Daré Bioscience Announces Positive Topline Data from the Exploratory Phase 2b RESPOND Study of Sildenafil Cream, 3.6% in Women with Female Sexual Arousal Disorder

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Sildenafil Cream-treated patients showed meaningful improvement in the co-primary endpoint assessment that evaluated change from baseline in the Arousal-Sensation Domain of the Sexual Function Questionnaire

Sildenafil Cream-treated patients also showed improvements in the secondary endpoint and pre-specified exploratory endpoints that evaluated sexual satisfaction, arousal lubrication, and achievement and pleasure of orgasm

Data support continued development of Sildenafil Cream and selection of proposed primary endpoint assessments for a Phase 3 study

Sildenafil Cream has the potential to be the first FDA-approved treatment for female sexual arousal disorder

SAN DIEGO, June 05, 2023 (GLOBE NEWSWIRE) -- Daré Bioscience, Inc. (NASDAQ: DARE), a leader in women's health innovation, and its collaborator Strategic Science & Technologies, LLC (SST), a Cambridge, MA based novel topical drug delivery company, today announced positive topline data from the exploratory Phase 2b RESPOND study evaluating topical Sildenafil Cream, 3.6% (Sildenafil Cream) as a treatment for female sexual arousal disorder (FSAD). The exploratory study was designed to test the sensitivity of several patient reported outcome (PRO) efficacy endpoints and their ability to determine a treatment effect of Sildenafil Cream compared to placebo to inform the ongoing development of Sildenafil Cream. The study also served as a validation study of exploratory endpoints that could be candidate endpoints in a Phase 3 study of Sildenafil Cream. Although the exploratory study was underpowered to assess statistical significance, certain endpoints achieved statistical significance.

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, a phosphodiesterase-5 (PDE-5) inhibitor, is the active ingredient in a tablet for oral administration currently marketed under the brand name Viagra® for the treatment of ED in men. Sildenafil Cream is an investigational proprietary topical cream formulation of sildenafil specifically designed to increase blood flow to the genital tissue in women. If development is successful, Sildenafil Cream has the potential to be the first FDA-approved treatment for FSAD. 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. In comparison, 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.

"We are very pleased with the topline data from the Phase 2b RESPOND study. Although the study was underpowered to assess statistical significance, we saw statistically significant results for certain of the endpoints, and the data indicate that, as compared to placebo, Sildenafil Cream had a therapeutic effect based on several PROs," said Sabrina Martucci Johnson, President and CEO of Daré Bioscience. "Because there are currently no FDA-approved treatments for FSAD, there are no efficacy endpoints that have been previously approved for use in a Phase 3 pivotal study for potential treatment for FSAD – but with the data from the Phase 2b RESPOND study we believe certain of the primary, secondary, and exploratory endpoints could be candidate endpoints in a Phase 3 study of Sildenafil Cream. Having now completed this pioneering work in the field of FSAD, we look forward to reviewing the data with the FDA, including discussing the data from assessments as early as the 4- and 8-week mark after randomization, and continuing the development of Sildenafil Cream, including our objective of initiating the first ever Phase 3 pivotal study for the treatment of FSAD. Following clinical development, Daré intends to leverage the existing safety and efficacy data on the active ingredient in Sildenafil Cream to utilize the FDA's 505(b)(2) pathway to obtain marketing approval of Sildenafil Cream in the U.S."

"The FDA has not approved any pharmacologic options for FSAD, a condition which significantly compromises a woman's ability to have a pleasurable sexual experience," commented Dr. Sheryl Kingsberg, Division Chief of Behavioral Medicine, Department of OBGYN, University Hospitals Cleveland Medical Center, Ohio, and Past President of The International Society for the Study of Women's Sexual Health, as well as co-editor of the Textbook of Female Sexual Function and Dysfunction: Diagnosis and Treatment. "Based on the topline data from the Phase 2b RESPOND study I am very excited about the potential for this topical Sildenafil Cream to address this critical unmet need in women's sexual health. Leveraging the known therapeutic benefit of the active ingredient in Viagra®, sildenafil, in a cream formulation to stimulate increased blood flow to the genital tissue, Sildenafil

Cream may offer women a safe, effective and ‘on demand' solution to difficulties with sexual arousal allowing for a more intense and enjoyable sexual experience."

