

To become the coordinating presence in women's health. We achieve this by identifying, unlocking and advancing innovation that improves health outcomes and promotes a better quality of life for women.

# DARÉ

IN ITALIAN, IT MEANS “**TO GIVE.**”

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

To us, Daré means to give women novel treatment options by **boldly addressing existing therapeutic gaps**. And that's exactly our mission.



March 16, 2020

# 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 key to our value creation strategy. We in-license products that meet a strict profile and drive commercial optionality (launch, partner or co-promote):

- Product candidates that are commercially viable and **attractive to strategic partners**
- Candidates that have a ***data package*** including a proof-of-concept and/or the ability to leverage a 505(b)(2) regulatory pathway
- Candidates with the potential to be ***first-in-category*** that *address persistent unmet needs* in women's health
- The ability to deliver products in a more ***personalized*** way **for women**

**DARE-BV1<sup>^</sup>**  
Bacterial Vaginosis

**Ovaprene<sup>®</sup>**  
Hormone-Free, Monthly Contraception  
Commercial License Agmt (U.S.): 

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

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

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

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

**Microchips**  
User-Controlled, Long-Acting  
Reversible Contraception

**ORB 204/214<sup>^</sup>**  
6 & 12 Month Injectable Contraception

**DARE-RH1**  
Non-Hormonal Male and Female  
Contraceptive Target



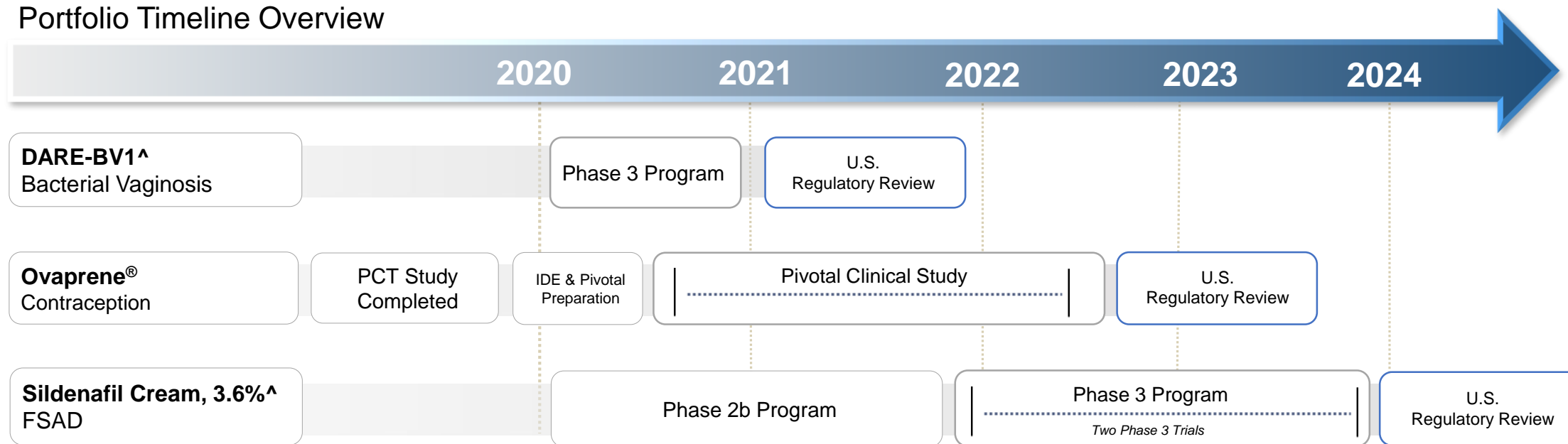
Timeline reflects management's current estimates and constitutes a forward-looking statement subject to qualifications noted elsewhere in this presentation. Actual development timelines may be substantially longer, and Daré is under no obligation to update or review these estimates. "First-in-category" statements are forward-looking statements relating to market potential of Daré's product candidates based on currently available, FDA-approved therapies.

<sup>^</sup>505(b)(2) regulatory pathway anticipated

<sup>‡</sup>DARE-HRT1 Phase 1 study to be conducted in Australia by Daré subsidiary

# WE ARE ACCELERATING INNOVATION IN WOMEN'S HEALTH

## Portfolio Timeline Overview



Timeline reflects management's current estimates and constitutes a forward-looking statement subject to qualifications noted elsewhere in this presentation. Actual development timelines may be substantially longer, and Daré is under no obligation to update or review these estimates.

<sup>^</sup>505(b)(2) regulatory pathway anticipated.



**DARE-BV1**

**Clindamycin 2% gel for Bacterial Vaginosis**



## Successful Proof of Concept

- Vaginal application of DARE-BV1 (clindamycin phosphate 2%) demonstrated effectiveness against BV in a proof-of-concept investigator-initiated study in women (n=30):<sup>1</sup>
- 86% of evaluable subjects met clinical cure endpoint at Test-of-Cure visit after single dose administered
- Favorable efficacy profile over currently approved treatments

## 505(b)(2) Regulatory Pathway

- QIDP and Fast Track Designation
  - **Five-year exclusivity** extension added to any exclusivity for which a QIDP qualifies upon FDA approval.
  - The **Fast Track** program is intended to facilitate development and expedite review of a Fast Track drug so that an approved product can reach the market expeditiously..
- Single Phase 3 clinical trial planned to support New Drug Application (NDA) for FDA approval – topline data anticipated by end of 2020.

