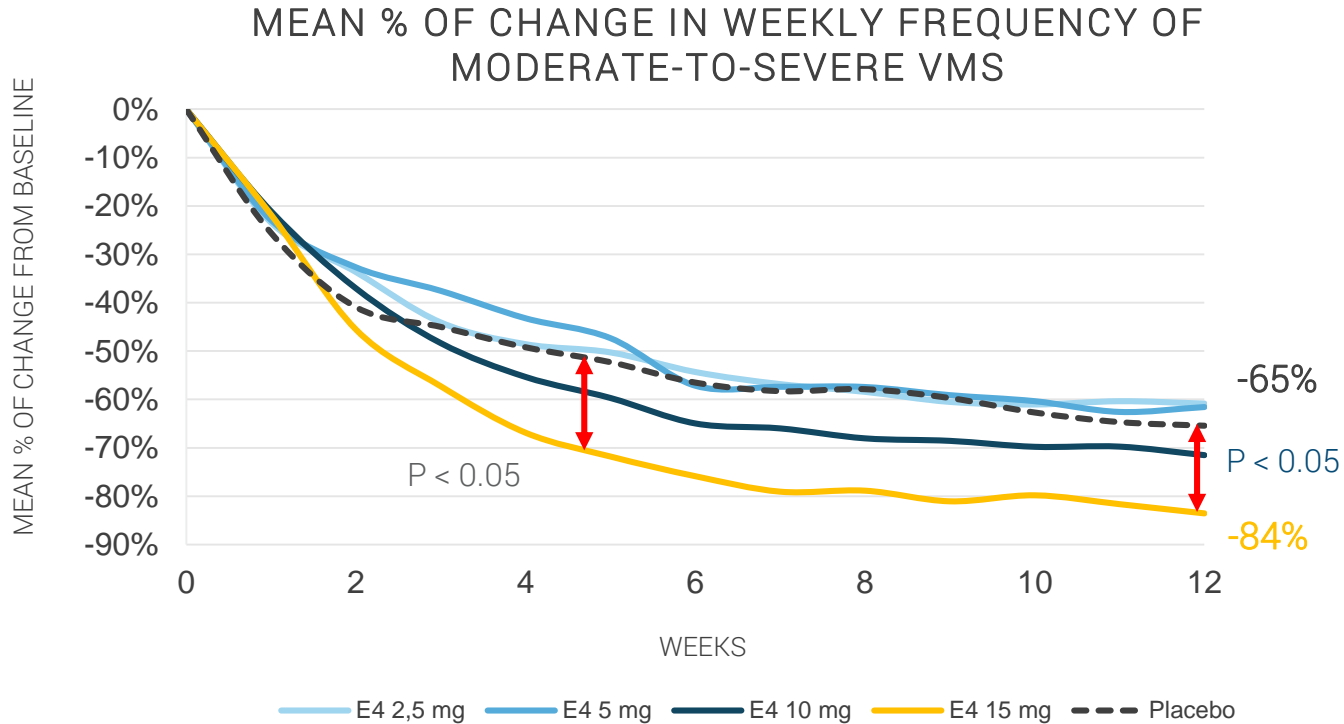
• Sources: (1) Transparency Market Research 2017; (2) KBC company report Aug 2015; (3) IMS link Q2 2016; (4) Datamonitor 2014

Donesta® Phase IIb: Positive Top-line Results – Optimal minimal dose & significant effect on VMS

