



Daré Bioscience Announces New Development Program, DARE-PDM1, as a Potential First-in-Category Treatment for Primary Dysmenorrhea

December 12, 2022

DARE-PDM1 Utilizes Proprietary Hydrogel Technology for Vaginal Delivery of Diclofenac, a Nonsteroidal Anti-Inflammatory; Phase 1 Study Targeted for 2023

2022 Daré Portfolio Accomplishments Include:

*Two Additional Portfolio Programs (DARE-GML and grant-funded DARE-LBT);
License Agreement with Organon to Commercialize XACIATO™;
Ovaprene® IDE Approval for Pivotal Contraceptive Efficacy Study;
Positive Phase 1/2 Data for both DARE-HRT1 and DARE-VVA1*

2023 Anticipated Milestones Include:

*XACIATO First Commercial Sale;
Sildenafil Cream, 3.6% for Female Sexual Arousal Disorder Phase 2b Topline Data;
Ovaprene Pivotal Study Recruitment; DARE-PDM1 Phase 1 Study*

SAN DIEGO, Dec. 12, 2022 (GLOBE NEWSWIRE) -- Daré Bioscience, Inc. (NASDAQ: DARE), a leader in women's health innovation, today announced a new development program targeted at treating primary dysmenorrhea by delivering the active pharmaceutical ingredient diclofenac, a nonsteroidal anti-inflammatory drug (NSAID), in a novel way. Daré's new investigational product, DARE-PDM1, will deliver diclofenac vaginally via the Company's proprietary hydrogel technology. A Phase 1 study of DARE-PDM1 is targeted for 2023. Because there are currently no FDA-approved vaginal diclofenac treatment options for primary dysmenorrhea, DARE-PDM1 has the potential to be a first-in-category product. Following clinical development, Daré intends to leverage the existing safety and efficacy data for diclofenac to utilize the U.S. Food and Drug Administration's (FDA) 505(b)(2) pathway to obtain marketing approval of DARE-PDM1 in the U.S.

"Calendar 2022 has been an incredibly successful year for our portfolio in terms of:

- 1) expanding our portfolio with additional differentiated product candidates that we believe further our leadership as an accelerator of innovative products in women's health;
- 2) securing a global commercialization collaboration for our first FDA-approved product, XACIATO (clindamycin phosphate) vaginal gel, 2%, a single-dose prescription medication for the treatment of bacterial vaginosis in females 12 years of age and older, which is the second commercial collaboration agreement for our portfolio (the first was entered into with Bayer in 2020 for Ovaprene); and
- 3) demonstrating clinical success (such as with DARE-HRT1 and DARE-VVA1) and advancing regulatory and clinical development to enable important 2023 milestones (such as the Sildenafil Cream Phase 2b topline data targeted for 2Q-2023 and Ovaprene pivotal study recruitment initiation targeted for mid-2023)," said Sabrina Martucci Johnson, President and CEO of Daré Bioscience.

"As a company, we are committed to addressing unmet needs in women's health. We believe that we have assembled a robust portfolio in women's health and that all of our programs have the opportunity to be either first-line or first-in-category, or both," Johnson added. "It is our belief that prioritizing women's health is not only good for the many women lacking effective or convenient therapeutic choices, but also for a broad set of stakeholders, because contraception, fertility, and vaginal and sexual health, our areas of focus, are compelling markets impacting millions of women and we have seen that innovation in these areas has led to commercially successful brands. Specifically, we find these market research statistics compelling: Only approximately 1% of healthcare research is invested in female-specific conditions beyond oncology, and women's health conditions outside of oncology comprise less than 2% of the current healthcare pipeline. Yet, women's health products outside of oncology make up 27% of the total number of blockbuster products (products that each have over \$500 million in annual sales) and contribute 35% of the total sales dollars generated by blockbuster products. This is why we believe investment in women's health will be efficient and disproportionately impactful in terms of translating dollars invested in R&D to ultimate revenue generated, and therefore, not only good for the 50% of the population to whom these products are targeted, but also a good business model."

