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): September 11, 2023

DARÉ BIOSCIENCE, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-36395**	**20-4139823**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS 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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock	**DARE**	**Nasdaq Capital Market**

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 7.01 Regulation FD Disclosure.

Exhibit 99.1 to this report is a copy of a presentation about Daré Bioscience, Inc. ("Daré" or the "Company") and its product and product candidates, dated September 11, 2023, 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 September 11, 2023.

The information in Item 7.01 of this report, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to liability under that Section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 7.01 and in Exhibit 99.1 shall not be incorporated by reference into any filing with the Securities and Exchange Commission made by Daré, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate presentation, dated September 11, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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.

Date: September 11, 2023

By: */s/ Sabrina Martucci Johnson*
Name: Sabrina Martucci Johnson
Title: President and Chief Executive Officer

Exhibit 99.1

DARÉ
IN ITALIAN, IT MEANS "TO GIVE."
IN ENGLISH, IT MEANS "TO BE BOLD."

Women

At Daré Bioscience, women's health is ***Our Sole Focus***.
Innovation in women's health needs to be a priority.
We are working hard to identify and advance new therapies that provide additional choices and improve outcomes so that we can make a difference in the lives of women everywhere.

Forward-Looking Statements; Disclaimers

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," or the negative of these terms and other similar expressions. Such statements include, but are not limited to, statements relating to the clinical and market potential of XACIATO™ (clindamycin phosphate) vaginal gel, 2% and Daré's product candidates, clinical trial advancement, timing and data, regulatory approval and commercialization, potential collaborations, expectations regarding existing collaborations, pipeline expansion, and potential funding and financing transactions. As used in this presentation, "first-in-category" is a forward-looking statement relating to market potential of a product candidate if it were to receive regulatory approval for the indication(s) for which it is being developed. None of the product candidates presented herein are approved for use outside of clinical trials. The timing of clinical trials, clinical trial data, FDA review and approval, collaborations and other milestones and events relating to development and commercialization of XACIATO and Daré's product candidates, other than those having occurred prior to the date of this presentation, are forward-looking statements. Forward-looking statements reflect management's estimates and expectations based on current information and 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: Daré's reliance on third parties to commercialize XACIATO and to manufacture and conduct clinical trials of its product and product candidates; the degree of market acceptance that XACIATO and any future product achieves; the coverage, pricing and reimbursement that XACIATO and any future product obtains from third-party payors; risks and uncertainties inherent in Daré's ability to successfully develop, obtain regulatory approval for and monetize its product candidates; Daré's need for additional capital to fund operations and execute its business strategy; and those risks and uncertainties described under the heading "Risk Factors" 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 are current only as of the date of this presentation. Daré does not undertake any obligation to update any forward-looking statement in this presentation to reflect new information, future developments or otherwise, except as required by law.

Experienced Management & Board of Directors

Sabrina Martucci Johnson, MSc, MIM
President & CEO

John Fair
Chief Commercial Officer

Lisa Walters-Hoffert
Chief Financial Officer

David Friend, PhD
Chief Scientific Officer

Christine Mauck, MD, MPH
Medical Director

Annie Thurman, MD, FACOG
Medical Director

Mark Walters
Vice President of Operations

William Rastetter, PhD
Chairman

Cheryl Blanchard, PhD

Jessica Grossman, MD

Susan Kelley, MD

Greg Matz, CPA

Sophia N. Ononye-Onyia, PhD, MPH, MBA

Robin Steele, JD, LLM

Sabrina Martucci Johnson, MSc, MIM
President & CEO

Management & Board Experience

Delivering **innovation** by **daring to be different®**

Advancing Products Women Want

How Daré Creates Value

- **Innovative women's health pipeline** with multiple upcoming program milestones anticipated.
- Every program, if approved, represents a potential **first-line or first-in-category** product opportunity.
- Experienced Board of Directors and Management Team with **demonstrated success in clinical and product development,** regulatory affairs, corporate strategy and financial operations.

Daré Commercial Collboarators

BAYER ORGANON

Examples of emerging and large pharmaceutical companies with branded women's health products.

abbvie Agile THERAPEUTICS astellas

FERRING PHARMACEUTICALS GSK mayne pharma

Gedeon Richter Ltd. Pfizer Theramex For Women. For Health

Daré Bioscience: Women's Health is our Sole Focus

Value Drivers

- **Meaningful market potential for differentiated products**
  First-line or first-in-category product opportunities across the portfolio
- **Diverse pipeline with independent outcomes**
  One FDA-approved product and several clinical development stage candidates utilizing different APIs and targeting different indications
- **505(b)(2) FDA pathway planned for most candidates**
  Use of well-characterized APIs expected to mitigate development risk, time, and cost – non-new molecular entities estimated to have a 23% probability of success of advancing from Phase 1 to approval and a 67% likelihood of approval for Phase 3 to approval, versus 6% and 38% for new molecular entities, respectively
- **Multiple novel delivery platforms**
  Persistent unmet needs require creative new approaches designed for her; Novel delivery platforms allow for first-in-category potential with well characterized APIs
- **Commercial value in women's health**
  Evidenced by differentiated brands and transformational pharma transactions

Innovation in Women's Health

Contraception	~73 million women ages 15-49 1st hormonal monthly IVR, NuvaRing, ~$900M at peak 1st hormonal IUD, Mirena franchise, ~$1.2B at peak 1st copper IUD, still ~$200M/yr 40 years post launch
Vaginal Health	Bacterial vaginosis affects ~23 million women in the US Rx clinical cure rates 37-68% (**excluding XACIATO™**)
Reproductive Health Menopause Sexual Health	Over 45 million women in the U.S. estimated to be in or approaching menopause 1st estrogen hormone therapy, Premarin, ~$2B at peak
	No FDA approved product for female sexual arousal disorder, **despite similar prevalence to erectile dysfunction (ED)** 1st drug indicated for ED, Viagra, $2B at peak
Fertility	U.S. fertility pharmaceutical sector estimated to be $1.5B 15M babies (11.1% of all live births) are born pre-term every year

Women's Health – An Efficient Investment Thesis

Approximately **1% of healthcare research** is invested in female-specific conditions beyond oncology.[1]

Women's health conditions outside of oncology **comprise less than 2%** of the current healthcare pipeline.[2]

We believe **investment** in women's health will be efficient and **disproportionately impactful**:

- Women's health products make up **27% of total blockbuster products** while contributing to 35% of total blockbuster sales.[3]
- **Women control 80% of U.S.** healthcare purchasing decisions.[1]

1 - McKinsey & Company, February 14, 2022, Unlocking Opportunities in Women's Healthcare
2 - GlobalData Drugs Database and McKinsey & Company
3 - IQVIA Monthly Global MIDAS $ Const-Exchng (MNF) 2013 – 2022
Blockbuster defined as $500 million dollar sales in a year Women's Health including conditions solely or disproportionately affecting women; excludes oncology conditions in women

Daré Portfolio – The Big Ideas*

Contraception

Ovaprene® - 1st Hormone-free, Monthly Contraceptive: *Commercialization Collaborator* *Grant funding*
- Pivotal Phase 3 subject enrollment to begin 4Q-2023+

DARE-204/214 - 1st 6 & 12-Month Injectable Contraceptive: *Grant funding*

DARE-LARC1 - 1st Long-Acting, Reversible Personal Contraceptive System: *Grant funding* ***foundation grant &***

DARE-RH1 - Hormone-free contraceptive target for women and men

Vaginal Health

XACIATO™ - Clindamycin phosphate vaginal gel, 2%, indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older^
- First Commercial Sale in 2023+ : *Commercialization Collaborator* ORGANON

DARE-VVA1 - 1st Hormone-free vulvovaginal atrophy therapy; potential option for women with HR+ breast cancer

DARE-CIN (formerly R-131-2) – 1st Non-surgical, pharmaceutical intervention for the treatment of high-grade CIN

DARE-GML - Novel multi-target antimicrobial

DARE-LBT - Novel hydrogel formulation for delivery of live biotherapeutics to support vaginal health: *Grant funding* ***foundation grant***

Reproductive Health
Menopause
Sexual Health

Sildenafil Cream, 3.6% - 1st Topical cream, same active ingredient as Viagra®
- Potential first-in-category treatment for female sexual arousal disorder (FSAD) and/or female sexual interest/arousal disorder (FSIAD)

DARE-HRT1 - 1st Hormone therapy estradiol + progesterone monthly intravaginal ring (IVR)

DARE-PDM1 - 1st Vaginal administration of diclofenac for primary dysmenorrhea
- Phase 1 study commenced; topline data 2023+

Fertility

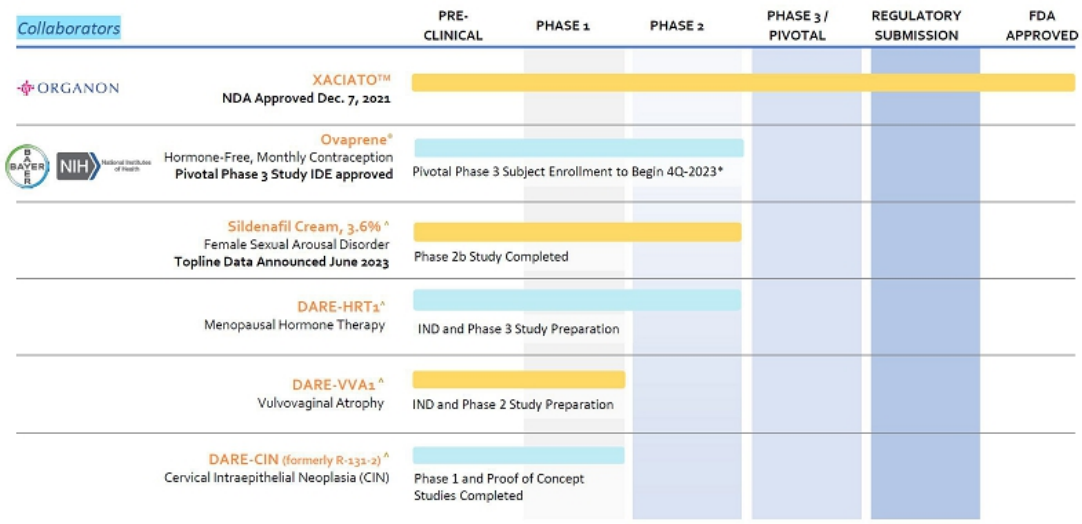
DARE-FRT1 / PTB1
- Progesterone delivery for pregnancy maintenance including the prevention of preterm birth (**DARE-PTB1**): *Grant funding*

– and for luteal phase support as part of an IVF regimen (**DARE-FRT1**).
- 1st IVR designed to release bio-identical progesterone over 14 days

DARE-PTB2
- Novel drug target validation studies to establish feasibility of a potential new therapeutic intervention for the prevention and treatment of idiopathic preterm birth: *Grant funding*

* The product candidates presented are in clinical or preclinical stage development and none are approved for use outside of a clinical trial. XACIATO is our only FDA approved product.
+ Currently anticipated timing
^ See Full Prescribing Information

Advancing Products Women Want – The Portfolio Snapshot



Organon and Daré are working towards a 2023 U.S. launch as soon as feasible*

^505(b)(2) regulatory pathway anticipated. ^ Currently anticipated timing

XACIATO is indicated for the treatment of bacterial vaginosis in females 12 years and older.
See Full Prescribing Information for the safe and effective use of XACIATO.
See XACIATO selected safety information on slide 24.

