UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM _____ TO_____**

Commission File No. 001-36395

DARÉ BIOSCIENCE, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-4139823**
(State or other jurisdiction of incorporation)	(IRS Employer Identification No.)
3655 Nobel Drive, Suite 260 **San Diego, CA** (Address of Principal Executive Offices)	**92122** (Zip Code)

Registrant's telephone number, including area code: **(858) 926-7655**

Securities registered under Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	**Name of each exchange on which registered**
Common Stock, Par Value $0.0001 Per Share	**DARE**	**Nasdaq Capital Market**

Securities registered under Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes x No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer	☐	Accelerated filer	☐
Non-accelerated filer	x	Smaller reporting company	x
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No x

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant on the last business day of the registrant's most recently completed second fiscal quarter (June 30, 2021), was approximately $85,850,000 based on the closing price of the registrant's common stock as reported on the Nasdaq Capital Market on such date. This excludes shares of common stock held by affiliates on such date. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power directly, or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant. The determination of affiliate status for this purpose may not be conclusive for other purposes.

As of March 30, 2022, there were 83,944,119 shares of the registrant's common stock, par value $0.0001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2022 annual meeting of shareholders (the "2022 Proxy Statement") are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2022 Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

Daré Bioscience, Inc. and Subsidiaries
Form 10-K – ANNUAL REPORT
For the Fiscal Year Ended December 31, 2021
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PART I

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, in particular ITEM 1. "BUSINESS," ITEM 7. "MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS," and the information incorporated by reference herein contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this report, including statements regarding our strategy, future operations, future financial position, projected revenue, funding and expenses, prospects, plans and objectives of management, 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," "pursue," "should," "would," "contemplate," "project," "target," "tend to," or the negative version of these words and similar expressions.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including those factors described in PART I, ITEM 1A, "RISK FACTORS," in this report, and elsewhere in this report. Given these uncertainties, you should not place undue reliance on any forward-looking statement. The following factors are among those that may cause such differences:

- *Inability to raise additional capital, under favorable terms or at all, and continue as a going concern;*
- *Failure to complete development of our product candidates, submit and obtain United States Food and Drug Administration, or FDA, or foreign regulatory authority approval and commercialize our products candidates on projected timelines or budgets, or at all;*
- *Inability to demonstrate sufficient safety and efficacy of our product candidates;*
- *The ability of third parties on which we rely to timely supply and manufacture our commercial product and our clinical trial supplies, including their components as well as the finished product, in the quantities needed in accordance with current good manufacturing practices, our specifications and other applicable requirements;*
- *The performance of third parties on which we rely to conduct nonclinical studies and clinical trials of our product candidates;*
- *The terms and conditions of our strategic collaborations, including our out-license agreements for commercialization of XACIATO™ and Ovaprene®;*
- *A decision by a commercial collaborator to discontinue its interest in our product or product candidate or to terminate our license agreement, or the failure of such license agreement to become fully effective;*
- *The performance of third parties on which we rely to commercialize, or assist us in commercializing, XACIATO and any future product;*
- *Difficulties with establishing and maintaining collaborations relating to the development and/or commercialization of our product candidates on a timely basis or on acceptable terms, or at all;*
- *Our loss of, or inability to attract, key personnel;*
- *The degree of market acceptance that XACIATO and any future product achieves;*
- *Coverage and reimbursement levels for XACIATO and any future product by government health care programs, private health insurance companies and other third-party payors;*
- *A change in the FDA's prior determination that the Center for Devices and Radiological Health would lead the review of a premarket application for potential marketing approval of Ovaprene;*
- *A change in regulatory requirements for our product candidates, including the development pathway pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or the FDA's 505(b)(2) pathway;*
- *Unsuccessful clinical trial outcomes stemming from clinical trial designs, failure to enroll a sufficient number of patients, higher than anticipated patient dropout rates, failure to meet established clinical endpoints, undesirable side effects and other safety concerns;*

- *Adverse differences between preliminary, interim or topline clinical study data reported by us and final study results;*
- *Communication from the FDA or another regulatory authority, including a complete response letter, that it does not accept or agree with our assumptions, estimates, calculations, conclusions or analyses of clinical or nonclinical study data regarding a product candidate, or that it interprets or weighs the importance of study data differently than we have in a manner that negatively impacts the candidate's prospects for regulatory approval in a timely manner, or at all;*
- *Failure to monetize our portfolio candidates through licenses, partnerships or other types of commercialization agreements;*
- *Failure to select product candidates that capitalize on the most scientifically, clinically or commercially promising or profitable indications or therapeutic areas within women's health due to limited financial resources;*
- *Loss or impairment of our in-licensed rights to develop and commercialize XACIATO and our product candidates ;*
- *Our payment and other obligations under our in-license and acquisition agreements for XACIATO and our product candidates;*
- *Developments by our competitors that make XACIATO or any potential product less competitive or obsolete;*
- *The impact of the macroeconomic conditions, geopolitical events, the COVID-19 pandemic and any future pandemic, epidemic, or similar public health threat or natural disasters on our business, operations and financial condition, or on those of third parties on which we rely;*
- *Cyber-attacks, security breaches or similar events compromising our technology systems or the technology systems of third parties on which we rely;*
- *Difficulty in introducing branded products in a market made up of generic products;*
- *Inability to adequately protect or enforce our, or our licensor's, intellectual property rights;*
- *Lack of patent protection for the active ingredients in XACIATO and certain of our product candidates that expose those product candidates to competition from other formulations using the same active ingredients;*
- *Higher risk of failure associated with product candidates in pre-clinical stages of development that may lead investors to assign them little to no value and make these assets difficult to fund;*
- *Dependence on grant funding for pre-clinical development of DARE-LARC1;*
- *Disputes or other developments concerning our intellectual property rights;*
- *Actual and anticipated fluctuations in our quarterly or annual operating results;*
- *Price and volume fluctuations in the stock market, and in our stock in particular, which could cause investors to experience losses and subject us to securities class-action litigation;*
- *Failure to maintain the listing of our common stock on the Nasdaq Capital Market or another nationally recognized exchange;*
- *Development of unexpected safety concerns related to our product or product candidates, or third-party products or product candidates that share similar characteristics or drug substances;*
- *Product liability claims or governmental investigations;*
- *Strict government regulations on our business, including various fraud and abuse laws, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act and the U.S. Foreign Corrupt Practices Act;*
- *Regulations governing the production or marketing of XACIATO and any future products; and*
- *Increased costs as a result of operating as a public company, and substantial time devoted by our management to compliance initiatives and corporate governance practices.*

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

All forward-looking statements in this report are current only as of the date of this report. We do not undertake any obligation to publicly update any forward-looking statement to reflect events or circumstances after the date on which any statement is made or to reflect the occurrence of unanticipated events, except as required by law.

ITEM 1. BUSINESS

The terms “we,” “us,” “our,” “Daré” or the “Company” refer collectively to Daré Bioscience, Inc. and its wholly-owned subsidiaries, unless otherwise stated or the context otherwise requires. All information in this report is based on our fiscal year. Unless otherwise stated, references to particular years, quarters, months or periods refer to our fiscal years ending December 31 and the associated quarters, months and periods of those fiscal years.