## Attractive Market Opportunity

- BV is the most common vaginal infection in women ages 15-44 <sup>2</sup>
- U.S. prevalence estimated to be ~21 million among women ages 14-49 <sup>2</sup>
- Approved prescription drugs have less than optimal clinical cure rates (37-68%) <sup>3</sup>
- Opportunity for significant upside and market expansion

## Patent Coverage

- Patents covering the licensed technology have been granted with terms through 2028
- Additional patents pending would have terms through 2035

1. Data on file

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

3. 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)

## DARE-BV1 Proof of Concept – Clinical Trial Design

Study Objective: Study the Efficacy and Safety of DARE-BV1 in the Treatment of Bacterial Vaginosis (n = 30)\*

Day 1 Baseline Visit	Day 7 - 14 Test-of-Cure Visit	Day 21 - 30 Continued Clinical Response Visit
<ul style="list-style-type: none"> <li>• <b>Single dose administered</b></li> </ul> <p>Tests Performed:</p> <ul style="list-style-type: none"> <li>• Physiological symptoms</li> <li>• pH</li> <li>• Saline “wet mount”</li> <li>• 10% KOH “whiff test”</li> <li>• Urine pregnancy (if needed)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Patients questioned regarding comfort level &amp; re-examined</b></li> </ul> <p>Tests Performed:</p> <ul style="list-style-type: none"> <li>• Physiological symptoms</li> <li>• pH</li> <li>• Saline “wet mount”</li> <li>• 10% KOH “whiff test”</li> <li>• Urine pregnancy (if needed)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Patients questioned regarding experience &amp; re-examined</b></li> </ul> <p>Tests Performed:</p> <ul style="list-style-type: none"> <li>• Physiological symptoms</li> <li>• pH</li> <li>• Saline “wet mount”</li> <li>• 10% KOH “whiff test”</li> <li>• Urine pregnancy (if needed)</li> </ul>
<ul style="list-style-type: none"> <li>• Eligibility: Female subjects 18 years or older with confirmed clinical diagnosis of BV</li> <li>• Primary Endpoint: Clinical Cure at Test-of-Cure visit (defined as resolution of clinical findings from baseline visit)</li> <li>• Secondary Endpoints: Proportion of patients with therapeutic and bacteriologic cures<sup>1,2</sup></li> <li>• Safety: Patients were questioned about their comfort level and adverse reactions they experienced</li> </ul>		

\*Investigator Initiated Proof of Principle Study Design

1. Therapeutic cure was a composite endpoint, which required both clinical cure (defined as resolution of all 4 Amsel criteria) and bacteriologic cure (Nugent score < 4). Bacteriologic cure required a Nugent score < 4.

2. Amsel & Gram Stain Criteria: <https://www.cdc.gov/std/tg2015/bv.htm>



## DARE-BV1 Proof of Concept - Trial Results

A single dose of **DARE-BV1** demonstrated **high clinical cure rate** compared to FDA-approved products<sup>1</sup>



Product	Clinical (Amsel) Cure	Bacteriologic (Nugent) Cure	Therapeutic Cure
<b>DARE-BV1</b> <small>novel gel (clindamycin)</small>	<b>86%</b>	<b>57%*</b>	<b>57%*</b>
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

- 28 of 30 women completed the study
- 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 cure rates presented for the products identified 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-BV1-001: Phase 3 Clinical Study Design\*

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

### Study Objectives:

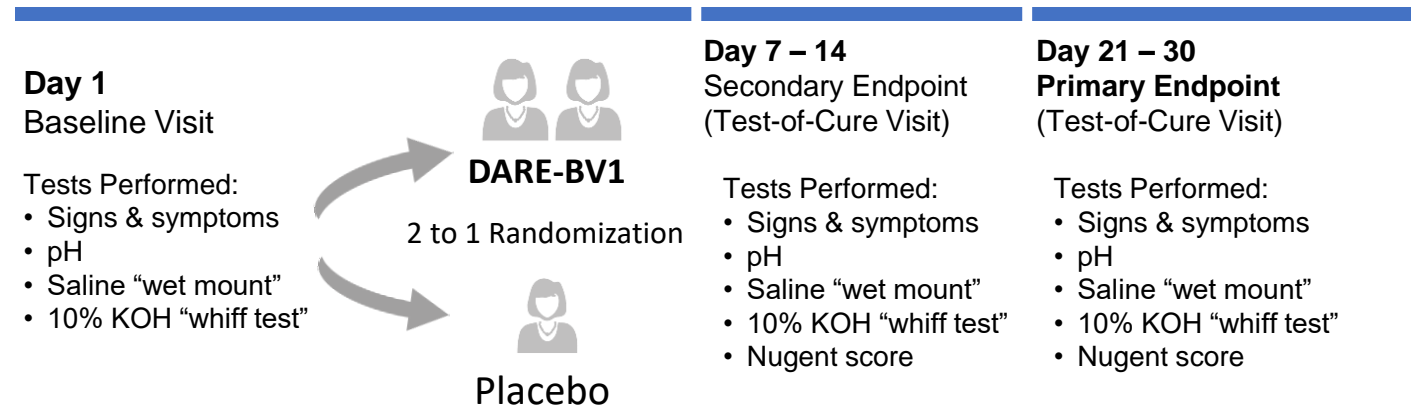
- **Primary endpoint:** Clinical Cure at Day 21-30 Visit
- **Secondary endpoints:**
  - Proportion of subjects with Clinical Cure at Day 7-14 Visit
  - Proportion of subjects with Bacteriological Cure at Day 7-14 and Day 21-30 Visits.
  - Proportion of subjects with Therapeutic Cure at Day 7-14 and Day 21-30 Visits.

### Definitions:

- Clinical Cure:
  - Return to normal physiological discharge as confirmed by the investigator;
  - Negative 10% KOH “whiff test”;
  - Clue cells < 20% of the total epithelial cells in the saline wet mount.
- Bacteriological Cure: a Nugent score < 4.
- Therapeutic Cure: both a Clinical Cure and Bacteriological Cure.

