

# DARÉ

IN ITALIAN, IT MEANS “**TO GIVE.**”

IN ENGLISH, IT MEANS “**TO BE BOLD.**”



# Forward-Looking Statements

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# WE ARE **ACCELERATING INNOVATION** IN WOMEN'S HEALTH

We're driven by a mission to accelerate a diverse portfolio of novel therapies for women that **expand treatment options, improve outcomes and facilitate convenience.**

With clinical trials underway, our initial **focus areas include contraception, fertility, and sexual and vaginal health.**



Partnering is core to our strategy

## We partner so we can...

**Accelerate** exciting new products

Develop new solutions to **address persistent unmet needs**

Become a **pipeline resource** for large and emerging commercial companies

Drive **new innovation**

## We look for...

Highly **differentiated products** with attractive market opportunities

**Proof-of-concept** and/or the ability to leverage a 505(b)(2) regulatory pathway

**First-in-category** or first-line opportunities

**Personalized** for women (non-systemic delivery)

## We partner with...



BILL & MELINDA  
GATES foundation



PARTNERS	ADVANCING PRODUCTS WOMEN WANT	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3 / PIVOTAL	REGULATORY FILING
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**DARE-BV1<sup>^</sup>**  
 Bacterial Vaginosis

Potential First-line Option for Bacterial Vaginosis (BV)  
*Bio-adhesive gel, clindamycin 2%*

**Ovaprene<sup>®</sup>**  
 Hormone-Free, Monthly Contraception

First-in-category Hormone-Free Monthly Contraception  
*Monthly, self-administered drug/device barrier IVR,*

**Sildenafil Cream, 3.6% <sup>^</sup>**  
 Female Sexual Arousal Disorder

First-in-category for Treatment Female Sexual Arousal Disorder (FSAD)  
*Topical Cream, same active ingredient as Viagra<sup>®</sup>*

**DARE-HRT1<sup>^‡</sup>**  
 Hormone Replacement Therapy

First-in-category Combination Hormone Delivery for VMS/HRT  
*IVR, combination bio-identical estradiol + bio-identical progesterone*

**DARE-FRT1<sup>^</sup>**  
 Pregnancy Maintenance (PTB & ART)

First-in-category Progesterone Delivery for Pregnancy Maintenance  
*IVR, bio-identical progesterone*

**DARE-VVA1<sup>^</sup>**  
 Vulvar and Vaginal Atrophy (HR+ Breast Cancer Population)

First-in-category Hormone-Free Vaginal Treatment for VVA  
*Proprietary formulation of tamoxifen for vaginal administration*

**DARE-LARC1<sup>^</sup>**  
 User-Controlled, Long-Acting, Reversible Contraceptive  
*Levonorgestrel Implant*

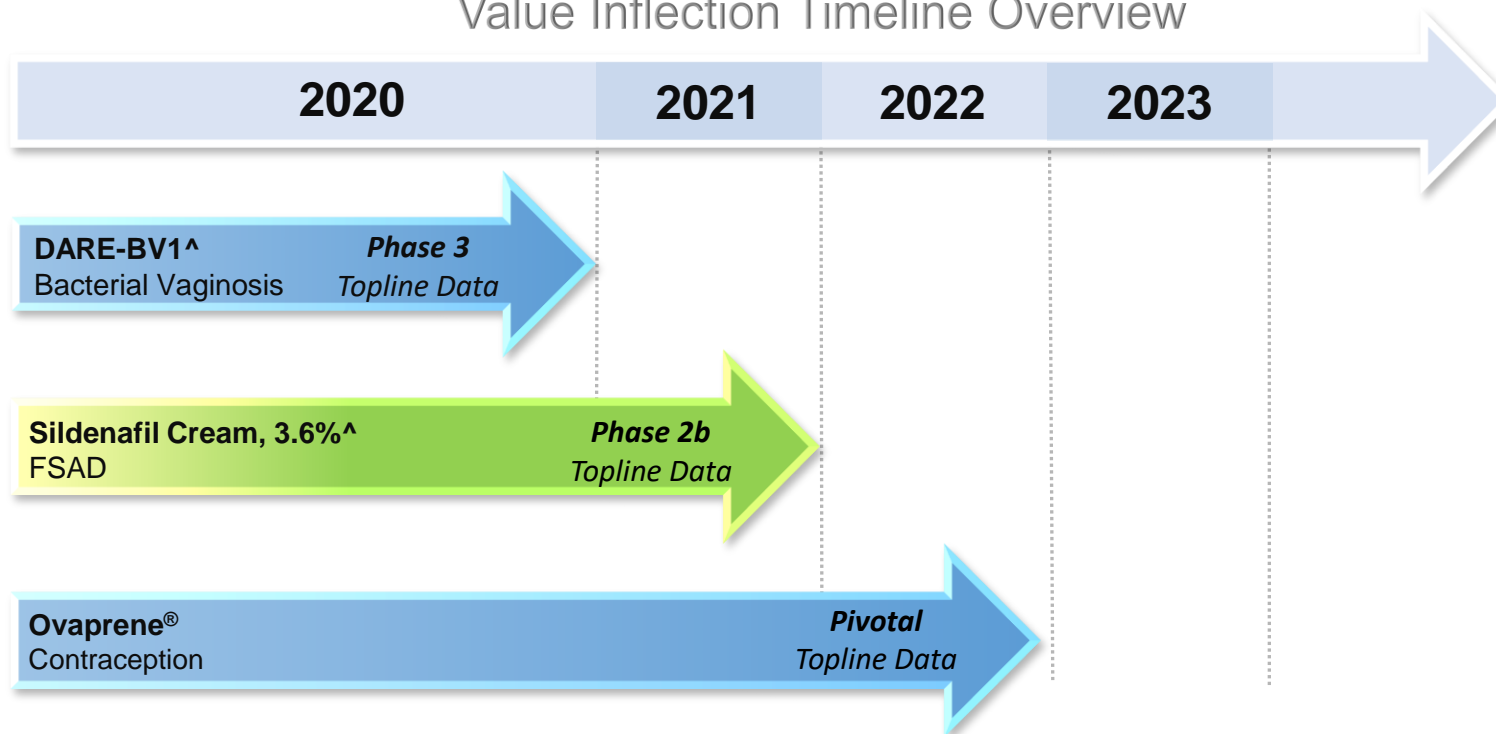
**DARE-RH1**      Male or Female Contraceptive Target  
**ORB 204/214<sup>^</sup>**    6 & 12 Month Injectable Contraception