Advancing Products Women Want – The Portfolio Snapshot

Grant funding / Development collaborator		PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3 / PIVOTAL	REGULATORY SUBMISSION	FDA APPROVED
	DARE-PDM1^ Primary Dysmenorrhea	Phase 1 Study Commenced 2023					
NIH	**DARE 204/214 ^** 6 & 12-Month Injectable Contraception	Phase 1 Study Preparation					
NIH	**DARE-FRT1/PTB1^** Preterm birth (DARE-PTB1) and for luteal phase support as part of an IVF regimen (DARE-FRT1)	Phase 1 Study Preparation					
NIH *foundation grant*	**DARE-LARC1 ^** Long-Acting, Reversible Personal Contraceptive System (grant funded program)						
foundation grant	**DARE-LBT** Novel hydrogel formulation for delivery of live biotherapeutics to support vaginal health (grant funded program)						
	DARE-GML Novel Antimicrobial Glycerol Monolaurate						
	DARE-RH1 Male or Female Contraceptive Target						
NIH	**DARE-PTB2** Potential New Therapeutic Intervention for the Prevention and Treatment of Idiopathic Preterm Birth						

^505(b)(2) regulatory pathway anticipated. * Currently anticipated timing.

FDA Approved – XACIATO

ORGANON

Commercialization Collaborator

XACIATO™ (Clindamycin Phosphate) Vaginal Gel, 2%

- XACIATO [zah-she-AH-toe] (clindamycin phosphate) vaginal gel, 2% is a lincosamide antibacterial indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older.*
- **Daré's first FDA-approved product**.
- Organon market access team meeting with customers to review XACIATO and obtain competitive coverage in the bacterial vaginosis marketplace.
- Organon will leverage the knowledge and experience of its established NEXPLANON sales team to accelerate XACIATO uptake at launch.
- Organon believes there is roughly a 90% overlap of those healthcare providers who prescribe NEXPLANON and who diagnose and treat BV. Because of the strong relationships the sales team has with these providers, we expect Organon to be well-positioned to inform them about XACIATO on day 1, ultimately providing benefits to patients
- Organon and Daré are working towards a 2023 U.S. launch as soon as feasible.

- The license became effective June 2022.
- **Daré received a $10 million upfront payment** in 3Q 2022 and a **$1 million payment in July 2023**.
- Daré is eligible to receive potential milestone payments of **up to $181.8 million and tiered double-digit royalties based on net sales.**

XACIATO is indicated for the treatment of bacterial vaginosis in females 12 years and older.
See Full Prescribing Information for the safe and effective use of XACIATO.
See XACIATO selected safety information on slide 24.

Advancing Products Women Want

Late-Stage Programs

Contraception

Ovaprene®

Collaborator & Grant funding

Investigational Hormone-Free, Monthly Contraceptive
Pivotal Phase 3 Study to Commence 2023*

Potential first-in-category hormone-free contraception

- Self-administered intravaginal drug/device
- Designed to be an easy-to-use monthly option with effectiveness approaching hormonal methods. There are currently no FDA-approved monthly, hormone-free contraceptives.
- Commercial license agreement with Bayer. Pivotal study collaboration with NICHD.

Sexual Health

Sildenafil Cream, 3.6% ^

FSAD/FSIAD
Phase 2b Study Topline Data Announced June 2023

Potential first-in-category treatment for female sexual arousal disorder (FSAD) and/or female sexual interest/arousal disorder (FSIAD).

- Investigational cream formulation of sildenafil, **the active ingredient in Viagra®**, for topical administration to treat FSAD/FSIAD.
- FSAD is a physiological condition characterized by the inability to attain or maintain sufficient genital arousal during sexual activity. FSIAD is defined in the DSM-5 as a lack of or significantly reduced sexual interest/arousal. There are currently no FDA-approved treatments.
- Of the various types of female sexual dysfunction disorders, FSAD is most analogous to erectile dysfunction in men.

* Anticipated timing
^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Late-Stage Programs

Menopause

Vaginal Health

DARE-HRT1^

Menopausal Hormone Therapy

Phase 1 / 2 Study Completed

IND and Phase 3 Study Preparations Underway

- **Potential first-in-category** vaginal combination hormone delivery for treatment of vasomotor symptoms due to menopause
- Self-administered 28-day IVR
- Intravaginal ring (IVR) designed to release bio-identical estradiol and bio-identical progesterone over 28 days.
- There are **no FDA-approved options** with both hormones in one monthly IVR.
- Potential to be the first convenient monthly format product with both hormones.

DARE-VVA1^

Vulvovaginal Atrophy (VVA)

Phase 1 / 2 Study Completed

IND and Phase 2 Study Preparations Underway

- Potential first-in-category hormone-free intravaginal treatment for VVA.
- Proprietary formulation of tamoxifen for vaginal administration.
- There are currently no FDA-approved vaginal hormone-free treatments for VVA.

^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Phase 2-Ready Program

Vaginal Health

DARE-CIN (formerly R-131-2)^

Cervical intraepithelial neoplasia (CIN)

Phase 1 and Proof-of-Concept Studies Completed

Activities to support IND filing to enable progression to Phase 2 clinical development underway

- Potential first-in-category, non-surgical, pharmaceutical intervention for the treatment of CIN and other HPV-related pathologies.
- Proprietary fixed-dose formulation of lopinavir and ritonavir in a soft gel vaginal insert.
- There are currently **no FDA-approved, non-surgical pharmaceutical interventions** to treat CIN2+.

^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Phase 1 Stage Program

Reproductive Health

DARE-PDM1^

Primary Dysmenorrhea

Phase 1 Study Topline Data in 2023*

- **Potential first-in-category** treatment for primary dysmenorrhea.
- Proprietary hydrogel formulation of diclofenac for vaginal administration.
- Alternative to oral nonsteroidal anti-inflammatory drugs and hormonal contraceptives, which often can produce undesirable side effects.
- There are currently **no FDA-approved** vaginal diclofenac treatment options for primary dysmenorrhea.

*Anticipated timing
^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Phase 1-Ready Programs

Contraception

Fertility

DARE 204/214^ *Grant funding* NIH National Institutes of Health

6 & 12-Month Injectable Contraception

Phase 1 Study Preparation

- **Novel 6 & 12-month injectable formulations** of etonogestrel being developed as a longer-acting, reversible method of contraception with a more predictable return to fertility.
- There are currently **no FDA-approved** injectable contraceptives available indicated for 6 & 12-months of protection.

DARE-FRT1/PTB1^ *Grant funding* NIH National Institutes of Health

Pregnancy Maintenance

Phase 1 Study Preparation

- **Potential first-in-category progesterone delivery** for pregnancy maintenance including the prevention of preterm birth (DARE-PTB1) and for luteal phase support as part of an IVF regimen (DARE-FRT1).
- IVR designed to release bio-identical progesterone for up to 14 days.
- Alternative to daily IM injections or vaginal gel. There are currently **no FDA-approved** products marketed in the U.S. that do not require daily dosing of progesterone.

^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Preclinical Stage Programs

Contraception

DARE-LARC1^ *Grant funding* *foundation grant* NIH

Long-Acting, Reversible Personal Contraceptive System

- **Potential first-in-category** Levonorgestrel-releasing, long-acting contraceptive implant that a woman can turn on and off herself, according to her own needs.
- Grant of up to $48.95 M to advance technology through non-clinical proof of principle to enable IND submission, and an NIH grant to explore device insertion/removal in non-clinical studies.
- There are currently **no FDA-approved** contraceptive implants available that allow one to remotely pause and resume dosing.

Vaginal Health

DARE-LBT *Grant funding* *foundation grant*

Novel Delivery of Live Biotherapeutics

- **Novel hydrogel formulation for delivery of live biotherapeutics** to support vaginal health, such as for administration following effective primary infection treatment to rebalance the vaginal microbiota disrupted by the infection.
- Grant funded program.
- There are currently **no FDA-approved** live biotherapeutics for vaginal health.

^505(b)(2) regulatory pathway anticipated.

Advancing Products Women Want

Preclinical Stage Programs

Vaginal Health

DARE-GML

Novel Antimicrobial Glycerol Monolaurate (GML)

- **A naturally occurring fatty acid monoester** that has shown broad antimicrobial activity, killing bacteria, fungi, and viruses, and represents a new class of antimicrobials.
- GML has the potential to be a first-in-category multi-target antimicrobial agent.

Contraception

DARE-RH1

Male or Female Contraceptive Target

- **A potential new rapidly reversible, non-hormonal contraceptive solution** with application for women and men.
- There are currently **no FDA-approved** contraceptives available that target sperm hypermotility required for implantation.

