

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**FORM 8-K**

**Current Report  
Pursuant to Section 13 or 15(d)  
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): **February 11, 2019**

**DARÉ BIOSCIENCE, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction  
of incorporation)

**001-36395**  
(Commission  
File Number)

**20-4139823**  
(I.R.S. Employer  
Identification No.)

**3655 Nobel Drive, Suite 260  
San Diego, CA 92122**  
(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(858) 926-7655**

**Not Applicable**  
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 8.01 Other Events**

Included as Exhibit 99.1 to this report is a presentation about Daré Bioscience, Inc. ("Daré") and its product candidates, dated February 11, 2019, which is incorporated herein by reference. Daré intends to use the presentation and its contents in various meetings with investors, securities analysts and others, commencing on February 11, 2019.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

<b>Exhibit Number</b>	<b>Description</b>
99.1	<a href="#">Corporate presentation, dated February 11, 2019</a>

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**DARÉ BIOSCIENCE, INC.**

Dated: February 11, 2019

By: /s/ Sabrina Martucci Johnson

Name: Sabrina Martucci Johnson

Title: President and Chief Executive Officer

Delivering innovation by  
daring to be different

February 11, 2019



## Forward Looking Statements

THIS PRESENTATION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT AN OFFER TO SELL OR A SOLICITATION OF AN OFFER TO BUY ANY SECURITIES OF DARÉ BIOSCIENCE, INC. ("DARÉ" OR THE "COMPANY"). THIS PRESENTATION INCLUDES CERTAIN INFORMATION OBTAINED FROM TRADE AND STATISTICAL SERVICES, THIRD PARTY PUBLICATIONS, AND OTHER SOURCES. DARÉ HAS NOT INDEPENDENTLY VERIFIED SUCH INFORMATION AND THERE CAN BE NO ASSURANCE AS TO ITS ACCURACY.

ALL STATEMENTS IN THIS PRESENTATION, OTHER THAN STATEMENTS OF HISTORICAL FACT, ARE FORWARD-LOOKING STATEMENTS WITHIN THE MEANING OF FEDERAL SECURITIES LAWS. IN SOME CASES, YOU CAN IDENTIFY FORWARD-LOOKING STATEMENTS BY TERMS SUCH AS "MAY," "WILL," "EXPECT," "PLAN," "ANTICIPATE," "STRATEGY," "DESIGNED," "COULD," "INTEND," "BELIEVE," "ESTIMATE," "TARGET," OR "POTENTIAL" AND OTHER SIMILAR EXPRESSIONS, OR THE NEGATIVE OF THESE TERMS. FORWARD-LOOKING STATEMENTS INVOLVE RISKS, UNCERTAINTIES AND ASSUMPTIONS THAT MAY CAUSE DARÉ'S ACTUAL RESULTS, PERFORMANCE OR ACHIEVEMENTS TO BE MATERIALLY DIFFERENT FROM THOSE EXPRESSED OR IMPLIED BY THE FORWARD-LOOKING STATEMENTS, INCLUDING, WITHOUT LIMITATION RISKS AND UNCERTAINTIES RELATING TO: THE OUTCOME OR SUCCESS OF CLINICAL TRIALS; DARÉ'S ABILITY TO RAISE ADDITIONAL CAPITAL AS NEEDED; DARÉ'S ABILITY TO OBTAIN AND MAINTAIN INTELLECTUAL PROPERTY PROTECTION FOR ITS PRODUCT CANDIDATES; DARÉ'S ABILITY TO DEVELOP PRODUCT CANDIDATES ON THE TIMELINES SET FORTH HEREIN; AND OTHER RISK FACTORS DESCRIBED IN DARÉ'S MOST RECENT ANNUAL REPORT ON FORM 10-K AND QUARTERLY REPORT ON FORM 10-Q FILED WITH THE SECURITIES AND EXCHANGE COMMISSION.

ALL FORWARD-LOOKING STATEMENTS IN THIS PRESENTATION ARE CURRENT ONLY AS OF THE DATE HEREOF AND DARÉ DOES NOT UNDERTAKE ANY OBLIGATION TO UPDATE ANY FORWARD-LOOKING STATEMENT TO REFLECT NEW INFORMATION, FUTURE DEVELOPMENTS OR OTHERWISE, EXCEPT AS REQUIRED BY LAW.

## What We Do



**Vision:** To become the coordinating presence in women's health.

**Mission:** We achieve this by identifying, unlocking and advancing innovation that improves health outcomes and promotes a better quality of life for women.

## Daré Highlights

### Daring to be different

A pure play biopharmaceutical company focused on improving the health and well being of women. At Daré, we focus on targeted delivery of products to address persistent unmet needs in women's health. Our focus areas include:

- Pregnancy Prevention
- Sexual Health
- Vaginal Health
- Fertility

#### Acquisition, Licensing & Partnering Strategy:

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

#### Value Creation Strategy:

- The portfolio is well positioned to drive upside value by capitalizing on market misalignments
- The majority of assets are well positioned to be first-in-category opportunities and are therefore attractive partnering candidates

Delivering clinical milestones are key value drivers for a development stage company. We expect to deliver against multiple milestones over the next 12 - 24 months including:

- Advancing our Bacterial Vaginosis (BV) program into a Phase 3 trial
- Topline readouts from our two pre-pivotal programs Ovaprene (2H 2019) and Sildenafil Cream, 3.6%, (4Q 2020)
- Initiating development activities on the DARE-IVR programs - Hormone Replacement Therapy (HRT/VMS) program phase 1 (2019)



# Coordinating Presence in Women's Health Market Misalignment = A Value Creation Opportunity

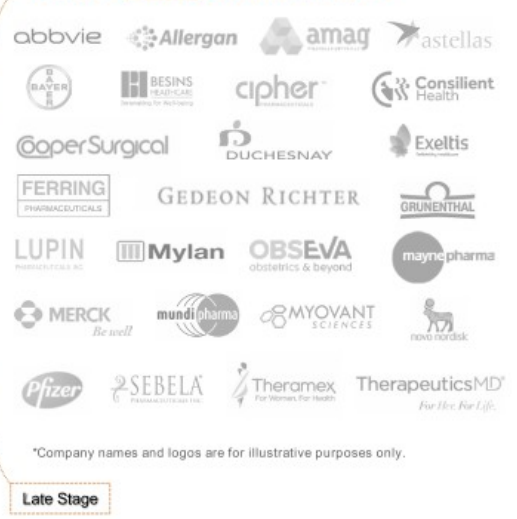
Innovators seeking development partners to advance products to commercialization in women's health.

Network of Product Developers



Large and mid-tier companies prefer to acquire or license products that are later-stage or ready for commercialization.

Network of Potential Commercial Partners\*

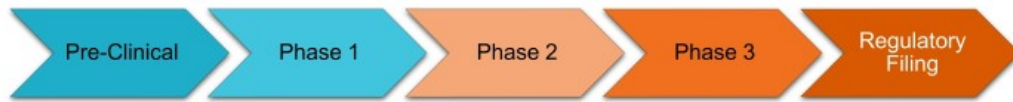


\*Company names and logos are for illustrative purposes only.

Global Women's Health Market Worth \$51 Billion  
by 2025 - CAGR: 3.9% <sup>1</sup>

<sup>1</sup> <https://www.prtnewswire.com/news-releases/womens-health-market-size-worth-51-billion-by-2025-cagr-39-grand-view-research-inc-651064753.html>





Vaginal Gel Clindamycin	DARE-BV1 <sup>†</sup> Formerly MP-101	Phase 3 Initiation 2H 2019		Bacterial Vaginosis
Barrier IVR Ferrous gluconate	Ovaprene® (PCT) <sup>*</sup>	Top line 2H 2019	CDRH / Device Lead	Non-Hormonal, Monthly Contraception
Topical Cream Sildenafil	Sildenafil Cream, 3.6% <sup>†</sup>	Top line 4Q 2020		Female Sexual Arousal Disorder
IVR Natural Estradiol + Natural progesterone	DARE-HRT1 <sup>††</sup> Topline 2H 2019	Formerly JNP-0201		Hormone Replacement Therapy

Accelerating pre-clinical programs with collaborations and non-dilutive funding whenever possible

IVR Natural progesterone	DARE-FRT1 <sup>*</sup>	Formerly JNP-0301		Pregnancy Maintenance (PTB & ART)
IVR Oxybutynin	DARE-OAB1 <sup>*</sup>	Formerly JNP-0101		Over-Active Bladder
Vaginal Insert SERM (tamoxifen)	DARE-VVA1 <sup>*</sup>	Formerly PT-101		Vulvar and Vaginal Atrophy (HR+ Breast Cancer Population)
Ca2+ Target	DARE-RH1	Formerly CatSper		Non-Hormonal Male & Female Contraceptive Target
Injectable Etonogestrel	ORB 204 & 214 <sup>*</sup>			6 & 12 Month Injectable Contraception

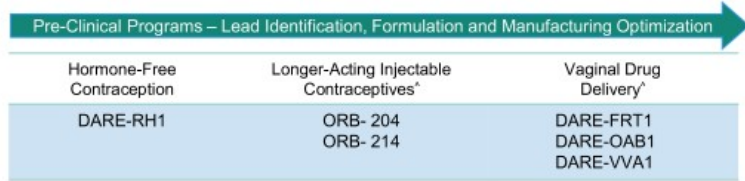
Timeline reflects management's current estimates and constitutes a forward looking statement subject to qualifications elsewhere in the presentation. Actual development timeline may be substantially longer, and Daré is under no obligation to update or review this estimate.

<sup>\*</sup>505(b)(2).

<sup>\*</sup>Ovaprene Post Coital Test (PCT) is a pre-pivotal clinical study.