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# WE ARE ACCELERATING INNOVATION IN WOMEN'S HEALTH

## Value Inflection Timeline Overview





WOMEN'S HEALTH  
IS OUR



SOLE FOCUS



DARE-BV1

Clindamycin 2% gel for Bacterial Vaginosis



# Bacterial Vaginosis (BV) - What is the clinical issue?

## Frequently recurring infection that can be difficult to treat

- The most common vaginal infection in women ages 15-44<sup>1</sup>
- Estimated to affect ~21 million women in the U.S.<sup>1</sup>
- Current prescription drugs are less than optimal with clinical cure rates ranging from 37-68%<sup>2</sup>



## BV increases clinical risks<sup>3</sup>

- **Preterm birth** – BV is linked to premature deliveries and low birth weight babies
- **Sexually transmitted infections** – BV makes women more susceptible to sexually transmitted infections, such as HIV, herpes simplex virus, chlamydia or gonorrhea
- BV may increase the risk of developing a **post-surgical infection** after gynecologic procedures
- BV can sometimes cause pelvic inflammatory disease (PID), an infection of the uterus and the fallopian tubes that can increase the risk of infertility

1. <https://www.cdc.gov/std/bv/stats.htm>

2. BV Product Data: <http://www.clindesse.com/pdf/PI.pdf>; [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/205223s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205223s000lbl.pdf); [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/205223s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205223s000lbl.pdf)

3. <https://www.mayoclinic.org/diseases-conditions/bacterial-vaginosis/symptoms-causes/syc-20352279>



# DARE-BV1

## CURATIVE POTENTIAL FOR THE MOST COMMON VAGINAL INFECTION (WOMEN AGES 15-44)

### Investigator Initiated Proof of Concept Study<sup>1</sup>



Product	Clinical (Amsel) Cure	Bacteriologic (Nugent) Cure	Therapeutic Cure
DARE-BV1	86%	57%*	57%*
Solosec <sup>®2</sup> <small>(secnidazole 2g oral granules)</small>	53-68%	40-46%	35-40%
Clindesse <sup>®3</sup> <small>clindamycin phosphate Vaginal Cream, 2%</small>	41-64%	45-57%	30-42%
Metronidazole gel, 1.3% <sup>4</sup>	37%	20%	17%

\* Based on data from 7 evaluable patients

DARE-BV1 is a thermosetting vaginal gel formulated with clindamycin phosphate 2%, a well known and well characterized antibiotic, that is designed for prolonged, localized release.

#### Proof of Concept Study: 28 of 30 women completed the study

Primary endpoint: Test-of-Cure Visit (Day 7 – 14)

- **24 of 28 (86%) women achieved clinical cure based on Amsel criteria**
- 4 of 7 (57%) women had bacteriologic cure and 4 of 7 (57%) had therapeutic cure

Continued clinical response visit (Day 21 – 30)

- **22 of 24 (92%) women showed continued clinical cure**
- 7 of 9 women had bacteriologic cure and 6 of 9 had therapeutic cure

1. No clinical studies have been conducted to evaluate the efficacy of DARE-BV1 compared to any FDA-approved products. The proof of concept study enrolled 30 women, ages 18-50, and assessed the safety and efficacy of DARE-BV1 to treat BV after a single administration. The cure rates presented for the FDA approved products identified in the table are based on information provided in the product's label.

2. <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=551e43d5-f700-4d6e-8029-026f8a8932ff&type=display>. Cure rate range reflects low and high cure rates across multiple studies.

3. <http://www.clindesse.com/pdf/PI.pdf>. Cure rate range reflects low and high cure rates across multiple studies

4. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/205223s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205223s000lbl.pdf)

# DARE-BV1

## Phase 3 Clinical Study Design

### Day 1 Baseline Visit

#### Tests Performed:

- Signs & symptoms
- pH
- Saline “wet mount”
- 10% KOH “whiff test”



**DARE-BV1**

2 to 1 Randomization



**Placebo**

Single administration of DARE-BV1 or placebo

### Day 7 – 14 Secondary Endpoint (Test-of-Cure Visit)

#### Tests Performed:

- Signs & symptoms
- pH
- Saline “wet mount”
- 10% KOH “whiff test”
- Nugent score

### Day 21 – 30 Primary Endpoint (Test-of-Cure Visit)

#### Tests Performed:

- Signs & symptoms
- pH
- Saline “wet mount”
- 10% KOH “whiff test”
- Nugent score

N ~220 subjects (age 12 and above)  
Duration ~30 days per subject  
Diagnosis - Bacterial vaginosis

#### Definitions:

**Primary Endpoint: Clinical Cure (Day 21-30):** Resolution of the abnormal vaginal discharge associated with BV; Negative 10% KOH “whiff test”; Clue cells < 20% of the total epithelial cells in the saline wet mount.

