VaRi Bioscience

VaRi Bioscience GmbH

Non-Confidential Company Presentation

February 2022

The Global Female Health Market

- The global female health market size was valued at around USD 32 billion in 2019 and is projected to increase with a CAGR of 7 % in the forecast period of 2019 - 2026
- After many years without research and innovation in female health, the market is hungry for new and innovative products
- Ideas for true innovations are scarce, but established companies are highly interested in licensing advanced, patent protected products
- VaRi Bioscience develops products using innovative vaginal ring delivery technology to address widespread medical need

Company at a Glance

Team:	• Founders Team consists of a group of senior executives and industry experts from leading female health companies (Schering, Organon and Bayer)
Technology:	• Women specific proprietary drug delivery technology of vaginal rings

Products and USP:	• VaRi Bioscience is developing innovative products for women not tolerating systemic estrogen application
	  • **VR103:** A well tolerated and efficient treatment of endometriosis with proven contraceptive efficacy
	  • **VR102**: A locally acting estriol (E3) releasing vaginal ring for the risk-free relief of symptoms of Vulvovaginal Atrophy (VVA) with 'first-in-class' potential
	  • **VR101**: A safe, long acting "progestin-only" contraceptive vaginal ring

Status of Clin. Development:	• All projects have demonstrated "Proof-of-Principle" with completed Phase I/IIa data
Operational Model:	• Capital-efficient virtual single asset development model ("VSAD" strategy)

VR103 – Endometriosis

Progestins are the therapeutic backbone based on their anti-inflammatory and anti-proliferative action

Disease Characteristics

- Endometriosis, a chronic and progressive inflammatory disease, affects about 10% of women of reproductive age. Recently, awareness of this debilitating and painful disease has been increasing
- Endometriosis is characterized by endometrial tissue growing outside the uterus. Deep infiltrating endometriosis may penetrate into adjacent organs (ovaries, gut, bladder) and eventually leads to infertility.
- The predominant symptom of endometriosis is pain which is not adequately controlled by NSAIDs
- Proliferation and growth of endometrial lesions is fueled by estrogens and cause inflammation and pain
- Progestins act as powerful counterparts to estrogen, inducing atrophy of the lesions. In the lesions, progestins are potent inhibitors of inflammation. About 70% of patients respond very well to progestins

VR103 – Current Treatment Options

Progestins are potent 1st line therapies but underutilized in the USA

Treatment options (USA)

- **Suspected patients** are usually treated with combined oral contraceptives (OCs). If pain persists, uninterrupted treatment (without placebo pills) may be tested.
- **First line therapy: progestin-only products**

  MPA (e.g., Provera®, Depo-subQ Provera 104®) and NETA (Aygestin®) were approved in the USA for several indications many years ago. They are highly effective in endometriosis but have inferior benefit-risk ratios because they were not dose-optimized for this indication. Continuous uninterrupted therapy is not possible.

  Progestins are highly effective in around 70% of patients, even in severe disease. Direct comparator trials revealed progestins to be equipotent to GnRH agonists. Therefore, long-acting progestin-only contraceptives such es, e.g., intrauterine devices (IUDs) and implants, are used off label.
- **Second line therapy: GnRH agonists and oral GnRH-Antagonists**

  The products inhibit stimulation of the ovaries to secret estrogens and progestins. Their therapeutic benefit solely relies on estrogen deprivation. Menopausal symptoms and bone loss are the consequence. To improve tolerability and safety, add-back therapy with estrogen and progestin, a triple therapy, is recommended. They are not reliably contraceptive, and fetus safety is not demonstrated. Therefore, non-hormonal contraception is required.