Advancing Products Women Want

Preclinical Stage Programs

Fertility

DARE-PTB2

Grant funding NIH National Institutes of Health

Prevention and Treatment of Idiopathic Preterm Birth (PTB)

- **Potential new approach for the prevention and treatment of idiopathic PTB** through a stress response protein target.
- Grant funding for proof-of-concept target validation studies in collaboration with the Lockwood Laboratory at the University of South Florida Morsani College Medicine.

Daré – Working to Accelerate Innovation in Women's Health

Upcoming Program Milestones*:

- **XACIATO™** (clindamycin phosphate) vaginal gel, 2%
  - First commercial sale in 2023
- **Ovaprene®** (hormone-free monthly contraception)
  - Pivotal Phase 3 subject enrollment to begin 4Q-2023
- **Sildenafil Cream, 3.6%** (FSAD/FSIAD)
  - Activities related to psychometric analyses to further refine the measures and resulting endpoints from the exploratory Phase 2b RESPOND study for use in a Phase 3 pivotal study and preparations for data review with FDA
- **DARE-PDM1** (primary dysmenorrhea)
  - Phase 1 study topline data 2023
- IND related activities for **DARE-HRT1** and **DARE-VVA1** and Phase 3 and Phase 2, respectively, clinical study initiation plans

* Anticipated timing

XACIATO™
(Clindamycin Phosphate) Vaginal Gel, 2%

One-time intravaginal administration

XACIATO is indicated for the treatment of bacterial vaginosis in females 12 years and older.
See Full Prescribing Information for the safe and effective use of XACIATO.
See XACIATO selected safety information on slide 24.

ORGANON

Commercialization Collaborator

Bacterial Vaginosis

Daré Innovation: XACIATO™ (Clindamycin Phosphate) Vaginal Gel, 2%*

Clinical Issue

- Recurring infection, difficult to treat effectively
- Most common vaginal condition in women ages 15-44
- Estimated to **affect ~23 million women in the US**[1]
- Bacterial Vaginosis increases health risks[2], including increased risk of preterm birth, sexually transmitted infections, post-surgical infection, and pelvic inflammatory disease that can increase the risk of infertility

Limitations with Rx standards of care

- Bacterial vaginosis is a disruption in the optimal vaginal microbiome and therefore recurrent in many women
- Women experiencing recurrence have three or more episodes in the same year, and may not prefer multiple doses of systemic antibiotics
- **Rx suboptimal:** clinical cure rates of 37-68% **(excluding XACIATO™)**[3]

Target Product Profile

- **Single self-administered dose**, any time of day
- Vaginal delivery of the antibiotic, with minimal systemic exposure
- Colorless, odorless gel
- Demonstrated equivalent cure rates in both women having her first occurrence of bacterial vaginosis as well as those with a history of multiple prior episodes
- Clear labeling for special populations such as pregnant and lactating women

1. https://www.cdc.gov/std/bv/stats.htm and https://www.census.gov/data/datasets/2017/demo/popproj/2017-popproj.html
2. https://www.mayoclinic.org/diseases-conditions/bacterial-vaginosis/symptoms-causes/syc-20352273
3. Bacterial vaginosis 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

XACIATO Overview

- **XACIATO [zah-she-AH-toe]** (clindamycin phosphate) vaginal gel, 2% is a lincosamide antibacterial indicated for the treatment of bacterial vaginosis in female patients 12 years of age and older.
- Daré's first FDA-approved product.
- Organon and Daré are working towards a 2023 U.S. launch as soon as feasible
  - To provide for continuity of supply to support a robust commercial launch, additional manufacturing related activities are being performed, including the production of additional commercial scale batches.
  - Organon market access team meeting with customers to review XACIATO and obtain competitive coverage in the bacterial vaginosis marketplace.
  - Organon will leverage the knowledge and experience of its established NEXPLANON sales team to accelerate XACIATO uptake at launch.
  - Organon believes there is roughly a 90% overlap of healthcare providers who prescribe NEXPLANON and who diagnose and treat BV. Because of the strong relationships the sales team has with these providers, we expect Organon to be well-positioned to inform them about XACIATO on day 1, ultimately providing benefits to patients.

QIDP, Fast Track and Priority Review Designations

NDA Approved December 7, 2021

XACIATO - Commercial License Agreement with Organon

- March 2022 – Organon and Daré announced they entered into an agreement whereby Organon will license global rights to XACIATO.[1] The license became effective June 2022.
- Organon is a global healthcare company formed through a spin-off from Merck & Co., Inc., Rahway, NJ, USA, (NYSE: MRK) known as MSD outside of the United States and Canada, to focus on improving the health of women throughout their lives.

- **Daré received a $10 million upfront payment** in 3Q 2022 and a **$1 million payment in July 2023.**
- Daré is eligible to receive potential milestone payments of **up to $181.8 million and tiered double-digit royalties based on net sales.**

We believe Organon shares our commitment to advance critically needed innovations in women's health. We are excited to be collaborating with one of the premier companies in women's health as we believe that Organon's commercial capabilities will ensure that XACIATO reaches the women most impacted by bacterial vaginosis.

1. https://ir.darebioscience.com/news-releases/news-release-details/organon-enters-global-license-agreement-commercialize-dare

XACIATO Selected Safety Information

- XACIATO is contraindicated in individuals with a history of hypersensitivity to clindamycin or lincomycin.
- Clostridioides difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhea to fatal colitis. Careful medical history is necessary since CDAD has been reported to occur over 2 months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial use not directed against C. difficile may need to be discontinued.
- Polyurethane condoms are not recommended during treatment with XACIATO or for 7 days following treatment. During this time period, polyurethane condoms may not be reliable for preventing pregnancy or for protecting against transmission of HIV and other sexually transmitted diseases. Latex or polyisoprene condoms should be used.
- XACIATO may result in the overgrowth of Candida spp. in the vagina resulting in vulvovaginal candidiasis, which may require antifungal treatment.
- The most common adverse reactions reported in >2% of patients and at a higher rate in the XACIATO group than in the placebo group were vulvovaginal candidiasis and vulvovaginal discomfort.
- XACIATO has not been studied in pregnant women. However, based on the low systemic absorption of XACIATO following the intravaginal route of administration in nonpregnant women, maternal use is not likely to result in significant fetal exposure to the drug.
- There are no data on the effect of clindamycin on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for clindamycin and any potential adverse effects on the breastfed child from clindamycin or from the underlying maternal condition.
- Please see the Prescribing Information, Patient Information, and Instructions for Use.

Ovaprene®

Investigational potential first-in-category, hormone-free, monthly birth control

U.S. Commercialization Collaborator

Phase 3 Development Collaborator

Contraception: Large Market Opportunity

Women in the Reproductive Health & Contraception Market Segment
(over 60 million women)

Population of women 15-44 years by age: US, 2020

Age (years)	US (Percent)	US (Count)
15-19 yrs	15.9	10,266,332
20-29 yrs	34.0	21,918,026
30-39 yrs	34.3	22,159,866
40-44 yrs	15.8	10,199,608
Total	100.0	64,543,832

Sources: US Census Bureau.
Population estimates based on bridged race categories released by the National Center for Health Statistics.
Retrieved June 17, 2020, from www.marchofdimes.org/peristats.

Successful Contraceptive Brands Peak Sales:

Mirena® Hormone IUD
(levonorgestrel-releasing intrauterine system) 52mg
- Physician inserted, long-acting, low/locally delivered hormone IUS
- 2020 worldwide sales: €1.2 billion (Bayer)[1]

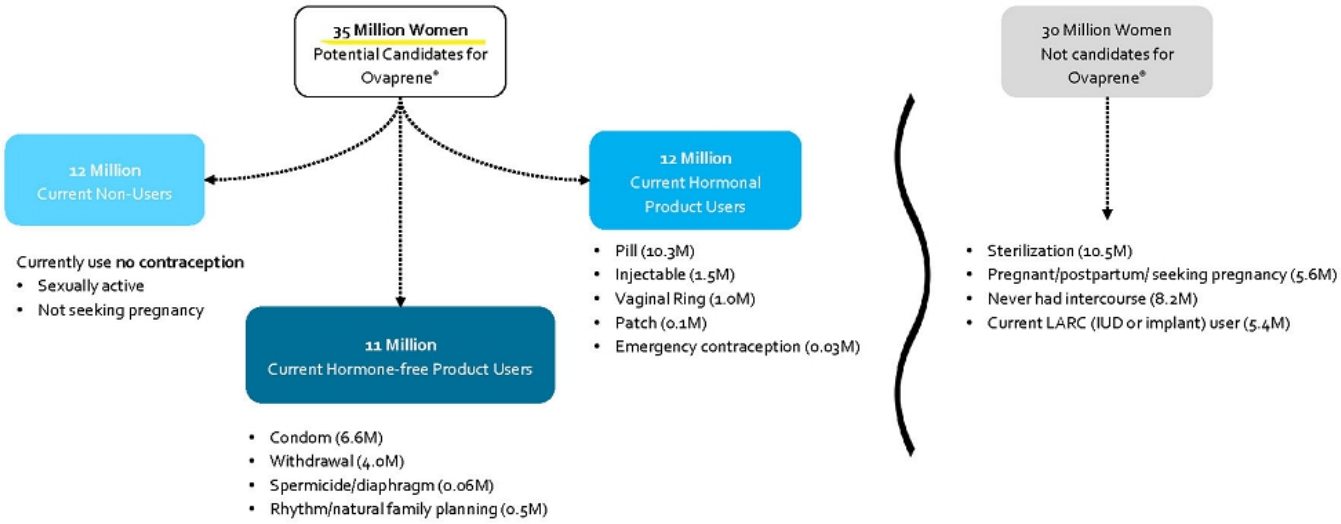
Lo Loestrin Fe

Lo Loestrin®
(norethindrone acetate and ethinyl estradiol, ethinyl estradiol tablets)
- Lowest amount of daily estrogen (10 micrograms) available in pill form
- 2019 US sales: $588 million (Allergan)[2]

NuvaRing®
(etonogestrel/ethinyl estradiol vaginal ring)
- Monthly vaginal ring
- 2018 worldwide sales: $900 million (Merck)[3]

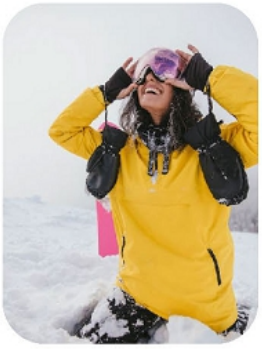
1.https://www.bayer.com/en/bayer-ag-annual-report-2019.pdfx. Includes sales for Mirena®, Kyleena® and Jaydess®/ Skyla®
2.https://www.prnewswire.com/news-releases/allergan-reports-fourth-quarter-and-full-year-2019-financial-results-301001646.html
3.https://www.sec.gov/Archives/edgar/data/0000310158/ 000031015819000014/mrk12312018 10k.htm

Ovaprene® - Potential Market Opportunity[1,2]



1. Market research study conducted in 2019 for Daré Bioscience
2. Contraceptive use data applied to 2019 population data from US Census

Contraception:
What's Missing from Current Hormone-Free Options?