**Secondary endpoints:** Proportion of subjects with Clinical Cure, Bacteriological Cure and Therapeutic Cure at Day 7-14 Visit

**Bacteriological Cure:** a Nugent score < 4.

**Therapeutic Cure:** both a Clinical Cure and Bacteriological Cure.

WOMEN'S HEALTH  
IS OUR

SOLE FOCUS



Ovaprene®

Investigational Hormone-Free, Monthly Contraceptive

*The U.S. contraceptive market size is projected to reach USD 9.6 billion by 2027 expanding at a CAGR of ~4.2%<sup>1</sup>  
~37 million U.S. women of reproductive age are estimated to currently use a contraceptive method<sup>2</sup>*

# Contraception – what kinds of products are successful?

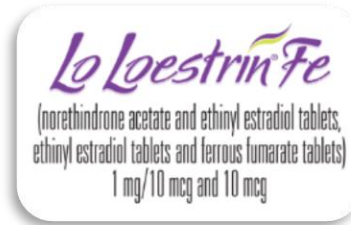


Mirena® Hormone IUD

(levonorgestrel-releasing intrauterine system) 52mg

Physician inserted, long-acting.  
low/locally delivered hormone IUS

2019 worldwide sales: **€1.2 billion** (Bayer)<sup>1</sup>



Lo Loestrin®

(norethindrone acetate and ethinyl estradiol, ethinyl estradiol tablets)

Lowest amount of daily estrogen  
(10 micrograms) available in pill form

2019 US sales: **\$588 million** (Allergan)<sup>2</sup>



NuvaRing®

(etonogestrel/ethinyl estradiol vaginal ring)

Monthly vaginal ring

2019 worldwide sales: **\$879 million** (Merck)<sup>3</sup>

## Lower hormone levels and more convenient delivery platforms

1. <https://www.bayer.com/en/bayer-ag-annual-report-2019.pdf>. Includes sales for Mirena®, Kyleena® and Jaydess® / Skyla®  
2. <https://www.prnewswire.com/news-releases/allergan-reports-fourth-quarter-and-full-year-2019-financial-results-301001646.html>  
3. [https://s21.q4cdn.com/488056881/files/doc\\_financials/2019/q4/2019-Form-10-K-Final.pdf](https://s21.q4cdn.com/488056881/files/doc_financials/2019/q4/2019-Form-10-K-Final.pdf).

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# Contraception – what kinds of features are women seeking ?

## Effective pregnancy prevention

## Less Hormones

- A majority of women prefer a monthly option with a lower hormone dose than the standard birth control pill.<sup>1</sup>

## Convenient dosing forms

- Independent surveys revealed that the vaginal ring has many of the features women deemed extremely important.<sup>2</sup>

## Defined coverage periods

- ~70% of women who practice contraception use non-coital (*not in the moment*) methods.<sup>3</sup>

CONTRACEPTIVE METHOD CHOICE				
Most effective method used in the past month by U.S. women, 2014				
METHOD	No. of women	% of women aged 15-44	% of women at risk of unintended pregnancy	% of contraceptive users
Pill	9,572,477	15.6	22.7	25.3
Tubal (female) sterilization	8,225,149	13.4	19.5	21.8
Male condom	5,496,905	8.9	13.0	14.6
IUD	4,452,344	7.2	10.6	11.8
Vasectomy (male sterilization)	2,441,043	4.0	5.8	6.5
Withdrawal	3,042,724	5.0	7.2	8.1
Injectable	1,481,902	2.4	3.5	3.9
Vaginal ring	905,896	1.5	2.1	2.4
Fertility awareness-based methods	832,216	1.3	2.0	2.2
Implant	965,539	1.6	2.3	2.6
Patch	69,106	0.1	0.2	0.2
Emergency contraception	69,967	0.1	0.2	0.2
Other methods*	234,959	0.4	0.6	0.6
No method, at risk of unintended pregnancy	4,408,474	7.2	10.5	na
No method, not at risk	19,302,067	31.4	na	na
Total	61,491,766	100.0	100.0	100.0

\*Includes diaphragm, female condom, foam, cervical cap, sponge, suppository, jelly/cream and other methods. NOTE: "At risk" refers to women who are sexually active; not pregnant, seeking to become pregnant or postpartum; and not noncontraceptively sterile. na=not applicable.

www.guttmacher.org

1. Hooper, DJ, Clin Drug Investig. 2010;30(11):74963  
2. Lessard, L, Perspectives on Sexual and Reproductive Health, Volume 44, Number 3, 9-2012  
3. <https://www.guttmacher.org/fact-sheet/contraceptive-use-united-states>