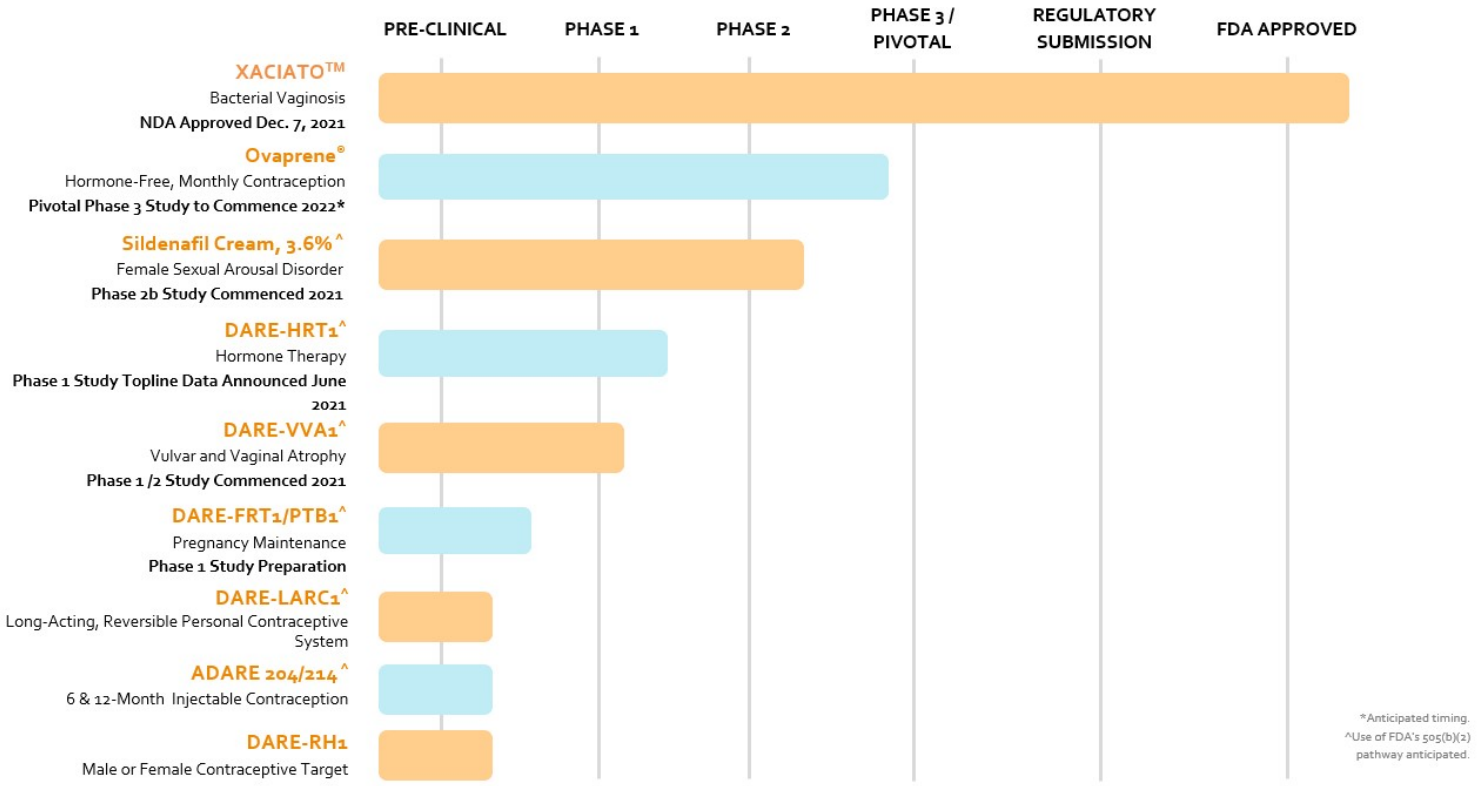
Overview

We are a biopharmaceutical company committed to advancing innovative products for women’s health. We are driven by a mission 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.

Our first product, XACIATO™ (clindamycin phosphate vaginal gel, 2%), was approved by the FDA in December 2021 for the treatment of bacterial vaginosis in females 12 years of age and older. In March 2022, we entered into an exclusive global license agreement with an affiliate of Organon & Co., Organon International GmbH, or Organon, to commercialize XACIATO. XACIATO is expected to be available commercially in the United States in the fourth quarter of 2022.

We began assembling our diverse portfolio of clinical-stage product candidates and pre-clinical programs in 2017 through acquisitions, exclusive in-licenses and other collaborations. Our programs target unmet needs in women’s health in the areas of contraception, fertility and vaginal and sexual health and aim to expand treatment options, enhance outcomes and improve ease of use for women. We are primarily focused on progressing the development of our existing product candidates. We are also exploring opportunities to expand our portfolio by leveraging assets to which we hold rights or obtaining rights to new assets, with continued focus solely on women's health. We believe the product candidates in our portfolio offer innovative approaches that may provide meaningful benefits over current therapeutic or contraceptive options. We evaluate potential new product candidates based on similar selection criteria as we applied in assembling our existing portfolio. Our product candidates, if approved for commercial sale, would be prescription products.

The following graphic summarizes our portfolio, including targeted indications, development status and milestones:


PRE-CLINICAL
PHASE 1
PHASE 2
PHASE 3 / PIVOTAL
REGULATORY SUBMISSION
FDA APPROVED
XACIATO™
Bacterial Vaginosis
NDA Approved Dec. 7, 2021
Ovaprene®
Hormone-Free, Monthly Contraception
Pivotal Phase 3 Study to Commence 2022*
Sildenafil Cream, 3.6%^
Female Sexual Arousal Disorder
Phase 2b Study Commenced 2021
DARE-HRT1^
Hormone Therapy
Phase 1 Study Topline Data Announced June 2021
DARE-VVA1^
Vulvar and Vaginal Atrophy
Phase 1 /2 Study Commenced 2021
DARE-FRT1/PTB1^
Pregnancy Maintenance
Phase 1 Study Preparation
DARE-LARC1^
Long-Acting, Reversible Personal Contraceptive System
ADARE 204/214^
6 & 12-Month Injectable Contraception
DARE-RH1
Male or Female Contraceptive Target
*Anticipated timing.
^Use of FDA's 505(b)(2) pathway anticipated.

Our Strategy

Our goal is to bring to market innovative products in women's health, primarily in the areas of contraception, fertility and vaginal and sexual health. We plan to achieve this goal by advancing the drug and drug/device combination product candidates in our portfolio through mid- to late-stage clinical development, and potentially regulatory approval, as well as by establishing and leveraging strategic partnerships and other collaborations to complete product development and commercialize our products, if approved. We are also exploring portfolio expansion through both business development activities that may result in acquiring, or acquiring access to, new product candidates through in-licensing or other collaborative arrangements, and leveraging assets we previously acquired or in-licensed from third parties. As with our current portfolio, we look for innovations in women's health that have (a) attractive market opportunities and potential to address an unmet medical need, including through new formulations, manners of application or delivery methods of well-known drug substances that result in novel, product candidates customized for women, (b) human proof-of-concept clinical data previously generated by third parties and/or potential to utilize the FDA's 505(b)(2) pathway, and (c) potential to become a first-in-category or first-line product.

We believe that there is an opportunity to fill the gap that exists in the development of innovations in women's health between (a) non-profit organizations, small private companies and individual entrepreneurs that discover, innovate and conduct early-stage research and clinical development of product candidates, and (b) pharmaceutical companies that conduct late-stage clinical development and commercialize approved products. We believe that the development activities between these two ends of this spectrum (early pre-clinical and clinical development of product candidates on the one hand and late-stage clinical trials and commercialization of product candidates on the other) are currently underserved. In addition, we believe there are gaps in treatment options in the women's health market and there is an opportunity to provide therapies that address persistent unmet needs. We intend to fill the mid-stage development gap and to expand treatment options for women.