VR103 - Competitive Landscape

VR103 has the potential to become the best-in-class 1st line therapy for approx. 70% of patients

	VR103	OCs	oral Progestin-only products NETA, Dienogest	Implant & IUD	GnRH ag.	GnRH antag.
Efficacy Endometriosis (pain scores)	**+++**	**++** limited evidence base, off-label use	**+++** Good evidence for Dienogest, NETA	**++/+++** evidence base limited	**+++** Evidence base	**+++** Excellent evidence base
Safety	**+++**	**Thrombosis Risk**	**+++**	**++** **surgical risks & penetration into tissue**	**bone loss** (reduced by add-back)	**bone loss** (reduced by add-back)
Efficacy Contraception (real world evidence)	**++/+++** **minimal user compliance needed**	**++**	**++** requires utmost compliance	**+++** no compliance required	**not established**	**not established**
Tolerability	**++**	**+++**	**+**	**++**	**major** (reduced by add-back)	**major** (reduced by add-back)
Irregular Bleeding / Spotting	**some**	**minimal**	**considerable**	upon insertion: **considerable** reduced over time	at treatment start: **considerable** later amenorrhea	at treatment start: **considerable** reduced over time
Hot Flushes / Night Sweats	**rarely**	**-**	**rarely**	**no - minimal**	**major** (reduced by add-back)	**major** (reduced by add-back)
Need for non-hormonal contraception	**no**	**no**	**no** if dosed same at time each day	**no**	**yes**	**yes**

Conclusion

- Progestin-only products are considered an excellent choice for the treatment of endometriosis in progestin-responsive patients (70%). Their efficacy is comparable to GnRH compounds. NETA (oral), Depot MPA (injection) and Dienogest (not available in USA) are approved for the indication

VR103 – The Opportunity

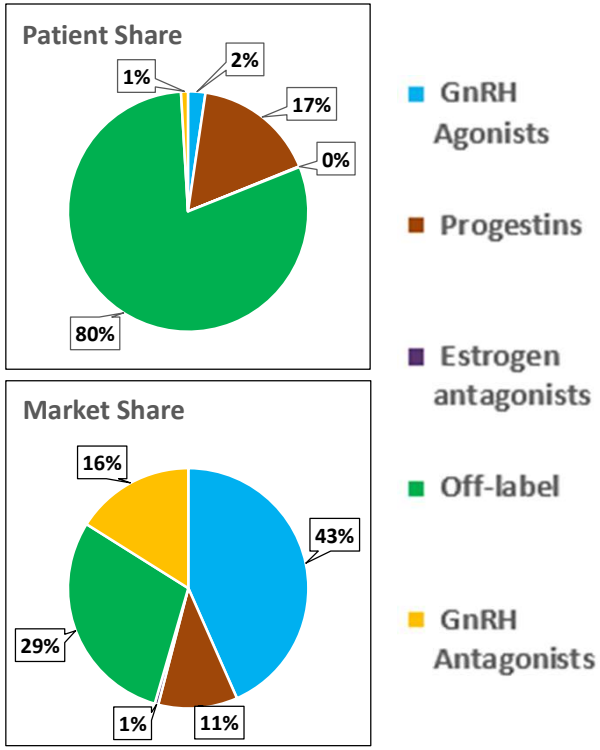
- VaRi's proprietary ring technology enables constant release of progestin over 3 months. Diligent dose finding will identify the release rate for optimal efficacy, tolerability and safety, also in severe patients. Excellent contraceptive efficacy is assured with minimal compliance requirements

VR103 – TPP Endometriosis

Indication:	• Endometriosis
Target Group:	• Consistent with guidelines, 1^{rst} line therapy for women suffering from endometriosis
USP:	• Highly effective non-invasive, long-acting endometriosis therapy with similar efficacy and superior safety compared to GnRH antagonists and agonists • Reliable contraception similar to other long-acting reversible progestin-only contraceptives (LARCs) • Constant release rates and diligent dose finding assures maximal potency AND safety
Route of Administration:	• Vaginal ring delivery
Dosing Frequency:	• 90-day treatment cycles / no therapy pause required
Efficacy:	• Similar to GnRH agonists and antagonists
Safety:	• No impact on bone mineral density due to limited reduction in plasma estrogen
Tolerability:	• Superior to approved progestin-only products: no / minimal estrogen withdrawal symptoms, such as, e.g., hot flashes, night sweats, vaginal dryness, and mood disorders
Additional product claims:	• Suitable for young women with suspected endometriosis suffering from pelvic pain or dysmenorrhea