# Contraception – what products are *hormone-free*?<sup>1,2</sup>



## Spermicides / Vaginal Gels

- Effectiveness (72% *Typical Use*)
- Woman controlled



## Condoms

- Effectiveness (82% *Typical Use*)
- Not woman controlled



## Diaphragms

- Effectiveness (88% *Typical Use*)
- Woman controlled



## Long-acting Copper IUD

- Effectiveness (99% *Typical Use*)
- Not woman controlled

Least Effective



Most Effective



# Contraception – what's **missing** from *hormone-free* options?



Spermicides / Vaginal Gels



Condoms



Diaphragms



Easy-to-use, monthly option with effectiveness approaching hormonal methods



Long-acting Copper IUD

Least Effective



Most Effective



# Ovaprene®

## Investigational Hormone-Free, Monthly Contraceptive

Desired Features of Birth Control Products: <sup>1-4</sup>	Design Features of Ovaprene: <sup>5-7</sup>
+ Efficacy	<b>86% - 91% Expected Typical Use Effectiveness</b> Approaching Hormone Contraception
+ Hormone Free	<b>No Hormones in the API</b> Unique dual action MOA (spermistatic & barrier)
+ Convenience	<b>Monthly Ring Form</b> Women choose monthly rings for the convenience of a non-daily option
+ Favorable Side Effect Profile	<b>No Colposcopic Abnormalities</b> No significant changes in vaginal flora and no serious adverse effects observed in prior published study
+ Easily Manage Fertility	<b>No Systemic/Long-term Activity</b> Inserted and removed without a provider allowing for immediate return to fertility

### Physical Barrier<sup>8</sup>

*Three-dimensional, knitted polymer barrier*



### Spermistatic Environment<sup>8</sup>

*Contraceptive-loaded silicone ring releasing non-hormonal active Ferrous gluconate*

## Investigational Hormone-Free, Monthly Contraceptive

### U.S. Regulatory Strategy<sup>1</sup>

Premarket approval (**PMA**) with the Center for Devices and Radiological Health (**CDRH**) as lead review division

#### Step 1 (Completed)

- Postcoital Test (PCT) Study - Completed 4Q 2019

#### Step 2 (Ongoing)

- File investigational device exemption (**IDE**) to support 2022 pivotal study readout
- Conduct pivotal study
  - Topline data expected by year-end 2022
  - ~250 completers up to 12 months of use
  - Primary endpoints: safety and efficacy (pregnancy probability)
  - Secondary endpoints: acceptability, product fit/ease of use and assessments of vaginal health

#### The PCT Clinical Study Met its Primary Endpoint<sup>2</sup>

Ovaprene prevented the requisite number of sperm from reaching the cervix across all women and all cycles evaluated.

- **Specifically, in 100% of women and cycles, an average of less than five (< 5) progressively motile sperm (PMS) per high-powered field (HPF) were present in the midcycle cervical mucus collected two to three hours after intercourse with Ovaprene in place.**
- Women enrolled in the study who completed at least one Ovaprene PCT (N=26) had a **mean of 27.21 PMS/HPF in their baseline cycle (without any contraceptive device)**, a mean of 0.22 PMS/HPF in their diaphragm cycle (in the presence of an FDA-cleared diaphragm with spermicide), **and a mean of 0.48 PMS/HPF in their Ovaprene PCT cycles (in the presence of the Ovaprene device), with a median of zero PMS.**

	Mean <small>Progressively Motile Sperm</small>	Median <small>Progressively Motile Sperm</small>	Standard Deviation	Interquartile Range
<b>Baseline PCT's</b>	27.21	23.20	17.88	24.80
<b>Ovaprene PCT's</b>	0.48	0.00	1.18	0.10

1. Anticipated regulatory pathway and timelines.

2. In PCT studies of similar size, products (diaphragms) that demonstrated no motile sperm in the cervical mucus during PCT assessments later demonstrated "typical use" contraceptive effectiveness of 86-91% in pivotal contraceptive studies evaluating pregnancy rates over six-month periods.

# Ovaprene®

## Investigational Hormone-Free, Monthly Contraceptive



### Ovaprene Commercial License Agreement with Bayer<sup>1</sup>

January 2020 - Bayer, marketers of the \$1 billion Mirena contraceptive franchise, and Daré announced that the companies signed a license agreement under which Bayer may commercialize Ovaprene in the United States once approved by the FDA.

Mirena® is the #1  
prescribed IUD  
in the US\*

- Bayer received the right to obtain exclusive rights to commercialize the product in the U.S. following completion of the pivotal clinical trial if Bayer, in its sole discretion, **makes payment to Daré of \$20 million.**
- Daré may receive **up to \$310 million in commercial milestone payments** plus tiered **royalties on net sales in the double-digits.**
- Bayer supports the development and regulatory process by **providing up to two full-time equivalents (internal experts), or FTEs**, in an advisory capacity, which gives us access to their global manufacturing, regulatory, medical and commercial internal expertise.