Key elements of our business strategy are as follows:

- *Advance clinical development of the product candidates in our portfolio through mid- to late-stage clinical development or regulatory approval*. We are targeting a 2022 commencement of a pivotal Phase 3 clinical study of Ovaprene in collaboration with the Eunice Kennedy Shriver National Institute of Child Health and Human Development, or NICHD. In addition, our Phase 2b RESPOND clinical study of Sildenafil Cream, 3.6% in women with female sexual arousal disorder, or FSAD, is ongoing. In 2022, we also expect to complete our ongoing Phase 1/2 clinical study of DARE-VVA1 and we are commencing a Phase 1/2 clinical study of DARE-HRT1.
- *Explore opportunities to expand our portfolio, with the women's health market as our sole focus*. While simultaneously advancing our current portfolio, we intend to continue to identify other important unmet needs in women's health and explore opportunities to build our product pipeline by acquiring or in-licensing new programs or leveraging assets we previously acquired or in-licensed to create new programs that meet our selection criteria.
- *Pursue strategic collaborations to enhance our development and commercialization capabilities*. We intend to develop and maintain strategic relationships with commercial stage companies that are leaders or emerging leaders in the women's health market, as well as with other entities, where we believe such collaborations will accelerate or otherwise improve upon our clinical development and/or product commercialization capabilities. Our license agreement with Bayer to commercialize Ovaprene, if approved, and our Cooperative Research and Development Agreement, or CRADA, with NICHD for the conduct of the Phase 3 clinical study of Ovaprene are examples of these efforts.
- *Seek non-dilutive funding to support product development.* We intend to advance development of our programs through a variety of means, including through non-dilutive funding. For example, technology development and other preclinical activities for DARE-LARC1 have been supported by funding under grant agreements with a private foundation and we anticipate that our 2021 grant agreement will continue to fund pre-clinical activities for that program through most of 2026, contingent upon the program's achievement of specified milestones. In addition, clinical development of Ovaprene and pre-clinical development activities for DARE-LARC1 and DARE-PTB1 have been supported by NICHD grant awards.

XACIATO

XACIATO [zah-she-AH-toe] (clindamycin phosphate) vaginal gel (formerly known as DARE-BV1), a lincosamide antibacterial, received FDA approval in December 2021 for the treatment of bacterial vaginosis in female patients 12 years of age and older. XACIATO is a clear, colorless, viscous gel, which contains clindamycin at a concentration of 2%. A single-dose user-filled disposable applicator delivers 5 g of vaginal gel containing 100 mg of clindamycin.

XACIATO is our first and only approved product. We achieved FDA approval of XACIATO three years after acquiring rights to the program. We commenced and completed a successful pivotal clinical study, prepared and filed a new drug application with the FDA and received notification from the FDA of U.S. marketing approval, all during the COVID-19 pandemic.

In March 2022, we entered into an exclusive license agreement with Organon pursuant to which Organon will obtain exclusive worldwide rights to develop, manufacture and commercialize XACIATO. XACIATO is expected to be available commercially in the United States in the fourth quarter of 2022. See "Strategic Agreements for Product Commercialization" below for further discussion of the terms of our agreement with Organon.

XACIATO previously received both Qualified Infectious Disease Product (QIDP) and Fast Track designations from the FDA for the treatment of bacterial vaginosis in women. As a result of the QIDP designation, XACIATO was eligible to receive a five-year extension of the three years of data exclusivity in the U.S. available to the product based on the submission of new clinical data that were essential to its approval. The FDA granted XACIATO for the treatment of bacterial vaginosis in female patients 12 years of age and older three years of data exclusivity, which was extended by five years, such that the data exclusivity period is set to expire on December 7, 2029. XACIATO has also been designated as a reference listed drug by the FDA for purposes of future generic drug development. The data exclusivity period should block the FDA from approving either a subsequent abbreviated NDA or 505(b)(2) NDA that relies in whole or in part on our protected clinical data. See also "Government Regulation - U.S. Government Regulation- New Drug Marketing Exclusivity under the Hatch-Waxman Act Amendments & GAIN Exclusivity Extension" below.

According to the Centers for Disease Control and Prevention, or the CDC, bacterial vaginosis is the most common vaginal condition in women ages 15-44. Bacterial vaginosis is a type of vaginal inflammation caused by the overgrowth of certain bacteria naturally found in the vagina. Symptoms include vaginal discharge, vaginal odor, vaginal pain, itching or burning, and burning during urination. We entered this therapeutic category because we felt there was a significant unmet need for better treatment. Branded prescription products that received FDA approval before XACIATO for the treatment of bacterial vaginosis have clinical cure rates (based on the Amsel criteria) ranging from 37-68%.

XACIATO is contraindicated in individuals with a history of hypersensitivity to clindamycin or lincomycin. Its prescribing information contains warnings and precautions about *clostridioides difficile*-associated diarrhea, XACIATO's incompatibility with and potential to weaken polyurethane condoms so as to make them unreliable for preventing pregnancy or protecting against sexually transmitted diseases (therefore, polyurethane condoms should not be used during treatment with XACIATO or for 7 days following treatment; latex or polyisoprene condoms should be used), and vaginal *candida* infections. The most common adverse reactions reported in >2% of patients and at a higher rate in the XACIATO group than in the placebo group in the pivotal DARE-BVFREE trial were vulvovaginal candidiasis and vulvovaginal discomfort. Systemic clindamycin has neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. It should be used with caution in patients receiving such agents.

Other clindamycin vaginal products have been used to treat pregnant women during the second and third trimester. XACIATO has not been studied in pregnant women. However, based on the low systemic absorption of XACIATO following the intravaginal route of administration in nonpregnant women, maternal use is not likely to result in significant fetal exposure to the drug. Similarly, because systemic absorption following intravaginal administration of clindamycin is low, transfer of the drug into breastmilk is likely to be low and adverse effects on the breastfed infant are not expected. The safety and effectiveness of XACIATO have not been established in pediatric patients younger than 12 years of age. XACIATO has not been evaluated in geriatric patients (65 years of age or older) to determine whether they respond differently than younger patients.

Clinical Data

The efficacy of XACIATO as a treatment of bacterial vaginosis in females 12 years of age and older was demonstrated in the Phase 3 DARE-BVFREE trial (NCT04370548), a randomized, double-blind, placebo-controlled clinical study that randomized 307 patients at 32 centers across the United States. A single dose of XACIATO was compared to a single dose of placebo vaginal gel (hydroxyethylcellulose [HEC] Universal Placebo Gel) for the treatment of bacterial vaginosis. Patients were evaluated at three timepoints: a Day 1 screening/randomization visit, a Day 7 to 14 Interim Assessment visit, and a Day 21 to 30 Test of Cure visit. The total study duration was up to approximately one month for each individual patient.

To be eligible, patients had to have a clinical diagnosis of bacterial vaginosis defined as an off-white (milky or gray), thin, homogeneous discharge with minimal or absent pruritus and inflammation of the vulva and vagina, clue cells > 20% of the total epithelial cells on microscopic examination of the saline wet mount, vaginal secretion pH of > 4.5, and a fishy odor of the vaginal discharge with the addition of a drop of 10% KOH (i.e., a positive whiff test). The 307 patients were randomized in a 2:1 ratio, with 204 in the XACIATO group and 103 in the placebo group. The modified Intent-To-Treat (mITT) Population excluded women with a positive test result for other concomitant vaginal or cervical infections at baseline, including a positive vaginal culture for *Candida* spp. or who had a baseline Nugent score of < 7.

Clinical Cure was defined as resolution of the abnormal vaginal discharge associated with bacterial vaginosis, a negative 10% KOH whiff test, and clue cells < 20% of the total epithelial cells in the saline wet mount. Bacteriological Cure was defined as a Nugent score < 4. Therapeutic Cure was defined as the presence of both a Clinical Cure and Bacteriological Cure. In the mITT population, a statistically significantly greater percentage of patients experienced Clinical Cure, Bacteriological Cure, and Therapeutic Cure at the Test of Cure (Day 21-30) visit in the XACIATO arm compared to placebo (Table 1). Statistically significant results for the endpoints were also achieved at the Interim Assessment visit (Day 7-14).