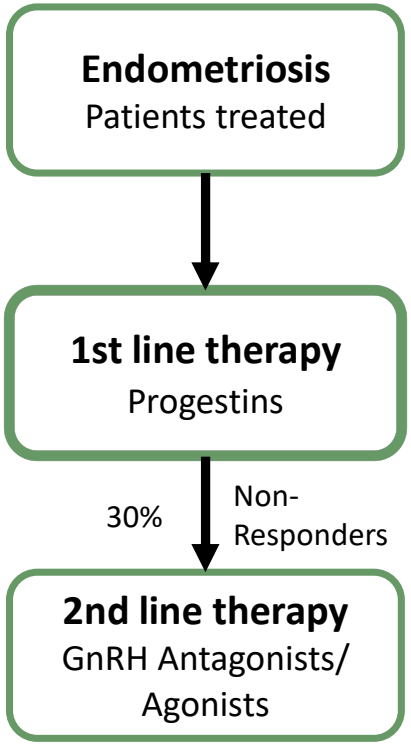
VR103 - Market Size & Potential (USA)

Endometriosis patient and market share by drug class in the US, 2020



Source: GlobalData, 2021

VR103 - Positioning



- The endometriosis market in the 7 major countries is forecasted to grow from 1.1 billion in 2020 to almost USD 3.0 billion in 2030 (**82% market growth over 10 years**).
- We strongly believe that **VR103 will lead to an increase of the progestin market share** due to the following reasons:
  - VR103 **is as effective as GnRH antagonists***, but offers a significantly superior side effect profile
  - VR103 **provides contraception** similar to oral contraceptives and long-acting products
  - VR103 is a **long-acting product for uninterrupted therapy** that allows patients to remain in control of their treatment
- Estimated price: **USD 10,000 annually** (Retail)
- Expected peak sales: **around USD 1.0 billion (US only)**

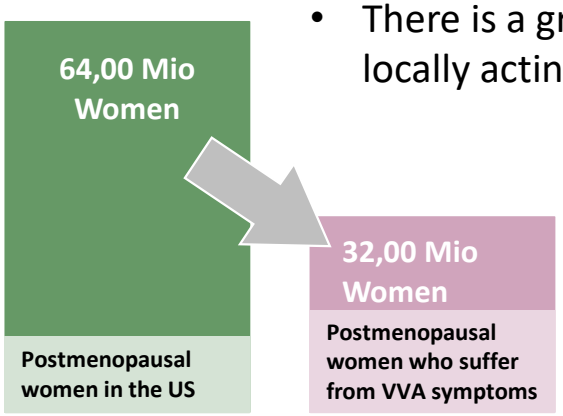
*Strowitzki, T., Marr, J., Gerlinger, C., Faustmann, T., & Seitz, C. (2010). Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial. Human reproduction (Oxford, England), 25(3), 633–641. https://doi.org/10.1093/humrep/dep469

VR102 – Vulvovaginal Atrophy

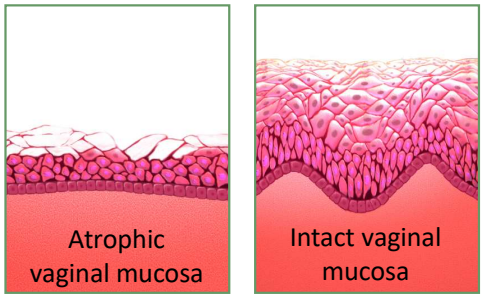
An unfavorable consequence of menopause and systemic anti-estrogenic therapy

Unmet need

- Vulvovaginal atrophy (VVA) is a common and underreported condition associated with the decrease of estrogen levels after menopause
- Symptoms of VVA have a significant influence on the quality of life of modern postmenopausal women.
- Treatment options for VVA in the US include estradiol preparations in outdated high strengths
- There is a growing market for locally acting “safe” preparations



Solution



- VR102 is a safe product due to use of low-dose E3
- VR102 would be the first FDA approved estriol preparation
- Estriol, a weak estrogen with low bioavailability, is perfectly suited for local therapy, being inherently safe so that it could even be considered for women under aromatase inhibitor therapy
- Long-acting (3-months) and “mess-free“ compared to creams or vaginal suppositories
- Initial development activities have been completed for VR102, making the realization tangible and further increasing the probability of success