- Anticipated aggregate costs of program through NDA filing, including Phase 3, nonclinical studies, manufacturing activities, and NDA filing, anticipated to be less than \$10 million.

## Phase 3 Clinical Study Design





Ovaprene®

Hormone-Free, Monthly Contraceptive

*The global contraceptive category is expected to reach \$33 billion by 2023<sup>1</sup>*

1. <https://www.globenewswire.com/news-release/2017/04/06/955073/0/en/Contraceptives-Market-worth-33bn-by-2023-Global-Market-Insights-Inc.html>

Advances in hormone products have largely focused on **reducing the hormone dosage**, adjusting or **extending the duration** of protection and **optimizing methods of administration**.



## Reduction of hormones and convenient product forms are driving new innovation

- Mirena® Product Family
  - Physician inserted, long-acting.
  - Low/locally delivered hormone IUS.
  - 2018 worldwide sales: \$1.14 billion (Bayer)<sup>1</sup>
- Lo Loestrin®
  - Pregnancy prevention with the lowest amount of daily estrogen (10 micrograms) available.
  - 2018 US sales: \$527 million (Allergan)<sup>2</sup>
- NuvaRing®
  - Monthly, convenient vaginal ring product form.
  - 2018 worldwide sales: \$902 million (Merck)<sup>3</sup>

1. <https://www.bayer.com/en/bayer-annual-report-2018.pdf>. Includes sales for Mirena®, Kyleena® and Jaydess® / Skyla®

2. <https://www.allergan.com/investors/news/thomson-reuters/allergan-reports-fourth-quarter-and-full-year-2018>

3. <https://investors.merck.com/news/press-release-details/2019/Merck-Announces-Fourth-Quarter-and-Full-Year-2018-Financial-Results/default.aspx>

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# Women's Preferences

1. Effective Pregnancy Prevention
2. Convenient Product Forms
  - Independent surveys revealed that the vaginal ring has many of the features women deemed extremely important.<sup>1</sup>
3. Method Mix
  - >70% of women who practice contraception currently use non-coital (*not in the moment*) methods.<sup>2</sup>
4. Less Hormones
  - A majority of women prefer a monthly option with a lower hormone dose than the pill.<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. Lessard, L, Perspectives on Sexual and Reproductive Health, Volume 44, Number 3, 9-2012

2. <https://www.guttmacher.org/fact-sheet/contraceptive-use-united-states>

3. Hooper, DJ, Clin Drug Investig. 2010;30(11):74963

Missing from the product mix are monthly, hormone-free alternatives that are effective and easy to use

## Least Effective Methods

Method	Perfect Use	Typical Use
Spermicide* / Vaginal Gels	82.00%	72.00%
Sponge-Parous*	80.00%	76.00%
Sponge-Nulliparous*	91.00%	88.00%
Condom (male)*	98.00%	82.00%
Diaphragm*	94.00%	88.00%
Combined Pill & Progestin only*	99.70%	91.00%
Evra Patch*	99.70%	91.00%
Nuva Ring*	99.70%	91.00%
Depo-Provera*	99.80%	94.00%
IUD- ParaGard (Copper T)*	99.40%	99.80%
IUD- Mirena (LNg)*	99.80%	99.80%
Implanon*	99.95%	99.95%
Female Sterilization*	99.50%	99.50%
Male Sterilization*	99.90%	98.85%

100% Effective = 0% Risk of Pregnancy

## Most Effective Methods

## Hormone Free Product Landscape<sup>1</sup>

Marketed or in development



### Spermicides / Vaginal Gels

- Effectiveness (72% Typical Use)
- Woman controlled
- Used "in the moment"



### Condoms

- Effectiveness (82% Typical Use)
- Not woman controlled
- Used "in the moment"



### Diaphragms

- Effectiveness (88% Typical Use)
- Woman controlled
- Used "in the moment"



### Long-acting IUD

- Effectiveness (99% Typical Use)
- Not woman controlled
- Physician inserted



## Ovaprene® Hormone-Free, Monthly Vaginal Contraceptive

### Successful postcoital test (PCT) Study using Predictive Contraceptive Endpoint

- ***The PCT Clinical Study Met its Primary Endpoint***
- Specifically, in 100% of women and cycles, an average of less than five (< 5) progressively motile sperm (PMS) per high power field (HPF) were present in the midcycle cervical mucus collected two to three hours after intercourse with Ovaprene in place – results consistent with other highly effective methods.\*

### CDRH (Device) Lead Review Division

- ***Single pivotal clinical trial planned to support application for FDA approval***

### Attractive Market Opportunity

- >\$6 billion in US Rx sales of contraceptive products (2016).<sup>2</sup>
- 40 million women of reproductive age currently use a contraceptive method.<sup>3</sup>

### Patent Coverage

- Patents covering the licensed technology have been granted with terms through 3Q 2028
- Opportunity for Patent Term Extension (PTE) and potential new patents

\* In PCT studies of similar size, products (diaphragms) with no motile sperm in the cervical mucus during their PCT assessments demonstrated “typical use” contraceptive effectiveness of 86-91% in pivotal contraceptive studies evaluating pregnancy rates over six-month period.

### Physical Barrier<sup>1</sup>

*Three-dimensional, knitted polymer barrier*



### Spermiostatic Environment<sup>1</sup>

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

1. Journal of Reproductive Medicine 2009; 54: 685-690

2. IMS NSP through Dec 2016

3. www.guttmacher.org, contraceptive fact sheet



## U.S. Regulatory Strategy\*

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

### Step 1 (Completed)

- **PCT Study - Completed 4Q 2019**
- Subjects evaluated over the course of five menstrual cycles. Each woman's cervical mucus was examined at several points during the study:
  - Cycle 1 - Baseline (excludes the use of any product)
  - Cycle 2 - Use of a barrier method (diaphragm)
  - Cycles 3,4 and 5 - Ovaprene vaginal ring
- Assess progressively motile sperm (**PMS**) per high powered field (**HPF**) in the cervical mucus, post coitus (primary endpoint <5 PMS per HPF).
- Safety assessments, PK, acceptability, fit, and ease of use.