Unlike the oral formulations of PDE-5 inhibitors, Sildenafil Cream is designed to be applied locally to the vulvar-vaginal tissue prior to sexual activity to facilitate vasodilation and increase blood flow directly to the genital tissue to improve the physical arousal response to address the lack of those genital arousal sensations commonly associated with FSAD. Increasing blood flow to the genital tissue, as Sildenafil Cream is designed to do, has the potential to improve genital arousal response and overall sexual experience for women. This is similar to the way ED medications work in men by directing blood flow to the genitals when taken prior to sexual activity.

“The topline data from the Phase 2b RESPOND study represent an important milestone in the field of female sexual dysfunction,” said Dr. Andrew Goldstein, Medical Advisor of Daré Bioscience and Past President of The International Society for the Study of Women's Sexual Health, as well as co-editor of the Textbook of Female Sexual Function and Dysfunction: Diagnosis and Treatment. “It is exciting to be working at the cutting edge of research focused on women’s sexual health and to advance a potential first-in-category treatment option for women suffering with FSAD.”

“It is encouraging to see sponsors such as Daré and SST developing endpoints that will foster approval of new medicines for women in FSAD. The previously completed content validation study and the exit interviews completed as part of the Phase 2b RESPOND study are significant steps to gaining regulatory approval of endpoints in this area. I look forward to continuing our collaboration by using the Phase 2b RESPOND study data to conduct psychometric analyses to further refine the measures and resulting endpoints for use in a Phase 3 pivotal study,” said Tara Symonds, Ph.D., Managing Director, UK, and Chief Scientific Officer at Clinical Outcomes Solutions, who is an advisor to Daré and SST and has extensive expertise in the development and validation of PROs for sexual health clinical trials, including establishing and leading Pfizer’s PRO Center of Excellence earlier in her career.

Daré plans to submit data from the Phase 2b RESPOND clinical study of Sildenafil Cream for publication in a peer-reviewed journal.

About the Exploratory Phase 2b RESPOND Study

Study Design

The exploratory Phase 2b RESPOND study was a multi-center, double-blind, randomized, placebo-controlled study to evaluate the efficacy and safety of Sildenafil Cream in premenopausal patients with FSAD. The study was a first of its kind Phase 2b clinical study that includes PRO instruments to screen eligible women with FSAD and included two co-primary endpoints, a secondary endpoint, and a number of exploratory endpoints to measure, among other things, improvement in localized genital sensations of arousal, reduction in the distress that women experience with FSAD and satisfactory sexual events. There are no FDA-approved treatments for FSAD and thus there are no efficacy endpoints that have been previously validated in a Phase 3 pivotal study for potential treatments for FSAD.

The FDA requested that any PROs for use in the assessment of efficacy in a Phase 3 study be adequately validated. Part of that validation of the PROs includes exit interviews performed as part of the Phase 2b RESPOND study to better understand qualitatively what constitutes a meaningful change to the subjects. These qualitative assessments of meaningful change were utilized to determine which endpoints achieved meaningful improvement in the Sildenafil Cream group. Additional psychometric analyses using the Phase 2b RESPOND study dataset is planned to further refine and validate the measures to inform the most appropriate endpoints for use in a Phase 3 pivotal study.

The Phase 2b RESPOND study began with 99 subjects in the Sildenafil Cream intent to treat population and 93 subjects in the placebo intent to treat population, with 70 subjects in the Sildenafil Cream intent to treat population and 60 subjects in the placebo intent to treat population completing the study, and therefore was underpowered to assess statistical significance. During the study, participants used Sildenafil Cream and a placebo cream in their home setting and documented their experience using PRO instruments. The study evaluated Sildenafil Cream compared to placebo cream over 12 weeks of dosing following both a non-drug and placebo run-in period.