About Primary Dysmenorrhea and DARE-PDM1

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. Recent market research suggests that the global market for dysmenorrhea treatment is estimated to be valued at USD \$11 billion and that the size of this market is expected to increase to USD \$25 billion by the year 2028. 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. Prevalence rates of dysmenorrhea vary but range from 50% to 90%. 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.

"Utilizing the same hydrogel technology found in XACIATO, and consistent with our portfolio of differentiated and novel product candidates, we are developing DARE-PDM1 to address a critical unmet medical need in women's health," said Dr. Annie Thurman, Medical Director of Daré Bioscience.

"The most common interventions for primary dysmenorrhea include oral NSAIDs and hormonal contraceptives which often can produce undesirable side effects. 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," continued Dr. Thurman.

Portfolio Updates Previously Announced in 2022:

XACIATO™ (clindamycin phosphate) vaginal gel, 2%, FDA-approved for treatment of bacterial vaginosis in females 12 years of age and older

Bacterial vaginosis is the most common cause of vaginitis worldwide and is estimated to affect approximately 21 million women in the U.S. The condition results from an overgrowth of bacteria, which upsets the balance of the natural vaginal microbiome and can lead to symptoms of odor and discharge.

In June, Daré [announced](#) that the exclusive license agreement entered into in March 2022 with [Organon](#) (NYSE: OGN), a global women's healthcare company, became fully effective. Under the agreement, Organon licensed global rights to XACIATO. Under the license agreement Daré received a \$10 million cash payment from Organon after the license became effective. Daré is eligible to receive potential milestone payments of up to \$182.5 million as well as tiered double-digit royalties based on net sales. Launch preparation activities are ongoing and the first commercial sale of XACIATO is anticipated in the first half of 2023 in the U.S.

Ovaprene® - investigational hormone-free monthly intravaginal contraceptive

In October, Daré [announced](#) that the FDA approved an Investigational Device Exemption (IDE) application allowing Daré to proceed with a single arm, open-label pivotal contraceptive efficacy study of Ovaprene. The multi-center, single arm, non-comparative, pivotal Phase 3 study will evaluate Ovaprene's effectiveness as a contraceptive device along with its safety and usability. If successful, Daré expects the pivotal study to support marketing approvals of Ovaprene in the U.S. and other countries. The Ovaprene investigator meeting for the pivotal study took place in December and initiation of recruitment for the study is targeted for mid-2023.

In January 2020, Daré and Bayer [announced](#) an exclusive licensing agreement for U.S. commercial rights to Ovaprene. Under the agreement, Daré received an upfront payment and access to Bayer's extensive clinical, regulatory, manufacturing and commercial expertise while retaining control over Ovaprene's development and regulatory approval process. Bayer received the right to obtain exclusive rights to commercialize the product in the U.S. following completion of the pivotal clinical trial being undertaken by Daré. If Bayer, in its sole discretion, makes payment to Daré of \$20 million, which Daré intends to apply to reimbursement of clinical study costs, then the exclusive license to commercialize Ovaprene in the U.S. will become effective. Daré will also be entitled to receive commercial milestone payments potentially totaling \$310 million, in addition to double digit tiered royalties on net sales.

If Ovaprene is approved by the FDA, it could be the first monthly non-hormonal contraceptive product for women and a first-in-category option for women seeking a hormone-free, self-administered and monthly birth control method.

Sildenafil Cream, 3.6% - investigational treatment for female sexual arousal disorder

In a joint communication released in November of this year, Daré and its development partner, Strategic Science and Technologies, LLC, [reported](#) that subject screening for the exploratory Phase 2b RESPOND clinical study of Sildenafil Cream, 3.6% had completed, allowing for a topline data announcement target of 2Q-2023. The Phase 2b RESPOND clinical study is a multi-center, double-blind, placebo-controlled study to evaluate the efficacy and safety of Sildenafil Cream, 3.6% in premenopausal patients with female sexual arousal disorder (FSAD). Approximately 160 to 170 subjects in total are expected to complete the study for inclusion in the topline data assessment targeted for 2Q-2023.