VR102 – TPP Vulvovaginal Atrophy

Indication:	•	Treatment of VVA caused by estrogen deficiency due to menopause
Target Group:	•	Postmenopausal women with symptoms of VVA
USP:	•	First-in-class long-acting local estrogen therapy that is safe (with proven safety) in women requiring systemic anti-estrogenic therapy because of breast cancer
Active ingredient(s):	•	Estriol (low-dose)
Route of Administration:	•	Vaginal ring delivery
Dosing Frequency:	•	90-day treatment cycles
Clinical efficacy:	•	Efficacy similar to other vaginally applied estrogen products (as indicated by influence on maturation index and pH, relief of symptoms of VVA)
Safety and Tolerability:	•	Well-tolerated, no systemic effects due to lack of increase of estriol plasma levels
Additional product claims:	•	The selected final dose is to show full local effects while not resulting in an increase of systemic E3 plasma levels which supports the claim of absence of systemic effects through treatment.

VR102 - Competitive Landscape

	Status	Active substance	Schedule	Dosage form
VR102	**Phase II**	**Estriol**	**90 day**	**Vaginal ring**
Intrarosa Theramex	Approved 2016	DHEA	Daily/ Bi-weekly	Vaginal Insert
Imvexxy TherapeuticsMD	Approved 2018	Estadiol	Daily/ Bi-weekly	Softgel Vaginal Insert
Osphema Duchesnay USA	Approved 2013	Ospemifene	Daily	Oral Tablet
DR 2041 TEVA	Phase III	Synt.Conj. estrogens	Daily	Vaginal Cream
WC 3037	Phase II	Estradiol	Daily	Vaginal Caps

- Estriol is a natural hormone that is quickly converted to an inactive metabolite after exerting its local effect
- No estriol product is approved for VVA in US
- Estriol is widely used by compounding pharmacies causing concerns by FDA
- No estriol VR is under development

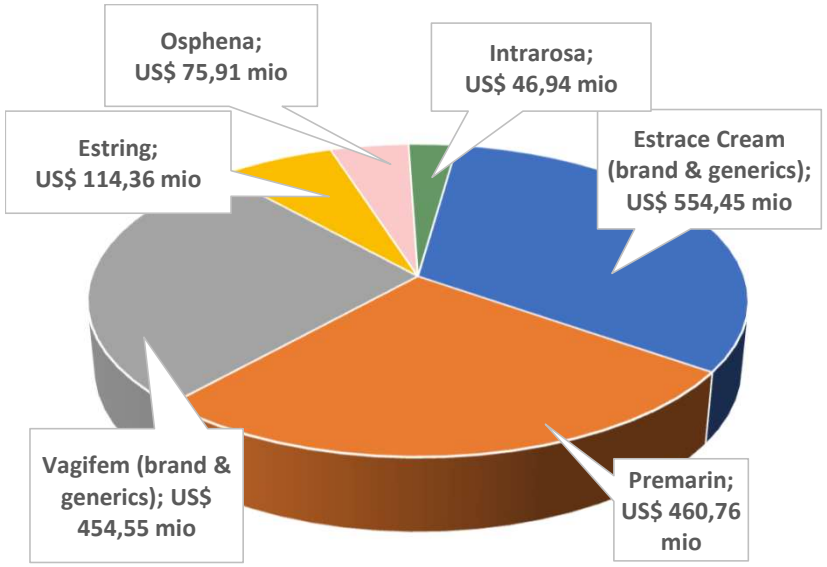
Advantages of VR102:

- Full local effect without any systemic activity
- ”mess free” application
- Convenient 3-month product

VR102 - Market Size & Potential (USA)

Local estrogen therapy currently represents over 95 % market share of VVA market

The VVA market exceeded US$ 1.7 bn of which individual sales in 2018:



Trend goes in direction of lowest possible dose and move away from semi-solids for better compliance

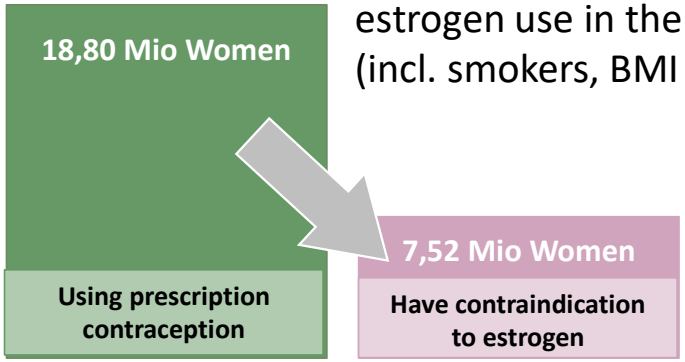
FDA is concerned about high number of prescriptions form compounding pharmacies