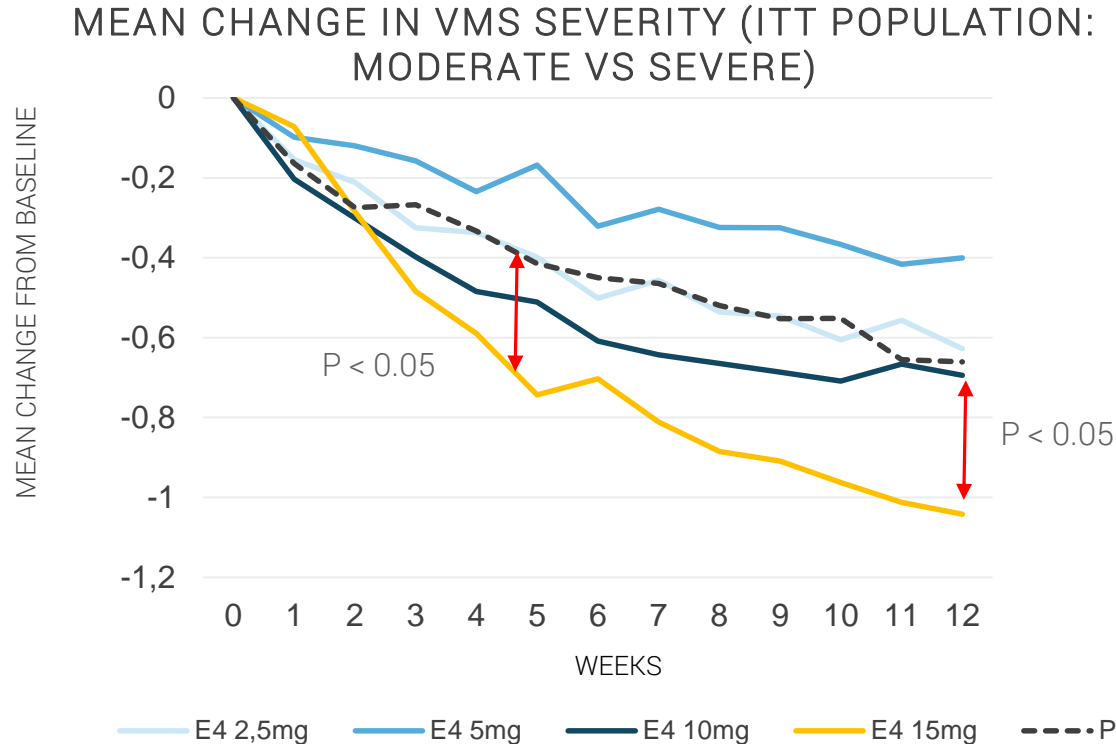


- **Primary study objective reached:**
optimal minimal effective dose defined at 15 mg
- **Frequency** and **severity** endpoints met,
despite not being powered for statistical significance:
- Proven Efficacy on **secondary endpoints** & promising safety profile

Donesta® Phase IIb: Positive Top-line Results: Significant effect on frequency of hot flushes



Donesta® Phase IIb: Positive Top-line Results: Significant effect on severity of hot flushes



















Donesta[®] Phase IIb: Summary and Next steps

- Launch of both an **E4 alone** and a **combination trial** (E4 + progestin) in order to maximize market potential of Donesta
- **Preparatory/bridging studies** to commence as early as Q4 2018 (e.g. food effect study), followed by initiation of recruitment for Phase III trials
- Detailed Phase III **design** is being discussed with **KOLs** and agencies

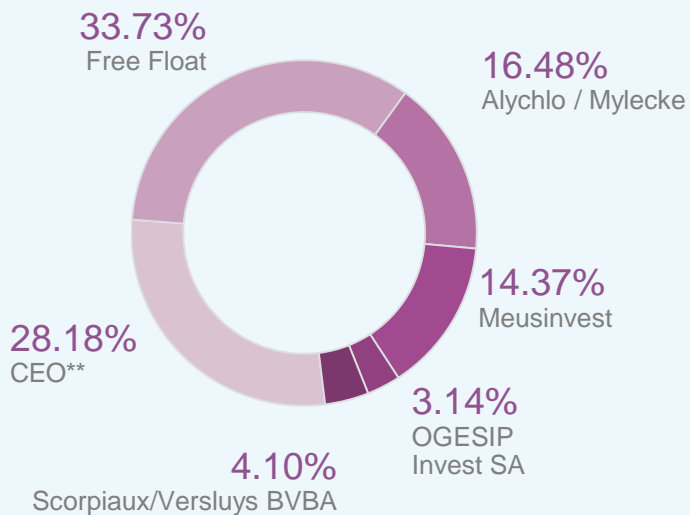
**Data strongly support further Donesta[®] development,
as a unique next-generation hormone therapy**