Sildenafil Cream is a proprietary topical formulation of sildenafil, a phosphodiesterase-5 (PDE-5) inhibitor, being developed as a first-in-category option for the treatment of FSAD. FSAD is the inability to reach or maintain a sufficient physical response to sexual stimulation and, of the various types of female sexual dysfunction disorders, FSAD is most analogous to erectile dysfunction (ED) in men. Sildenafil is the active ingredient in a tablet for oral administration currently marketed under the brand name Viagra® for the treatment of ED in men. Market research suggests that 16% of women in the U.S. ages 21 to 60, or approximately 10 million women, are distressed from experiencing symptoms associated with FSAD, including lack of or low sexual arousal, and are actively seeking solutions to improve their condition. For context on the potential market opportunity for an FDA-approved treatment for FSAD, the prevalence of complete ED in men is estimated to be about 5% of men at age 40, increasing to about 15% at age 70.

If clinical development is successful, Sildenafil Cream, 3.6% has the potential to be the first FDA-approved FSAD treatment option.

DARE-HRT1 & DARE-VVA1 Phase 1/2 data

In April, Daré [announced](#) the initiation of a Phase 1/2 clinical study of DARE-HRT1, a novel, investigational intravaginal ring (IVR) designed to deliver bio-identical 17β-estradiol and bio-identical progesterone continuously over a 28-day period as part of a hormone therapy (HT) regimen following menopause. HT is used to treat the vasomotor symptoms (VMS) and genitourinary syndrome associated with menopause. Positive efficacy results from this study were [announced](#) in October, including statistically significant results for improvement in both the vasomotor and vaginal symptoms of menopause. Daré anticipates that the topline pharmacokinetics (PK) data from the study will be available and reported later in the fourth quarter of 2022.

"The levels of estradiol released from both the lower and higher dose formulations of DARE-HRT1 achieved statistically significant improvement in VMS as well as the genitourinary symptoms of menopause, and vaginal pH and maturation index," said David Friend PhD, Chief Scientific Officer of Daré Bioscience. "DARE-HRT1 also had a high level of acceptability in the study, with 100% of subjects reporting that the IVR was comfortable to wear and no reports of expulsion during use and over 95% of subjects stated they would be either somewhat or very likely to use the IVR for a women's health condition or unrelated disease if needed."

The North American Menopause Society's (NAMS) guidance on hormone therapy states that dosing estrogen and progestogen in combination may offer important benefits to women, and NAMS observed that non-oral routes of administration may offer advantages over orally administered therapies.

DARE-HRT1 has the potential to be the first FDA-approved monthly IVR delivering both estrogen and progestogen hormone therapy.

Positive topline results from a Phase 1/2 clinical study of DARE-VVA1 were also [announced](#) this year, in November. The Phase 1/2 study evaluated different doses of DARE-VVA1, a tamoxifen vaginal insert, in 17 postmenopausal women with vulvar and vaginal atrophy (VVA). DARE-VVA1 is an investigational, proprietary formulation of tamoxifen for intravaginal administration with the potential to be a first-in-category treatment of VVA for women with or at-risk of hormone receptor-positive (HR+) breast cancer. Tamoxifen is a well-known and well-characterized selective estrogen receptor modulator (SERM) that has been prescribed by oncologists for decades for the treatment of breast cancer. In breast tissue, tamoxifen acts as an estrogen antagonist. In contrast, in other tissues such as vaginal tissues, tamoxifen has been reported to exert an estrogen-like response on vaginal cytology.