Hormone-free Options	Pregnancies Expected (per 100 women) [1,*]
Spermicides & Vaginal Gels [2]	>27
Condoms (male)	18
Diaphragms (with a spermicide)	12
Easy-to-use monthly option	**Effectiveness approaching hormonal methods**
Copper IUD	<1

Least Effective

Most Effective

1.U.S. Food and Drug Administration. Birth Control Guide dated 6/14/2021: https://www.fda.gov/consumers/free-publications-women/birth-control-chart

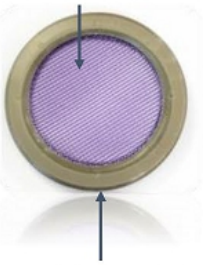
2.U.S. Food and Drug Administration. Drug Data Prescribing Information for a vaginal gel approved in 2020, Phexxi™ provides that in a multicenter, open-label, single-arm clinical trial in the U.S. (AMP002; NCT03243305), the 7-cycle cumulative pregnancy rate was 13.7% (95% CI: 10.0%, 17.5%), excluding cycles with back-up contraception, cycles <21 or > 35 days in length and cycles in which no intercourse was reported. The estimated Pearl Index, calculated based on data from the 7-cycle study, was 27.5 (95% CI: 22.4%, 33.5%). https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208352s000lbl.pdf

* Pregnancy rates tell you the number of pregnancies expected per 100 women during the first year of typical use. Typical use shows how effective the different methods are during actual use (including sometimes using a method in a way that is not correct or not consistent). For more information on the chance of getting pregnant while using a method or on the risks of a specific product, please check the product label or Trussell, J. (2011). "Contraceptive Failure in the United States." Contraception 83(5):397-404.

Ovaprene® Investigational Hormone-Free, Monthly Contraceptive

Physical Barrier [6]

Three-dimensional, knitted polymer barrier



Spermiostatic Environment[6]

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

Desired Features of Birth Control Products:[1-4]	Design Features of Ovaprene:[5-7]
+Efficacy	86% - 91% Expected Typical Use Effectiveness Approaching User-Controlled Hormone Contraception
+Hormone Free	No Hormones in the API Unique dual action MOA (spermiostatic & barrier)
+Convenience	Monthly Ring Form Women choose monthly intravaginal products for the convenience of a non-daily option
+Favorable Side Effect Profile	Safety Profile Similar to a Diaphragm No significant changes in vaginal flora and no serious adverse effects observed in studies to date
+Easily Manage Fertility	No Systemic/Long-term Activity Inserted and removed without a provider allowing for 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):743-63
4.Ersek, J, Matern Child Health J (2011) 15:497–506
5.In PCT studies of similar size, products (diaphragms) that demonstrated no motile sperm in the cervical mucus during PCT assessments later demonstrated "typical use" contraceptive effectiveness of 86-91% in pivotal contraceptive studies evaluating pregnancy rates over six-month periods. Mauck C, Vincent K. Biology of Reproduction, Volume 103, Issue 2, August 2020, Pages 437–444
6.Journal of Reproductive Medicine 2005; 54: 685-690
7.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 2020 - **Bayer,** which markets the $1 billion **Mirena contraceptive franchise,** and Daré announced the execution of a license agreement under which Bayer may commercialize Ovaprene investigational contraceptive in the US once approved by FDA[1].

Mirena* is the #1 prescribed IUD in the U.S.*

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

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

* https://www.mirena-us.com/, supported by 2014-2016 SHS data.
1.https://ir.darebioscience.com/news-releases/news-release-details/bayer-and-dare-bioscience-announce-exclusive-licensing-agreement

Ovaprene® - Collaborative Research Agreement with NIH

- July 2021 – Daré announced that funding and clinical operations support for the Phase 3 will be provided by the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under the CRADA[1]

NIH Cooperative Research and Development Agreement (CRADA) for the Pivotal Phase 3 Study

"This collaboration between Daré and NICHD marks an important milestone in Women's Healthcare Innovation. Women are at the center of everything we do and we are so pleased to continue to partner with Daré in support of our mission We're For Her to provide women with education and access to contraceptive options," ***said John Berrios, Bayer's Head of Women's Healthcare.***

- The pivotal Phase 3 study will be supported by the NICHD's Contraceptive Development Program which oversees the Contraceptive Clinical Trials Network (CCTN) established in 1996 to conduct studies of investigational contraceptives. The Phase 3 study will be conducted within the CCTN with the NICHD's CRO.
- Daré will be responsible for providing clinical supplies of Ovaprene® and coordinating interactions with and preparing and submitting supportive regulatory documentation to the FDA.
- Under the CRADA, Daré also agreed to contribute $5.5 million toward the total estimated cost to conduct the pivotal Phase 3 study. Three payments totaling $5 million have been made. Daré and NICHD are in discussions regarding an amendment to the CRADA.

1. https://ir.darebioscience.com/news-releases/news-release-details/dare-announces-collaborative-research-agreement-crada-pivotal

Ovaprene® - U.S. Regulatory Strategy[1]

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

	Mean *Progressively Motile Sperm*	Median *Progressively Motile Sperm*	Standard Deviation	Interquartile Range
Baseline PCT's	27.21	23.20	17.88	24.80
Ovaprene PCT's	0.48	0.00	1.18	0.10

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

Premarket approval (PMA) strategy

The Center for Devices and Radiological Health (CDRH) as lead review division

Step 1 (Completed)

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

Step 2 (Ongoing)

1. FDA approval of investigational device exemption (IDE) for pivotal study start – Obtained 4Q-2022
2. Review and implement additional FDA study design recommendations
3. Conduct pivotal study - Subject enrollment anticipated 4Q-2023
   - This is a non-comparative study meaning all women will use Ovaprene – *there is no placebo*
   - Target approximately 250 subjects to complete ~12 months (13 menstrual cycles), of use.
   - Primary objective: typical use pregnancy rate over 13 menstrual cycles (estimated Pearl Index)
   - Secondary objectives:
     - 13-cycle typical use cumulative pregnancy rate
     - Safety, acceptability, product fit/ease of use, vaginal health

1 Anticipated regulatory pathway and timelines.
2 Mauck C., Vincent K. Biology of Reproduction, Volume 103, Issue 2, August 2020, Pages 437–444

Sildenafil Cream, 3.6%

Potential First-In-Category treatment for Female Sexual Arousal Disorder (FSAD), and/or Female Sexual Interest/Arousal Disorder (FSIAD), which have no FDA-approved therapies

Novel cream formulation of sildenafil, the **active ingredient in Viagra®**

FSAD/FSIAD – The Clinical Issue & Prevalence

- **Female Sexual Arousal Disorder (FSAD)** is characterized primarily by inability to attain or maintain sufficient genital arousal during sexual activity and, **Female Sexual Interest/Arousal Disorder (FSIAD)** is defined in the DSM-5 as lack of, or significantly reduced, sexual interest/arousal [1]
- Of female sexual function disorders, these conditions are those **most analogous to erectile dysfunction (ED) in men**.
- Arousal disorders in women should be distinguished from a general loss of interest in sexual activity and from other sexual dysfunctions, such as orgasmic disorder (anorgasmia) and hypoactive sexual desire disorder (HSDD), which is characterized in DSM-IV-TR as lack or absence of sexual fantasies and desire for sexual activity for some period of time.[2,3]

- Meta-analysis of 95 studies from 2000-2014 indicated prevalence of Female Sexual Dysfunction in premenopausal women worldwide is 41%, and difficulty with arousal alone is 23%.[4]
- Market research estimates:
- 33% of US women aged 21 to 60 (~ 20 million women), experience symptoms of low or no sexual arousal.[5,6]
- 10 million women are considered distressed and actively seeking treatment.[5]

There are **no FDA-approved treatments** for FSAD/FSIAD

1. Diagnostic and Statistical Manual (DSM) 4th Edition Text Revision (DSM IV TR) defines FSAD 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. As described in the fifth edition of the DSM (DSM 5), which was published in 2013, FSIAD is characterized as lack of, or significantly reduced, sexual interest and/or arousal for at least six months and the symptoms must be severe enough to cause clinically significant distress. Patients could meet the DSM 5 criteria for FSIAD if they predominantly have symptoms of low sexual interest, if they predominantly have symptoms of low sexual arousal, or if they predominantly have symptoms of both low sexual desire and low sexual arousal.
2. https://labs.la.utexas.edu/meston/lab/female-sexual-interest-arousal-disorders/, accessed 8 August 2023
3. https://my.clevelandclinic.org/health/diseases/24640-anorgasmia, accessed 8 August 2023
4. McCool et al. Sex Med Rev 2016;4:197-212. DOI: 10.1016/j.sxmr.2016.03.002
5. Ad Hoc Market Research: FSAD Prevalence Report (Oct 2015) conducted for SST LLC.
6. Based on US Census projections for 2016.