- VR102 has “first-in-class” potential: the first estriol product on the VVA market with no systemic estrogenic activity.
- Estimated peak sales around **US$ 500 mio (USA only)**
- Estimated annual treatment price (Retail): **USD 2,300**

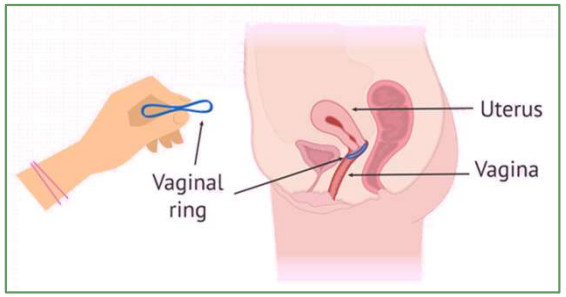
VR101 – Progestin-only Contraceptive

Unmet need

- Although hormonal contraceptives are well tolerated in general, the risk of developing deep vein thrombosis (DVTs) is still an unresolved problem
- New research suggests that estrogens are causing the problem
  - The prevalence of the target group of women with contraindications to estrogen use in the US is > 40% (incl. smokers, BMI >30, age > 35)



Solution



- Giving women the choice: VR101 is long-acting, reversible & self administered
- VR101, a progestin-only product, can be used by women with an estrogen sensitivity without increased risk of DVTs
- Long-acting (3-months)
- Initial development activities have been completed for VR101, making the realization tangible and further increasing the probability of success

VR101 - TPP

Indication:	• Contraception
Target Group:	• Premenopausal women especially with contraindications to use estrogen
Route of Administration:	• Vaginal ring delivery
Dosing Frequency:	• 90-day treatment cycles
Efficacy:	• Superior efficacy compared to oral progestin only contraceptives POPs
Safety and Tolerability:	• Well tolerated in line with current standards
Additional product claims:	• Superior bleeding profile (i.e. less irregular bleeding) than existing products compared to existing progestin only contraceptives • Better treatment compliance • Less mood-related side effects

VR101 - Competitive Landscape

Progestin-only Contraceptives

	Status	Schedule	Dosage form
VR101	**Phase II**	**90 days**	**Vaginal Ring**
Slynd® Exeltis	Approved	24+4 days	Tablet
LNG Navad	Phase II	28 days	Tablet
LNG VR Chemo	Phase II	28 days	Vaginal Ring

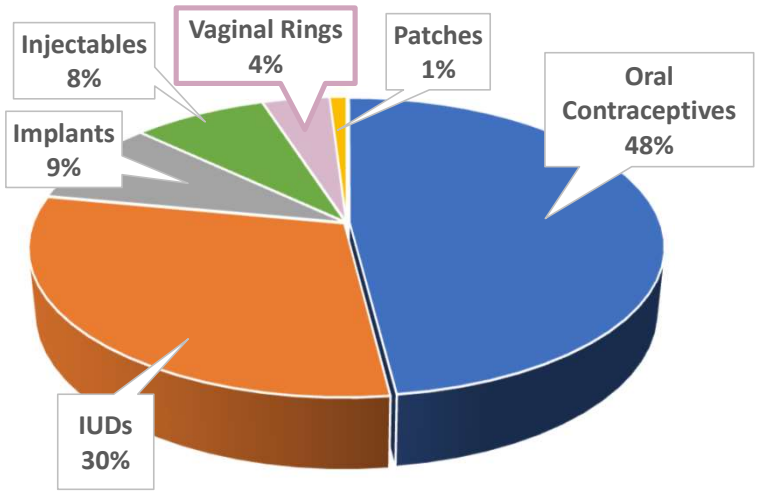
Advantage of VR101:

- 3-month product is considered a LARC (long-acting reversible contraceptive)
- Better bleeding profile than oral product expected

VR101 - Market Size & Potential (USA)

Of 72 mio women aged 15-50, 26 % use prescription contraception → 18.8 mio women

% of women using prescription contraception by method:



CDC strongly recommends the use of LARCs (long-acting reversible contraceptives) due to their high efficacy in preventing pregnancy

- VR101 targets two categories of women:
  - Women with contraindications to estrogen use (smoker, age >35 and BMI >30) → 30 - 40 % of population
  - Women seeking LARC but are afraid of invasive procedures (around 40 %)
- VR101 will take market share from all non oral subsegments, mainly (nominal)
  - Vaginal rings 1.0 – 1.5%
  - Injectables 2.0 – 2.5%
  - IUDs 2.0 – 2.5%
  - Implants 2.5 – 3.0 %
- Estimated peak market share between 7.5-10 %
- Estimated **peak sales** based on an annual sales price of US$ 1,200 could range between **US$ 1.7 - 2.25 bn**

Company & Financing History

- **VaRi Bioscience** has been founded in August 2021 by a group of industry veterans with extensive experience in the development of female health products
- Vaginal rings were selected as core technology because of the avoidance of daily fluctuations of drug plasma levels and the convenient long-term use
- VaRi Bioscience has done an extensive screening of suitable APIs
- Innovative formulation concepts for VR103, VR102 and VR101 have been developed and patent applications have been filed
- Seed phase financing has been secured by the founders

Management Team

CEO
K. Nickisch, PhD

Board Member
L. Lingnau

API Sourcing
O. Petrov, PhD

VR Development
H. Vromans, PhD

Finance & Business Operations
M. Blankenburg

Corporate Development
K. Bode-Greuel, MD, PhD

CMO
n.n.

CEO & Board

Senior Management

IP Status and Freedom to Operate

- All projects will be covered by a combination of formulation and process patents
- Innovative formulation concepts for VR103, VR102 and VR101 have been developed by VaRi Bioscience
- Patent applications have been filed with the European Patent Office by November 2021
- First filing will be in USA followed by international applications in selected countries
- Process patents will be added after clinical batches have been produced

Operational Model

Internal Functions:
- Management
- Project Management
- Marketing & Business Development
- Finance

External Partner:
Cooperation with experienced CROs and leadership through a knowledgeable management team provide the expertise to design streamlined, cost-efficient development programs.

External Partner

Research & Development
- Process / analytical development, non GMP
- Stabilization tests

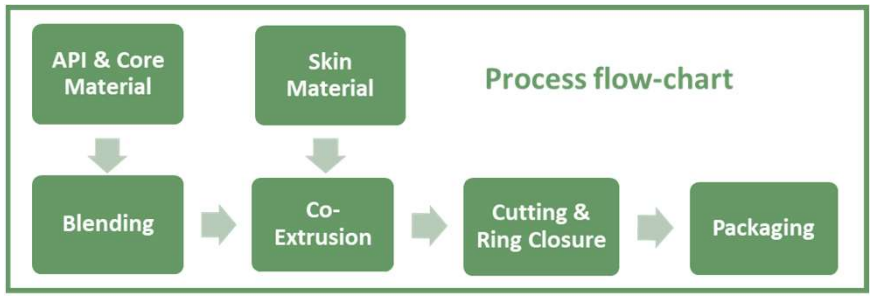
API Supply
- API supply

Manufacturing of clinical supply
- Clinical Supply
- Commercial supply
- QC

Clinical Research Organization
- Phase II, clinical studies
- IND preparation

Technology & Manufacturing Plans

- Two core technologies are needed for the manufacturing of vaginal rings:
  - Extrusion
  - Ring-closure molding technology
- Extrusion is based on long-lasting experience in the plastic industry
- Various approaches for the molding technology have been developed
- Specialized CMOs are available and have been evaluated for clinical & commercial supply



Technology Platform Provides Additional Upside

- Innovative drug delivery technology has significant potential outside female health („roll out“)
- Focus on indications that require long-term treatment and that benefit from low day to day plasma level variations as well as sustained drug exposure
- Published data confirm approach and support positioning and development strategy
  - https://doi.org/10.1016/j.contraception.2020.06.006
  - https://doi.org/10.1080/13625187.2021.1884219
  - https://doi.org/10.1002/cpdd.968
  - https://doi.org/10.1111/bcp.13822
- Corporate partners might be interested in getting access to this innovative drug delivery technology

Thank you!

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