#### The PCT Clinical Study Met its Primary Endpoint

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) PMS per 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

### Step 2 (Ongoing)

File investigational device exemption (IDE) - Planned for 1H 2020

- Pivotal Study - Planned for 2H 2020
  - N= ~250 completers upto 12 months of use
  - Primary Endpoints: safety and efficacy (pregnancy probability)
  - Secondary Endpoints: acceptability, product fit/ease of use and assessments of vaginal health

\*Anticipated regulatory pathway and timelines.

## OUR PIPELINE: OVAPRENE®

Features Desired Most in Birth Control: <sup>1-4</sup>	Design Features of Ovaprene: <sup>5,6</sup>
+ Convenience (Easy to Use & Easy to Remember)	Monthly Ring Product Form  Women chose monthly rings for the convenience of a non-daily option.
+ Hormone Free	No Hormones in the API  Unique dual action MOA (spermistatic & barrier).
+ Efficacy	<u>Expected</u> Typical Use Effectiveness Comparable to Hormone Contraception (86% vs 91%).
+ Favorable Side Effect Profile	No Colposcopic Abnormalities  No significant changes in vaginal flora.  No serious adverse effects observed in prior published study.
+ Easily Manage Fertility	No Systemic Activity  Inserted and removed without a provider.  Immediate return to fertility.

1. <https://www.urban.org/urban-wire/women-want-effective-birth-control>  
2. Lessard, L, Perspectives on Sexual and Reproductive Health, Volume 44, Number 3,9-2012  
3. Hooper, DJ, Clin Drug Investig. 2010;30(11):74963  
4. Ersek, J, Matern Child Health J (2011) 15:497–506  
5. Journal of Reproductive Medicine 2009; 54: 685-690  
6. Trussell J. Contraceptive Efficacy. In Hatcher RA, Trussell J, Nelson AL, Cates W, Kowal D, Policar M. Contraceptive Technology: Twentieth Revised Edition. New York, NY: Ardent Media, 2011.



## Ovaprene® Commercial License Agreement with Bayer

- January 13, 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.
- 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 will support the development and regulatory process by providing up to two fulltime 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 strategy and confirmation of Ovaprene's market potential as the first monthly non-hormonal contraceptive product.

- Bayer is committed to bringing to market innovation in women's health and is the only company to have built a contraceptive brand family in excess of \$1 billion.
- We believe partnering now with Bayer is a means to commercially de-risk the program and unlock the program's full value.



# 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>

1. <https://www.businesswire.com/news/home/20190628005277/en/Global-Female-Sexual-Dysfunction-Treatment-Market-2019-2023>

## Successful Proof of Concept

- Sildenafil Cream, 3.6% improved genital blood flow (n=31)<sup>1</sup> and increased genital temperature (n=6)<sup>2</sup> in proof of concept studies
  - Efficacy signal observed in both pre and postmenopausal patients
  - Excellent systemic/local safety and tolerability profile

## 505(b)(2) Regulatory Pathway

- Ability to leverage the safety profile of sildenafil (Viagra®) for FDA submission package
- Alignment with the FDA on Phase 2b study design and novel primary endpoint PRO instruments

## Attractive Market Opportunity<sup>3</sup>

- 33% of women in the U.S. (21 to 60 years old) experience symptoms of low or no sexual arousal
- 16% (~10m women) are considered distressed and are seeking a solution to improve their condition

## Patent Coverage

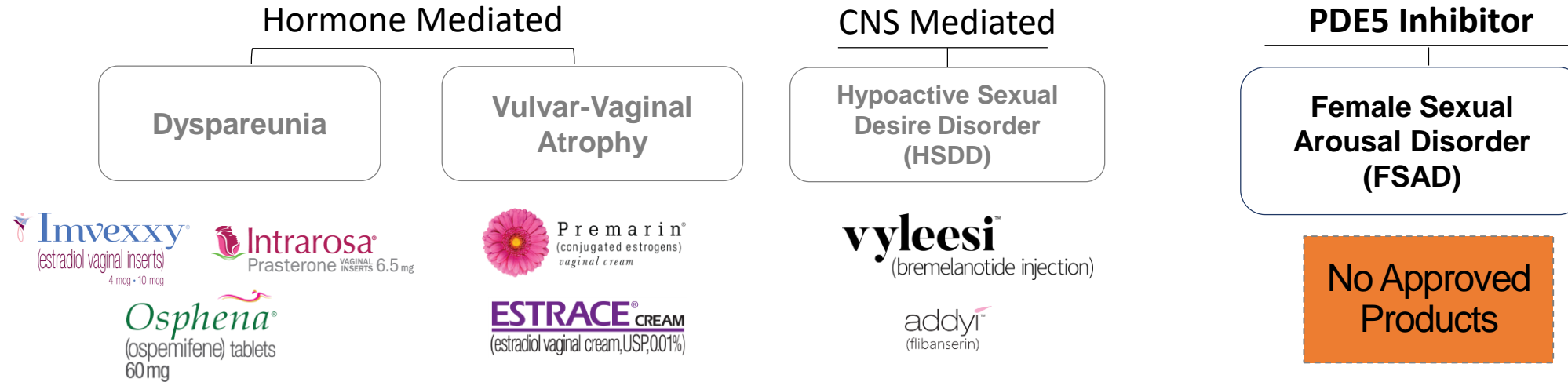
- Patents covering the licensed technology have been granted with terms through 2031 (through June 2029 in the U.S.)
- No ANDA route: ANDA is not currently an option for topicals that result in low systemic uptake

1. Data on file

2. Data on file

3. Ad Hoc Market Research: FSAD Prevalence Report (Oct 2015) conducted for SST LLC. Based on US Census projections for 2016.