Sildenafil Cream, 3.6% - Product Profile

Topically-administered investigational Sildenafil Cream[1] is…

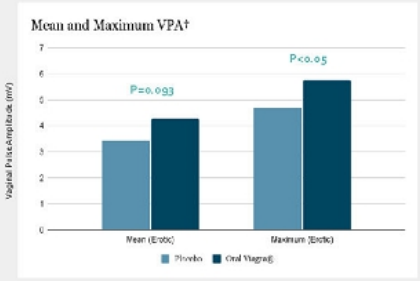
- A PDE5 inhibitor utilized in ED medications for men – ED product **Viagra® peaked at $2.05 billion in sales in 2012**.[2]
- Designed to increase local blood flow to promote improved genital arousal response.
- Applied topically, avoiding hepatic first-pass metabolism response, resulting in lower systemic exposure potentially resulting in reduced side effects vs. oral sildenafil, including Viagra®.
- Given similarities between ED and FSAD, sildenafil - the active ingredient in Viagra® - may improve genital arousal response and overall sexual experience for women as it does in men.
- There are no FDA-approved treatments for FSAD or FSIAD.

1 Sildenafil Cream, 3.6% (formerly SST-6007)
2 https://qz.com/quartz/1298763/its-the-20th-anniversary-of-viagra-heres-how-its-changed-the-world

Oral Sildenafil provided a compelling proof of concept for FSAD/FSIAD

Statistically significant increases in Vaginal Pulse Amplitude (VPA)[1]

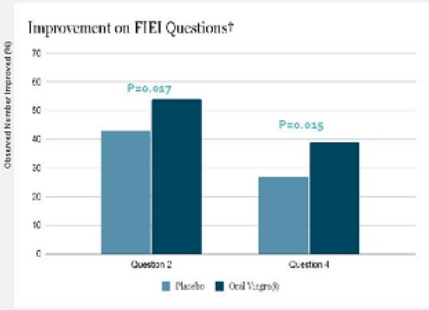
***Pfizer** VPA Clinical Lab Study – Oral Viagra*



† Twelve healthy premenopausal women were studied.

Statistically significant improvement in genital stimulation (FIEI)[2]

***Pfizer** Clinical Field Study – Oral Viagra*



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

Question #4 – "After taking the study medication, intercourse and/or foreplay was: (a) pleasant and satisfying; better than before taking the study medication, (b) unpleasant; worse than before taking study medication, (c) unchanged; no difference, or (d) pleasant; but still not like it used to be or I would like it to be."

202 postmenopausal women with FSAD who had protocol specified estradiol and free testosterone concentrations, and/or were receiving estrogen and/or androgen replacement therapy were studied.

Key Takeaways of Viagra® studies:

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

1.The Enhancement of Vaginal Vasocongestion by Sildenafil in Healthy Premenopausal Women. Journal of Women's Health & Gender-Based Medicine. Vol. 11, No. 4. 2002
2.Safety and Efficacy of Sildenafil Citrate for the Treatment of FSAD: A Double-Blind, Placebo Controlled Study. The Journal of Urology. Vol 170, 2333-2338, December 2003.

Sildenafil Cream, 3.6% - Phase 1 and Phase 2a Study Results

Phase 1 Study of SST-6007 (Sildenafil Cream, 3.6%)[1]

- Normal healthy postmenopausal women were dosed with escalating doses of Sildenafil Cream, 3.6%, using a cross-over study design.
- Sildenafil Cream had significantly lower systemic exposure compared to a 50 mg oral sildenafil dose:
  - AUC – 3-6%
  - Cmax – 1-2%
- Sildenafil Cream was safe and well tolerated at clinically relevant doses (1-2g):
  - Favorable product characteristics as self-reported by subjects
  - Easy to use
  - Readily absorbed

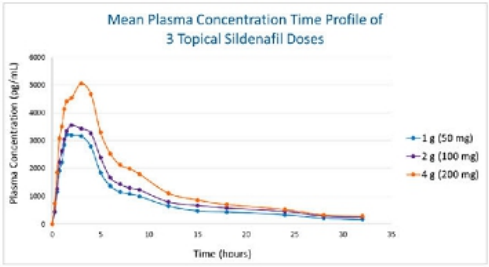
Phase 2a Study of SST-6007(Sildenafil Cream, 3.6%)[1]

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

Phase 1 Study

Parameter	Treatment Level		
	1 g cream (36mg sildenafil), n=20	2 g cream (71mg sildenafil), n=20	4 g cream (142mg sildenafil), n=19
Cmax (ng/mL)	3.61	4.10	5.65
AUC0-t(h*ng/mL)	27.45	33.32	45.33
Tmax (hr)	2.56	2.60	2.42

Phase 1 Study



1. Data on file. Sildenafil Cream, 3.6% was previously known as SST-6007.

Sildenafil Cream, 3.6% - Thermography Study Results*

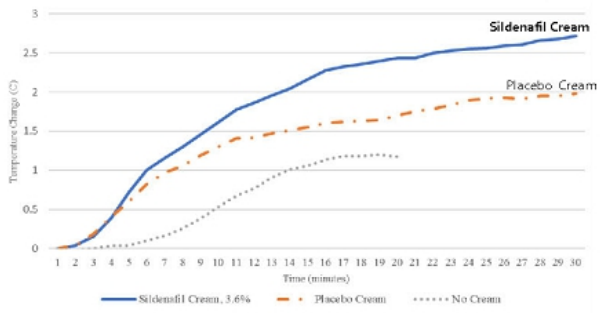
Demonstrated time to effect

(See Figure 1)

- Positive cognitive arousal responses were noted.
- Significantly greater increases in genital temperature after application of Sildenafil Cream compared to placebo cream.
- Significantly greater self-reported arousal responses reported during Sildenafil Cream visits compared to placebo cream visits.

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

Figure 1. Clitoral temperature change during the sexually explicit film



Thermography Study Design & Methodology (N=6)[1]

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

1. Data on file.
* Thermography utilizes sensitive cameras capable of detecting and recording temperature variations over time. Genital temperature changes are a surrogate for genital blood flow.

Sildenafil Cream, 3.6% - Phase 2b RESPOND Study - Overview

Exploratory Phase 2b clinical study designed to evaluate **Sildenafil Cream vs. placebo** over 12 weeks of double-blinded dosing following both a non-drug and placebo run-in period

- Compared Sildenafil Cream vs. placebo used in patients' home setting.
- Co-primary endpoints: patient reported outcome (PRO) instruments measured improvement in localized genital sensations of arousal (**Arousal-Sensation Domain of the Sexual Function Questionnaire**) and reduction in FSAD related distress (**Female Sexual Distress Scale**).
- Secondary endpoint: measured change in the number of **satisfactory sexual events**
- Exploratory endpoints: **Several efficacy endpoints measured and could be candidate endpoints in a Phase 3 study. Efficacy assessments were administered both on an electronic diary to be completed within 24 hours of a sexual event and via 28-day recall assessments**.

Topline data of exploratory Phase 2b RESPOND study announced June 2023.

Sildenafil Cream, 3.6% - Phase 2b RESPOND Study – Highlights

Positive findings from the exploratory Phase 2b RESPOND study of Sildenafil Cream, 3.6% in women with Female Sexual Arousal Disorder **support continued development of Sildenafil Cream and selection of proposed primary endpoint assessments for a Phase 3 study**

- Sildenafil Cream-treated group showed meaningful improvement in the co-primary endpoint assessment that evaluated change from baseline in the Arousal-Sensation Domain of the Sexual Function Questionnaire, although the endpoint did not achieve statistical significance.[1]
- **Sildenafil Cream-treated group also showed improvements** in the secondary endpoint and pre-specified exploratory endpoints that evaluated various aspects of the sexual experience:
  - **Sexual satisfaction**
  - **Arousal lubrication**
  - **Achievement and pleasure of orgasm**
  - **Sexual desire**

Preparing to Request End-of-Phase 2 Meeting with FDA

1.The study did not demonstrate statisitcal significance for the co-primary or secondary efficacy endpoints.

DARE-HRT1

Potential **first-in-category 28-day intravaginal ring** (IVR) combination bio-identical estradiol and bio-identical progesterone menopausal hormone therapy for **treatment of vasomotor symptoms**

There are no FDA approved options with both hormones in one monthly IVR.

Intravaginal Ring (IVR) Technology Highlights

The Vaginal Route of Drug Administration[1]

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

Our IVR Technology Design Features:

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

1 Sonia, T.A. & Sharma, C.P., "Routes of administration of insulin – Vaginal route," Oral Delivery of Insulin, 2014, https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/vaginal-drug-delivery

Vasomotor Symptoms of Menopause

Daré Innovation: DARE-HRT1 Monthly Vaginal Ring

Clinical Issue

- In the US, over 45M women are estimated to be in or approaching menopause; symptoms can last up to 10 years[1]
- ~75% of menopausal women experience hot flashes[2]
- 3 in 5 menopausal women felt that they were adversely affected by symptoms while at work[3]
- 35% of menopausal women reported that they had experienced 4+ symptoms of menopause, but only 44% said they had discussed their symptoms with a doctor[4]

Limitations with current standards of care

- Hormone therapy is the most effective treatment for VMS and other symptoms of menopause according to the North American Menopause Society (NAMS)[5].
- NAMS recommends delivering both estrogen and progesterone, simultaneously, for women with an intact uteri and NAMS states that non-oral routes of administration may offer potential advantages.
- There are no FDA-approved products that combine both estradiol and progesterone in a non-oral monthly form.
- Many treatments do not offer bioidentical hormones to most closely mimic the natural hormones in a woman's body.

Target Product Profile

- A single, non-oral, non-daily, monthly product that can deliver both bioidentical estradiol and progesterone.
- Non-oral routes of administration bypass the liver[5] and may reduce the risk of blood clots[6].
- A vaginal ring is a preferred form factor, due to the convenience, discrete administration, and ease of use [7]. According to a survey of women who switched from an oral contraceptive to an intravaginal ring (IVR), 71% of reported they would continue to use the IVR after the study[8].

[1] https://my.clevelandclinic.org/health/diseases/21861-menopause
[2] https://www.hopkinsmedicine.org/health/conditions-and-diseases/introduction-to-menopause
[3] OPINIUM RESEARCH https://www.vodafone.com/sites/default/files/2021-10/menopause-global-research-report-2021.pdf
[4] https://www.healthyagingpoll.org/reports-more/report/womens-health-sex-intimacy-and-menopause
[5] https://www.menopause.org/docs/default-source/professional/nams-2022-hormone-therapy-position-statement.pdf
[6] https://www.reuters.com/article/us-blood-clot/study-finds-no-blood-clot-risk-with-hormone-patch-idINTRE6BU1Z720101231
[7] Source: Internal Qualitative Market Research, Mar-Apr 2017
[8] Creinin MD, Multicenter comparison of the contraceptive ring and patch: a randomized controlled trial. Obstet Gynecol. 2008;111(2 Pt 1): 267-77.