Table 1: Summary of Clinical Cure, Bacteriological Cure, and Therapeutic Cure (mITT Population)

	Interim Assessment visit (day 7-14)			**Test of Cure visit (day 21-30)**		
Parameter	XACIATO (N = 122) n (%)	Placebo (N = 59) n (%)	Treatment Difference (%) [95% Confidence Interval]	XACIATO (N = 122) n (%)	Placebo (N = 59) n (%)	Treatment Difference (%) [95% Confidence Interval]
Clinical Cure	93 (76.2)	14 (23.7)	52.5 (38.0, 67.0)	86 (70.5)	21 (35.6)	34.9 (19.0, 50.8)
Bacteriological Cure	50 (41.0)	2 (3.4)	37.6 (26.5, 48.7)	53 (43.4)	3 (5.1)	38.4 (26.7, 50.1)
Therapeutic Cure	43 (35.2)	0	32.5 (25.5, 45.0)	45 (36.9)	3 (5.1)	31.8 (20.3, 43.3)

The percentage of patients with Clinical Cure at the Test of Cure visit was also significantly higher in the XACIATO group compared to the placebo group among the subsets of patients defined by prior episodes of bacterial vaginosis (≤ 3 episodes and >3 episodes in the previous 12 months) at 71.3% (72/101) for XACIATO and 39.1% (18/46) placebo, and 70.0% (14/20) for XACIATO and 23.1% (3/13) placebo, respectively.

The median age of the patients in the trial was 35 years (range 15-59 years). The population was 56% Black or African American and 41% White. Persons of Hispanic or Latino ethnicity made up 25% of the population. A history of prior bacterial vaginosis was noted in 89% of the population. XACIATO was well-tolerated in the trial.

Our Pipeline: Clinical-Stage Programs

Ovaprene®

We believe the need for more effective and convenient options is particularly true with contraception. While a variety of hormonal and non-hormonal options exist, there is a notable void: an effective, short-acting, hormone-free method of contraception that does not require intervention at the time of intercourse.

Ovaprene is a novel, investigational hormone-free monthly intravaginal contraceptive designed to be worn conveniently over multiple weeks (one menstrual cycle) and with the potential to achieve “typical use” contraceptive

efficacy approaching that of current FDA-approved non-implanted hormonal contraceptive methods (pills, patches and vaginal rings), which is approximately 91% typical use efficacy. Typical use contraceptive efficacy refers to the expected rate of pregnancy prevention during the first year of actual use of a method, including sometimes using the method in a way that is not correct or not consistent. Ovaprene features a proprietary knitted polymer barrier to physically block sperm from entering the cervical canal within a silicone-reinforced ring that releases non-hormonal agent ferrous gluconate to impede sperm motility. Unlike current FDA-approved monthly intravaginal contraceptives, Ovaprene does not contain hormones, but, consistent with those monthly intravaginal contraceptives, including Merck's NuvaRing®, Ovaprene is designed to be a "one size fits most" monthly, self-administered product. If approved, Ovaprene could be the first hormone-free, monthly contraceptive option for women.

Ovaprene is composed of both device and drug components and is considered a combination product by the FDA. Ovaprene previously underwent a request for designation process with the FDA that determined that the Center for Devices and Radiological Health, or CDRH, would lead the review of a premarket approval, or PMA, for potential marketing approval in the U.S.

Clinical Data

In a postcoital test, or PCT, pilot clinical study conducted by the previous sponsor in 20 women and published in The Journal of Reproductive Medicine® in 2009, Ovaprene demonstrated the ability to immobilize sperm and prevent their progression into the cervical mucus. The study also demonstrated the acceptability of the device to both partners. No colposcopic abnormalities, no significant changes in vaginal flora and no serious adverse effects were observed.

In November 2019, we announced positive topline results of our PCT clinical trial of Ovaprene. We designed the PCT clinical trial to assess general safety and effectiveness in preventing progressively motile sperm from reaching the cervical canal following intercourse and acceptability of the product to the patient. The study evaluated 23 women over the course of five menstrual cycles, with each woman assessed over approximately 21 visits. Each woman's cervical mucus was measured at several points during the study, including a baseline measurement at menstrual cycle 1 that excluded the use of any product. Subsequent cycles and visits included the use of a diaphragm during intercourse (menstrual cycle 2) and Ovaprene (menstrual cycles 3, 4 and 5). The primary endpoint of the study was to evaluate changes from baseline in PCT results due to device use, as represented by the proportion of women and cycles with an average of fewer than five progressively motile sperm (PMS) per high power field (HPF) in midcycle cervical mucus collected two to three hours after intercourse with Ovaprene in place.

Our PCT clinical trial met its primary endpoint: Ovaprene prevented the requisite number of sperm from reaching the cervix across all women and all cycles evaluated. Specifically, in 100% of women and cycles, an average of less than five PMS per HPF were present in the midcycle cervical mucus collected two to three hours after intercourse with Ovaprene in place. To calculate the average number of PMS, PMS were counted across each of nine HPFs and averaged. Women enrolled in the study who completed at least one Ovaprene PCT (N=26) had a mean of 27.21 PMS/HPF in their baseline cycle when no contraception was used, a mean of 0.22 PMS/HPF in their diaphragm cycle, which was anticipated based on published studies, and a mean of 0.48 PMS/HPF in their Ovaprene PCT cycles, with a median of zero PMS. No serious or severe adverse events were reported or observed.

PCT clinical trials have been used as a surrogate marker for contraceptive effectiveness. Infertility research suggests that higher rates of pregnancy are associated with PMS per HPF of from greater than one to greater than 20 sperm, and less than five PMS per HPF is considered indicative of contraceptive effectiveness.

Pivotal Phase 3 Clinical Study

In January 2022, we initiated an Investigational Device Exemption, or IDE, review process with the FDA for a multi-center, non-comparative, pivotal Phase 3 clinical study of the safety and efficacy of Ovaprene to prevent pregnancy. Our IDE submission was subsequently converted to an IDE pre-submission so that the FDA could engage in a collaborative discussion with us regarding items that must be addressed prior to enrollment of any subjects in the Phase 3 study. This process is ongoing and we believe it will allow us to finalize the protocol and design of the study as the registration study to support a future PMA submission. Based on communications with the FDA, in terms of study sample size and duration, we expect that at least 200 subjects completing 12 months of Ovaprene use will be adequate. We are targeting commencement of the Phase 3 study during 2022.

In July 2021, we entered into the CRADA with the U.S. Department of Health and Human Services, as represented by NICHD, part of the National Institutes of Health, for the conduct of the Phase 3 study, which will be conducted within NICHD's Contraceptive Clinical Trial Network with NICHD contractor Health Decisions Inc., a

contract research organization, providing clinical coordination and data collection and management services. We and NICHD will each provide medical oversight and final data review and analysis for the study and will work together to prepare the final report of the results of the study. We are responsible for providing clinical supplies of Ovaprene, coordinating interactions with the FDA, preparing and submitting supportive regulatory documentation, and providing a total of $5.5 million in payments to NICHD to be applied toward the costs of conducting the Phase 3 study. NICHD will be responsible for the other costs related to the conduct of the Phase 3 study and will manage the payment of expenses to Health Decisions Inc., the clinical sites, and other parties involved with the study. If the planned Phase 3 study is successful, we expect the data to support a pre-market approval submission, or PMA, to the FDA, as well as regulatory filings in Europe and other countries worldwide, to allow for marketing approvals of Ovaprene.

In addition to the CRADA, we are collaborating with ADVA-Tec, Inc. and Bayer HealthCare LLC, or Bayer, for the development and commercialization of Ovaprene as part of two strategic collaborations announced in March 2017 and January 2020, respectively. See "Strategic Agreements for Pipeline Development" and "Strategic Agreements for Product Commercialization" below for discussion of the terms of each collaboration.