*We believe the licensing agreement with Bayer is validation of our broader corporate strategy and confirmation of Ovaprene's market potential as the first monthly non-hormonal contraceptive product in the US market.*



## Sildenafil Cream, 3.6% Female Sexual Arousal Disorder (FSAD)

*The global female sexual dysfunction treatment market is expected to grow at ~37% CAGR from 2019 - 2023<sup>1</sup>*

# Sildenafil Cream, 3.6%

## FSAD - what is the clinical issue?

Female Sexual Arousal Disorder (FSAD), is characterized primarily by an **inability to attain or maintain sufficient genital arousal** during sexual activity and, of the female sexual function disorders, is the analogous to erectile dysfunction (ED) in men.\*

The condition should be distinguished from a general loss of interest in sexual activity and from other sexual dysfunctions, such as the orgasmic disorder (anorgasmia) and hypoactive sexual desire disorder (HSDD), which is characterized as a lack or absence of sexual fantasies and desire for sexual activity for some period of time.<sup>1,2</sup>

\*Diagnostic and Statistical Manual 4th Edition Text Revision (DSM IV TR), defines female sexual arousal disorder as a persistent or recurrent inability to attain or to maintain until completion of the sexual activity, an adequate lubrication-swelling response of sexual excitement. The diagnostic criteria also state that the inability causes marked distress or interpersonal difficulty, is not better accounted for by another Axis I disorder (except another sexual dysfunction) and is not due exclusively to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

1. <https://drgeo.com/womens-sexual-health-overview/>

2. <https://health.usnews.com/conditions/sexual-disorder-dysfunction>





# Topically administered Sildenafil Cream<sup>1</sup> is...

- # There are no FDA-approved Treatments for FSAD

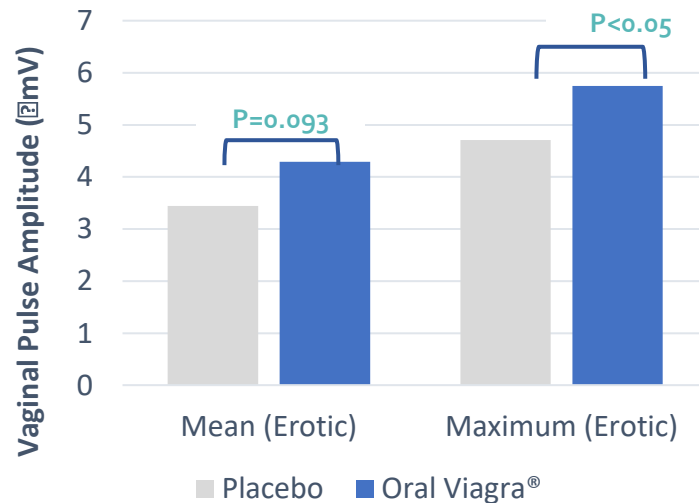


# Sildenafil Cream, 3.6%

## Statistically significant increases in Vaginal Pulse Amplitude (VPA)<sup>1</sup>

*Pfizer VPA Clinical Lab Study – Oral Viagra*

Mean and Maximum VPA<sup>†</sup>

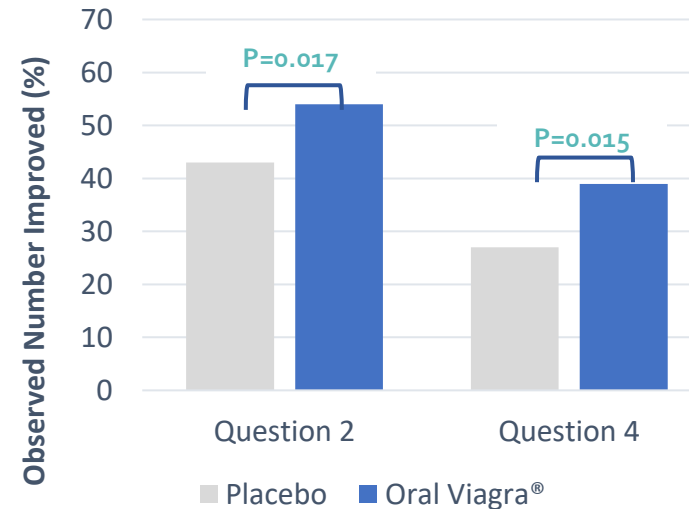


<sup>†</sup> Twelve healthy premenopausal women were studied.

## Statistically significant improvement in genital stimulation (FIEI)<sup>2</sup>

*Pfizer Clinical Field Study – Oral Viagra*

Improvement on FIEI Questions<sup>†</sup>



## Female Intervention Efficacy Index (FIEI)

<sup>†</sup> **Question #2** – “After taking study medication, the sensation/feeling in my genital (vaginal, labia, clitoris) area during intercourse or stimulation (foreplay) seemed to be: (a) more than before, (b) less than before, or (c) unchanged”. **Question #4** – “After taking the study medication, intercourse and/or foreplay was: (a) pleasant and satisfying; better than before taking the study medication, (b) unpleasant; worse than before taking study medication, (c) unchanged; no difference, or (d) pleasant; but still not like it used to be or I would like it to be.” 202 postmenopausal women with FSAD who had protocol specified estradiol and free testosterone concentrations, and/or were receiving estrogen and/or androgen replacement therapy were studied.

### Key Takeaways of Viagra® studies:

- Increased blood flow and clinical efficacy observed with oral sildenafil (Viagra®) in women.
- The side effect profile of the oral formulation was not optimal for women - leading to the exploration of alternative delivery options including a topical route of administration.

# Sildenafil Cream, 3.6%

## Phase 1 Study of SST-6007 (Sildenafil Cream, 3.6%)<sup>1</sup>

Normal healthy postmenopausal women were dosed with escalating doses of Sildenafil Cream, 3.6%, using a cross-over study design.