The DARE-VVA1 study was a randomized, multi-center, double-blind, parallel-arm, placebo-controlled, dose-ranging study that evaluated the safety, tolerability, plasma PK and pharmacodynamics (PD) of DARE-VVA1. Eligible participants were randomly allocated to one of five treatment groups (approximately 4 participants per group) that evaluated four dose levels (1 mg, 5 mg, 10 mg, and 20 mg) and a placebo. Following a screening visit, DARE-VVA1 was self-administered intravaginally once a day for the first two weeks, and then twice a week for the following six weeks for a total treatment period of 56 days. Intravaginal administration of DARE-VVA1 was well tolerated and all treatment emergent adverse events were mild or moderate and equally distributed between participants randomized to study drug treatment versus placebo. DARE-VVA1 demonstrated improvements in vaginal cytology parameters and self-assessed most bothersome symptoms of VVA (vaginal dryness or pain with intercourse) that support ongoing development.

VVA is a common condition in postmenopausal women as well as women diagnosed with, or with a history of, HR+ breast cancer, who often report VVA as one of the most unpleasant side effects of their cancer treatment. The prevalence of VVA in postmenopausal breast cancer patients is estimated to be between 42 and 70 percent. Products containing estrogen are commonly used to treat VVA. However, the use of estrogen-containing products for the treatment of VVA is often contraindicated for HR+ breast cancer patients and survivors because of the concern that estrogen use will promote recurrence of disease.

There are currently no FDA-approved products labeled for VVA treatment for patients with or at risk of recurrence of HR+ breast cancer.

New Portfolio Candidates – DARE-LBT and DARE-GML

DARE-LBT - novel hydrogel formulation for delivery of live biotherapeutics

In November, Daré [announced](#) it received a grant of \$584,986 to support activities related to development of a vaginal thermosetting gel formulation that can be reconstituted at the point of care for the 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. 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 or where extended storage may be required. There are currently no FDA approved live biotherapeutics for vaginal health.

DARE-GML - novel antimicrobial glycerol monolaurate

In August, Daré [announced](#) it entered into a license agreement with Hennepin Life Sciences LLC under which Daré acquired the exclusive global rights to develop and commercialize treatments delivering the novel antimicrobial glycerol monolaurate (GML) intravaginally for a variety of vaginal health conditions including bacterial, fungal, and viral infections. 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 antimicrobials. GML has the potential to be a first-in-category multi-target antimicrobial agent.

About Daré Bioscience

Daré Bioscience is a biopharmaceutical company committed to advancing innovative products for women's health. The company's mission is to identify, develop and bring to market a diverse portfolio of differentiated therapies that prioritize women's health and well-being, expand treatment options, and improve outcomes, primarily in the areas of contraception, fertility, and vaginal and sexual health.

Daré's first FDA-approved product, XACIATO™ (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, which is under a global license agreement with Organon. XACIATO is a clear, colorless, viscous gel, to be administered once intravaginally as a single dose. Daré's portfolio also includes potential first-in-category candidates in clinical development: Ovaprene®, a novel, hormone-free monthly intravaginal contraceptive whose U.S. commercial rights are under a license agreement with Bayer; Sildenafil Cream, 3.6%, a novel cream formulation of sildenafil to treat female sexual arousal disorder utilizing the active ingredient in Viagra®; and DARE-HRT1, a combination bio-identical estradiol and progesterone intravaginal ring for hormone therapy following menopause. To learn more about XACIATO, Daré's full portfolio of women's health product candidates, and Daré's mission to deliver differentiated therapies for women, please visit www.darebioscience.com.

Daré may announce material information about its finances, product and product candidates, clinical trials and other matters using the Investors section of its website (<http://ir.darebioscience.com>), SEC filings, press releases, public conference calls and webcasts. Daré will use these channels to distribute material information about the company, and may also use social media to communicate important information about the company, its finances, product and product candidates, clinical trials and other matters. The information Daré posts on its investor relations website or through social media channels may be deemed to be material information. Daré encourages investors, the media, and others interested in the company to review the information Daré posts in the Investors section of its website and to follow these Twitter accounts: @SabrinaDareCEO and @DareBioscience. Any updates to the list of social media channels the company may use to communicate information will be posted in the Investors section of Daré's website.