<sup>†</sup>HRT Phase 1 study to be conducted in Australia by Daré subsidiary.

## Portfolio Timeline Overview



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



<sup>A</sup>505(b)(2).

<sup>\*</sup>Ovaprene Post Coital Test (PCT) is a pre-pivotal clinical study.

<sup>†‡</sup>HRT Phase 1 study to be conducted in Australia by Daré subsidiary.



# Investment Highlights

## Financial Profile

### Background

- NASDAQ:DARE
- Publicly traded via reverse merger that closed July 19, 2017

### Balance sheet, September 30, 2018:

- \$9.5 million in cash
- Non-dilutive NIH SBIR Award:
  - In Q2-2018, Daré received a Notice of Award for the first \$224,665 of an anticipated \$1.9 million in grant funding from a division of the National Institutes of Health.
- 11.4 million common shares and 3.7 million warrants outstanding
- No debt

# Management Team

## Daré Bioscience

Sabrina Martucci Johnson, MSc, MIM President and CEO	Cypress Bioscience, Calibr, Advanced Tissue Sciences, WCG, Baxter Healthcare
Lisa Walters-Hoffert Chief Financial Officer	ROTH Capital Partners, Citicorp Securities, Bank of America, Oppenheimer & Co.
David Friend, PhD Chief Scientific Officer	Evoform, CONRAD, Elan Corporation
John Fair Chief Business Officer	Evoform, WCG, Gemini Healthcare, Aegis plc
Mark Walters Vice President, Operations	Pacira, SkyePharma, Alliance Pharmaceuticals, American Home Products
Mary Jarosz, RPh, RAC, FTOPRA Global Head of Regulatory Affairs	Evoform, WCG, Abbott Laboratories
Christine Mauck, MD, MPH Medical Director	CONRAD, Population Council, RW Johnson, FDA
Bridget Martell, MD, MA Medical Affairs	Juniper Pharmaceuticals, Purdue Pharma, Pfizer
Nadene Zack, MSc Sr. Director Clinical Operations	Retrophin, Aragon, Cypress Bioscience, Pfizer

# Board of Directors

## Daré Bioscience

Roger Hawley (Chairman)	Zogenix, Allos Biopharma, Cypress Bioscience, InterMune, Elan Corporation, GSK
Jessica Grossman, MD	Medicines360, Sense4Baby, Johnson & Johnson
Susan Kelley, MD	Bayer, BMS, ArQule, Cerulean
Greg Matz	CooperSurgical - Cooper Companies, Agilent, Hewlett Packard
William Rastetter, PhD	Neurocrine Biosciences, IDEC, GRAIL, Receptos, Illumina, Cerulean
Robin Steele, JD, LL.M.	InterMune, Elan Corporation, Alveo, Allos Biopharma
Sabrina Martucci Johnson, MSc, MIM	Cypress Bioscience, Calibr, Advanced Tissue Sciences, WCG, Baxter Healthcare

# Program Overview





**DARE-BV1** (Formerly MP-101)  
Clindamycin 2% gel for Bacterial Vaginosis



# DARE-BV1 Overview

## Bacterial Vaginosis (BV)

### 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>
  - 88% 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

- Single Phase 3 clinical trial planned for FDA approval

### Attractive Market Opportunity

- BV is the most commonly reported 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 (37-67%) <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)

# Bacterial Vaginosis

## Symptoms & Causes of BV

- BV is the most commonly reported vaginal infection in women ages 15-44.<sup>1</sup> BV is characterized by a shift in the vaginal flora from the dominant Lactobacillus to a polymicrobial flora.<sup>2</sup>
- BV has been associated with serious health issues, including preterm births, pelvic inflammatory disease, increased susceptibility to sexual transmitted infections (including HIV infection) and other chronic health problems.<sup>1,2</sup>
- A number of potential microbial pathogens, singly and in combinations, have been implicated in the disease process.
  - The list of possible agents includes Gardnerella, Atopobium, Prevotella, Peptostreptococcus, Mobiluncus, Sneathia, Leptotrichia, Mycoplasma, and BV-associated bacterium 1 (BVAB1) to BVAB3.<sup>1</sup>

# Bacterial Vaginosis

## Symptoms & Causes of BV

- BV is characterized by the presence of three of the following four criteria:
  - Vaginal pH of >4.5
  - Clue cells on saline wet mount
  - Release of a fish amine odor
  - A characteristic thin, homogenous vaginal discharge
    - In 1991, Nugent et al. described a Gram stain scoring system of vaginal smears to diagnose BV.<sup>1,3</sup>
- The Nugent score is calculated by assessing for the presence of large gram-positive rods (*Lactobacillus* morphotypes; decrease in *Lactobacillus* scored as 0 to 4), small gram-variable rods (*G. vaginalis* morphotypes; scored as 0 to 4), and curved gram-variable rods (*Mobiluncus* spp. morphotypes; scored as 0 to 2) and can range from 0 to 10. A score of 7 to 10 is consistent with BV.<sup>1,3</sup>
- BV is not considered to be a sexually transmitted infection, but it is more common in women who are sexually active.





# Bacterial Vaginosis

## Market Opportunity

- In the US, an estimated 21 million women aged 14-49 years (approximately 29%) are infected with BV.<sup>1,2</sup>
  - BV leads to symptoms including abnormal vaginal discharge and odor that are unpleasant and disrupt and interfere with a woman's relationships and general quality of life.
  - BV has been associated with serious health issues, including preterm births, pelvic inflammatory disease, increased susceptibility to sexual transmitted infections (including HIV infection) and other chronic health problems.<sup>3,4</sup>
  - IMS/IQVIA
    - According to IMS/IQVIA data, the 2016 U.S. annual sales figures for BV prescriptions were in excess of \$150m including utilization of oral and vaginal forms of Clindamycin and Metronidazole.<sup>5</sup>
  - Lupin Inc., the U.S. subsidiary of India-based Lupin, acquired Symbiomix, the maker of secnidazole (a 5-nitroimidazole antibiotic granular powder) for the treatment of BV in a transaction valued at \$150m.<sup>6</sup>
    - Lupin's 1x oral Solosec® (secnidazole) launched in May of 2018.<sup>7</sup>

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

2. Suher, Allana et al., "Bacterial Vaginosis: A Review," US Pharmacist 2018; 43(9):32-33

3. Center for Disease Control and Prevention (CDC). [www.cdc.gov/std/bv/stats.htm](http://www.cdc.gov/std/bv/stats.htm)

4. Onderdonk, A. et al. "The Human Microbiome during Bacterial Vaginosis," Clinical Microbiology Reviews, April 2016 Volume 29 Number 2

5. IMS/IQVIA data (2016). Data on file

6. <http://www.pharmalive.com/lupin-coughs-up-150-million-cash-for-new-jersey-based-biopharma-company-symbiomix/>

7. <http://www.lupinpharmaceuticals.com/lupin-launches-solosec-secnidazole-2g-oral-granules-in-the-us.htm>

# Bacterial Vaginosis

## DARE-BV1 (Formerly MP-101) Proof of Principle Study Design

Study Objective: Study the Efficacy and Safety of DARE-BV1 in the Treatment of Bacterial Vaginosis

Proof of Principle Study Design (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>• Single dose administered</li></ul>	<ul style="list-style-type: none"><li>• Patients questioned regarding comfort level &amp; re-examined</li></ul>	<ul style="list-style-type: none"><li>• Patients questioned regarding experience &amp; re-examined</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>	<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>	<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>		

1. Therapeutic cure was a composite endpoint, which required both clinical cure (defined as clinical cure: 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>

# Bacterial Vaginosis

## DARE-BV1 (Formerly MP-101) Proof-of-Principle Study Summary

A single dose of DARE-BV1 demonstrated high clinical cure rate compared to other approved products

Product	Clinical (Amsel) Cure	Bacteriologic (Nugent) Cure	Therapeutic Cure
 DARE-BV1 <small>novel gel (clindamycin)</small>	88%	57%*	57%*
 Solesec® <sup>1</sup> <small>(secnidazole 2g oral granules)</small>	53-68%	40-46%	35-40%
 Clindesse® <sup>2</sup> <small>clindamycin phosphate Vaginal Cream, 2%</small>	41-64%	45-57%	30-42%
 Metrogel, 1.3% <sup>3</sup>	37%	20%	17%

\* Based on data from 9 evaluable patients

- 26 of 30 women completed the study
- Test-of-Cure Visit (Day 7 – 14)
  - 23 of 26 (88%) 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)
  - 23 of 24 (96%) women showed continued clinical cure
  - 8 of 9 women had bacteriologic cure and 7 of 9 had therapeutic cure

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

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

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



# Contraception

Expected to be a \$33 billion global category by 2023<sup>1</sup>



1. Global Market Insights, <https://globenewswire.com/news-release/2016/05/19/841462/0/en/Contraceptives-Market-size-to-exceed-33-Billion-by-2023-Global-Market-Insights-Inc.html>



# New Contraceptive Option

## Ovaprene® Overview

### Successful Proof of Concept Study

- Ovaprene demonstrated effectiveness in preventing sperm from entering the cervical canal in a proof-of-concept study in women (n=20):<sup>1</sup>
  - No viable sperm in the cervical mucus
  - No colposcopic abnormalities

### CDRH (Device) Regulatory Pathway

- Single pivotal clinical trial expected 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

# New Contraceptive Option

## Ovaprene® Overview

### Innovation in Contraception

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



### Convenience is driving new innovation

- NuvaRing®
  - Monthly, convenient vaginal ring product form.
  - 2017 worldwide sales: \$761 million (Merck)<sup>5</sup>
- Mirena® Product Family
  - Physician inserted, long-acting.
  - Low/locally delivered hormone IUS.
  - 2017 worldwide sales: \$1.12 billion (Bayer)<sup>7</sup>

1. Lo Loestrin Fe contains a low-dose combination of two female hormones. <https://www.loloestrin.com/loloestrin/about-lo-estrin>. Lo Loestrin® and its design are registered trademarks of Allergan Pharmaceuticals International Limited.