Partnering with leaders in Women's Health at key value inflection points

	EU	US	RoW
Estelle®	 GEDEON RICHTER	Partnering intended for commercialization	Partnering ongoing   Fuji Pharma Co., Ltd.    Brazil Japan & ASEAN Canada South Korea BeLux*
Donesta®	Partnering intended for co-development Phase III		Partnering ongoing  Fuji Pharma Co., Ltd. Japan & ASEAN
Myring™	Partnering discussions ongoing     Austria Czech Republic Russia Denmark		Partnering discussions ongoing  Chili
Other products (incl. Zoreline®; Tibelia®)	Partnering discussions ongoing**  	Partnering discussions ongoing	Partnering discussions ongoing 

Summary Financial Information

Share capital as of June 2018*



IFRS P&L and cash balance (in m€, FY as of 06/30/2018)**

	HY 2017	HY 2018
Revenues	12.7	12.6
R&D Expenses	(25.5)	(19.4)
G&A	(5.2)	(4.5)
Selling expenses	(2.4)	(2.4)
REBITDA	(23.2)	(11.5)
	Dec 2017	June 2018
Cash & Equivalents	36.2	85.8

➤ Revenues stable :

- Decreased Benelux sales compensated by
- Increased Licensing revenues (Libbs – Estelle)

➤ Costs controlled:

lower R&D Expenses because end of clinical studies Phase III for Estelle

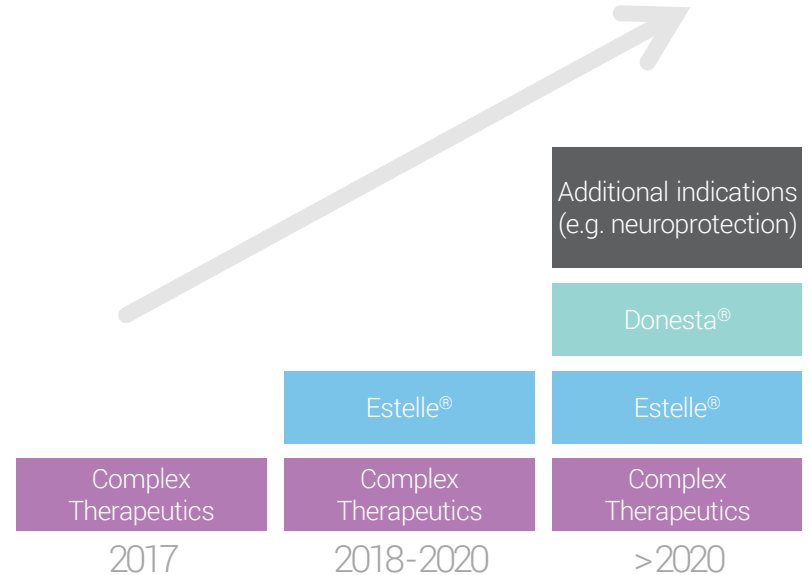
- **Cash:** EUR 77.5m private placement in May 2018

* Shareholdership in accordance with transparency declarations received by the company and notified managers' transactions. Market Cap: €1.1bn as of June 2018 (Euronext: MITRA)

** CEO (François Fornieri) holds warrants for 1,023,000 additional shares of Mithra

Building a transformative Women's Health company

- Multiple prospective near- and mid-term milestones and launches to drive long-term growth
- Estelle® and Donesta® – late-stage potential blockbusters built on unique E4 platform
- Acceleration of **business development** including partnerships for E4-based programs
- **Industry partner** with specialist research, development and manufacturing capabilities
- **Diversified model** spreads risk and maximizes product opportunities through collaborations



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Thank you

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