## OUR PIPELINE: SILDENAFIL CREAM, 3.6%



Of the various types of female sexual dysfunction disorders, FSAD is most analogous to erectile dysfunction (ED) in men and is characterized primarily by an inability to attain or maintain sufficient genital arousal during sexual activity that causes distress or interpersonal difficulty. Despite several approved prescription products for ED, no pharmacologic options have yet been approved by the FDA for FSAD. Sildenafil, the active ingredient in Sildenafil Cream, is marketed in an oral dosage form under the brand name Viagra® for the treatment of ED in men.

With its approval of Addyi®, FDA acknowledged and formally classified the distinct and separate disorders that comprise Female Sexual Dysfunction. Where HSDD is characterized primarily by a lack of sexual desire, **FSAD is characterized primarily by an inability to attain or maintain sufficient physical sexual arousal.**

FSAD is characterized primarily by an inability to attain or maintain sufficient physical sexual arousal; it is also characterized by distress or interpersonal difficulty.\*

- Estimated 23-33% of women suffer from arousal disorder:
  - Meta-analysis of 95 studies from 2000-2014 indicated the prevalence of Female Sexual Dysfunction in premenopausal women worldwide is 40.9%, and difficulty with arousal alone is 23%.<sup>1</sup>
  - **33% of women in the U.S. age 21 to 60** (approximately 20 million women), experience symptoms of low or no sexual arousal.<sup>2,3</sup>
  - **10 million women are considered distressed and actively seeking treatment.**<sup>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.

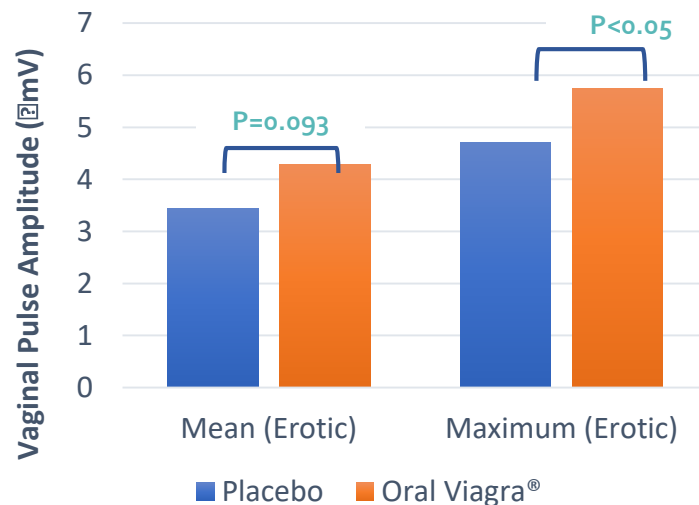


Increased blood flow and clinical efficacy with oral sildenafil (Viagra®) in women:

- Statistically significant increases in Vaginal Pulse Amplitude (VPA)<sup>1</sup>
- Statistically significant improvement in genital stimulation (FIEI)<sup>2</sup>

Pfizer VPA Clinical Lab Study – Oral Viagra

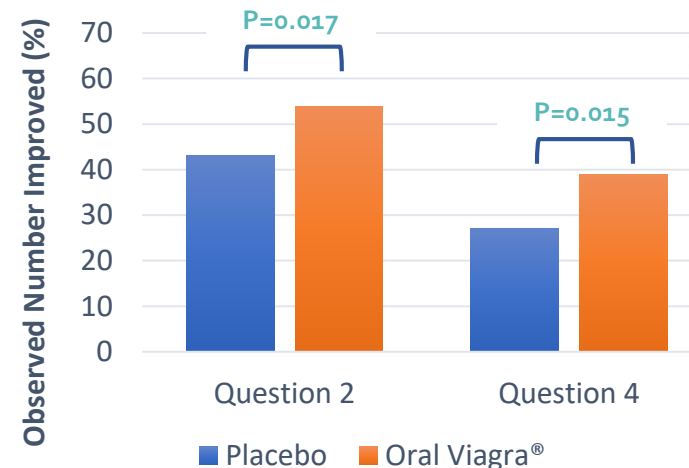
### Mean and Maximum VPA†



† Twelve healthy premenopausal women were studied.

Pfizer Clinical Field Study – Oral Viagra

### Improvement on FIEI Questions†



### Female Intervention Efficacy Index (FIEI)

† 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:

- Oral sildenafil (same active as Viagra) demonstrated statistically significant activity
- Side effects of the oral formulation led to the investigation of a **new topical route of administration**