Menopause – Hormone Therapy Position Paper

NAMS POSITION STATEMENT

2022 hormone therapy position statement of The North American Menopause Society[2]

- Hormone therapy remains the **most effective treatment** for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause and has been shown to prevent bone loss and fracture.
- The risks of hormone therapy differ depending on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used. Treatment should be individualized using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation of the benefits and risks of continuing therapy.
- Non-oral routes of administration (eg, transdermal, vaginal) may offer potential advantages because non-oral routes bypass the first-pass hepatic effect.

3 in 4[1] **Women**

say menopause has interfered with their lives. **64% of women** say they feel unprepared to handle their symptoms.

1. https://www.sri.com/story/menopause-goes-high-tech-understanding-your-menopause-journey-by-leveraging-ai-and-wearable-sensing-technology/
2. https://www.menopause.org/docs/default-source/professional/nams-2022-hormone-therapy-position-statement.pdf

DARE-HRT1*

Completed Phase 1 STUDY [1,2]

- Open-label, 3-arm, parallel group study evaluated the pharmacokinetics (PK) and safety of DARE-HRT1 in healthy postmenopausal women
- First arm received one 28-day DARE-HRT1 IVR (17β2-estradiol (E2) 80 µg/d with progesterone (P4) 4 mg/d); second arm received one 28-day DARE-HRT1 IVR (E2 160 µg/d with P4 8 mg/d); third arm received oral Estrofem (1 mg E2) and Prometrium (100 mg P4) both daily for 29 days
- **PK**: Both DARE-HRT1 IVRs gave similar steady-state concentrations of E2 as seen with drug products approved by the FDA for treatment of VMS and genitourinary symptoms of menopause. The E2 concentrations of this study support the potential of DARE-HRT1, a promising new option for hormone therapy for treatment of VMS and vaginal symptoms associated with menopause.
- **Safety**: Both DARE-HRT1 IVRs were safe and well tolerated. Treatment emergent adverse events were comparable to the referent oral regimen.

Completed Phase 1 / 2 STUDY [3,4]

- Open-label, 2-arm, parallel group study evaluated the safety, PK, preliminary efficacy and usability of DARE-HRT1 IVRs over 12 weeks in 21 healthy postmenopausal women
- Women were randomized (1:1) to either DARE-HRT1 IVR1 (E2 80 µg/d with P4 4 mg/d) or DARE-HRT1 IVR2 (E2 160 µg/d with P4 8 mg/d) and used the IVR for three 28-day cycles, inserting a new IVR monthly.
- **Preliminary Efficacy**: Preliminary local genitourinary syndrome of menopause (GSM) treatment efficacy was supported by significant decreases in vaginal pH and % parabasal cells, and significant increases in the overall vaginal maturation index (VMI) and % superficial cells for both IVR groups (all P values <0.01). Preliminary VMS efficacy was supported by significant decreases in all domains of the Menopause-Specific Quality of Life (MENQOL) questionnaire from baseline for both IVR groups (all P values <0.01). There was significant improvement in hot flashes and night sweats among both IVR groups. Data from this study support further development of DARE-HRT1 for the treatment of menopausal symptoms.
- **Safety and PK**: Both DARE-HRT1 IVRs were safe and released E2 in systemic concentrations, which were in the low, normal premenopausal range. Systemic P4 concentrations predict endometrial protection. Data from this study support further development of DARE-HRT1 for the treatment of menopausal symptoms.

*505(b)(2) regulatory pathway anticipated

1. Hull, et al., (2023) Climacteric, DOI: 10.1080/13697137.2023.2194526
2. Hull, et al., *Menopause* 30 (4): p 427-436, April 2023
3. Thurman, et al., *Menopause* 30 (8): p 817-823, August 2023. DOI: 10.1097/GME.0000000000002210
4. Thurman, et al., *Menopause* 30 (9), 2023. DOI: 10.1097/GME.0000000000002230

DARE-HRT1 - U.S. Regulatory Strategy[1]

- Following clinical development, Daré intends to leverage the existing safety and efficacy data on the active ingredients in DARE-HRT1, estradiol and progesterone, to utilize the FDA's 505(b)(2) pathway to obtain marketing approval of DARE-HRT1 in the U.S.
- Daré intends to seek FDA approval of DARE-HRT1 for the treatment of moderate to severe VMS due to menopause in women with intact uteri.
- Based on pre-IND communications with the FDA and the topline PK data from the DARE-HRT1 Phase 1 / 2 study, **Daré believes FDA approval of DARE-HRT1 for that indication is achievable via the 505(b)(2) pathway supported by a single, placebo-controlled, Phase 3 clinical trial of DARE-HRT1** and a scientifically justified PK "bridge" (via a relative bioavailability trial) between DARE-HRT1 and the selected listed estradiol and progesterone drugs.
- Ongoing activities to support progressing directly into a single Phase 3 study to support registration include manufacturing and non-clinical studies to support the IND submission and the planned IND-opening Phase 3 study.

1.Anticipated regulatory pathway and timelines.

DARE-VVA1

Potential **first-in-category hormone-free vaginal treatment for VVA.**
Proprietary formulation of tamoxifen for intravaginal administration.

There are currently no FDA-approved vaginal hormone-free treatments for VVA.

DARE-VVA1*

Proprietary tamoxifen formulation for intravaginal administration for vulvovaginal atrophy (VVA), a chronic condition characterized by pain during intercourse, vaginal dryness and irritation.

- There are currently no FDA-approved vaginal, hormone-free treatments for VVA.
- Approximately 4 million US women have a history of invasive breast cancer; HR+ is the most common type.[1]
- Localized estrogen therapy for VVA is often contraindicated for women diagnosed with, or at risk of recurrence of, ER-positive and PR-positive breast cancer.
- VVA prevalence in postmenopausal breast cancer survivors is estimated at 42 to 70%.[2]
- There is a clear unmet medical need for an effective non-hormonal treatment for VVA

*505(b)(2) regulatory pathway anticipated.

1. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2022-2024-breast-cancer-fact-figures-acs.pdf
2. Clinical Breast Cancer, Dec 2017. https://www.sciencedirect.com/science/article/pii/S1526820917300552

DARE-VVA1 - Proof of Concept

- This exploratory study[1] 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)
Median Vaginal pH Normal vaginal pH is usually less than 4.5.[2]	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 Lower pH value is a measure of symptom relief
Vaginal Dryness Rated using a visual analogue scale (VAS) that ranged from: 0 = Not bothered by dryness 10 = Extremely bothered by dryness	8.0 range of 7.5 to 9.0	3.0 range 2.0 to 3.0	-5.5 median range -6.0 to -4.5 Decreased vaginal dryness is a measure of symptom relief

In addition, systemic absorption of tamoxifen was not significant:

- After 8 weeks of study treatment with vaginal tamoxifen, 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),[3] 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

DARE-VVA1 Phase 1/2 Study

Completed Phase 1 / 2 Study

***Pharmacokinetics, safety and preliminary pharmacodynamic evaluation of DARE-VVA1: a soft gelatin capsule containing tamoxifen for the treatment of vulvovaginal atrophy*[1]**

Objective:

- This study aimed to measure safety, systemic pharmacokinetics and preliminary efficacy of a vaginal tamoxifen capsule (DARE-VVA1) among postmenopausal women with moderate-to-severe VVA.

Methods:

- This was a randomized, placebo-controlled, double-blind, phase 1/2 study of DARE-VVA1, in four doses (1, 5, 10 and 20 mg).

Results:

- Seventeen women were enrolled and 14 completed the 8-week treatment. DARE-VVA1 was safe.
  - All adverse events were of mild or moderate severity and distributed similarly among active and placebo groups.
  - Plasma tamoxifen concentrations were highest among women using DARE-VVA1 20 mg, but the maximum mean (standard deviation) plasma tamoxifen concentrations on day 1 (2.66 ± 0.85 ng/ml) and day 56 (5.69 ± 1.87 ng/ml) were <14% of those measured after one oral tamoxifen dose.
  - **Active study product users had significant decreases from pre-treatment baseline in vaginal pH and proportion of vaginal parabasal cells** ($p = 0.04$ for both endpoints), with women randomized to the 10 mg or 20 mg dose experiencing the largest treatment impact.
  - The severity of vaginal dryness and dyspareunia decreased significantly from baseline with active study product use ($p = 0.02$ for both endpoints).

Conclusions:

- DARE-VVA1 was safe and resulted in minimal systemic exposure to tamoxifen. Preliminary efficacy data support further development of DARE-VVA1.

1. Thurman, et al., *Climacteric* (2023) https://doi.org/10.1080/13697137.2023.2211763

DARE-CIN

(formerly R-131-2)

Potential **first-in-category non-surgical, pharmaceutical intervention for the treatment of CIN2+.**
Proprietary fixed-dose formulation of lopinavir and ritonavir in a soft gel vaginal insert.

There are currently no FDA-approved, pharmaceutical interventions for the treatment of CIN2+.

DARE-CIN* (formerly R-131-2, lopinavir/ritonavir vaginal insert)

DARE-CIN is a proprietary fixed-dose formulation of lopinavir and ritonavir in a soft gel vaginal insert being developed for the treatment of CIN, also referred to as cervical dysplasia, and other HPV-related pathologies.