Sildenafil Cream, 3.6%

While numerous pharmaceutical products have been developed and approved to treat erectile dysfunction in men, women continue to lack effective options for female sexual arousal disorder, or FSAD, the most analogous condition of the various types of female sexual dysfunction disorders. We are developing Sildenafil Cream, 3.6%, an investigational proprietary cream formulation of sildenafil, a phosphodiesterase-5 inhibitor and the active ingredient in the male erectile dysfunction drug Viagra®, for topical administration to the vulva and vagina for treatment of FSAD. Today, there are no FDA-approved products that specifically address the symptoms or underlying pathology of FSAD. We plan to leverage the existing data and established safety profile of sildenafil and the Viagra® brand to utilize the FDA's 505(b)(2) pathway to obtain marketing approval of Sildenafil Cream, 3.6% in the U.S. for the treatment of women suffering from FSAD. If approved, Sildenafil Cream, 3.6% could be the first FDA-approved FSAD treatment option for women.

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. This is distinct from hypoactive sexual desire disorder (HSDD) in women, which is characterized primarily by a lack of sexual desire. As with erectile dysfunction in men, FSAD in women is associated with insufficient blood flow to the genitalia. Sildenafil Cream, 3.6% is designed to facilitate vasodilation and increase genital blood flow, and, as a result, to provide improvements in the female genital arousal response, while avoiding systemic side effects observed with oral formulations of sildenafil.

Clinical Data

In a Phase 1 clinical study of three escalating doses of topical sildenafil cream (1 g cream with 35 mg sildenafil; 2 g cream with 71 mg sildenafil; and 4 g cream with 142 mg sildenafil) in 20 healthy post-menopausal women using a crossover study design, topical sildenafil cream demonstrated significantly lower systemic exposure to sildenafil compared to a 50 mg oral sildenafil dose, and topical sildenafil cream was safe and well tolerated at clinically relevant doses (1-2 g cream). Study subjects reported favorable product characteristics: easy to use and readily absorbed.

In a Phase 2a, single center, single-dose, double-blind, placebo-controlled, 2-way crossover study, women with FSAD, ages 21 to 60, received a single 2 g dose of Sildenafil Cream, 3.6%. Of the 35 women enrolled, 31 (15 pre-menopausal and 16 post-menopausal) completed the study. The primary objective was to evaluate the efficacy of Sildenafil Cream, 3.6% compared to placebo cream assessed by participant-reported levels of subjective cognitive sexual arousal and by physiological genital arousal response. Sildenafil Cream, 3.6% demonstrated increases in measurable blood flow to the genital tissue compared to placebo (mean change in vaginal pulse amplitude analysis) using a vaginal photoplethysmograph approximately 30 minutes post-dosing.

A Phase 1, single-dose, double-blind, placebo-controlled, two-way crossover study to evaluate the feasibility of using thermography to assess the pharmacodynamics of Sildenafil Cream, 3.6% in normal healthy women was conducted at a single center. During the thermography study, genital temperature, a surrogate for genital blood flow, was captured and recorded utilizing an infrared camera capable of detecting heat patterns from blood flow in body tissues. The study, which was designed to evaluate up to 10 subjects, achieved the study objectives based on a planned interim analysis of the first six completed subjects, and thus additional subjects were not enrolled. In this study, Sildenafil Cream, 3.6% demonstrated significantly greater increases in genital temperature compared to

placebo cream, indicating a positive impact on genital blood flow during the 30-minute post-dosing testing session, with statistical separation from placebo cream within the first 15 minutes after dosing. Additionally, significantly greater self-reported arousal responses were reported during Sildenafil Cream, 3.6% visits compared to placebo cream visits.

In 2019, as part of our Phase 2b clinical program for Sildenafil Cream, 3.6%, we completed a non-interventional study, or the content validity study, designed to identify and document the genital arousal symptoms that are most important and relevant to women with FSAD. Participants who met the eligibility criteria participated in one-on-one, in-depth interviews conducted by subject matter experts in the field of clinical outcome assessments and female sexual medicine. The findings of that study helped facilitate alignment with the FDA on acceptable efficacy endpoints in our Phase 2b clinical study and future Phase 3 program, including with respect to the patient reported outcome, or PRO, instruments to be used to screen eligible patients with FSAD and to measure achievement of the primary efficacy endpoint in the Phase 2b study.

Phase 2b RESPOND Clinical Study

In March 2021, we announced initiation of our Phase 2b RESPOND clinical study of Sildenafil Cream, 3.6% in women with FSAD. During the Phase 2b RESPOND clinical study, subjects will use Sildenafil Cream, 3.6% and placebo cream in their home setting and will document genital arousal symptoms and distress using PRO instruments. The primary efficacy endpoint of the study is a composite endpoint that includes patient-reported improvement in genital sensations of arousal and reduction in distress associated with FSAD. The Phase 2b RESPOND clinical study is designed to evaluate Sildenafil Cream, 3.6% compared to placebo cream over 12 weeks of dosing following both a non-drug and placebo run-in period. The study is expected to randomize 400 to 590 subjects into the double-blind dosing period at 40 to 50 clinical sites in the U.S. to ensure a total of 300 (150:150) to 440 (220:220) subjects complete the 12-week double-blind dosing period. The final size of the study will be determined by a single interim analysis for unblinded sample size re-estimation, based on the study's adaptive design. An adaptive design implemented in accordance with the FDA's Guidance for Industry on adaptive designs for clinical trials of drugs mitigates the risk of the study being underpowered if the true treatment effect and variability are significantly different from estimates based on published data but are still clinically meaningful. The pace of enrollment of participants in the trial has been slower than initially expected. While the COVID-19 pandemic contributed in part to the slower pace of enrollment, we identified a number of other contributing factors, and we implemented mitigation strategies and adapted certain requirements to increase study subject recruitment. We do not expect these changes to impact trial results. We anticipate that the planned interim analysis will be conducted in 2022, after which we will be able to predict the timeframe for announcement of topline data from this trial.

We are developing Sildenafil Cream, 3.6% with Strategic Science & Technologies-D LLC under our license and collaboration agreement announced in February 2018. See "Strategic Agreements for Pipeline Development" below for discussion of the terms of this collaboration.

DARE-HRT1

DARE-HRT1 is a unique intravaginal ring, or 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 to treat the vasomotor symptoms, or VMS, and genitourinary syndrome associated with 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 vaginal ring technologies, ours is designed to release drugs via a solid ethylene vinyl acetate polymer matrix without the need for a membrane or reservoir to contain the active drug or control the release, allowing for sustained drug delivery over time periods ranging from weeks to months. Hormone therapy is considered the most effective treatment for vasomotor symptoms, commonly referred to as hot flashes, and the genitourinary syndrome of menopause, and it has been shown to prevent bone loss and fracture.

Following clinical development, we intend to leverage existing safety and efficacy data on estradiol and progesterone, the active ingredients in DARE-HRT1, to utilize the FDA's 505(b)(2) pathway to obtain marketing approval in the U.S.

There are currently no FDA-approved IVRs that deliver bio-identical progesterone in combination with bio-identical estradiol. As such, DARE-HRT1 has the potential to be a first-in-category product that offers monthly convenience for women.

Clinical Data

In June 2021, we announced positive topline results from our Phase 1 clinical trial of DARE-HRT1. The randomized, open-label, three-arm, parallel group trial evaluated the pharmacokinetics, or PK, and safety of DARE-HRT1 in approximately 30 healthy, post-menopausal women with intact uteri, and was conducted by our wholly owned Australian subsidiary at specialty women's health sites in Australia. The primary objective of the study was to describe the PK parameters of two different dose combinations (estradiol 80 µg/progesterone 4 mg IVR and estradiol 160 µg/progesterone 8 mg IVR) over 28 days. Secondary endpoints of the study were to assess the safety and tolerability of DARE-HRT1 and compare the systemic exposure of estradiol, estrone, and progesterone of DARE-HRT1 over 28 days against a daily combination of oral estrogen (Estrofem®) and oral progesterone (Prometrium®). Baseline-corrected steady state release level data from the study demonstrate that both the lower (IVR1) and higher (IVR2) dose versions of DARE-HRT1 successfully delivered the bio-identical estradiol and bio-identical progesterone over the 28-day evaluation period (Table 2).