- Sildenafil Cream had significantly lower systemic exposure compared to a 50 mg oral sildenafil dose
  - AUC – 3-6%
  - C<sub>max</sub> – 1-2%
- Sildenafil Cream was safe and well tolerated at clinically relevant doses (1-2g)
- Favorable product characteristics as self-reported by subjects
  - Easy to use
  - Readily absorbed

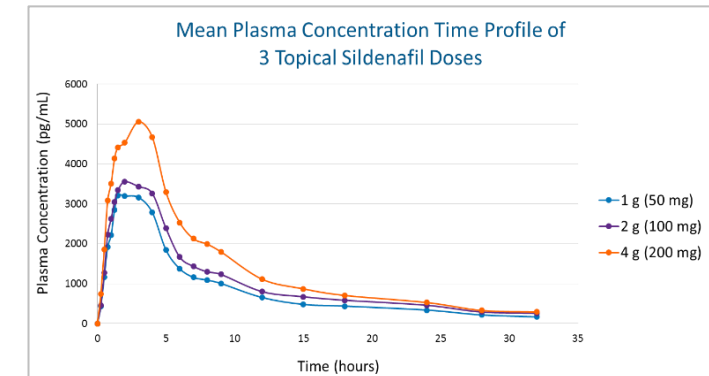
## Phase 2a Study of SST-6007 (Sildenafil Cream, 3.6%)<sup>1</sup>

**Demonstrated increased blood flow** in the genital tissue **compared to placebo** (mean change in VPA analysis) in 31 women (pre and postmenopausal) ~30 minutes post dosing.

Phase 1 Study

Treatment	N=59	Sildenafil Single Dose	C <sub>max</sub> (ng/ml)	T <sub>max</sub> (hr)	AUC <sub>last</sub> (h*ng/ml)
Topical Sildenafil 1 g of cream	20	35 mg	3.4	2.37	25.6
Topical Sildenafil 2 g of cream	20	71 mg	3.8	2.27	30.8
Topical Sildenafil 4 g of cream	19	142 mg	5.3	2.22	42.5

Phase 1 Study



# Sildenafil Cream, 3.6%

## Positive Data – Thermography Study\*

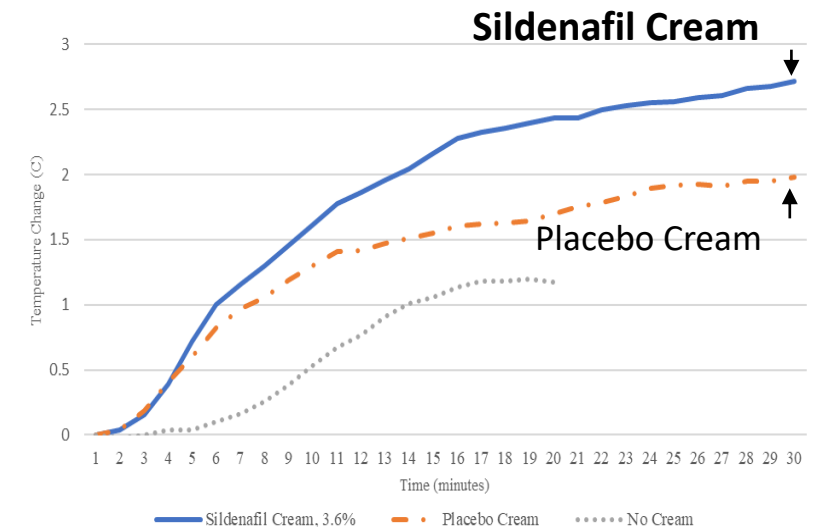
### Positive findings for Sildenafil Cream, 3.6% (as shown in Figure 1.)

- Positive cognitive arousal responses were noted.
- Significantly greater **increases in genital temperature** after application of Sildenafil Cream compared to placebo cream and no cream.
- Significantly **greater self-reported arousal responses** reported during Sildenafil Cream visits compared to placebo cream visits.

### Thermography Study Design & Methodology (N=6)<sup>1</sup>

Phase 1, single-dose, double-blind, placebo-controlled, 2-way crossover study evaluating the feasibility of using thermography to assess the pharmacodynamics of Sildenafil Cream, 3.6% in normal healthy women. The study required 3 visits and a follow up contact: Visit 1 (screening), Visits 2-3 (double-blind dosing) and a phone call (safety follow-up).

Figure 1. Clitoral temperature change during the sexually explicit film



**Statistically significant greater linear slope during minutes 11-15 of the sexually explicit stimuli as compared to the placebo cream for the vestibule.**

# Sildenafil Cream, 3.6%

## Phase 2b – At Home Study

The Phase 2b study is designed to evaluate Sildenafil Cream versus placebo over twelve weeks of dosing following both a non-drug and placebo run-in period.

- In the Phase 2b study women will use Sildenafil Cream and placebo in their home setting.
- Primary endpoint patient reported outcome (PRO) instruments to measure **improvement in localized genital sensations of arousal** and **reduction in the distress** that women with FSAD experience.
- Several exploratory efficacy endpoints will be measured and could potentially prove to be additional measurements of efficacy in a future Phase 3 program.