2. Minastrin <https://www.minastrin24.com>. Minastrin® is a registered trademark of Allergan Pharmaceuticals International Limited.

3. <https://www.nuvaring.com/how-nuvaring-works/>

4. <https://www.mirena-us.com/about-mirena/>

5. Annual Report on Form 10-K for fiscal year ended December 31, 2017

6. Bayer Annual Report 2017. Includes sales for Mirena®, Kyleena® and Jaydess® / Skyla®

# New Contraceptive Option

## Ovaprene® Overview

### Women's Preferences

- Effective Pregnancy Prevention
- Convenient Product Forms
  - Independent surveys revealed that the vaginal ring has many of the features women deemed extremely important.<sup>1</sup>
- Less Hormones
  - A majority of women prefer a monthly option with a lower hormone dose than the pill.<sup>2</sup>
- Methods **not in the moment** (noncoital)
  - 77% of women who practice contraception currently 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.gutmacher.org



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

# What's Missing in Contraception?

## Hormone free alternatives that are effective and easy to use

Least Effective

100% Effective = 0% Risk of Pregnancy <sup>1,2</sup>

Birth Control Effectiveness		
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%

Most Effective

### Hormone Free Product Landscape <sup>4</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

# New Contraceptive Option

## Ovaprene® Overview

### Ovaprene® Non-hormonal, Monthly Vaginal Ring

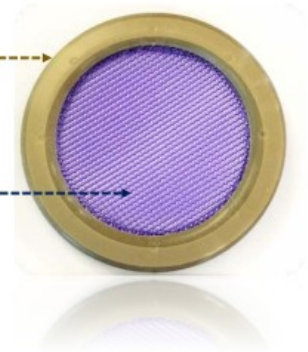
#### Spermiostatic Environment<sup>1</sup>

- Achieved through a contraceptive-loaded silicone ring matrix.
- Releasing non-hormonal active Ferrous gluconate.

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

- 3-D, non-braided, fluid-permeable mesh barrier.

Rx distribution (OB/GYN) – anticipated upon approval.



# New Contraceptive Option

## Ovaprene® Overview

Ovaprene successfully prevented sperm from reaching the cervical canal in a previous human postcoital test (PCT) clinical study.

- 2009 - Postcoital Assessment:<sup>1</sup>
  - Open-label, single-arm, pilot safety and tolerability study.
  - Published in the Journal of Reproductive Medicine, 2009.
- Patients:
  - N= 20; all women completed one cycle of use.
- Results:
  - **Postcoital testing revealed no viable sperm in the cervical mucus.**
  - No colposcopic abnormalities, no significant changes in vaginal flora and no serious adverse effects observed.

2.3

Birth Control Effectiveness		
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%
Eura Patch*	99.70%	91.00%
Nova 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%

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 88% in pivotal contraceptive studies evaluating pregnancy rates over time.



# New Contraceptive Option

## Ovaprene® Overview

### U.S. Regulatory Strategy

- PMA with CDRH (Medical Device Division) as lead review division.
- Pathway expected to be based on similar CDRH approvals - Example: Caya® diaphragm.\*

#### Step 1 – Postcoital test (PCT) 2018 / 2019\*

- The study is enrolling 50 couples.
  - 25 women complete a total of 21 visits
- Evaluated over the course of five menstrual cycles.
- Each woman's cervical mucus will be 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 motile sperm per high powered field (HPF) in the cervical mucus, post coitus.
- Safety assessments, PK, acceptability, fit, and ease of use.





- Data from the study is expected to be available in the second half of 2019.
- If there is demonstration of feasibility in the PCT clinical trial, the Company intends to prepare and file an Investigational Device Exemption (IDE) with the FDA to commence a pivotal clinical trial to support marketing approvals of Ovaprene in the United States, Europe and other countries worldwide.

#### Step 2 – Pivotal Study 2020 / 2021\*

- Single pivotal clinical (expected).
- N= ~250 completers over 6 months of use.
  - Primary Endpoints: Safety & Efficacy
    - Pregnancy probability.
  - Secondary Endpoints:
    - Acceptability/product fit/ease of use.
    - Assessments of vaginal health.

# New Contraceptive Option

## Ovaprene® Overview

Features Desired Most in Birth Control: <sup>1-4</sup>	Design Features of Ovaprene: <sup>5,6</sup>
 <b>Convenience</b> (Easy to Use & Easy to Remember)	<b>Monthly Ring Product Form</b> Women chose rings for the convenience of a non-daily option.
 <b>Hormone Free</b>	<b>No Hormones in the API</b> Unique dual action MOA (spermiostatic & barrier).
 <b>Efficacy</b>	<u>Expected</u> Typical Use Effectiveness Comparable to Hormone Contraception (88% vs 91%).
 <b>Favorable Side Effect Profile</b>	<b>No Colposcopic Abnormalities</b> No significant changes in vaginal flora. No serious adverse effects observed in prior published study.
 <b>Easily Manage Fertility</b>	<b>No Systemic Activity</b> 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):749-63  
 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.





# Women's Sexual Health & Wellness Female Sexual Arousal Disorder (FSAD)

World market for both male and female sexual dysfunction drugs will reach 7.7 billion in 2019<sup>1</sup>



1. <https://www.visiongain.com/sexual-dysfunction-drugs-market-will-reach-7-7bn-in-2019-predicts-a-new-visiongain-study/>

# Female Sexual Arousal Disorder (FSAD)

Sildenafil Cream, 3.6%

## Successful Proof of Concept

- Sildenafil Cream, 3.6% improved genital blood flow in a proof-of-concept study (n=35):<sup>1</sup>
  - 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

## Attractive Market Opportunity<sup>2</sup>

- 33% of females 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. Ad Hoc Market Research: FSAD Prevalence Report (Oct 2015) conducted for SST LLC. Based on US Census projections for 2016.

# Female Sexual Arousal Disorder (FSAD)

Sildenafil Cream 3.6%

Dyspareunia

Vulvar-Vaginal  
Atrophy

Hypoactive Sexual  
Desire Disorder  
(HSDD)

Female Sexual  
Arousal Disorder  
(FSAD)

 **Intrarosa**  
Prasterone 0.65% 6.5 mg

**ESTRACE**<sup>®</sup> CREAM  
(estradiol vaginal cream, USP, 0.01%)

**addyi**<sup>®</sup>  
(flibanserin)

 **Imvexxy**  
(estradiol vaginal insert)

 **Osphena**  
(ospemifene) tablets  
60mg

 **Premarin**<sup>®</sup>  
(conjugated estrogens)  
vaginal cream

**Rekynda**  
(bremelanotide)

**No Approved  
Products**

With its approval of Addyi®, FDA has now 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.

- INTRAROSA is a registered trademark of Endoceutics, Inc.
- Imvexxy is a trademark of TherapeuticsMD, Inc.
- Osphena is a registered trademark of Duchesnay USA, Pennsylvania, USA.
- ESTRACE® is a registered trademark of Allergan Pharmaceuticals International Limited.
- Premarin is a registered trademark of Pfizer Inc.
- Addyi is a registered trademark of Sprout Pharmaceuticals, Inc.
- Bremelanotide is a registered trademark of Palatin Technologies, Inc.

# Female Sexual Arousal Disorder (FSAD)

Sildenafil Cream 3.6%

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.

1. McCool et al. Sex Med Rev 2016;4:197-212.

2. Ad Hoc Market Research: FSAD Prevalence Report (Oct 2015) conducted for SST LLC.

3. Based on US Census projections for 2016.

# Female Sexual Arousal Disorder (FSAD)

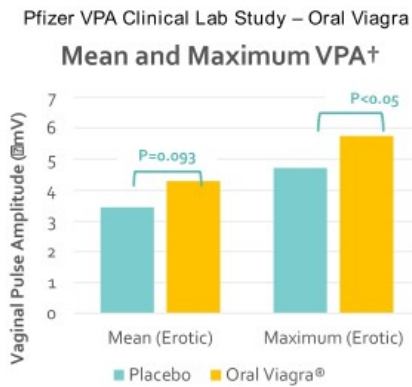
## Sildenafil Cream 3.6%

Key Takeaways of Viagra® studies:

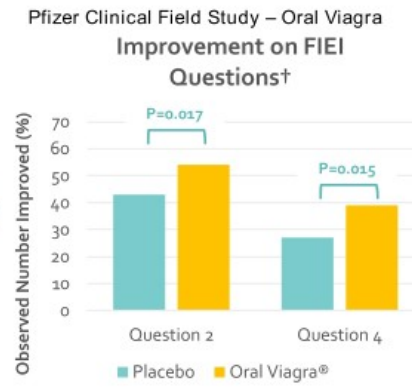
- Oral sildenafil (Viagra) demonstrated statistically significant activity
- Side effects of the oral formulation led to the investigation of a new route of administration

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

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



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



Female Intervention Efficacy Index (FIEI)

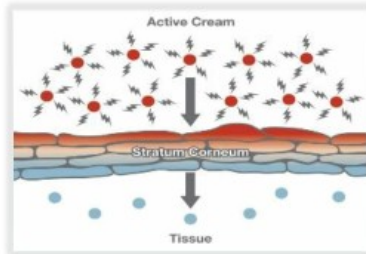
<sup>‡</sup> Question #2 – “After taking study medication, the sensation/feeling in my genital (vaginal, labia, clitoris) area during intercourse or stimulation (foreplay) seemed to be: (a) more than before, (b) less than before, or (c) unchanged”. Question #4 – “After taking the study medication, intercourse 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.

