Daré Bioscience Announces Publication in Menopause: The Journal of The North American Menopause Society of Data from Phase 1 Trial of DARE-HRT1 that Support the Potential of DARE-HRT1 as an Effective Hormone Therapy for both Vasomotor and Vaginal Symptoms

January 26, 2023

Daré Plans to Advance DARE-HRT1 into Single Phase 3 Efficacy Trial for Treatment of Vasomotor Symptoms (VMS) due to Menopause

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

SAN DIEGO, Jan. 26, 2023 (GLOBE NEWSWIRE) -- Daré Bioscience, Inc. (NASDAQ: DARE), a leader in women's health innovation, today announced the publication of data from a Phase 1 trial evaluating the pharmacokinetics of DARE-HRT1, an 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 regimen, in the journal *Menopause*, which is the journal of the North American Menopause Society. Daré previously reported positive topline results from this study, as well as from a subsequent Phase 1 / 2 clinical trial of DARE-HRT1. The journal article entitled "Evaluation of 28-Day Estradiol and Progesterone Vaginal Rings in a Phase 1 Clinical Pharmacokinetic Study" is available at the *Menopause* journal's website in the Latest Articles section.

Hormone therapy is used to treat the vasomotor symptoms (VMS) and genitourinary syndrome associated with menopause. DARE-HRT1 has the potential to be the first FDA-approved product to offer vaginal delivery of combination bio-identical estradiol and bio-identical progesterone hormone therapy in a convenient monthly format. Daré plans to advance DARE-HRT1 into a single Phase 3 clinical trial to support a new drug application for DARE-HRT1 for the treatment of moderate to severe VMS due to menopause in women with intact uteri.

"We are excited to have this peer-reviewed article published in the North American Menopause Society's journal as we believe that the delivery of hormone therapy over 28-days utilizing a novel intravaginal ring which requires no daily action on the part of the patient, or the provider, supports DARE-HRT1's potential to be a first-in-category, convenient non-oral and non-daily option for women suffering from menopausal symptoms," said Sabrina Martucci Johnson, President and CEO of Daré Bioscience.

"The North American Menopause Society believes that hormone therapy is the most effective treatment for VMS and the genitourinary symptoms of menopause and has stated that a non-oral route of administration may offer potential advantages over oral routes of administration. If successful, DARE-HRT1 could be the first product approved to continuously deliver non-oral hormone therapy with both estradiol and progesterone together over multiple weeks," said David Friend PhD, Chief Scientific Officer for Daré Bioscience. "In this open-label, three-arm study, the DARE-HRT1 IVRs were able to demonstrate steady-state plasma concentrations of estradiol similar to those seen with drug products approved by the FDA for treatment of VMS and genitourinary symptoms of menopause."

The IVR technology used in DARE-HRT1 was developed by Dr. Robert Langer from the Massachusetts Institute of Technology and Dr. William Crowley from Massachusetts General Hospital and Harvard Medical School. Unlike other IVR technologies, Daré's IVR drug delivery technology is designed to release more than one active ingredient via a solid ethylene vinyl acetate polymer matrix without the need for a membrane or reservoir to contain the active drug or to control the release, allowing for sustained drug delivery.

Thirty-two (32) healthy postmenopausal women, with an average age of 57 years, were recruited at two Australian sites to participate in this open-label, three arm study. The first arm received one DARE-HTR1 ring for 28 days designed to release 17β-estradiol (E2) at a rate of 80 µg/day and progesterone (P4) at 4mg/day. The second arm received an alternative DARE-HRT1 ring for 28 days releasing E2 at 160 µg/day and P4 at 8mg/day. The third arm received both oral Estrofem (1mg E2) and Prometrium (100 mg P4) daily for 29 days. Blood samples were taken predose then intensively over the first day (day 1) and periodically thereafter over the remaining 27 days. After removal of the DARE-HRT1 rings on the morning of day 29, intensive samples were collected. Similar procedures were conducted with women enrolled in the oral group. The plasma samples were analyzed for E2, estrone (E1), and P4 using validated bioanalytical methods.

DARE-HRT1 505(b)(2) Regulatory Pathway

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 U.S. Food and Drug Administration's (FDA) 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.

About Menopause

Menopause is defined as the final menstrual period and is typically confirmed after a woman has missed her period for 12 consecutive months. Most women experience menopause between ages 40 and 58.[1] An estimated 45 million women in the U.S. are approaching or in menopause, which results in a decrease in estrogen and other hormones.[1,2] Hot flashes, vaginal dryness and loss of bone density are frequently associated with menopause.

Night sweats (hot flashes that occur during sleep) often cause sleep disturbance, and vaginal atrophy (the drying and thinning of vaginal tissues) can cause a feeling of vaginal tightness during sex along with pain, burning, or soreness.[1] Hence, management of menopausal symptoms can impact quality of life, productivity and health. The North American Menopause Society (NAMS) believes that hormone therapy is the most effective treatment for VMS and the genitourinary syndrome of menopause and observes that a non-oral route may offer potential advantages over oral routes of administration because non-oral routes bypass the first-pass hepatic effect.[2]

1. Menopause 101: A primer for the perimenopausal. NAMS, accessed 6 January 2023. http://www.menopause.org/for-women/menopauseflashes/menopause-symptoms-and-treatments/menopause-101-a-primer-for-the-perimenopausal.
2. NAMS Position Statement. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause: The Journal of The North American Menopause Society* Vol. 29, No. 7, pp. 767-794 DOI: 10.1097/GME.0000000000002028. https://www.menopause.org/docs/default-source/professional/nams-2022-hormone-therapy-position-statement.pdf

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 DARE-HRT1's potential as a safe and effective hormone therapy for symptoms of menopause, DARE-HRT1's potential to be the first FDA-approved monthly IVR product delivering both estrogen and progestogen hormone therapy for symptoms of menopause, the importance of the results of the Phase 1 and Phase 1 / 2 clinical studies to Daré and DARE-HRT1, the anticipated regulatory approval pathway for DARE-HRT1, and the potential for FDA approval of DARE-HRT1 for the treatment of moderate to severe VMS due to menopause in women with intact uteri based on a single Phase 3 clinical trial together with study data that establishes a scientific bridge to the selected listed drugs. 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: 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; 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; the risk that development of a product candidate requires more clinical or nonclinical studies than Daré anticipates, or that the duration of a study or number of study subjects must be significantly greater than anticipated; 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 such as inflation, rising interest rates 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 commence, 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 impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; 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.

Contacts:

Investors on behalf of Daré Bioscience, Inc.:
Lee Roth
Burns McClellan
lroth@burnsmc.com
212.213.0006

OR

Media on behalf of Daré Bioscience, Inc.:
Jake Robison
Evoke Canale
jake.robison@evokegroup.com
619.849.5383

Source: Daré Bioscience, Inc.

Source: Daré Bioscience, Inc.