Study Efficacy Results and Safety

Summary of Topline Data
A co-primary endpoint of the Phase 2b RESPOND study was to evaluate the efficacy of Sildenafil Cream compared to placebo as measured by change from baseline to the end of the study in the Arousal-Sensation Domain of the 28-item Sexual Function Questionnaire (SFQ28). The endpoint did not achieve statistical significance. However, the change at the end of the study in the group treated with Sildenafil Cream was consistent with how women reported meaningful improvement in an exit interview at the end of the study.

The other co-primary endpoint was to evaluate the efficacy of Sildenafil Cream compared to placebo as measured by change from baseline to the end of the study in the score for feeling concerned by difficulties with sexual arousal. The change was assessed using the previously validated Female Sexual Distress Scale – Desire, Arousal and Orgasm (FSDS-DAO) Survey. This assessment did not differentiate Sildenafil Cream from placebo.

The secondary endpoint of the study was to evaluate the efficacy of Sildenafil Cream compared to placebo as measured by change from baseline to the end of the study in the number of satisfactory sexual events based on the subjects' response to a question answered and recorded via electronic diary within 24 hours after each sexual event. The endpoint was selected because it can serve as a primary endpoint in a Phase 3 study based on the FDA draft 2016 guidance document for female sexual dysfunction. When measured at the 4- and 8-week mark after randomization, subjects treated with Sildenafil Cream had a higher proportion of satisfying sexual events during the prior month (68.6% and 74.1% at the 4- and 8-week mark, respectively) compared to those treated with placebo (47.9% and 67.9% at the 4- and 8-week mark, respectively) (week 4 P value = 0.04).

The exploratory endpoints (selected based on the Content Validity study conducted by SST and Daré) included endpoints related to genital arousal, genital blood flow, lubrication, orgasm, concerns about difficulties with sexual arousal, and other assessments including questions regarding satisfying sexual events. The exploratory endpoints were assessed at multiple periods over the course of the study via electronic diary.

- An exploratory endpoint regarding concerns about difficulties with sexual arousal differentiated Sildenafil Cream versus placebo. Specifically, when asked about their overall impression of change regarding their concerns about difficulties with sexual arousal, women treated with Sildenafil Cream were more likely to report an overall improvement. Based on responses to the question at the 4-, 8- and 12-week mark after randomization, 44% to 49% of the subjects treated with Sildenafil Cream reported an overall improvement compared to 37% to 44% of the subjects treated with placebo (P value < 0.01).
- Exploratory endpoints related to arousal lubrication and achievement and pleasure of orgasm also demonstrated important differences between the subjects treated with Sildenafil Cream compared to placebo as measured by change from baseline to the 8-week mark after randomization, at P value = 0.059 and P value = 0.066, respectively (trending toward significance despite the small number of subjects in each group, n=73 in the Sildenafil Cream intent to treat group and n=64 in the placebo intent to treat group for these assessments).
- 48.7% of the subjects treated with Sildenafil Cream reported an increase in their overall satisfaction with sexual activity measured at the end of the study, compared to 42.6% of the subjects treated with placebo.

Summary of Cited Top Line Data
The exploratory Phase 2b RESPOND study was underpowered to assess statistical significance, although statistical significance was achieved on certain assessments. The following table sets forth certain data regarding the co-primary endpoints, the secondary endpoint, and certain exploratory endpoints:

Objective/Endpoint	Measured At	Sildenafil Cream, N(1)	Placebo, N(1)	P value
Co-Primary: SFQ28 Arousal Sensation Domain	End of study (week 12)	70	60	>0.05
Co-Primary: FSDS-DAO Survey (Q14 only (Concerned by difficulties with sexual arousal))	End of study (week 12)	70	60	>0.05
Secondary: Proportion of Satisfactory Sexual Events per Month during Double Blind Treatment Period	Week 4	78	68	0.04
	Week 8	73	64	>0.05
	Week 12	71	61	>0.05
Exploratory: Arousal Lubrication PROs	Week 8	73	64	0.059
Exploratory: Orgasm PROs	Week 8	73	64	0.066
Exploratory: Regarding Concern for FSAD Symptoms(2)	Weeks 4 - 12	78	68	<0.01
Exploratory: Regarding Satisfactory Sexual Activity(2)	Weeks 4 - 12	78	68	<0.01

(1) The numbers in this column represent the number of subjects included in the assessment at the indicated time point.
(2) This exploratory endpoint was measured periodically beginning at week 4 after randomization through the end of the study.

Safety
Sildenafil Cream was generally safe and well-tolerated. There were no treatment related serious adverse events and the majority of treatment related adverse events were mild in severity.

About FSAD and Sildenafil Cream, 3.6%

FSAD is distinct from hypoactive sexual desire disorder (HSDD) in women, which is characterized primarily by a lack of sexual desire. FSAD is a condition characterized primarily by a persistent or recurrent inability to attain or maintain sufficient genital arousal (an adequate lubrication-swelling response) during sexual activity, frequently resulting in distress or interpersonal difficulty. As with ED in men, FSAD is associated with insufficient blood flow to the genitalia.

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. In comparison, 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. Daré believes the potential market opportunity for an FDA-approved treatment for FSAD is comparable in size to the market for FDA-approved treatments for ED in men.

Sildenafil Cream, 3.6% is an investigational proprietary cream formulation of sildenafil, a PDE-5 inhibitor, designed for topical administration to the vulvar-vaginal tissue to increase genital blood flow and provide improvements in the female genital arousal response, while avoiding systemic side effects observed with oral formulations of sildenafil. Sildenafil Cream has been previously evaluated in Phase 1 and Phase 2a clinical studies. In a Phase 1 clinical study in 20 healthy post-menopausal women, topical Sildenafil Cream was safe and well tolerated at clinically relevant doses, and study subjects reported favorable product characteristics: easy to use and readily absorbed. In a Phase 2a study in women with FSAD (15 pre-menopausal and 16 post-menopausal), Sildenafil Cream increased measurable blood flow to the genital tissue compared to placebo cream. Further, data from a thermography study in six healthy women demonstrated significantly greater increases in genital temperature after administration of Sildenafil Cream compared to placebo cream, indicating a positive impact on genital blood flow during the 30-minute testing session, with statistical separation from placebo within the first 15 minutes of dosing.

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, vaginal health, reproductive health, menopause, sexual health and fertility.

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 menopausal hormone therapy. 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 Sildenafil Cream's potential as a safe and effective therapy for FSAD, Daré's plans for continued clinical development of Sildenafil Cream, the anticipated regulatory pathway for Sildenafil Cream, the potential for Sildenafil Cream to be the first FDA-approved treatment for FSAD, and the potential market opportunity for Sildenafil Cream. 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 2b RESPOND study, are based on Daré's preliminary analysis of key efficacy and safety data and, following a comprehensive review of the study data, topline results may not accurately reflect the complete results from the study and the differences between topline results and complete results may be significant and may adversely impact the continued clinical development of the investigational product, including anticipated time and expense of continued development; the risk that data from the Phase 2b RESPOND study, which assessed multiple patient reported outcomes at 4, 8 and 12 weeks after randomization, may not be predictive of results of any future clinical study that assesses safety and efficacy of Sildenafil Cream at time points beyond 12 weeks after randomization, and the double-blind dosing period the FDA may require for a pivotal Phase 3 study of Sildenafil Cream is unknown at this time; the risk that the FDA, other regulatory authorities, members of the scientific or medical communities or investors 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, execute its business strategy and continue as a going concern; 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 development of a product candidate requires more clinical or nonclinical studies than Daré anticipates; 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 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 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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