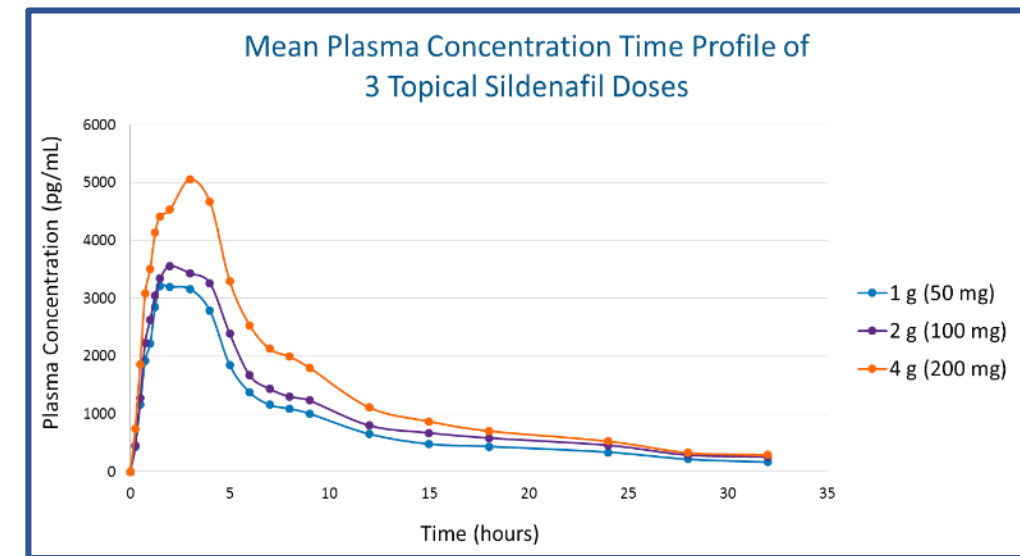
## Phase 1 Study of SST-6007 (Sildenafil Cream, 3.6%)<sup>1</sup>

- Normal healthy postmenopausal women were dosed with escalating doses of Sildenafil Cream, 3.6%, using a cross-over study design.
- Topical sildenafil had significantly lower systemic exposure compared to a 50 mg oral sildenafil dose
  - AUC – 3-6%
  - C<sub>max</sub> – 1-2%
- Safe and very 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

Treatment	N	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



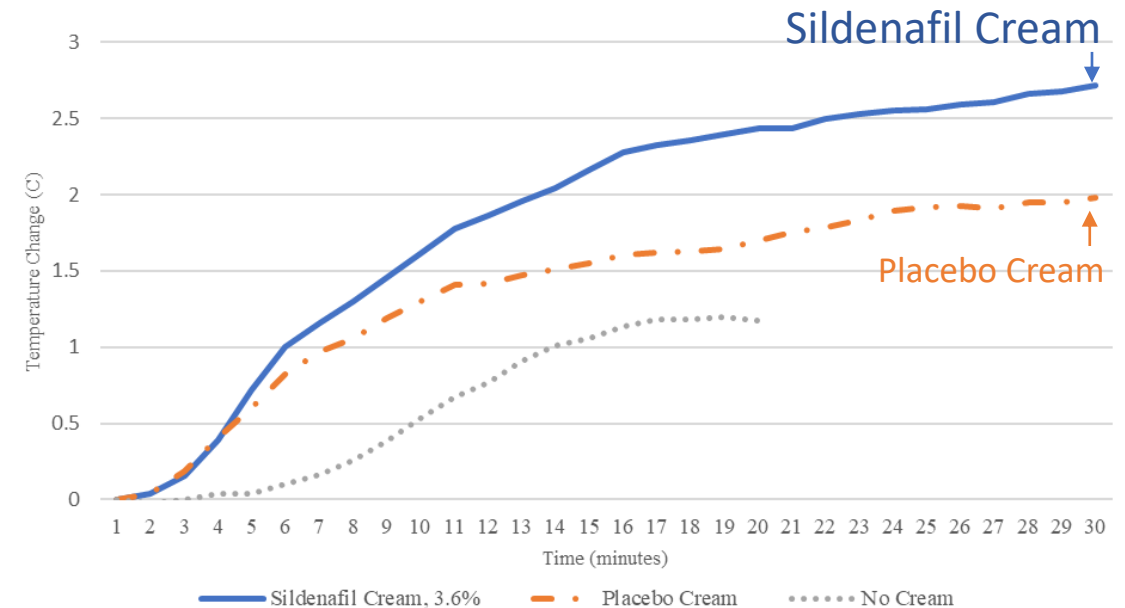
# Positive Data - Thermography Study

"The results from the first six subjects to complete all assessments indicate the utility of thermography technology to detect statistically meaningful differences in genital temperature changes, a surrogate for genital blood flow, and support the ongoing evaluation of Sildenafil Cream as a treatment for FSAD."

*Dr. Tuuli Kukkonen, C.Psych., an Associate Professor in the Department of Family Relations and Applied Nutrition at the University of Guelph in Ontario, Canada*

- Thermography utilizes sensitive cameras capable of detecting and recording temperature variations over time.
  - Genital temperature changes are a surrogate for genital blood flow.
- 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 consisted of three phases, Screening Phase (Visit 1), the Double-Blind Dosing Phase (Visits 2-3) and a Safety Follow-up Phase (Phone Call).
- Findings:
  - The thermography study yielded positive findings for Sildenafil Cream, 3.6% (blue line), 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.

*Figure 1. Clitoral temperature change during the sexually explicit film*



*Sildenafil Cream produced a statistically significant greater linear slope during minutes 11-15 of the sexually explicit stimuli as compared to the placebo cream for the vestibule.*

## OUR PIPELINE: SILDENAFIL CREAM, 3.6%

### Content Validity

Completed 3Q 2019

- A content validity study was designed to help ensure the concepts we plan to measure are the most important and relevant to our target population.
- This was a non-interventional study – participants were not asked to use or evaluate any products.

### Type C Meeting

Completed 4Q 2019

- Type C meeting with the FDA completed and alignment was reached on the design of the Phase 2b clinical study of Sildenafil Cream, 3.6% (Sildenafil Cream), including the patient reported outcome (PRO) instruments that will be used to screen eligible patients with FSAD and to assess the efficacy of Sildenafil Cream in treating FSAD.