# Female Sexual Arousal Disorder (FSAD)

## Sildenafil Cream 3.6%

### Formulation Innovation

- Sildenafil Cream, 3.6% designed to directly increase local blood flow to the genital tissue.
- The formulation delivers localized action, with minimal systemic uptake of the active drug.<sup>1</sup>



### SST Formulation Technology

6 issued patents in the U.S. on the topical delivery of Sildenafil and other PDE-5 inhibitors.

- Leveraging the known therapeutic benefit of oral sildenafil to stimulate increased blood flow to the genital tissue.
- If approved, Sildenafil Cream, 3.6% may offer a safe, effective and 'on demand' solution to difficulties with sexual arousal.



# Female Sexual Arousal Disorder (FSAD)

## Sildenafil Cream 3.6%

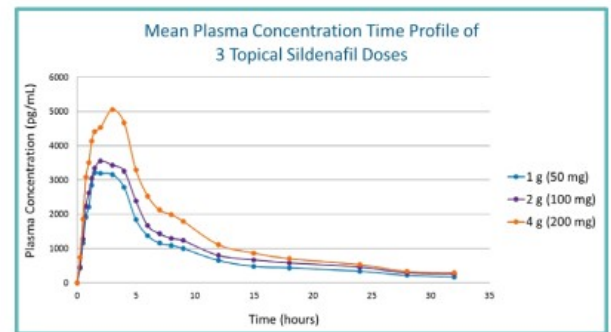
### Phase 1 Study of Sildenafil Cream, 3.6%<sup>1</sup>

- 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 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

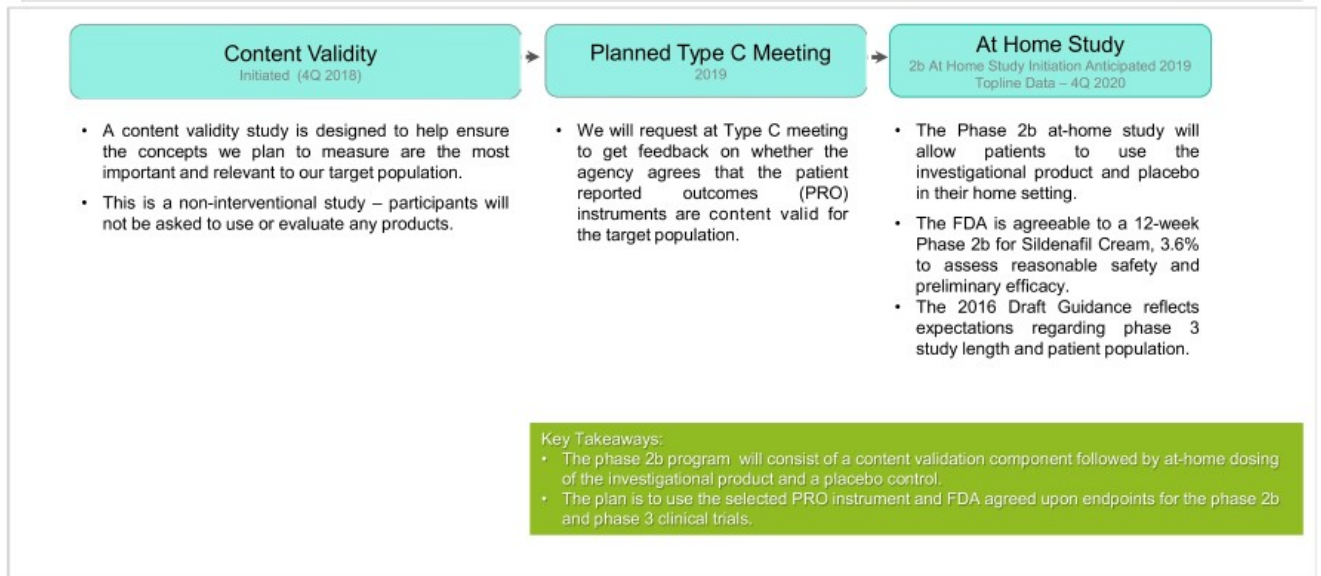
Treatment	N	Sildenafil Single Dose	C <sub>max</sub> (ng/ml)	T <sub>max</sub> (hr)	AUC <sub>last</sub> (h*ng/ml)
Topical Sildenafil 1 g of cream	20	35 mg	3.4	2.37	25.6
Topical Sildenafil 2 g of cream	20	71 mg	3.8	2.27	30.8
Topical Sildenafil 4 g of cream	19	142 mg	5.3	2.22	42.5



# Female Sexual Arousal Disorder (FSAD)

## Sildenafil Cream 3.6%

Phase 2b Program: Continue to explore additional clinical and non-clinical work that might be valuable or required to support the overall program and the anticipated design of the Phase 2b.





# Female Sexual Arousal Disorder (FSAD)

Sildenafil Cream 3.6%

Dyspareunia

Vulvar-Vaginal  
Atrophy

Hypoactive Sexual  
Desire Disorder  
(HSDD)

Female Sexual  
Arousal Disorder  
(FSAD)

 **Intrarosa**  
Prasterone *intra* 6.5 mg

**ESTRACE** CREAM  
(estradiol vaginal cream, USP, 0.01%)

**addyi**  
(flibanserin)

 **Imvexxy**  
(estradiol vaginal insert)

**Osphena**  
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60mg

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(conjugated estrogens)  
vaginal cream

**Rekynda**  
(bremelanotide)

**Sildenafil Cream, 3.6%**  
(If approved)

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- Bremelanotide is a registered trademark of Palatin Technologies, Inc.



# Innovative Vaginal Drug Delivery

Well characterized therapeutic options



# Intravaginal Ring (IVR) Technology Platform

Daré has an exclusive, global license to Juniper's novel IVR technology originally developed by Dr. Robert Langer from MIT<sup>1</sup> and Dr. William Crowley<sup>2</sup> from Massachusetts General Hospital and Harvard Medical School. Daré's exclusive license covers all rings in development as well as additional applications of the IVR technology platform in other therapeutic areas.

- Features of the Juniper 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 licensed from Juniper include:
  - DARE-OAB1
    - Formerly JNP-0101, an oxybutynin ring for the treatment of overactive bladder;
  - DARE-HRT1
    - Formerly JNP-0201, a combination bio-identical estradiol + progesterone ring for hormone replacement therapy.
  - DARE-FRT1
    - Formerly JNP-0301, a natural progesterone ring for the prevention of preterm birth and for fertility support as part of an IVF treatment plan.



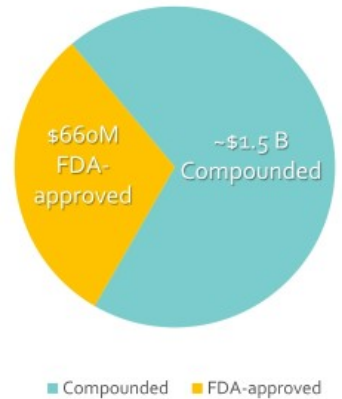
# Hormone Replacement Therapy (HRT)

DARE-HRT1

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>
- 2012 NAMS consensus statement 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>



# Hormone Replacement Therapy (HRT)

DARE-HRT1

## Phase 1 - Hormone Replacement Therapy (HRT)

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 Intravaginal ring (IVR):
    - 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

# Vaginally Delivered Tamoxifen for VVA

## DARE-VVA1

### Vaginally Delivered Tamoxifen to treat VVA in HR+ Breast Cancer Patients

- DARE-VVA1 (Formerly PT-101)
  - A proprietary vaginal formulation of tamoxifen, has the potential to be a first-in-class treatment for 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 hormone-receptor-positive 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 reported to be between 42 and 70 percent.<sup>2</sup>
- If approved, DARE-VVA1 has the potential to be the first treatment specifically developed for VVA in patients with HR+ breast cancer.



1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2800285/#S16title>  
2. Clinical Breast Cancer: <https://www.sciencedirect.com/science/article/pii/S1526820917300952>





# Strategic Pre-Clinical Candidates

Contraceptives that address global gaps





**Dare's Innovation Engine**

Reproductive Health  
Public & Private  
Sector Funding



**daré**  
bioscience  
Daring to be different

"Innovative partnerships increase access to family planning, helping more women plan their lives and shape their futures."

Chris Elias, President Global Development Program, Bill & Melinda Gates Foundation



Major foundations contribute hundreds of millions of dollars to fund new innovation in women's reproductive health.

Development organizations screen and advance promising new innovation.






Daré has emerged as the coordinating presence among these organizations and is well positioned to partner on the product candidates with significant market potential.

# Value Creation in Women's Reproductive Health

Addressing Global Needs  
in Contraception



Daring to be different

Organization	Funding Source / Donor	Product Name	License Holder / Partner	Form	Indication	Annual Sales / Corporate Value
The Population Council	USAID Gates Foundation	Anovera 	Therapeutics MD	Ring	Pregnancy Prevention	2018 \$20M upon FDA approval; \$20M first commercial batch, milestones + royalties <sup>1</sup>
	USAID	Paragard 	Cooper Surgical	IUD	Pregnancy Prevention	2017 Cooper Surgical \$1.1B Acquisition from Teva <sup>1</sup>
	USAID	Mirena 	Bayer	IUS	Pregnancy Prevention	2017 >\$1.1B (Global sales) <sup>2</sup>
	USAID	Jadelle 	Bayer	Implant	Pregnancy Prevention	2014 ~\$400M (Global sales) <sup>1</sup>
Medicines360	Large Anonymous Donor	Liletta 	Allergan	IUS	Pregnancy Prevention	2013 \$50M upfront; \$125M milestones + royalties <sup>1</sup>

<sup>1</sup> SEC Filing/IMS Data;  
<sup>2</sup> Bayer Annual Report 2017. Includes sales for Mirena®, Kyleena® and Jaydess® / Skyla®

# A New Contraceptive Target

DARE-RH1 CatSper

A Novel Approach To Male And Female Contraception.