- There are currently no FDA-approved, pharmaceutical interventions for the treatment of cervical intraepithelial neoplasia (CIN) grade 2 or greater (CIN2+).
- Human papillomavirus, or HPV, is the most common sexually transmitted infection (STI) in the United States. About 80% of women will get at least one type of HPV at some point in their lifetime.[1]
  - About 250,000 to 1 million women in the U.S. get diagnosed with cervical dysplasia each year. The condition occurs most often among women of childbearing age, particularly aged 25 to 35.[2]
- A persistent HPV infection is a prerequisite for development of most CIN and cervical cancer.
  - Together, HPV types HPV-16, HPV-18, HPV-45, HPV-31, and HPV-33 account for ~85% of invasive cervical cancer worldwide.[3]
- In the United States, in 2016, an estimated 196,000 cases of CIN2+ were diagnosed.[4]
  - For CIN2+, the only FDA-approved intervention is a loop electrosurgical excision procedure (LEEP).
- The key value proposition for DARE-CIN is that it is a pharmacological approach in CIN2+, to avoid LEEP surgery.
  - A LEEP procedure uses a wire loop heated by electric current to remove cells and tissue in a woman's lower genital tract and is generally considered an effective treatment but may have negative long-term effects on a woman's fertility (preterm birth).[5]

*505(b)(2) regulatory pathway anticipated.

1. https://www.womenshealth.gov/a-z-topics/human-papillomavirus#:~:text=Genital%20HPV%20is%20the%20most,79%20million%20Americans%20have%20HPV. &text=It%20is%20so%20common%20that,some%20point%20in%20their%20lifetime.
2. https://my.clevelandclinic.org/health/diseases/15678-cervical-intraepithelial-neoplasia-cin#:~:text=How%20common%20is%20cervical%20dysplasia,particularly%20aged%2025%20to%2035.
3. Skinner, et al. Int J Cancer. 2016 May 15; 138(10): 2428–2438. https://doi.org/10.1002/ijc.29971
4. McClung, et al. MMWR Morb Mortal Wkly Rep 2019;68:337–343. DOI: http://dx.doi.org/10.15585/mmwr.mm6815a1
5. https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/loop-electrosurgical-excision-procedure-leep

Proof of Concept

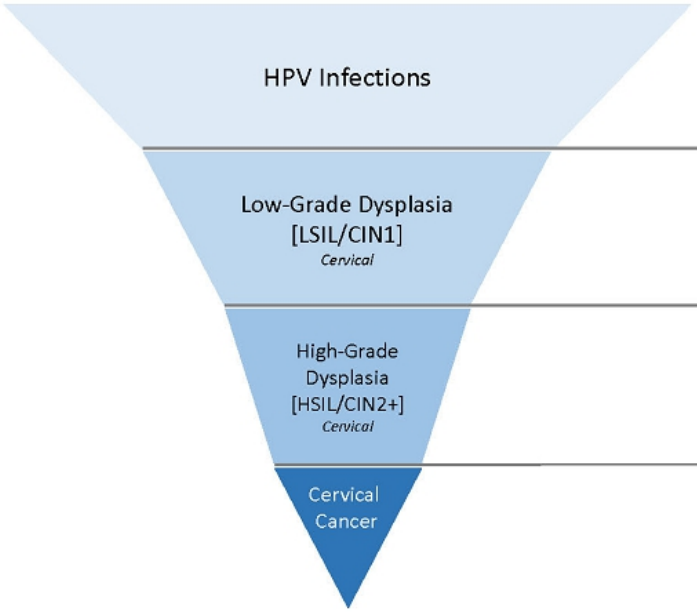
- A Single-Arm, Proof-Of-Concept Trial of Lopinavir/Ritonavir[1] as a Treatment for HPV-Related Pre-Invasive Cervical Disease.[2]
- A total of 23 women with HSIL‡ were treated with lopinavir/ritonavir during which time no adverse reactions were reported.
  - A maximum concentration of 10 ng/ml of lopinavir was detected in patient plasma 1 week after starting treatment.
  - HPV was no longer detected in 12/23 (52.2%, 95%CI: 30.6–73.2%).
  - Post-treatment cytology at 12 weeks on women with HSIL, showed 14/22 (63.6%, 95%CI: 40.6–82.8%) had no dysplasia and 4/22 (18.2%, 95%CI: 9.9–65.1%) were now low grade demonstrating a combined positive response in 81.8% of women of which 77.8% was confirmed by histology.
  - These data are supported by colposcopic images, which show regression of cervical lesions.
- These results demonstrate the potential of lopinavir/ritonavir as a self-applied therapy for HPV infection and related cervical lesions.

‡ HSIL = (CIN2/3)

*505(b)(2) regulatory pathway anticpated

1. Lopimune soft gel capsules (133 mg lopinavir/33 mg ritonavir) for vaginal insertion
2. Hampson L., et al. (2016) PLoS ONE 11(1): e0147917. doi:10.1371/journal.pone.0147917

HPV Associated Conditions In the United States



HPV Infections[1]
- ~42.5 M Americans infected with HPV
- ~13 M new infections annually

Low-Grade Dysplasia[2]
- ~1.5 M women diagnosed annually

High-Grade Dysplasia[3]
- 196,000 CIN2+ cases annually (74% were women aged 18–39 years)

Cervical Cancer[4]
- ~14,000 cases annually

1. Estimated prevalence and incidence in 2018. CDC STI Fact Sheet (2021) https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/2018-STI-incidence-prevalence-factsheet.pdf
2. Chang, et al. Vaccine 27 (2009) 4355–4362. https://noelbrewer.web.unc.edu/wp-content/uploads/sites/16987/2018/10/2009_Chang.pdf
3. Based on estimated 2016 cases. McClung, et al. MMWR Morb Mortal Wkly Rep 2019;68:337–343. DOI: http://dx.doi.org/10.15585/mmwr.mm6815a1
4. Based on American Cancer Society's estimated new cases for 2023 (Jan 12, 2023). https://www.cancer.org/content/dam/CRC/PDF/Public/8599.00.pdf

Phase 1 & Phase 1-Ready Programs
Preclinical Programs

Advancing Products Women Want

Phase 1 & Phase 1 Ready Programs

DARE-PDM1^
Primary Dysmenorrhea
Phase 1 Study Commenced

1. First-in-category treatment for primary dysmenorrhea.
2. Proprietary hydrogel formulation of diclofenac for vaginal administration.
3. Alternative to oral nonsteroidal anti-inflammatory drugs and hormonal contraceptives, which often can produce undesirable side effects.

There are currently no FDA-approved vaginal diclofenac treatment options for primary dysmenorrhea.

DARE 204/214^
6 & 12-Month Injectable Contraception
Phase 1 Study Preparation

Novel 6 & 12-month injectable formulations of etonogestrel being developed as a longer-acting, reversible method of contraception with a more predictable return to fertility.

There are currently no FDA-approved injectable contraceptives available indicated for 6-12 months protection.

DARE-FRT1/PTB1^
Pregnancy Maintenance
Phase 1 Study Preparation

1. First-in-category progesterone delivery for pregnancy maintenance including the prevention of preterm birth (DARE-PTB1) and for luteal phase support as part of an IVF regimen (DARE-FRT1).
2. IVR designed to release bio-identical progesterone up to 14 days.
3. Alternative to daily IM injections or vaginal gel.

There are currently no FDA-approved products marketed in the U.S. that do not require daily dosing of progesterone.

Preclinical Programs

DARE-LARC1^
Long-Acting, Reversible Personal Contraceptive System

Levonorgestrel-releasing, long-acting contraceptive implant that a woman can turn on and off herself, according to her own needs. Grant of up to $4 8.95 M to advance technology through non-clinical proof of principle to enable IND submission, and an NIH grant to explore device insertion/removal in non-clinical studies.

There are currently no FDA-approved contraceptive implants available that allow one to remotely pause and resume dosing.

DARE-GML
Novel Antimicrobial Glycerol Monolaurate

A naturally occurring fatty acid monoester that has shown broad antimicrobial activity, killing bacteria, fungi, and viruses, and represents a new class of antimicrobials.

GML has the potential to be a first-in-category multi-target antimicrobial agent.

DARE-LBT
Novel hydrogel formulation for delivery of live biotherapeutics

Novel hydrogel formulation for delivery of live biotherapeutics to support vaginal health such as for administration following effective primary infection treatment to rebalance the vaginal microbiota disrupted by the infection.

Grant-funded program.

There are currently no FDA-approved live biotherapeutics for vaginal health.

DARE-RH1
Male or Female Contraceptive Target

A potential new rapidly reversible, non-hormonal contraceptive solution with application for women and men.

There are currently no FDA-approved contraceptives available that target sperm hypermotility required for implantation.

DARE-PTB2
Prevention and Treatment of Idiopathic Preterm Birth

Proof-of-concept target validation studies in support of a potential new approach for the prevention and treatment of idiopathic preterm birth.

There are currently no marketed FDA-approved products indicated for the prevention of preterm birth

^505(b)(2) regulatory pathway anticipated.

DARE-PDM1*

Proprietary hydrogel formulation of diclofenac for vaginal administration. Alternative to oral nonsteroidal anti-inflammatory drugs (NSAIDs) and hormonal contraceptives, which often can produce undesirable side effects.

- There are currently no FDA-approved vaginal diclofenac treatment options for primary dysmenorrhea.
- Market research suggests that the global market for dysmenorrhea treatment was estimated to be valued at USD $13 billion in 2022 and that the size of this market is expected to increase to USD $28.5 billion by the year 2029[1]
- Primary dysmenorrhea is defined as painful menstruation in women with normal pelvic anatomy, typically described as cramping pain in the lower abdomen before or during the menstrual period. Primary dysmenorrhea usually begins during adolescence and is a leading cause of recurrent short-term school absence in adolescent girls and a common problem in women of reproductive age.[2]
  - According to the American College of Obstetricians and Gynecologists' Committee on Adolescent Health Care, dysmenorrhea is the most common menstrual symptom among adolescent girls and young women, and most adolescents experiencing dysmenorrhea have primary dysmenorrhea.[3]
  - Prevalence rates of dysmenorrhea vary but range from 50% to 90%.[3]
  - A prospective study of college students found that 72% of monitored periods were painful, most commonly during the first day of menses, and 60% of the women studied reported at least one episode of severe pain.[4]

By incorporating diclofenac into our proprietary hydrogel for vaginal administration, we believe we can provide a treatment option that addresses the pain-related symptoms of the condition while minimizing side effects commonly seen with use of oral NSAIDs.