### Phase 2b At Home Study

Initiation Planned 2020

- **The Phase 2b at-home study will allow patients to use the investigational product and placebo in their home setting.**
- **Primary endpoint 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 in our Phase 2b study and could potentially prove to be additional measurements of efficacy in a future Phase 3 program.**
- **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.**

## OUR PIPELINE: SILDENAFIL CREAM, 3.6%



With its approval of Addyi®, FDA acknowledged and formally classified the distinct and separate disorders that comprise Female Sexual Dysfunction. Where HSDD is characterized primarily by a lack of sexual desire, **FSAD is characterized primarily by an inability to attain or maintain sufficient physical sexual arousal.**



# Microchips Program

User-Controlled Long Acting Reversible Contraception

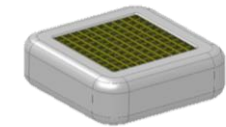
(UC-LARC)

# WE ARE ACCELERATING INNOVATION IN WOMEN'S HEALTH

## How the Microchips Technology is Designed to Work

### Drug Storage

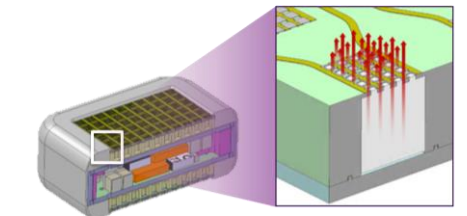
- Individual doses are stored in micro-reservoir arrays
- Reservoirs are hermetically sealed at room temperature
- Thin metallic membranes over each reservoir protect drug post-sealing



Microchip-based Implant

### Drug Release

- Drug doses are initiated automatically on schedule or wirelessly on-demand by patient or clinician
- Reservoirs are opened via electrothermal ablation of membranes
- Upon opening, interstitial fluid diffuses in and drug diffuses out



Pre-programmed or  
wireless activation



# WE ARE ACCELERATING INNOVATION IN WOMEN'S HEALTH

The Bill & Melinda Gates Foundation has strong interest in family planning. An estimated 215m women in developing countries don't 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**

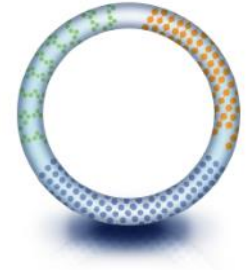
Currently executing a 4<sup>th</sup> supplemental grant funding to demonstrate multiple drug releases *in vivo*, after successfully completing additional market research and concept development in the 3<sup>rd</sup> supplemental grant funding



# Innovative Vaginal Drug Delivery Technology

Well characterized therapeutic options for innovation in Women's Health

1



# Innovation in Drug Delivery

- Features of the intravaginal ring technology include:
  - Sustained drug delivery
  - Variable dosing and duration
  - Single or multiple drug delivery via a solid ethylene vinyl acetate polymer matrix (without the need for a membrane or reservoir to contain the active drug or control the release)
- Current 505(b)(2) candidates include:<sup>1</sup>
  - **DARE-HRT1**
    - A combination bio-identical estradiol + bio-identical progesterone ring for hormone replacement therapy
  - **DARE-FRT1**
    - A bio-identical progesterone ring for the prevention of preterm birth and for fertility support as part of an IVF treatment plan

*Daré has an exclusive, global license to novel IVR technology originally developed by Dr. Robert Langer from MIT and Dr. William Crowley from Massachusetts General Hospital and Harvard Medical School that has been further developed by Juniper Pharmaceuticals.<sup>2,3</sup> Daré's exclusive license covers the candidates described above, as well as additional applications of the IVR technology platform in other therapeutic areas.*

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

2. <http://www.ibtimes.com/robert-langer-top-mit-biomedical-engineer-father-30-companies-how-launch-successful-2141263>

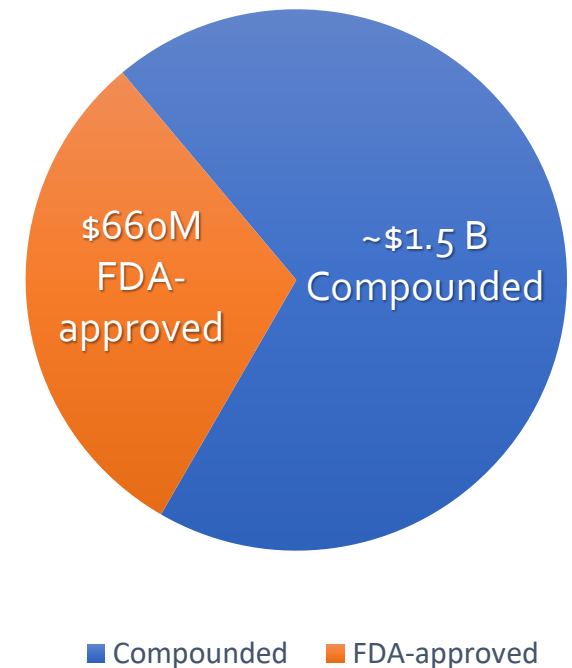
3. <https://reproendo.mgh.harvard.edu/programs/research-investigators/dr-william-crowley/>

## DARE-HRT1 - Treating Vasomotor / Menopause Related Symptoms

Hormone Replacement Therapy (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>1</sup>

- 45M women in U.S. approaching or in menopause.<sup>2</sup>
- The 2017 Hormone Therapy Position Statement of The North American Menopause Society (NAMS), which provides evidence-based and current best clinical practice recommendations for the use of hormone therapy (HT) for the treatment of menopause-related symptoms and reviews the effects of HT on various health conditions at different stages of a woman's life, supports HRT in peri- and post-menopausal women – estrogen to reduce symptoms and progesterone to prevent thickening of uterine wall.<sup>3</sup>
- **NAMS recommends non-oral route over oral.**<sup>3</sup>
- 2002 Women's Health Initiative (WHI) study showed that the long-term use of certain synthetic hormones (a combination of medroxyprogesterone and conjugated equine estrogens) increased the risk of breast cancer, stroke, heart attack and blood clots.

