Daré Bioscience Announces Positive Phase 1 Results for DARE-HRT1

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Results Support Potential as the First Monthly Therapy for both the Vasomotor and the Vaginal Symptoms of Menopause

The First Clinical Study Using the Novel Segmented Intravaginal Ring (IVR) Technology Validates its Potential to Provide a Versatile Convenient Drug Delivery Solution

SAN DIEGO, June 28, 2021 (GLOBE NEWSWIRE) -- Daré Bioscience, Inc. (NASDAQ:DARE), a leader in women's health innovation, today announced positive topline results from its Phase 1 clinical trial of DARE-HRT1. DARE-HRT1 is a novel 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 to treat the vasomotor symptoms (VMS) and genitourinary syndrome associated with menopause. The topline data from the study support DARE-HRT1's 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 to treat both VMS as well as vaginal symptoms of menopause. The North American Menopause Society's guidance on hormone therapy includes 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 demonstrated the ability to deliver two different active pharmaceutical ingredients, in this case two bio-identical hormones, reliably over a 28-day period. Generating positive topline data in our first Phase 1 study utilizing our novel IVR technology represents an important clinical achievement for Daré and for the IVR platform," said Sabrina Martucci Johnson, President and CEO of Daré Bioscience. "For some women, hormone therapy is a highly effective treatment for the symptoms associated with menopause, such as hot flashes and vaginal dryness, and may also prevent bone loss and fracture. The delivery of hormone therapy over 28 consecutive days with 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."

"We are highly encouraged by these Phase 1 data as they demonstrate DARE-HRT1's ability to achieve our dual release objectives," said David Friend, PhD, Chief Scientific Officer of Daré Bioscience. "In addition to delivering hormone therapy, we believe the IVR technology used in DARE-HRT1 is an important platform technology with the potential to offer a versatile vaginal drug delivery solution to address a variety of unmet needs in women's health through its ability to release one or more drugs at desired rates over time and with the added benefit of convenience."

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 vaginal ring 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.

DARE-HRT1 Phase 1 Clinical Trial Study Design

The randomized, open-label, three-arm, parallel group Phase 1 study was designed to evaluate the pharmacokinetics (PK) of DARE-HRT1 in approximately 30 healthy, post-menopausal women with intact uteri. The primary objective of the study was to describe the PK parameters of two different dose combinations over 28 days. Secondary objectives of the study were to assess the safety and tolerability of DARE-HRT1 and to compare the systemic exposure of estradiol (the active form for therapeutic hormone therapy purposes), estrone, and progesterone of DARE-HRT1 over 28 days against a daily combination of FDA-approved oral estrogen and oral progesterone products evaluated in the Phase 1 study.

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

Topline Results of the Phase 1 Clinical Trial

Data from the study demonstrate that DARE-HRT1 successfully delivered estradiol and the progesterone over the 28-day 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 over 28 days as shown in the table below:

	Steady State (Standard Deviation)
DARE-HRT1 IVR1 (n=10)	
Estradiol	20.6 (16.8) pg/mL
Progesterone	1.32 (0.20) ng/mL
DARE-HRT1 IVR2 (n=11)	
Estradiol	32.5 (9.3) pg/mL
Progesterone	2.23 (0.61) 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 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.[2]

In addition, the study treatment was well tolerated with the most common adverse events consistent with other vaginal products. There was only one early discontinuation due to an adverse event, which was found to be unrelated to study treatment or participation, and no serious adverse events were reported. The proportion of participants reporting adverse events was similar across all dose groups, the two DARE-HRT1 groups as well as the group receiving a daily combination of FDA-approved oral estrogen and oral progesterone products, with 89% of adverse events mild in severity and all other adverse events (11%) rated as moderate.

DARE-HRT1 had a high level of acceptability in the study, with over 80% of subjects on the lower and higher dose versions of DARE-HRT1 reporting the IVR as comfortable or very comfortable. Additionally, over 80% of subjects in each IVR dose group stated they were either somewhat or very likely to use the IVR for a women's health condition or disease if needed.

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

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.

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.[3] An estimated 45 million women in the U.S. are approaching or in menopause, which results in a decrease in estrogen and other hormones.[1,3] 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.[3] 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.[1]

1. The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017 Jul;24(7):728-753. DOI: 10.1097/GME.0000000000000921
2. Kuhl, H. (2005) Pharmacology of estrogens and progestogens: influence of different routes of administration. *Climacteric,* 8:sup1, 3–63. DOI: 10.1080/13697130500148875
3. Menopause 101: A primer for the perimenopausal. NAMS, accessed 25 June 2021. http://www.menopause.org/for-women/menopauseflashes/menopause-symptoms-and-treatments/menopause-101-a-primer-for-the-perimenopausal.

About Daré Bioscience

Daré Bioscience is a clinical-stage biopharmaceutical company committed to the advancement of 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 expand treatment options, improve outcomes and facilitate convenience for women, primarily in the areas of contraception, vaginal health, sexual health, and fertility.

Daré's product portfolio includes potential first-in-category candidates in clinical development: Ovaprene®, a novel, investigational 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®; DARE-BV1, a unique hydrogel formulation of clindamycin phosphate 2% to treat bacterial vaginosis via a single

application; and DARE-HRT1, a combination bio-identical estradiol and progesterone intravaginal ring for hormone therapy following menopause. To learn more about Daré's full portfolio of women's health product candidates, and mission to deliver differentiated therapies for women, please visit www.darebioscience.com.

Daré may announce material information about its finances, 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 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 on the investor relations page of Daré's website mentioned above.

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," "tend to," 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 monthly therapy for VMS and vaginal symptoms of menopause, the potential of Daré's IVR technology to provide a platform for development of other vaginally delivered therapies, the importance of the Phase 1 clinical study results to Daré, DARE-HRT1 and the IVR platform, and the anticipated regulatory approval pathway for DARE-HRT1. 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 future results, performance or achievements expressed or implied by the forward-looking statements in this press release, including, without limitation, risk and uncertainties related to: the risk that topline results from a clinical trial, including the Phase 1 study of DARE-HRT1, are based on Daré's preliminary analysis of key data and, following a comprehensive review of study data, such results may change and topline results may not accurately reflect the complete results from the clinical trial; the risk that the FDA, other regulatory authorities or members of the scientific or medical communities may not accept or agree with Daré's interpretation of or conclusions regarding the study data; Daré's ability to raise additional capital when and as needed to advance its product candidates and continue as a going concern; the effects of the COVID-19 pandemic 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, including its clinical trials, to fulfill their contractual obligations to Daré; Daré's ability to develop, obtain regulatory approval for, and commercialize its product candidates; the failure or delay in starting, conducting and completing clinical trials or obtaining FDA or foreign regulatory approval for Daré's product candidates in a timely manner; 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; 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 candidates less competitive or obsolete; failure of Daré's product candidates, if approved, to gain market acceptance or obtain adequate coverage from third-party payers; Daré's ability to retain its licensed rights to develop and commercialize a 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 candidates; Daré's failure to timely establish or leverage third-party partnerships or collaborations to commercialize its product candidates, if approved; Daré's dependence on third parties to conduct clinical trials and manufacture clinical trial material; 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; cyberattacks, 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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