- The identification of the CatSper target represents the potential to develop a novel class of non-hormonal contraceptive products for both men and women.
  - The discovery of a sperm-specific ion channel, CatSper, was validated in animal models where it was demonstrated that male mice lacking CatSper have poor sperm motility.
- CatSper proteins are ion channels expressed solely in the membranes of sperm flagellum and are essential to sperm motility.
- Pre-clinical research has demonstrated CatSper mediates hyperactive motility of sperm.
  - Sperm hyperactivity is necessary to penetrate the physical barrier known as the zona pellucida which encloses the ovum and protects the egg.<sup>1</sup>
  - The contraceptive benefit of targeting CatSper is achieved by inhibiting sperm hyperactivity and preventing egg fertilization.

# A New Long Acting Contraceptive Option

## Microparticle 6 & 12 Month Injectable Contraception

### ORB-204 and ORB-214, injectable etonogestrel<sup>1</sup>

The initial development on Orbis' long-acting injectable contraceptive program was carried out under a subcontract funded by Family Health International (FHI 360) through a grant from the Bill & Melinda Gates Foundation.

- Pre-clinical studies for the 6- and 12- month formulations have been completed to date:
  - Establishing pharmacokinetics and pharmacodynamics profiles.

An injectable contraceptive is designed to provide discreet, non-invasive protection over several months

- Limitations of the currently marketed injectable contraceptive: provides contraceptive protection for only three months, and can delay the ability to get pregnant for up to ten months after receiving the injection.

Target product profile of long-acting injectable

- Prolonged duration (6 to 12 months), improved ease of use, with an improved side effect profile and predictable return to fertility.

# Corporate & Investor Communications

NASDAQ: DARE  
Trading as DARE since July 20, 2017



[www.darebioscience.com](http://www.darebioscience.com)





# Appendix

Daré Programs: Consumer & Market Insights





## Bacterial Vaginosis Market Insights

American Sexual Health Association (ASHA), in conjunction with Harris Poll, conducted a national survey of 304 women ages 18 to 49 who have had bacterial vaginosis (BV). The survey was conducted online by Harris Poll on behalf of Symbiomix Therapeutics, LLC, a Lupin company, and the ASHA within the United States between September 14 and 29, 2017 among 304 US women aged 18-49 who have been diagnosed by a healthcare professional with BV within the past 2 years ("women with bacterial vaginosis").

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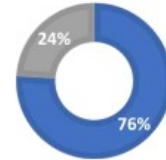
# Bacterial Vaginosis Market Insights

## American Sexual Health Association (ASHA) National Bacterial Vaginosis Survey

- 76% of women with BV stated they would have gone to see a healthcare professional sooner if they were aware of the risks associated with BV if left untreated
- Only 43% of women with BV are aware that if left untreated, BV can cause an increased risk of sexually transmitted infections (STIs)

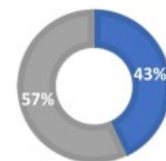
### IF BV RISK FACTORS WERE KNOWN

- Would Seek Treatment Sooner
- Would Not Seek Treatment Sooner



### AWARE OF LINK TO STI

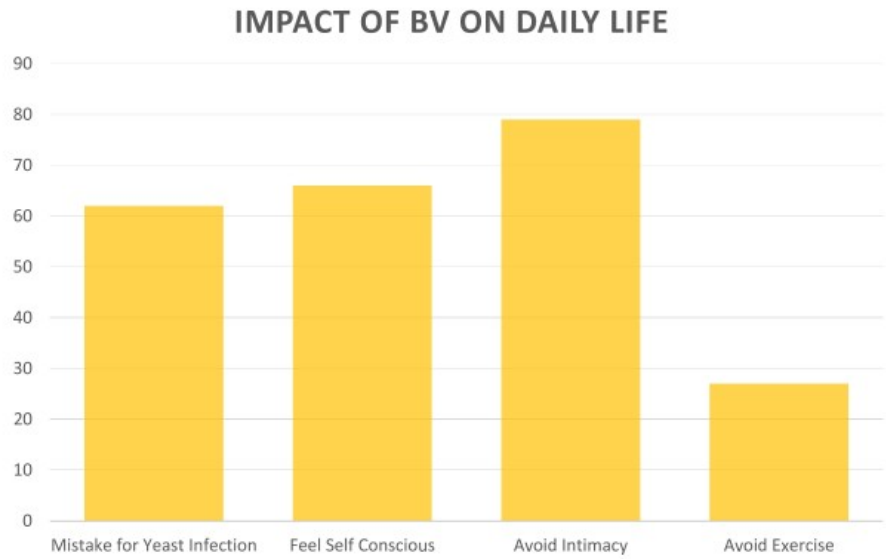
- Aware BV Can Increase Risk of STI
- Unaware BV Can Increase the Risk of STI



# Bacterial Vaginosis Market Insights

## American Sexual Health Association (ASHA) National Bacterial Vaginosis Survey

- According to the ASHA survey, 62% of women mistake BV for a yeast infection prior to diagnosis
- Most women with BV feel self-conscious (68%) and/or embarrassed (66%) due to their condition
- Women with BV avoid everyday activities including being intimate with their spouse/partner (79%), working out (27%), or going on a first date (17%)



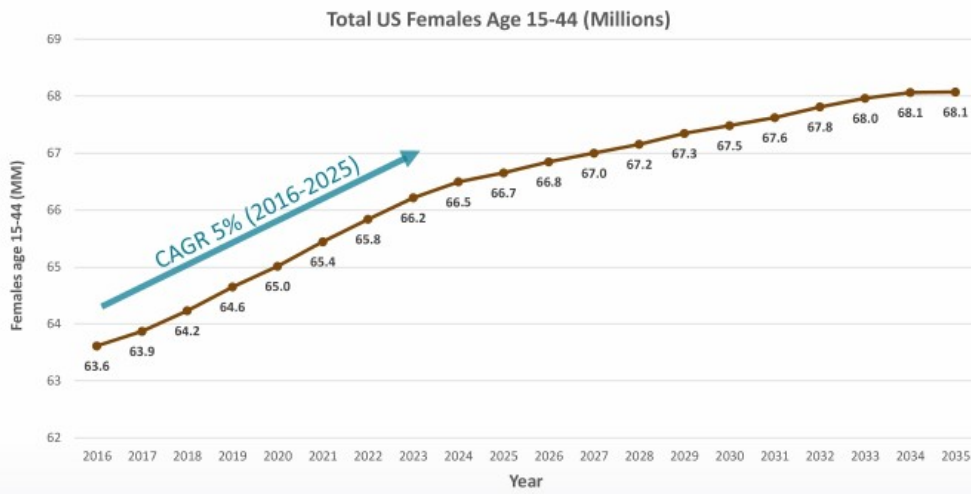


# Ovaprene Market Insights

Secondary Market Research & Market Sizing Data Prepared by SmartPharma, February 2019.  
Data on File.

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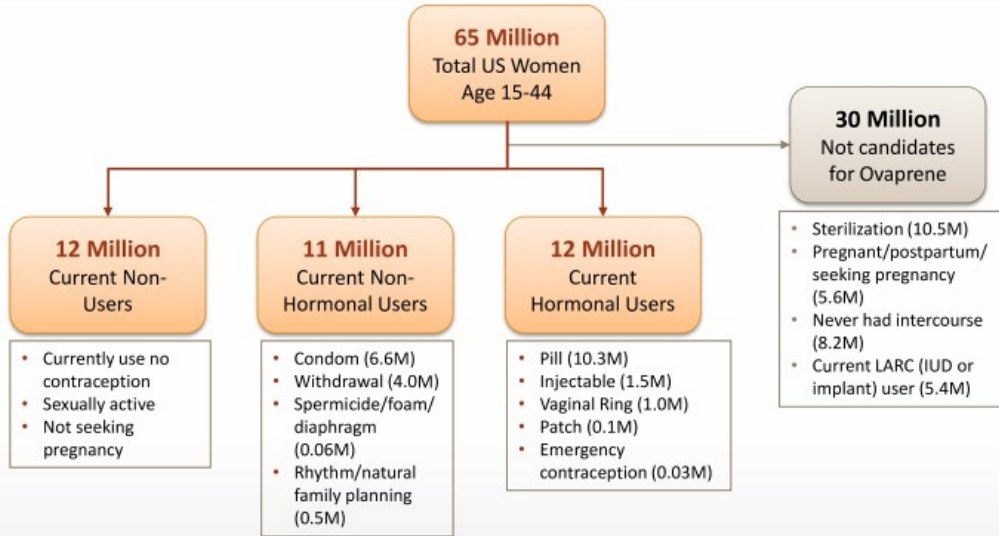
# US Contraceptive Population is Over 60 million and Continues to Grow



Source: US Census Bureau, 2017 National Dataset (2016 is base population estimate for projection)  
<https://www.census.gov/programs-surveys/popproj.html>

# Ovaprene Potential – Total Market Size

There are currently 35 million US women who could potentially choose Ovaprene for contraception



Source: CDC National Survey for Family Growth, 2013-2015 dataset, cdc.gov. Contraceptive use data applied to 2019 population data from US Census

# Negative Information About Hormones is Persistent in the Public Domain

*As a non-hormonal option, Ovaprene does not have to overcome myths or negative “press”*