**\$2.2 Billion U.S. Market<sup>4</sup>**



1. The 2017 hormone therapy position statement of The North American Menopause Society; Menopause: The Journal of The North American Menopause Society Vol. 24, No. 7, pp. 728-753

2. U.S. Census Bureau, Population Division. Table 2. 2015 to 2060 (NP2012-T2). Released Dec. 2012.

3. <https://www.menopause.org/docs/default-source/2017/nams-2017-hormone-therapy-position-statement.pdf>

4. U.S. 2014. Source: Symphony Health Solutions Report

## Phase 1 – VMS/HRT STUDY

DARE-HRT1 for the treatment of VMS due to menopause – combination bio-identical estradiol and progesterone in a convenient 28-day IVR

- Proposed 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.
- Primary Objectives:
  - To describe the PK parameters over 28 days using two different dose combinations of DARE-HRT1:
    - Estradiol 80 µg/Progesterone 4 mg IVR
    - Estradiol 160 µg/Progesterone 8 mg IVR
  - Identify the steady-state PK after 28 days of each DARE-HRT1
- N=30
- Topline data anticipated by the end of 2020

# Pregnancy Maintenance

- Prevention of Pre-term Birth (PTB)
  - In the US, approximately 12% of pregnancies are preterm (less than 37 weeks)<sup>1</sup>
  - Standard interventions include steroids, hormones and tocolytic agents to stop/slow the frequency and duration of contractions<sup>2</sup>
- Assisted Reproductive Technologies (ART)
  - The global ART market is expected to reach **USD 45 billion by 2025**, according to a May 2018 report by Grand View Research, Inc.<sup>3</sup>
    - Childbearing postponement is a high impact driver of the infertility treatment market.
    - Increasing marital age, rising tobacco and alcohol consumption, and increasing obesity rates are some of the other factors contributing to the market growth.
    - Furthermore, increasing incidence rate of conditions such as poly-cystic ovarian syndrome, tubal factors and endometriosis are other drivers of the market.
  - Record number of babies born using (ART) <sup>4</sup>
    - From 1996 to 2016, there was a greater than a three-fold increase in the number of U.S. births incorporating ART.

1. <https://www.stanfordchildrens.org/en/topic/default?id=prematurity-90-P02401>

2. <https://www.uptodate.com/contents/preterm-labor-beyond-the-basics>

3. <https://www.grandviewresearch.com/press-release/global-assisted-reproductive-technology-market>

4. <https://www.pewresearch.org/fact-tank/2018/07/17/a-third-of-u-s-adults-say-they-have-used-fertility-treatments-or-know-someone-who-has/>

# Vaginally Delivered Tamoxifen to treat VVA in Hormone-Receptor Positive (HR+) Breast Cancer Patients

- DARE-VVA1
  - A proprietary formulation of tamoxifen for vaginal administration.
  - 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.
- VVA is a chronic condition characterized by pain during intercourse, vaginal dryness and irritation.
  - Most women use localized estrogen therapy which is contraindicated for the more than two million women diagnosed with, or at risk of recurrence of, ER-positive and PR-positive breast cancer.<sup>1</sup>
  - Daré intends to develop this novel local application of tamoxifen to mitigate the symptoms of VVA for patients with or at risk for HR+ breast cancer, including women currently on anti-cancer therapy.
  - Due to the use of aromatase inhibitors for the treatment of HR+ breast cancer, the prevalence of VVA in postmenopausal breast cancer patients is estimated to be between 42 and 70 percent.<sup>2</sup>

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2800285/#S16title>

2. Clinical Breast Cancer: <https://www.sciencedirect.com/science/article/pii/S1526820917300952>



# 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>  Lower pH value is a measure of symptom relief 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	-2.0 median range -2.5 to -1.5
<b>Vaginal Dryness</b>  Rated using a visual analogue scale (VAS) that ranged from: 0 = Not bothered by dryness 10 = Extremely bothered by dryness  Decreased vaginal dryness is a measure of symptom relief	8.0 range of 7.5 to 9.0	3.0 range 2.0 to 3.0	-5.5 median range -6.0 to -4.5

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)

# NASDAQ: DARE

## Q4-2019: Acquisition of Microchips Biotech

- **Closing cash acquired (less transaction related expenses): \$5.7 million**
- Issuance of ~3 million DARE common shares
- Cash resources that are not committed to funding the contraceptive program activities under the grant from the Bill & Melinda Gates Foundation will be used by Daré for working capital and general corporate purposes

## Q1-2020 (through January 31<sup>st</sup>): **\$7.8 million Cash Raised**

- ATM sales: \$5.1 million
- Warrants exercised: \$1.7 million
- License fees: \$1.0 million

## At January 31, 2020:

- Common shares o/s: 24.5 million
- Warrants o/s: ~2 million

## NIH SBIR Grant:

- \$1.9 million - aggregate grant funding for Ovaprene research and development expenses from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), a division of the National Institutes of Health (NIH).
- \$730,722 - remaining portion of award available in 2020 contingent upon NIH approval.

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## Balance Sheet September 30, 2019

- Cash: \$2.4 million
- Common shares o/s: 16.7 million
- Warrants o/s: 3.75 million
- No debt

MOVE THE

FIELD FORWARD

## EXECUTIVE MANAGEMENT TEAM



Sabrina Martucci Johnson MSc, MIM  
President & CEO



David Friend, PhD  
Chief Scientific Officer



Lisa Walters-Hoffert  
Chief Financial Officer



John Fair  
Chief Business Development Officer



Mary Jarosz, RPh, RAC, FTOPRA  
Global Head of Regulatory Affairs



Mark Walters  
Vice President of Operations



Christine Mauck, MD, MPH  
Medical Director



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President & CEO





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