Daré Bioscience Announces Positive Pharmacokinetic (PK) Results from the DARE-HRT1 Phase 1 / 2 Study that Support the Potential of DARE-HRT1 as an Effective Hormone Therapy for both Vasomotor and Vaginal Symptoms of Menopause

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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. 09, 2023 (GLOBE NEWSWIRE) -- Daré Bioscience, Inc. (NASDAQ: DARE), a leader in women's health innovation, today announced topline PK results from its Phase 1 / 2 clinical trial of DARE-HRT1 that support the potential of DARE-HRT1 as an effective hormone therapy (HT) based on the levels of hormones released. DARE-HRT1 is 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 HT regimen. HT 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.

"The delivery of hormone therapy over a 12-week study via a 28-day intravaginal ring which requires no daily intervention supports DARE-HRT1's potential to be a first-in-category option, offering ease-of-use and consistent dosing to women suffering from menopausal symptoms. There are currently no FDA-approved products that continuously deliver hormone therapy with both estradiol and progesterone together over multiple consecutive weeks," said Dr. Annie Thurman, Medical Director of Daré Bioscience. "We believe these Phase 1 / 2 topline data support progressing directly into a single Phase 3 study following the Investigational New Drug (IND) submission to and clearance from the FDA."

Previously reported topline efficacy data from the Phase 1 / 2 study demonstrated improvement in both VMS as well as vaginal symptoms of menopause. 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.

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.

Data from a prior randomized, open-label, three-arm, parallel group Phase 1 study that evaluated the PK of DARE-HRT1 in approximately 30 healthy, post-menopausal women with intact uteri demonstrated that DARE-HRT1 successfully delivered both estradiol and progesterone over the 28-day evaluation period. The estradiol PK data in that prior DARE-HRT1 Phase 1 study support the potential of DARE-HRT1 as an effective hormone therapy for both VMS and vaginal symptoms associated with menopause.

DARE-HRT1 Phase 1 / 2 Clinical Trial Study Design

The randomized, open-label, two-arm, parallel group Phase 1/2 study was designed to evaluate DARE-HRT1's safety, PK, and preliminary efficacy in improving the VMS as well as the vaginal symptoms of menopause in approximately 20 healthy, post-menopausal women (age range 51-65 years, mean 59 years) with intact uteri over approximately three consecutive months of use. The primary objective of the study was to describe the safety, tolerability, and PK of two different dose combinations (estradiol 80 µg/progesterone 4 mg IVR and estradiol 160 µg/progesterone 8 mg IVR) over 12 weeks of use. Secondary objectives of the study were to assess the usability, participant tolerability, and preliminary effectiveness of DARE-HRT1 for both the VMS and vaginal symptoms of menopause.

The study was conducted by Daré's wholly owned subsidiary in Australia.

Topline Results of the Phase 1 / 2 Clinical Trial

Topline data from the study demonstrate that DARE-HRT1 successfully delivered estradiol and progesterone over the 12-week evaluation period. The baseline-corrected steady state release of estradiol and progesterone from both the lower (IVR1) and higher (IVR2) dose versions of DARE-HRT1 evaluated in the study demonstrated steady state release levels in month 3 of the 12-week study as shown in the table below:

	Steady State C_{avg} (standard deviation)
DARE-HRT1 IVR1 (n=11)	
Estradiol	22.17 (4.47) pg/mL
Progesterone	1.25 (0.34) ng/mL
DARE-HRT1 IVR2 (n=10)	
Estradiol	38.97 (10.79) pg/mL

Progesterone	1.80 (0.28) ng/mL

The levels of estradiol released from both the lower and higher dose formulation of DARE-HRT1 evaluated in the study achieved or exceeded the levels that were targeted for hormone therapy. Target levels of estradiol for hormone treatment for either the VMS or vaginal symptoms of menopause were established by reviewing PK levels published for FDA-approved products for both the treatment of VMS as well as the genitourinary symptoms of menopause. Based on the estradiol PK data in the DARE-HRT1 Phase 1 / 2 study, the results support the potential of DARE-HRT1 as an effective hormone therapy for both VMS and vaginal symptoms associated with menopause. The levels of progesterone released from both versions of DARE-HRT1 evaluated in the study met the objectives of releasing progesterone. Progesterone is used in hormone therapy to reduce the impact of estrogen on nontarget sites, such as the endometrium, to prevent estrogen-induced endometrial hyperplasia.

The levels of estradiol released from both the lower and higher dose formulation of DARE-HRT1 evaluated in the study achieved statistically significant improvement in VMS as well as the genitourinary symptoms of menopause, and vaginal pH and maturation index.

Menopausal symptoms, including hot flashes and night sweats, were reduced compared with baseline in both DARE-HRT1 dose groups ($p<0.01$). Participants also showed significant improvement from baseline in all measures surveyed on The Menopausal Quality of Life Survey (MENQOL), which surveys not only parameters of VMS, but also physical, psychosocial and sexual symptoms ($p<0.01$ on all domains). With DARE-HRT1 use, vaginal pH significantly decreased compared to baseline ($p<0.01$) and cytologic tests of the vaginal epithelium (vaginal maturation index) showed significant normalization (all p values <0.01 for increases in superficial cells, increases in intermediate cells and decreases in parabasal cells from baseline) among all participants. Finally, the most common genitourinary symptom, vaginal dryness, which was reported by 70% of participants at baseline, showed significant improvement in both DARE-HRT1 groups ($p<0.01$) and this subset also experienced significant decreases in vaginal pain with DARE-HRT1 use ($p<0.01$).

The study treatment was well tolerated with the types of most common adverse events consistent with other vaginal products. There were only two early discontinuations due to an adverse event, and no serious adverse events were reported.

DARE-HRT1 had a high level of acceptability in the study, with 100% of subjects reporting that the IVR was comfortable to wear, and there were no reports of the IVR being expelled from the vagina during use. Additionally, 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.

Daré plans to submit data from the Phase 1 / 2 clinical study of DARE-HRT1 for publication in a peer-reviewed publication.

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 advantages over oral routes of administration.[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 Phase 1 / 2 clinical study results 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.

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