*505(b)(2) regulatory pathway anticipated. Daré has not had any communications with the FDA regarding the specific marketing approval requirements for DARE-PDM1

1 - https://www.reanin.com/report-store/healthcare/pharmaceuticals-and-therapeutics/dysmenorrhea-treatment/global-dysmenorrhea-treatment-market

2 - https://www.aafp.org/pubs/afp/issues/2005/0315/p1885.html

3 - https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/12/dysmenorrhea-and-endometriosis-in-the-adolescent

4 - https://www.aafp.org/pubs/afp/issues/1999/0801/p489.html

DARE-FRT1 and DARE-PTB1*

Grant funding NIH National Institutes of Health

Bio-identical progesterone up to 14-day IVR for prevention of preterm birth and luteal phase support as part of an IVF treatment plan.
There are currently no FDA-approved products marketed in the U.S. that do not require daily dosing of progesterone.

Prevention of Preterm Birth (PTB)

- After steadily declining from 2007 to 2014[1], the US premature birth rate rose for the fourth straight year in 2018 with ~10% of babies born preterm (<37 weeks).[2]

NIH Grant Funding for PTB Program

- Potential for up to $2.3 million in NIH grant funding to support DARE-PTB1 development
- Notice of award for initial $300,000 in grant funding announced Aug 2020. Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health Award Number R44 HD101169.

Assisted Reproductive Technologies (ART)/IVF

- As women wait longer to have children, infertility risk increases
- ~12-15% of couples cannot conceive after 1-year of unprotected sex.[3]
- ~20% of US women have their first child after age 35; ~1/3 of couples in which the woman is older than 35 years have fertility problems.[4]

- Current products for delivery of progesterone for prevention of preterm birth, as well as luteal phase support in ART, are limited to daily vaginal or intramuscular injectable dosage forms, which have limitations in patient comfort, convenience, and outcomes.
- The IVR is designed to deliver bio-identical progesterone continuously over an up to 14-day period and is being developed as a more convenient treatment option for the prevention of preterm birth (DARE-PTB1) and broader luteal phase support as part of an in vitro fertilization regimen (DARE-FRT1).

*505(b)(2) regulatory pathway anticipated.

1 2019 March of Dimes Report Card, https://www.marchofdimes.org/mission/reportcard.aspx
2 CDC's National Center for Health Statistics, National Vital Statistics Reports, Births: Final Data for 2018, Nov 27, 2019, https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf
3 https://www.nichd.nih.gov/health/topics/infertility/conditioninfo/common accessed January 8, 2021
4 https://www.cdc.gov/reproductivehealth/infertility/index.htm accessed January 8, 2021

DARE 204/214*

Grant funding NIH National Institutes of Health

Novel 6 & 12-month injectable formulations of etonogestrel being developed as a longer-acting, reversible method of contraception with a more predictable return to fertility.

- There are currently no FDA-approved injectable contraceptives available indicated for 6 & 12 months of protection.
- The only approved injectable contraceptive product in the U.S. is DEPO-PROVERA CI (medroxyprogesterone acetate) injectable suspension, which is indicated as every 3 months (13 weeks) administered by deep, intramuscular injection in the gluteal or deltoid muscle.[2]

Some of the **limitations with DEPO-PROVERA** include the following:[2,3]

1. Requires an injection 4 times per year.
2. Unpredictable return to fertility. After stopping Depo-Provera, the median time to conception for those who do conceive is 10 months following last injection (range is 4 to 31 months).
3. Research suggests that Depo-Provera and Depo-SubQ Provera 104 might cause a loss of bone mineral density. This loss might be especially concerning in teens who haven't reached their peak bone mass. And it's not clear whether this loss is reversible. Thus, Depo-Provera is not indicated for longer term use (i.e. more than 2 years).

The target product profile potential for DARE204/214 are 6- and 12- month formulations, minimizing the number of injections required per year, and with a predictable return to fertility relative to the 6- or 12- month contraceptive window. API is etonogestrel which does not have same black box warning regarding bone loss as medoxyprogesterone acetate.[4]

~65M women in U.S. are in the reproductive health and contraception market segment[1]

*505(b)(2) regulatory pathway anticipated. Daré has not had any communications with the FDA regarding the specific marketing approval requirements for DARE-204/214.

1 - CDC National Survey for Family Growth, 2013-2015 dataset, cdc.gov.
2 - https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/e2046s016lbl.pdf
3 - https://www.mayoclinic.org/tests-procedures/depo-provera/about/pac-20392204#:~:text=Among%20the%20things%20to%20consider,birth%20control%20method%20for%20you
4 - https://www.organon.com/product/usa/pi_circulars/n/nexplanon/nexplanon_pi.pdf

DARE-LARC1*

Grant funding foundation grant NIH National Institutes of Health

- Long-Acting, Reversible Personal Contraceptive System – levonorgestrel-releasing implant drug delivery system designed to store and precisely deliver hundreds of therapeutic doses over years that a woman can turn on and off herself, according to her own needs, without further healthcare provider intervention.
- There are currently no FDA-approved contraceptive implants available that allow one to remotely pause and resume dosing.

*505(b)(2) regulatory pathway anticipated. Daré has not had any communications with the FDA regarding the specific marketing approval requirements for DARE-LARC1

DARE-GML

Glycerol monolaurate (GML) is a naturally occurring fatty acid monoester that has shown broad antimicrobial activity, killing bacteria, fungi and viruses, and represents a new class of antimicrobial agents. **GML has the potential to be a first-in-category multi-target antimicrobial**.

- Bacterial vaginosis and vulvovaginal candidiasis represent the two most common vaginal infections in the United States, leading to over 30 million treatment visits per year [1,2]

Women often experience multiple episodes of vaginal infection in a year, and treatments for one condition may increase the likelihood of developing another condition.[3] GML has multiple properties that make it an attractive active pharmaceutical ingredient (API) to potentially treat and/or prevent vaginal infections of various sources.

1. Proven activity against the key culprit microbial species (Gardnarella and Candida) that cause most vaginal infections[4]
2. Potential to inhibit bacterial biofilm formation and disrupt already formed biofilms[5]
3. Unique microbicidal mechanism of action, targeting bacterial surface signal signaling by plasma membrane disruption, potentially preventing development of microbial resistance[5]

GML has been shown both *in vitro* and in women to reduce both bacterial and fungal colonization without affecting the healthy bacteria that maintain vaginal health[4] and has also been shown *in vivo* to inhibit viral transmission.[6]

1. https://www.cdc.gov/std/bv/stats.htm
2. Benedict K, Jackson BR, Chiller T, Beer KD. Estimation of direct healthcare costs of fungal diseases in the United States. Clin Infect Dis. 2018 Sep 10.
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3827168/
4. Antimicrob Agents Chemother. 2010 Feb;54(2):597-601
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3194780/
6. 2009. Glycerol monolaurate prevents mucosal SIV transmission. Nature;458:1034-1038.

DARE-LBT

Grant funding foundation grant

Novel hydrogel formulation for delivery of live biotherapeutics to support vaginal health.
There are currently no FDA-approved live biotherapeutics for vaginal health.

- Grant from the **Bill & Melinda Gates Foundation for $584,986** to support activities related to development of a vaginal thermosetting gel formulation for the delivery of live biotherapeutics that can be reconstituted at the point of care.

Vaginal health conditions, **such as bacterial vaginosis, remain prevalent and serious problems** that can negatively impact a woman's quality of life and create economic burden for women, employers, and the broader healthcare system.

- Scientific evidence suggests that there may be benefits to following an effective primary bacterial infection treatment with administration of live bacterial cultures to rebalance the vaginal microbiota disrupted by the infection. It is believed that addressing the vaginal dysbiosis by reconstituting the vaginal microbiota could reduce recurrence and reduce susceptibility to other infections and conditions, including sexually transmitted infections and preterm labor and birth.
- A barrier to development of live biotherapeutic products for vaginal administration in low- and middle-income countries is the identification of a delivery vehicle capable of maintaining the viability of the live microbes during product storage, shipment and distribution.

If successful, the formulation could be carried forward for further development as a delivery vehicle with potential to enhance the availability of novel therapeutics for vaginal health in the United States and worldwide, including in countries with varying climatic conditions and/or where extended storage may be required.

DARE-PTB2

Grant funding NIH National Institutes of Health

Proof-of-concept target validation studies in support of a new approach for the prevention and treatment of idiopathic PTB. There are currently no marketed, FDA-approved products indicated for the prevention of preterm birth.

- Grant from the **Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH)** to support activities related to the conduct and completion of proof-of-concept target validation studies in support of a potential new approach for the prevention and treatment of idiopathic preterm birth.

Preterm birth is defined as a live birth before 37 completed weeks of gestation.[1,2] Premature babies often have serious health problems. These problems can vary in severity and the earlier a baby is born, the higher the risk of health-related complications, including difficulty maintaining normal body temperature, difficulty breathing or feeding, and susceptibility to severe infections and brain disorders.[2,3]

According to the World Health Organization (WHO), **an estimated 13.4 million babies were born preterm in 2020**.[4] Preterm birth complications were responsible for the deaths of approximately 900,000 children in 2019 and complications from preterm birth are the leading cause of death among children under 5 years of age.[4]

1. March of Dimes PeriStats™, Preterm Birth, accessed 28 July 2023. https://www.marchofdimes.org/peristats/data?reg=99&slev=4&top=3
2. Mayo Clinic, Diseases & Conditions, Premature birth, accessed 28 July 2023. https://www.mayoclinic.org/diseases-conditions/premature-birth/symptoms-causes/syc-20376730
3. WHO, Newsroom, Questions and answers, Newborn health: Challenges facing preterm babies, accessed 28 July 2023. https://www.who.int/news-room/questions-and-answers/item/newborn-health-challenges-facing-preterm-babies
4. WHO, Newsroom, Fact sheets, Detail, Preterm birth, accessed 28 July 2023. https://www.who.int/news-room/fact-sheets/detail/preterm-birth

DARÉ
IN ITALIAN, IT MEANS "TO GIVE."
IN ENGLISH, IT MEANS "TO BE BOLD."

Women

At Daré Bioscience, women's health is ***Our Sole Focus***.
Innovation in women's health needs to be a priority.
We are working hard to identify and advance new therapies that provide additional choices and improve outcomes so that we can make a difference in the lives of women everywhere.

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