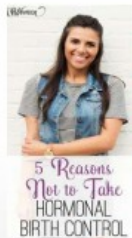
## 5 Reasons Women Avoid Birth Control

- Reason #1: “I don’t want to get fat”
- Reason #2: “It might make me depressed”
- Reason #3: “Birth control causes cancer”
- Reason #4: “I don’t want to put chemicals in my body”
- Reason #5: “I’m not at risk for getting pregnant”

## 6 Reasons Why You Shouldn’t Take The Pill Long Term

April 4, 2017 by [Fertility Friday](#) / 91 Comments

- The pill lowers your sex drive
- The pill shrinks your clitoris and causes painful sex
- The pill causes depression and anxiety
- Long term pill use puts you at an increased risk of cervical cancer
- Long term pill use is associated with a delay in your return to fertility



1. Hormonal Birth Control Comes with Side Effects
2. Birth Control is Full of Hormones/Chemicals
3. Birth Control Works Against Your Body
4. Birth Control \*May\* Cause Abortions
5. A Whole Host of Other Reasons

### Sources:

HelloFlo, Mar 22, 2017, [www.helloflo.com](http://www.helloflo.com)

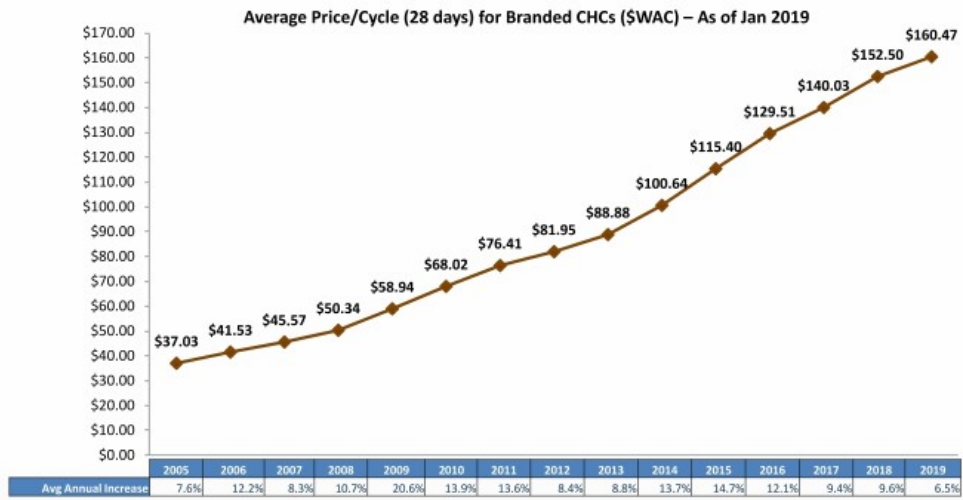
Fertility Friday, April 4, 2017, [www.fertilityfriday.com](http://www.fertilityfriday.com)

Equipping Godley Women, April 15, 2015, [www.equippinggodleywomen.com](http://www.equippinggodleywomen.com)

# Contraceptive Pricing and Reimbursement

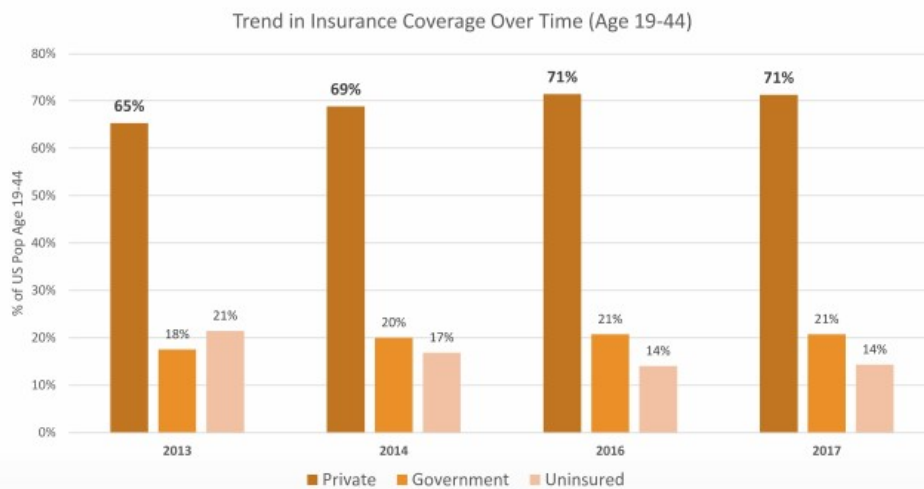


# Brand Contraceptives Have Consistently Increased in Price



Source: MediSpan PriceRx, accessed Jan 2019. Average of 13 available branded contraceptives available in US market. Only three of these brands have no generic equivalent, and the average price/cycle for those 3 = \$171.06

# Over 70% of Reproductive-Aged Women in the US Have Private Insurance

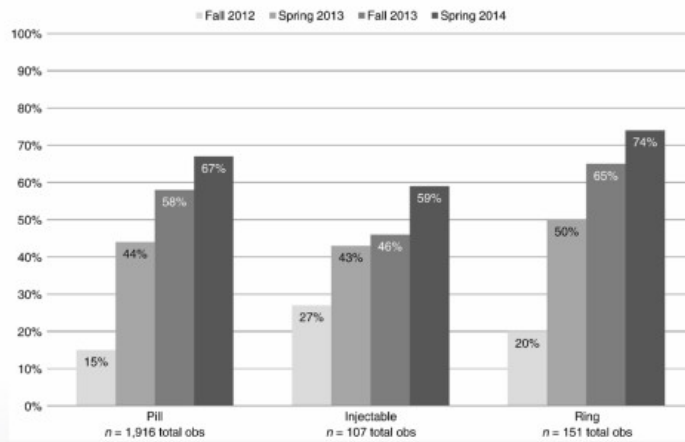


\*Patients can have more than one form of insurance, so totals may exceed 100%

Source: Berchick et al. US Census Bureau, Health Insurance Coverage in the US: 2017, Issued Sep 2018

# Most Women Pay \$0 For Birth Control Since the ACA Was Enacted

**Percent of Women with \$0 Copay for Birth Control Over Time**  
 (n=892 women age 18-39 with private health insurance who used a prescription contraceptive method)



By spring 2014, mean and median out-of-pocket costs for the pill were \$6.48 and \$0 per month, respectively

HHS issued a clarification in May 2015 that required coverage of at least 1 product per method with \$0 copay – therefore the percentages have likely increased since this data

Sources:  
 Guttmacher Institute Continuity and Change in Contraceptive Use Study in: Sonfeld A, et al. Contraception 2015;91:44-48  
 US Dept of Health and Human Services (HHS) FAQs About ACA Implementation (Part XXVI), www.cms.gov

# ACA Contraceptive Mandate: Current Status of Contraceptive Policy

- Insurance plans must cover all FDA-approved methods with no copay or cost sharing to patients<sup>1</sup>
  - They must cover at least one type of each method in each category
- 62.8 million women (age 18-64) now have birth control coverage with no cost sharing<sup>2</sup>
  - Exemptions and accommodations for religious and moral objections are in place, but they affect only 6,400 to 127,000 women<sup>3</sup>
  - The latest attempts by the current administration to broaden the exemption has been blocked by two federal courts<sup>4</sup>
- If Ovaprene is approved, it has the potential to be the only product in the category, as it is a vaginal ring with a spermistatic active.

<sup>1</sup>[www.HealthCare.gov/coverage/birth-control-benefits/](http://www.HealthCare.gov/coverage/birth-control-benefits/)

<sup>2</sup>National Women's Law Center Fact Sheet, Nov 2018

<sup>3</sup>HHS Fact Sheet, Nov 7 2018

<sup>4</sup>National Women's Law Center Fact Sheet, Oct 2018 and Washington Post, Jan 14, 2019



# Sildenafil Cream, 3.6% FSAD Demographic Insights & Concept Test

Market Research Report Conducted by Ad Hoc Research on behalf of Strategic Science & Technologies, LLC. 222 Third Street, Suite 2242 Cambridge, MA 02142 – December 2015

# FSAD - Psychological & Physiological Impact



## The Current Experience of FSAD Sufferers

(Physical and Psychological)



# Experience of FSAD Sufferers

- The concept definitely **has potential**. FSAD sufferers are likely to purchase it and are willing to give it a try.
- A few questions remain:

## 1. What do they currently experience during sexual activity that they are hoping the cream will rectify?

They often feel....	They do not often feel...
The inability to attain an adequate level of sexual excitement	Genital tenseness or tightness
The lack of desire for intimacy	Genital pulsing or throbbing
Lack of genital or clitoral fullness, pressure or engorgement	The feeling of muscle contractions in their genitals
Lack of genital wetness or lubrication	The feeling of readiness
	Satisfaction with their level of physical arousal

## 2. What are their main physical desires when it comes intimacy?

- They are **desperate for their bodies to respond**, be it to...
  - Intimacy;
  - An intimate touch;
  - Touch.



# Experience of Female Sexual Arousal Disorder (FSAD) Sufferers

## 3. What is the psychological impact of this disorder?

- The impact appears to be immense. Emotions run the gamut from **dissatisfaction with** to **anger about their sex lives**.
- The **most frequent** feelings include:
  - **Dissatisfaction** with their sex lives;
  - **Bothered** by their low sexual desire;
  - **Unhappiness** about their sexual relationships; and
  - **Frustration** due to their sexual problems.
- Thus, conveying an understanding of these feelings, either in claims, in communications or both, will promote interest in the product.