Table 2: Baseline-Corrected Steady State Levels of Estradiol and Progesterone

	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 each 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 Phase 1 study, the results support further development of DARE-HRT1 as a potentially effective hormone therapy for both VMS and vaginal symptoms associated with menopause. The levels of progesterone released from each version 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 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.

Phase 1/2 Clinical Study

We are commencing a Phase 1/2 clinical study of DARE-HRT1 in Australia in the second quarter of 2022. The open-label study will evaluate the PK of the lower and higher dose versions of DARE-HRT1 in approximately 20 healthy, post-menopausal women with intact uteri over approximately three consecutive months of use. The study will also collect safety, usability, acceptability and symptom-relief data.

We are developing DARE-HRT1 under our license agreement with Catalent JNP, Inc. See “Strategic Agreements for Pipeline Development” below for discussion of the terms of that agreement.

DARE-VVA1

DARE-VVA1 is a proprietary formulation of tamoxifen for vaginal administration. We are developing DARE-VVA1 as an alternative to estrogen-based therapies for the treatment of moderate to severe vulvar and vaginal atrophy, or VVA, in women with or at risk for hormone-receptor positive (HR+) breast cancer, including women on anti-cancer therapy, to treat the symptoms of VVA. Tamoxifen is a well-known and well-characterized selective estrogen receptor modulator, or SERM. Tamoxifen has unique properties that produce different effects in different types of tissues. In breast tissue, tamoxifen acts as an estrogen antagonist, meaning that it can inhibit estrogen's effect and hence why it may be effective in treating HR+ breast cancer. However, in other tissue, including vaginal tissue, tamoxifen has been reported to exert an estrogen-like response. This has the potential to have a favorable effect on vaginal cytology. VVA is an inflammation of the vaginal epithelium due to the reduction in levels of circulating estrogen, which is characterized by pain during intercourse, vaginal dryness and irritation. Commonly used therapies for VVA are estrogen-based and often contraindicated in HR+ breast cancer patients, or patients with a genetic predisposition or history of familial disease, because of the concern that estrogen use will promote recurrence or occurrence of disease. Due to the prevalence of aromatase inhibitors for the treatment of HR+ breast cancer, the prevalence of VVA in post-menopausal breast cancer patients is estimated to be between 42 and 70 percent. We intend to leverage the existing safety and efficacy data for tamoxifen to utilize the FDA's 505(b)(2) pathway to obtain marketing approval of DARE-VVA1 in the U.S.

An exploratory study of vaginal administration of tamoxifen in four healthy postmenopausal women diagnosed with VVA published in *Clinical and Experimental Obstetrics & Gynecology* demonstrated that tamoxifen self-administered intravaginally for three months clinically benefited women with symptoms of VVA without significant systemic absorption of the study drug. In the open-label prospective cohort study with no placebo arm, participants were instructed to self-administer a vaginal suppository containing tamoxifen (20 mg) daily for one week and twice weekly for three months. The study treatment was effective in reducing vaginal pH and vaginal dryness. When measured after eight weeks on the study treatment, serum tamoxifen levels were negligible, 5.8 ng/ml (median), with a range of 1.0 to 10.0 ng/ml. In comparison, after three months of once daily administration of oral dose of 20-mg tamoxifen, Nolvadex® (tamoxifen citrate) tablets, the average steady state plasma concentration of tamoxifen is 122 ng/ml (range of 71 to 183 ng/ml).

In September 2021, we announced initiation of our Phase 1/2 clinical study of DARE-VVA1. The randomized, multi-center, double-blind, parallel-arm, placebo-controlled, dose-ranging study is designed to evaluate the safety, tolerability, PK, and pharmacodynamics (PD) of DARE-VVA1 in postmenopausal participants with moderate to severe VVA and is being conducted by our wholly owned Australian subsidiary. We expect the study will enroll approximately 40 postmenopausal women with VVA, including a cohort of women with a history of hormone-receptor positive breast cancer, at approximately three study sites. Eligible participants will be randomly allocated to one of the five treatment groups (approximately 8 participants per group) that will evaluate four dose levels (1 mg, 5 mg, 10 mg, and 20 mg) and a placebo. Following a screening visit, DARE-VVA1 will be 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. In each treatment group, participants will have serial blood sampling for PK analysis and undergo safety evaluations and preliminary assessments of effectiveness. Following the completion of the treatment period, participants will attend a safety follow-up visit. The primary endpoints of the study will evaluate the safety and tolerability of DARE-VVA1 by vaginal administration and determine the plasma PK of DARE-VVA1 after intravaginal application. Secondary endpoints will evaluate the preliminary efficacy and PD of DARE-VVA1 in terms of the most bothersome symptom and changes in vaginal cytology and pH. We anticipate reporting topline data from the study in the second half of 2022.

We acquired the DARE-VVA1 program through our acquisition of Pear Tree Pharmaceuticals in 2018. See "Strategic Agreements for Pipeline Development" below for discussion of that merger agreement.

DARE-FRT1 and DARE-PTB1

DARE-FRT1 and DARE-PTB1 are IVRs designed to release bio-identical progesterone over a 14-day period. DARE-FRT1 is being developed for broader luteal phase support as part of an in vitro fertilization, or IVF, treatment plan. DARE-PTB1 is being developed for the prevention of preterm birth. Each of DARE-FRT1 and DARE-PTB1 was developed from the same IVR technology platform as DARE-HRT1. We are conducting development activities in preparation for Phase 1 clinical studies of these product candidates. We intend to leverage the existing safety and efficacy data for progesterone to utilize the FDA's 505(b)(2) pathway to obtain marketing approval of DARE-FRT1 and DARE-PTB1 in the U.S.

We are developing DARE-FRT1 and DARE-PTB1 under our license agreement with Catalent JNP, Inc. See "Strategic Agreements for Pipeline Development " below for discussion of the terms of that agreement.

Our Pipeline: Pre-Clinical Stage Programs

Our pre-clinical stage programs are:

- **DARE-LARC1**, a contraceptive implant delivering levonorgestrel with a woman-centered design that has the potential to be a long-acting, yet convenient and user-controlled contraceptive option;
- **ADARE-204 and ADARE-214**, injectable formulations of etonogestrel designed to provide contraception over 6-month and 12-month periods, respectively; and
- **DARE-RH1**, a novel approach to non-hormonal contraception for both men and women by targeting the CatSper ion channel.

DARE-LARC1, our potential user-controlled, long-acting reversible contraceptive, is designed to store and precisely deliver hundreds of therapeutic doses of the contraceptive levonorgestrel over a period of years and to be controlled by the user, without further intervention by a healthcare provider. DARE-LARC1's woman-centered design seeks to offer the benefits of traditional long-acting reversible contraceptives with the added flexibility and convenience for the user to pause and resume release of levonorgestrel, depending on her desire for fertility or contraceptive protection. Under a grant agreement we entered into in June 2021, we may receive up to $48.95 million, payable over approximately five years, to advance development of the technology through nonclinical proof of principle studies to enable an investigational new drug, or IND, submission. We received an initial payment under that grant of $11.45 million in 2021. Additional payments are contingent upon the DARE-LARC1 program's achievement of development and reporting milestones specified in the grant agreement. Additionally in 2021, we received an unrelated NICHD grant award of approximately $300,000 to be used to explore device insertion and removal in nonclinical studies.