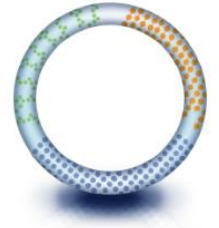




## Vaginal Drug Delivery

New prescription drug delivery options for women

# Vaginal Drug Delivery Technology - IVR



## The Vaginal Route of Drug Administration<sup>1</sup>

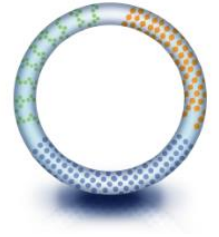
- Vaginal drug delivery offers many potential advantages due to the large surface area, a dense network of blood vessels and high elasticity due to presence of smooth muscle fibers
- Recognized advantages include: comparable ease of administration and ability to bypass hepatic first-pass metabolism

## Our Intravaginal Ring (IVR) Technology – Design Features:

- Sustained drug delivery
- Variable dosing and duration
- Solid ethylene vinyl acetate (EVA) polymer matrix that can contain and release a single or multiple active drugs
- No need for a membrane or reservoir to contain the active drug(s) or control the release



# Vaginal Drug Delivery Technology - IVR



## DARE-HRT1

A combination bio-identical estradiol + bio-identical progesterone IVR for hormone replacement therapy

## Hormone Replacement Therapy (HRT)

HRT remains the most effective treatment for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause (GSM) and has been shown to prevent bone loss and fracture.<sup>2</sup>

- The 2017 Hormone Therapy Position Statement of The **North American Menopause Society** (NAMS), supports HRT in peri-and post-menopausal women.<sup>2</sup>

NAMS recommends **non-oral route** over oral.<sup>2</sup>

### Planned Phase 1 VMS/HRT STUDY

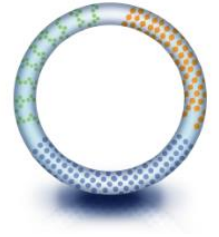
A Phase 1, Open-Label, 3-arm Parallel Group Study to Evaluate the Pharmacokinetics and Safety of DARE-HRT1 (80 µg and 160 µg Estradiol/ 4 mg and 8 mg Progesterone Intravaginal Rings) in Healthy Post-Menopausal Women.

N=30

45M women in U.S. approaching or in menopause.<sup>3</sup>



# Vaginal Drug Delivery Technology - IVR



## DARE-FRT1

A bio-identical progesterone IVR for the prevention of preterm birth and IVF/fertility support

## Prevention of Preterm Birth (PTB)

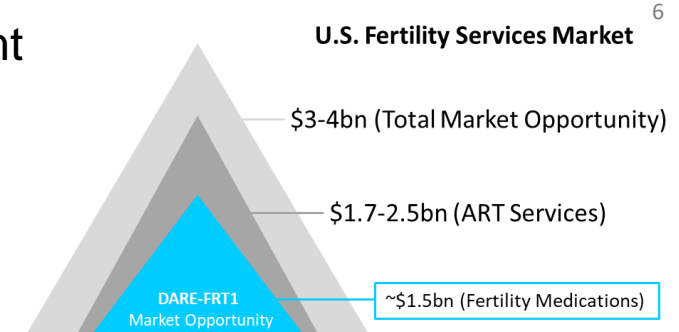
The rate of premature birth in the United States rose in 2018 for the fourth straight year after a steady decline from 2007 to 2014.<sup>2</sup>

- In 2018, ~10% of babies were born preterm (less than 37 weeks) in the US.<sup>3</sup>

## Assisted Reproductive Technologies (ART)/IVF

An estimated 12-15% of couples are unable to conceive after 1-year of unprotected sex.<sup>4</sup>

As women wait longer to have children, they increase their risk of infertility. Approximately 20% of U.S. women have their first child after age 35 and about 1/3 of couples in which the woman is older than 35 years have fertility problems.<sup>5</sup>



<sup>1</sup>  
505(b)(2) candidate

<sup>2</sup> Anticipated regulatory pathway. Daré has not had any communications with the FDA regarding the specific marketing approval requirements for DARE-HRT1 or DARE-FRT1

<sup>3</sup> 2019 March of Dimes Report Card, <https://www.marchofdimes.org/mission/reportcard.aspx>

<sup>4</sup> CDC's National Center for Health Statistics, National Vital Statistics Reports, Births: Final Data for 2018, Nov 27, 2019, [https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68\\_13-508.pdf](https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf)

<sup>5</sup> Retrieved May 26, 2020 from <https://www.nichd.nih.gov/health/topics/infertility/conditioninfo/common>

<sup>6</sup> Retrieved May 26, 2020 from <https://www.cdc.gov/reproductivehealth/infertility/index.htm>

<sup>7</sup> Harris Williams & Co. Fertility market overview. May 2015.

# Vaginal Drug Delivery

## DARE-VVA1

A proprietary formulation of tamoxifen for vaginal administration

## Vulvar and vaginal atrophy (VVA)

A chronic condition characterized by pain during intercourse, vaginal dryness and irritation

Potential to be the first treatment specifically approved for the treatment of vulvar and vaginal atrophy (VVA) in patients with hormone-receptor positive (HR+) breast cancer.

- Approximately 3.8 million women in the U.S. have a history of breast cancer and HR+ is the most common type.<sup>2</sup>
- Localized estrogen therapy for VVA may be contraindicated for women diagnosed with, or at risk of recurrence of, ER-positive and PR-positive breast cancer.

VVA prevalence in postmenopausal breast-cancer survivors is estimated to be between **42 and 70%**.<sup>3</sup>



Daré is developing this novel local application of tamoxifen to mitigate the symptoms of VVA for patients HR+ breast cancer, including women currently on anti-cancer therapy.