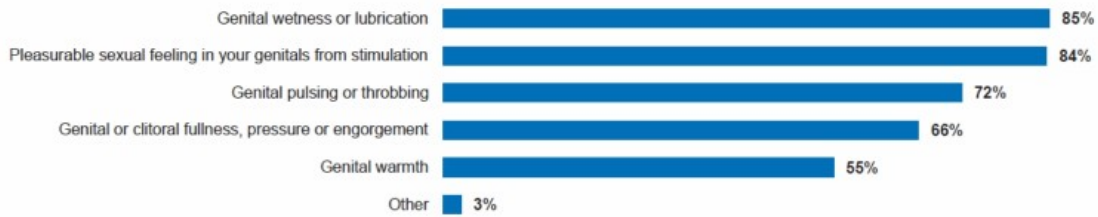


## 4. What “remedies” have they tried to combat the disorder?

**3** the average number of remedies tried to combat FSAD

- **Almost all FSAD sufferers surveyed have tried “something”** to treat their difficulties getting or staying physically aroused.
- The most common are **topical lubricants** and a **vibrator/other accessory** for stimulation.

# Female Sexual Arousal Disorder (FSAD) Respondents Indicators of Sexual Arousal

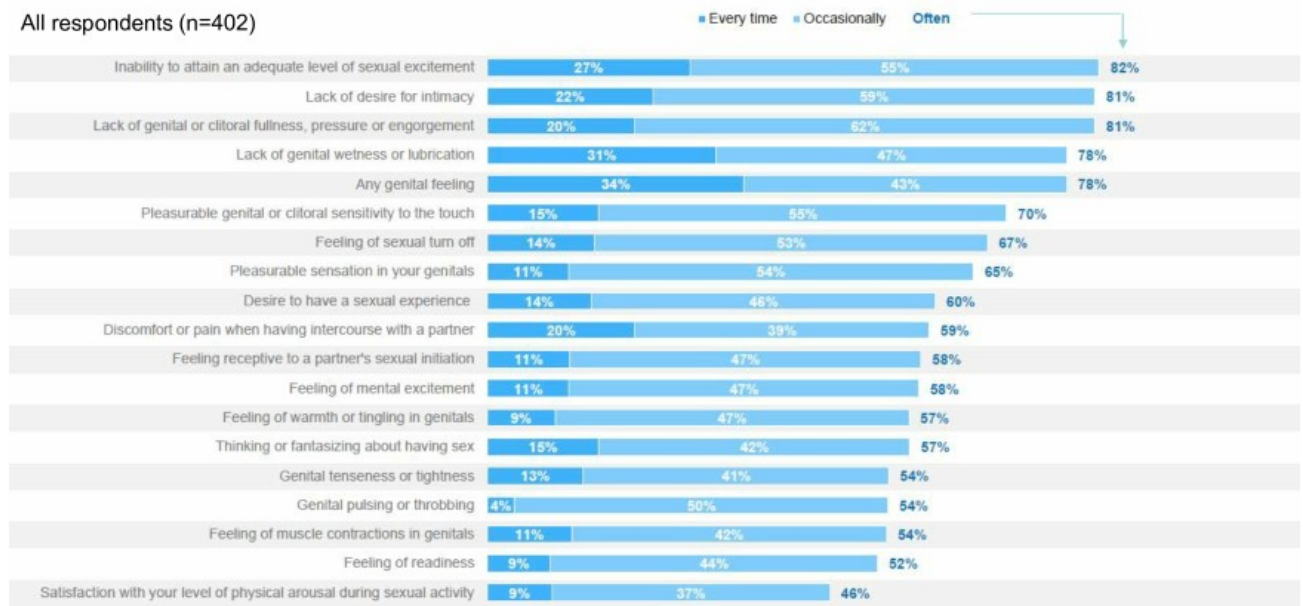


All respondents (n=402)	Age group		FSAD LT SA 35-54 *	
	21-44 n=195	45-60 n=207	Yes n=120	No n=282
Genital wetness or lubrication	87%	81%	83%	85%
Pleasurable sexual feeling in your genitals from stimulation	84%	84%	85%	84%
Genital pulsing or throbbing	75%	69%	69%	74%
Genital or clitoral fullness, pressure or engorgement	65%	68%	66%	66%
Genital warmth	58%	50%	51%	56%
Other	3%	2%	2%	3%

\* LT- in a long-term relationship  
SA - currently sexually active  
35-54 - ages of 35 to 54

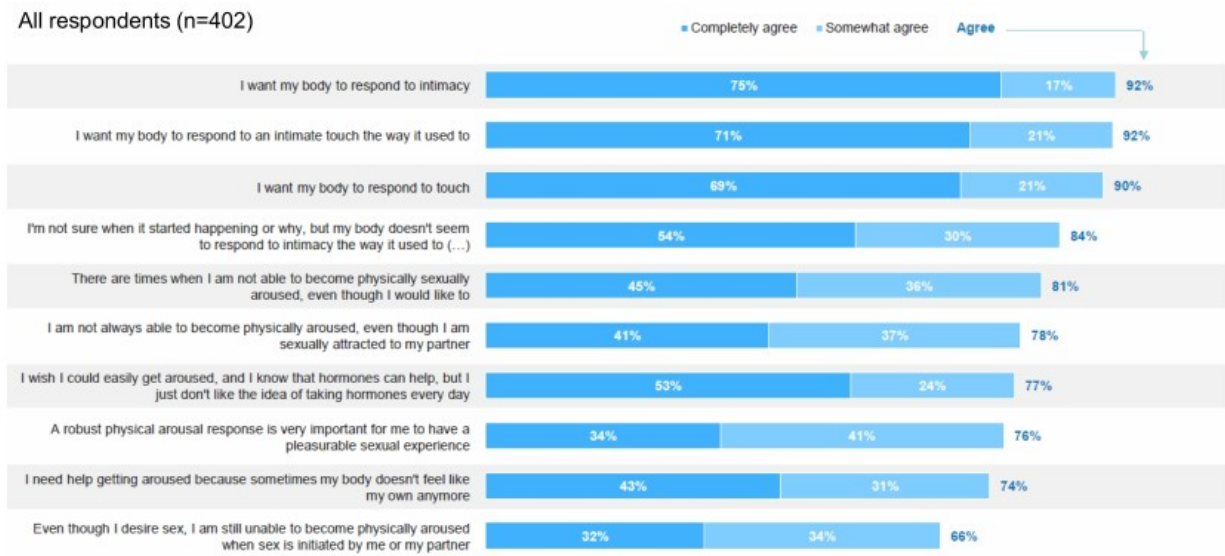
# Female Sexual Arousal Disorder (FSAD) Respondents Signs & Symptoms

All respondents (n=402)



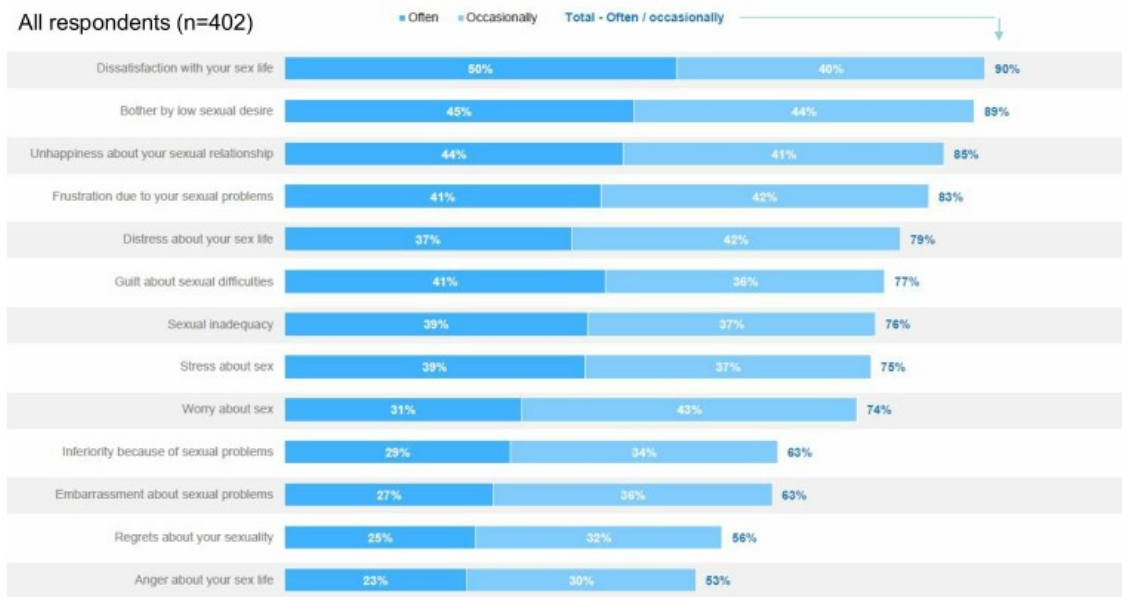
# Psychological Impact of FSAD

All respondents (n=402)



# Psychological Impact of FSAD

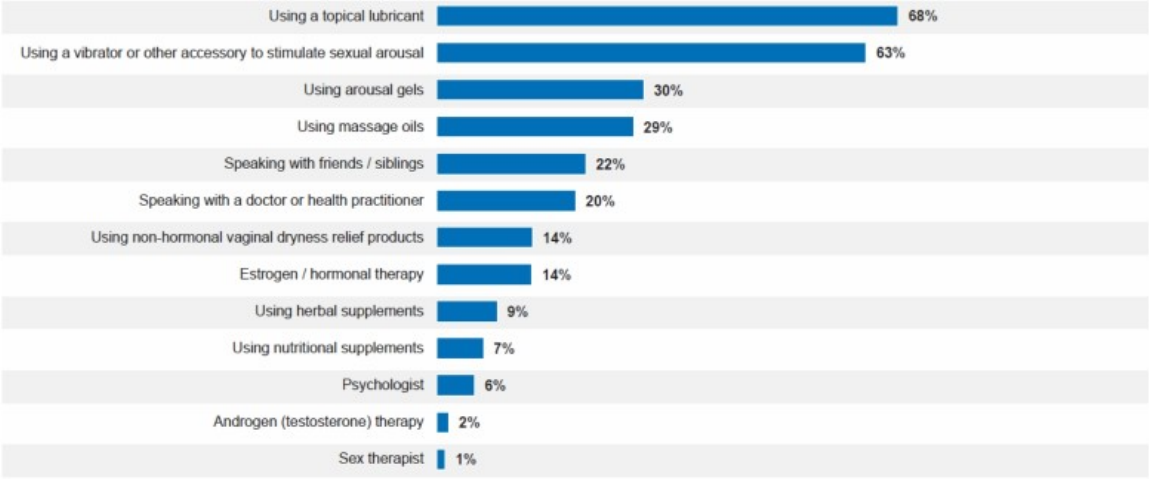
All respondents (n=402)



# Without an FDA Approved Product for FSAD, Women's Options are Suboptimal



All respondents (n=402)



Source data on File: Research Report –December 2015; AD Hoc research - Sildenafil Topical Cream for Women Concept Test, slide 41-47.