Sales and Marketing

We do not have established marketing, sales or distribution infrastructure or capabilities. In order to commercialize any of our product candidates if approved for commercial sale, we must either establish a sales and marketing organization with technical expertise and supporting distribution capabilities or collaborate with third-parties that have sales and marketing experience. Our approach is to develop an appropriate commercialization strategy for each of our product candidates based on the size of the market opportunity, the level of competition and the anticipated complexity of the launch. As we move our product candidates through development toward, and in some cases, through regulatory approval, we evaluate several options for each product candidate's commercialization strategy. These options include building our own sales force and other commercial infrastructure, entering into strategic marketing partnerships with third parties, including commercial sales organizations or other pharmaceutical or biotechnology companies, out-licensing the product to other pharmaceutical or biotechnology companies, and combinations of these strategies. We have entered into an exclusive license agreement with Organon to out-license worldwide commercialization of XACIATO and an exclusive license agreement with Bayer to out-license U.S. commercialization of Ovaprene. Each of these licensees has established marketing, sales and distribution capabilities in women's health. We expect to continue to evaluate each product opportunity and pursue the commercialization strategy that we believe will maximize the return on our assets in and outside of the U.S. for our stockholders. We have engaged third parties to assist in commercial planning and other commercial readiness activities for our product candidates and intend to continue to do so, as needed.

See “Strategic Agreements for Product Commercialization” below for a discussion of the terms of our out-license agreements.

Manufacturing and Supply

We do not own or operate, nor do we expect to own or operate, facilities for manufacturing, storage and distribution, or testing of our product or product candidates. We rely on third parties to supply and manufacture our product candidates and other materials necessary to conduct pre-clinical testing, clinical trials and other activities required for regulatory approval of our product candidates, and expect to continue to do so in the future. In addition, to the extent our commercialization strategy for a product requires that we undertake commercial supply obligations, we intend to rely on contract manufacturers and suppliers for manufacture, storage, distribution and testing of our finished commercial products and their respective components, including the active pharmaceutical ingredients, or API. These arrangements require less upfront capital expenditure and allow us to maintain a smaller and more flexible infrastructure.

Under the terms of our license agreement with Organon, we will be responsible for providing product supply of XACIATO on an interim basis until Organon assumes such responsibility. In March 2022, we entered into a long-term supply and manufacturing agreement with the contract manufacturing organization, or CMO, that provided clinical supplies of XACIATO for our pivotal Phase 3 DARE-BVFREE clinical study. This CMO currently is our sole source for commercial supplies of XACIATO. Under the terms of our agreement, the CMO is responsible for obtaining supplies, at our expense, of all the components necessary for the manufacture of XACIATO, including the API, clindamycin. Our agreement contemplates potential assignment by us to a commercial collaborator. We expect to have sufficient quantities of XACIATO finished product to support commercial launch in 2022.

Under our agreements with ADVA-Tec and SST, respectively, ADVA-Tec is responsible for providing all clinical trial and commercial supplies of Ovaprene, either directly or through a CMO, and SST is responsible for providing Sildenafil Cream, 3.6% for the Phase 2b clinical study. Other than our agreement with ADVA-Tec, we have no long-term arrangements for the production or supply of our product candidates or the materials required to produce them.

We expect that our current arrangements will meet our foreseeable needs for clinical trial materials or, generally, that alternative supply sources will be readily available. However, we may experience manufacturing and supply delays and disruptions in connection with CMOs scaling up production to meet our clinical supply requirements for later stage clinical studies. In addition, some key raw materials or components of our clinical-stage product candidates, including Ovaprene and Sildenafil Cream, 3.6%, have only a single source of supply and alternative supply sources may not be readily available. Global supply chain disruptions related to the COVID-19 pandemic and recent geopolitical events may contribute to manufacturing and supply delays. See ITEM 1A. "RISK FACTORS – Risks Related to Product Research & Development and Regulatory Approval – Manufacturing and supply delays and disruptions may significantly delay our clinical studies and be expensive for us to resolve" below.

Strategic Agreements for Product Commercialization

Organon License Agreement

On March 31, 2022, we entered into an exclusive license agreement with Organon pursuant to which Organon will obtain exclusive worldwide rights to develop, manufacture and commercialize XACIATO and other future intravaginal or urological products for human use formulated with clindamycin that rely on intellectual property we control. Under the agreement, we will receive a $10.0 million non-refundable and non-creditable payment following the effective date of the agreement and will be entitled to receive tiered double-digit royalties based on net sales and up to $182.5 million in milestone payments as follows: $2.5 million following the first commercial sale of a licensed product in the United States, which is expected to occur during the fourth quarter of 2022; and up to $180.0 million in tiered commercial sales milestones and regulatory milestones. Royalty payments will be subject to customary reductions and offsets. The royalty period for each licensed product will continue on a country-by-country basis from the first commercial sale of the licensed product in the country until the expiration of the later of (i) the date that no valid patent claim would be infringed in the absence of the license granted under the agreement by the sale of the licensed product in the country, (ii) 10 years after the end of the month in which the first commercial sale of the licensed product in the country occurred, and (iii) the expiration of regulatory market exclusivity for the licensed product in that country.

Under the agreement, we will be responsible for regulatory interactions and for providing product supply on an interim basis until Organon assumes such responsibilities. Until such time, Organon will purchase all of its product requirements of XACIATO from us at a transfer price equal to our manufacturing costs plus a single-digit percentage markup.

The effective date of the agreement will occur following the satisfaction of closing conditions that include receipt of all applicable approvals, or the expiration or termination of all applicable waiting periods, required under applicable antitrust laws, including the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended. Unless terminated earlier, the agreement will expire on a product-by-product and country-by-country basis upon expiration of the applicable royalty period for each licensed product. In addition to customary termination rights for both parties, following the first anniversary of the effective date of the Agreement, Organon may terminate the Agreement in its entirety or on a country-by-country basis at any time in Organon's sole discretion on 120 days' advance written notice.

The agreement includes customary representations and warranties, covenants and indemnification obligations of each party.

In addition, the terms of the agreement provide Organon exclusive worldwide rights of first negotiation for specified potential future products of ours.

Bayer License Agreement

In January 2020, we entered into a license agreement with Bayer regarding the further development and commercialization of Ovaprene in the U.S. We received a $1.0 million upfront non-refundable payment from Bayer and Bayer agreed to support us in development and regulatory activities by providing the equivalent of two experts to advise us in clinical, regulatory, preclinical, commercial, CMC and product supply matters. Bayer, in its sole discretion, has the right to make the license effective by paying us an additional $20.0 million, referred to as the Clinical Trial and Manufacturing Activities Fee. Such license would be exclusive with regard to the commercialization of Ovaprene for human contraception in the U.S. and co-exclusive with us with regard to development.

The following is a summary of the other terms of the Bayer license agreement:

Milestone Payments Paid by Bayer. We will be entitled to receive (a) a milestone payment in the low double-digit millions upon the first commercial sale of Ovaprene in the U.S. and escalating milestone payments based on annual net sales of Ovaprene during a calendar year, totaling up to $310.0 million if all such milestones, including the first commercial sale, are achieved, (b) tiered royalties starting in the low double digits based on annual net sales of Ovaprene during a calendar year, subject to customary royalty reductions and offsets, and (c) a percentage of sublicense revenue.

Efforts. We will be responsible for the pivotal trial for Ovaprene and for its development and regulatory activities and we have product supply obligations. After payment of the Clinical Trial and Manufacturing Activities Fee, Bayer will be responsible for the commercialization of Ovaprene for human contraception in the U.S.

Term. The initial term of the agreement, which is subject to automatic renewal terms, continues until the later of (a) the expiration of any valid claim covering the manufacture, use, sale or import of Ovaprene in the U.S.; or (b) 15 years from the first commercial sale of Ovaprene in the U.S. In addition to customary termination rights for both parties, Bayer may terminate the agreement at any time on 90 days' notice and the agreement will automatically terminate if we do not receive the Clinical Trial and Manufacturing Activities Fee if and when due.