# Vaginal Drug Delivery

## Vaginal Tamoxifen – Proof of Concept Study<sup>1</sup>

**This exploratory study** in four postmenopausal women diagnosed with VVA demonstrated that a self-administered vaginal suppository containing tamoxifen (20mg) dosed daily for one week and twice weekly for three months **was effective in reducing vaginal pH and vaginal dryness.**

Vaginal Tamoxifen	Enrollment (Baseline)	On Treatment (Month 3)	Paired Difference (Baseline vs. Month 3)
<b>Median Vaginal pH</b> Normal vaginal pH is usually less than 4.5. <sup>2</sup>	7.1 range 6.5 to 7.5	5.0 range 5.0 to 5.2	<b>-2.0 median</b> <b>range -2.5 to -1.5</b>  Lower pH value is a measure of symptom relief
<b>Vaginal Dryness</b> Rated using a visual analogue scale (VAS) that ranged from: 0 = Not bothered by dryness 10 = Extremely bothered by dryness	8.0 range of 7.5 to 9.0	3.0 range 2.0 to 3.0	<b>-5.5 median</b> <b>range -6.0 to -4.5</b>  Decreased vaginal dryness is a measure of symptom relief

In addition, systemic absorption of tamoxifen was not significant.

- After 8 weeks of study treatment with vaginal tamoxifen, the median plasma concentration of tamoxifen was 5.8 ng/ml, with a range of 1.0 to 10.0 ng/ml
- In comparison, after 3 months of administration of 20mg, once-daily oral tamoxifen citrate (Nolvadex),<sup>3</sup> the average steady state plasma concentration of tamoxifen is 122 ng/ml with a range of 71 to 183 ng/ml

1. Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663 XLVI, n. 2, 2019

2. <https://www.medicalnewstoday.com/articles/322537.php>

3. US Food and Drug Administration: "Drug Approval Package: Nolvadex (Tamoxifen Citrate) NDA# 21-109.2002". Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2002/21109\\_Nolvadex.cfm](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21109_Nolvadex.cfm)



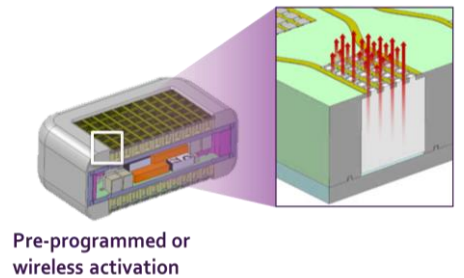
User-Controlled Long Acting Reversible Contraception  
(UC-LARC) / Microchips Technology

# DARE-LARC1

## User-Controlled Long Acting Reversible Contraception

### Design Features of the Technology:

- Drug Storage
  - Individual doses are stored in micro-reservoir arrays
  - Reservoirs are hermetically sealed at room temperature
  - Thin membranes over each reservoir protect drug post-sealing
- Drug Release
  - Drug doses are initiated automatically on schedule or wirelessly on-demand by a patient
  - Reservoirs are opened via electrothermal ablation of membranes
  - Upon opening, interstitial fluid diffuses in and drug diffuses out



# DARE-LARC1

## User-Controlled Long Acting Reversible Contraception

The Bill & Melinda Gates Foundation has strong interest in family planning.  
An estimated 215 million women in developing countries do not have access to contraception.

Up to \$20.5m

### Funding 2013

**Grant to understand user needs and define the product concept**

Favorable response from Sub-Saharan Africa

- Sub-dermal implant use is growing
- **87% of women surveyed said they would use the proposed implant**
- 74% of healthcare workers said they would use the proposed implant in their practice

### Funding 2014 – 2021

**Grant to develop implant concept and technology**

Currently executing a 4<sup>th</sup> supplemental grant funding to demonstrate multiple drug releases *in vivo*, after successfully completing additional market research and concept development in the 3<sup>rd</sup> supplemental grant funding

# Daré Financial Summary

## Q1-2020 Financial Highlights:

- Net cash raised from stock sales, warrant exercises and license fee: \$7.9 million
- Cash and equivalents (3/31/2020): \$5.0 million

## Updates through May 12, 2020:

- Net cash raised from stock sales: \$2.0 million
- Common shares o/s: 26.6 million
- Warrants o/s: ~2 million
- Purchase agreement executed for potential stock sales of up to \$15 million over a 36-month period ending May 2023

## Non-dilutive Grant Funding:

- NIH SBIR: \$730,722 final award notice (announced 4/1/2020) of a \$1.9 million grant for Ovaprene R&D expenses from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), a division of the National Institutes of Health.
- Bill & Melinda Gates Foundation: eligible for up to \$2.5 million in additional funding to support development of a wireless, patient controlled, implantable long-acting, reversible contraceptive technology; \$17.9 million of up to \$20.5 million in total grant funding previously received.

































# WE ARE ACCELERATING INNOVATION IN WOMEN'S HEALTH

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	<b>David Friend, PhD, Chief Scientific Officer</b>    
	<b>Lisa Walters-Hoffert, Chief Financial Officer</b>    
	<b>John Fair, Chief Strategy Officer</b>   
	<b>Mary Jarosz, RPh, RAC, FTOPRA, Global Head of Regulatory Affairs</b>   
	<b>Mark Walters, Vice President of Operations</b>    
	<b>Christine Mauck, MD, MPH, Medical Director</b>   

## BOARD OF DIRECTORS

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