Forward-Looking Statements

Daré cautions you that all statements, other than statements of historical facts, contained in this press release, are forward-looking statements. Forward-looking statements, in some cases, can be identified by terms such as "believe," "may," "will," "estimate," "continue," "anticipate," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would," "contemplate," "project," "target," "objective," or the negative version of these words and similar expressions. In this press release, forward-looking statements include, but are not limited to, statements relating to plans and expectations with respect to Daré's product candidates, including anticipated timing for commencement and conduct of clinical trials and clinical trial data readouts, potential regulatory approval pathways, potential for FDA approval based on a single pivotal clinical study, and potential to be first-line and/or first-in-category products, expectations regarding the commercial launch of XACIATO in the U.S., expectations regarding commercial

collaborations and potential payments under commercial collaboration agreements, expectations regarding market potential for women's health products outside of oncology, expectations regarding potential for investment in women's health product candidates to be efficient and disproportionately impactful in terms of translating dollars invested in research and development to sales revenue, and expectations regarding Daré's business model. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause Daré's actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements in this press release, including, without limitation: Daré's ability to develop, obtain FDA or foreign regulatory approval for, and commercialize its product candidates and to do so on communicated timelines; failure or delay in starting, conducting and completing clinical trials of a product candidate; Daré's ability to design and conduct successful clinical trials, to enroll a sufficient number of patients, to meet established clinical endpoints, to avoid undesirable side effects and other safety concerns, and to demonstrate sufficient safety and efficacy of its product candidates; Daré's dependence on third parties to conduct clinical trials and manufacture and supply clinical trial material and commercial product; Daré's ability to raise additional capital when and as needed to advance its product candidates, execute its business strategy and continue as a going concern; the loss of, or inability to attract, key personnel; the effects of the COVID-19 pandemic, macroeconomic conditions and geopolitical events on Daré's operations, financial results and condition, and ability to achieve current plans and objectives, including the potential impact of the pandemic on Daré's ability to timely enroll, conduct and report results of its clinical trials and on the ability of third parties on which Daré relies to assist in the conduct of its business to fulfill their contractual obligations to Daré; the risk that positive findings in early clinical and/or nonclinical studies of a product candidate may not be predictive of success in subsequent clinical and/or nonclinical studies of that candidate; the risk that developments by competitors make Daré's product or product candidates less competitive or obsolete; difficulties establishing and sustaining relationships with development and/or commercial collaborators; failure of Daré's product or product candidates, if approved, to gain market acceptance or obtain adequate coverage or reimbursement from third-party payers; Daré's ability to retain its licensed rights to develop and commercialize a product or product candidate; Daré's ability to satisfy the monetary obligations and other requirements in connection with its exclusive, in-license agreements covering the critical patents and related intellectual property related to its product and product candidates; Daré's ability to adequately protect or enforce its, or its licensor's, intellectual property rights; the lack of patent protection for the active ingredients in certain of Daré's product candidates which could expose its products to competition from other formulations using the same active ingredients; product liability claims; governmental investigations or actions relating to Daré's product or product candidates or the business activities of Daré, its commercial collaborators or other third parties on which Daré relies; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; cyber attacks, security breaches or similar events that compromise Daré's technology systems or those of third parties on which it relies and/or significantly disrupt Daré's business; and disputes or other developments concerning Daré's intellectual property rights. Daré's forward-looking statements are based upon its current expectations and involve assumptions that may never materialize or may prove to be incorrect. All forward-looking statements are expressly qualified in their entirety by these cautionary statements. For a detailed description of Daré's risks and uncertainties, you are encouraged to review its documents filed with the SEC including Daré's recent filings on Form 8-K, Form 10-K and Form 10-Q. You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date on which they were made. Daré undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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