# Sildenafil Cream, 3.6% Product Profile Market Research

# Sildenafil Cream, 3.6% Concept Testing



402 American women between the ages of 21 and 60 and suffering from *Female Sexual Arousal Disorder (FSAD)* were surveyed via web panel between November 18 and 23, 2015.



The purpose of this study is to measure the market potential of a topical cream version of *sildenafil* targeting women as a potential remedy for FSAD.

1

## What degree of consumer interest is there in this product idea?

- **A significant degree.** Many FSAD sufferers have been experiencing symptoms for more than a year. In addition to the physical symptoms they experience, the psychological impact of the disorder is quite burdensome.
- On average, FSAD sufferers have tried approximately 3 different remedies – chief among them topical lubricants and vibrators. However, they have found little to no relief.
- FSAD sufferers like the idea. They perceive it to be different from other remedies they have put to the test and they believe it will meet their needs.
- FSAD sufferers are ready to try something new – especially one that promises no side effects.

2

## What are the potential drivers of and barriers to adoption of the product?

Potential Drivers	Potential Barriers
They want to give it a try. They are ready to try something new.	<b>Embarrassment</b> (in front of their partners, doctors and pharmacists).
They want to increase their sex drive/sexual arousal.	<b>Believability:</b> will it work? They have tried many other "remedies" that have not.

# Sildenafil Cream, 3.6% Concept Testing

3

## What are the most motivating claims?

- In concrete terms, the elements of the concept they like the most are:

- ✓ No side effects (the #1 claim, by a very wide margin);
- ✓ Proven safe;
- ✓ Clinically tested;
- ✓ Odorless;
- ✓ Absorbs completely;
- ✓ Available without a prescription.

- Any support point that enhances the legitimacy of the product is naturally motivating, be it:

- ✓ Doctor recommended;
- ✓ Available by prescription only for two years before being available without a prescription;
- ✓ The same active ingredient as in *Viagra* (although slightly less so than the previous two).



# Sildenafil Cream, 3.6% Concept Testing – Cream Formulation



Source data on File: Research Report –December 2015; AD Hoc research - Sildenafil Topical Cream for Women Concept Test, slide 10.

# Sildenafil Cream, 3.6% Concept Testing – Concept Acceptors

5

## What is the profile of *Concept Acceptors* (in terms of symptoms experienced, relationship to the condition of FSAD, etc.)?

- Concept Acceptors are **not widely different** from FSAD sufferers as a whole. However, they do appear to be the **most severe sufferers** of FSAD:
  - **The intensity of their symptoms and feelings is much stronger.**
    - They experience some of the **physical symptoms more frequently**, such as:
      - Lack of genital wetness or lubrication;
      - Lack of genital or clitoral fullness, pressure or engorgement;
      - Lack of desire for intimacy and;
      - Genital tenseness or tightness.
    - Not surprisingly, they have an **even deeper desire:**
      - **For their bodies to respond to touch and intimacy**, the way they used to;
      - **To have help becoming/staying physically aroused.**
    - On an emotional level, they are **even MORE...**
      - **Bothered** by their low sexual desire;
      - **Dissatisfied** with their sex lives;
      - **Frustrated** with their sexual problem;
      - Engulfed by **guilt** about their sexual difficulties;
      - **Worried** about sex;
      - Likely to feel sexually **inadequate/inferior** and;
      - **Embarrassed.**
  - One potential reason they are Concept Acceptors is they **tend to have sex more often** than FSAD sufferers in general – Their need for relief is even greater than those who have sex less frequently.



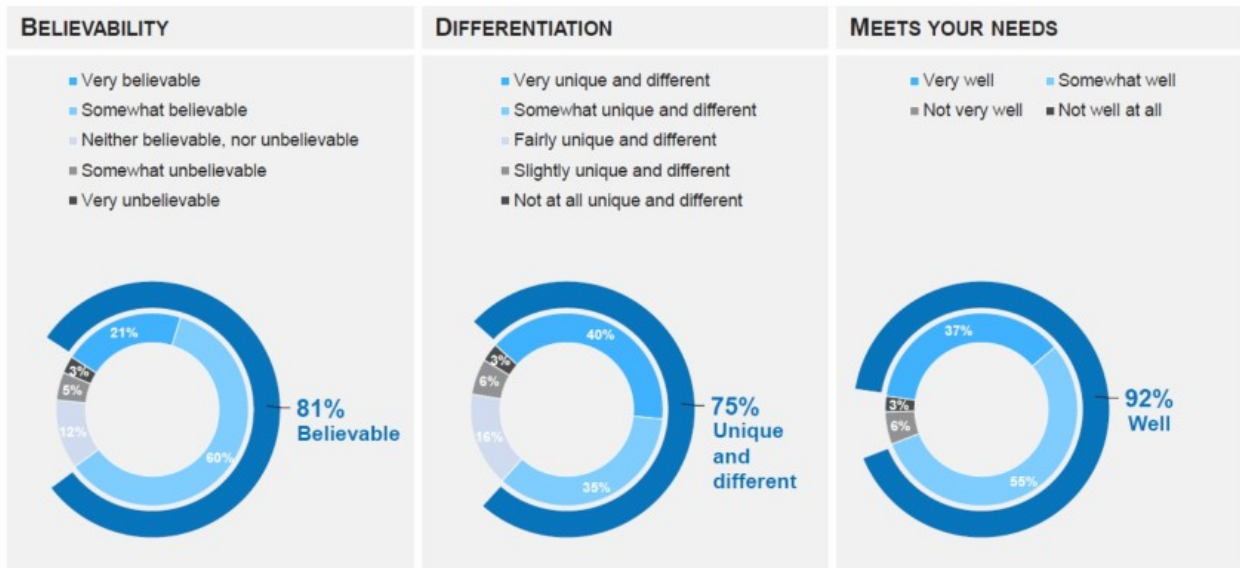
## Sildenafil Cream, 3.6% Concept Testing – Purchase Interest

- 82% of respondents indicated they would be likely to purchase the product if it were currently available.
- A subgroup of respondents aged 35-54 had a higher purchase interest (86%) vs. the aggregate (82%).

	Total n=402	Age group		FSAD LT SA 35-54*	
		21-44 n=195	45-60 n=207	Yes n=120	No n=282
<b>Likely</b>	<b>82%</b>	<b>81%</b>	<b>84%</b>	<b>86%</b>	<b>80%</b>
<i>Very likely</i>	35%	31%	39%	46% ↑	29% ↓
<i>Somewhat likely</i>	47%	50%	44%	40% ↓	51% ↑
Neither likely, nor unlikely	10%	9%	12%	10%	10%
<b>Unlikely</b>	<b>8%</b>	<b>11%</b> ↑	<b>5%</b> ↓	<b>4%</b>	<b>10%</b>
<i>Somewhat unlikely</i>	4%	6%	3%	2%	6%
<i>Very unlikely</i>	4%	5%	2%	2%	4%

\* LT- in a long-term relationship  
SA - currently sexually active  
35-54 - ages of 35 to 54

# Sildenafil Cream, 3.6% Concept Testing – Believability & Viability





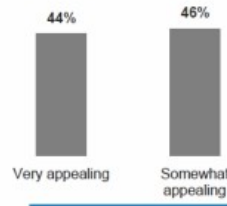
# Sildenafil Cream, 3.6% Concept Testing – Concept Appeal

- The majority of respondents (89%) considered the concept appealing.
- The largest proportion of respondents to consider the concept very appealing were women between the ages of 35-54.

	Total n=402	Age group		FSAD LT SA 35-54*	
		21-44 n=195	45-60 n=207	Yes n=120	No n=282
<b>Appealing</b>	<b>89%</b>	<b>88%</b>	<b>91%</b>	<b>95%</b> ↑	<b>87%</b> ↓
<i>Very appealing</i>	44%	41%	48%	50%	41%
<i>Somewhat appealing</i>	46%	47%	44%	45%	46%
<b>Neither appealing, nor unappealing</b>	<b>6%</b>	<b>6%</b>	<b>7%</b>	<b>4%</b>	<b>8%</b>
<b>Unappealing</b>	<b>4%</b>	<b>6%</b> ↑	<b>2%</b> ↓	<b>2%</b>	<b>6%</b>
<i>Somewhat unappealing</i>	3%	4%	2%	1%	4%
<i>Very unappealing</i>	1%	2% ↑	0% ↓	1%	2%

\* LT- in a long-term relationship  
SA - currently sexually active  
35-54 - ages of 35 to 54

## 89% Appealing



## 4% Unappealing