Strategic Agreements for Pipeline Development

Hammock/MilanaPharm Assignment and License Agreement

In December 2018, we entered into (a) an Assignment Agreement with Hammock Pharmaceuticals, Inc., or the Assignment Agreement, and (b) a First Amendment to License Agreement with TriLogic Pharma, LLC and MilanaPharm LLC, or the License Amendment. Both agreements relate to the Exclusive License Agreement among Hammock, TriLogic and MilanaPharm dated as of January 9, 2017, or the MilanaPharm License Agreement. Under the Assignment Agreement and the MilanaPharm License Agreement, as amended by the License Amendment, we acquired an exclusive, worldwide license under certain intellectual property to, among other things, develop and commercialize products for the diagnosis, treatment and prevention of human diseases or conditions in or through any intravaginal or urological applications. The licensed intellectual property relates to the hydrogel drug delivery platform of TriLogic and MilanaPharm known as TRI-726. In XACIATO, this proprietary technology is formulated with clindamycin for the treatment of bacterial vaginosis. In December 2019, we entered into amendments to each of the Assignment Agreement and License Amendment. In September 2021, we entered into another amendment to the License Agreement.

The following is a summary of other terms of the License Amendment, as amended:

License Fees. A total of $235,000 in license fees were payable to MilanaPharm, the final installment of which was $110,000 paid in 2020.

Milestone Payments. We paid MilanaPharm $300,000 in the aggregate upon achievement of certain clinical and regulatory development milestones, $50,000 of which was paid in 2020, and $250,000 of which was paid in 2021. We may also pay MilanaPharm up to $1.75 million in the aggregate upon achieving certain commercial sales milestones.

Foreign Sublicense Income. We will pay MilanaPharm a low double-digit percentage of all income received by us or our affiliates in connection with any sublicense granted to a third party for use outside of the United States, subject to certain exclusions.

Royalty Payments. During the royalty term, we will pay MilanaPharm high single-digit to low double-digit royalties based on annual worldwide net sales of licensed products and processes. The royalty term, which is determined on a country-by-country basis and licensed product-by-product basis (or process-by-process basis), begins with the first commercial sale of a licensed product or process in a country and terminates on the latest of (1) the expiration date of the last valid claim of the licensed patent rights that cover the method of use of such product or process in such country, or (2) 10 years following the first commercial sale of such product or process in such country. Royalty payments are subject to reduction in certain circumstances, including as a result of generic competition, patent prosecution expenses incurred by us, or payments to third parties for rights or know-how required for us to exercise the licenses granted to it under the MilanaPharm License Agreement or that are strategically important or could add value to a licensed product or process in a manner expected to materially generate or increase sales.

Efforts. We must use commercially reasonable efforts and resources to (1) develop and commercialize at least one licensed product or process in the United States and at least one licensed product or process in at least one of Canada, the United Kingdom, France, Germany, Italy or Spain, and (2) continue to commercialize that product or process following the first commercial sale of a licensed product or process in the applicable jurisdiction.

Term. Unless earlier terminated, the license term continues until (1) on a licensed product-by-product (or process-by-process basis) and country-by-country basis, the date of expiration of the royalty term with respect to such licensed product in such country, and (2) the expiration of all applicable royalty terms under the MilanaPharm License Agreement with respect to all licensed products and processes in all countries. Upon expiration of the term with respect to any licensed product or process in a country (but not upon earlier termination of the MilanaPharm License Agreement), the licenses granted to us under the MilanaPharm License Agreement will convert automatically to an exclusive, fully paid-up, royalty-free, perpetual, non-terminable and irrevocable right and license under the licensed intellectual property.

In addition to customary termination rights for all parties, MilanaPharm may terminate the license granted to us solely with respect to a licensed product or process in a country if, after having launched such product or process in such country, (1) we or our affiliates or sublicensees discontinue the sale of such product or process in such country and MilanaPharm notifies us of such termination within 60 days of having first been notified by us of such discontinuation, or (2) we or our affiliates or sublicensees (A) discontinue all commercially reasonable marketing efforts to sell, and discontinue all sales of, such product or process in such country for nine months or more, (B) fail to resume such commercially reasonable marketing efforts within 120 days of having been notified of such failure by MilanaPharm, (C) fail to reasonably demonstrate a strategic justification for the discontinuation and failure to resume to MilanaPharm, and (D) MilanaPharm gives 90 days' notice to us.

The following is a summary of other terms of the Assignment Agreement, as amended.

Assignment; Technology Transfer. Hammock assigned and transferred to us all of its right, title and interest in and to the MilanaPharm License Agreement and agreed to cooperate to transfer to us all of the data, materials and the licensed technology in its possession pursuant to a technology transfer plan to be agreed upon by the parties, with a goal for us to independently practice the licensed intellectual property as soon as commercially practical in order to develop and commercialize the licensed products and processes.

Fees. A total of $512,500 in fees were payable to Hammock, the final installment of which was paid in 2020.

Milestone Payments. We will pay Hammock up to $1.1 million in the aggregate upon achievement of certain clinical and regulatory development milestones, $100,000 of which was paid in 2020 and $750,000 of which was paid in 2021. The remaining milestone does not relate to a bacterial vaginosis product.

Term. The Assignment Agreement will terminate upon the later of (1) completion of the parties' technology transfer plan, and (2) payment to Hammock of the last of the milestone payments.

ADVA-Tec License Agreement

In March 2017, we entered into a license agreement with ADVA-Tec, Inc., under which we were granted an exclusive license to develop and commercialize Ovaprene for human contraceptive use worldwide. We must use commercially reasonable efforts to develop and commercialize Ovaprene, and must meet certain minimum spending amounts per year, including $2.5 million per year to cover such activities until a final PMA is filed, or until the first commercial sale of Ovaprene, whichever occurs first. ADVA-Tec will conduct certain research and development work as necessary to allow us to seek a PMA from the FDA and will provide us with clinical trial and commercial supplies of Ovaprene, either directly or through a CMO, on commercially reasonable terms.

Under the license agreement, in addition to an exclusive license to ADVA-Tec's and its affiliates' intellectual property rights for all uses of Ovaprene as a human contraceptive device, we have a right of first refusal to license these patents and patent applications for additional indications.

The following is a summary of other terms of the ADVA-Tec license agreement:

Milestone Payments. We will pay to ADVA-Tec: (1) up to $14.6 million in the aggregate based on the achievement of specified development and regulatory milestones, $200,000 of which was paid in 2021; and (2) up to $20 million in the aggregate based on the achievement of certain worldwide net sales milestones. The remaining development and regulatory milestones include: the FDA's approval to commence a pivotal clinical trial; successful completion of such pivotal clinical trial; the FDA's acceptance of a PMA filing for Ovaprene; the FDA's approval of the PMA for Ovaprene; CE Marking of Ovaprene in at least three designated European countries; obtaining regulatory approval in at least three designated European countries; and obtaining regulatory approval in Japan.

Royalty Payments. After the commercial launch of Ovaprene, we will pay ADVA-Tec royalties based on aggregate annual net sales of Ovaprene in specified regions at a royalty rate that will vary between 1% and 10% and will increase based on various net sales thresholds.

Term. Unless earlier terminated, the license we received under the agreement continues on a country-by-country basis until the later of the life of the licensed patents or our last commercial sale of Ovaprene. In addition to customary termination rights for both parties: (A) we may terminate the agreement with or without cause in whole or on a country-by-country basis upon 60 days prior written notice; and (B) ADVA-Tec may terminate the agreement if we develop or commercialize any non-hormonal ring-based vaginal contraceptive device competitive to Ovaprene or if we fail to: (1) in certain limited circumstances, commercialize Ovaprene in certain designated countries within three years of the first commercial sale of Ovaprene; (2) satisfy the annual spending obligation described above, (3) use commercially reasonable efforts to complete all necessary pre-clinical and clinical studies required to support and submit a PMA, (4) conduct clinical trials as set forth in the development plan to which we and ADVA-Tec agree, and as may be modified by a joint research committee, unless such failure is caused by events outside of our reasonable control, or (5) enroll a patient in the first non-significant risk medical device study or clinical trial as allowed by an institutional review board within six months of the production and release of Ovaprene, unless such failure is caused by events outside of the our reasonable control.

Cooperative Research and Development Agreement with NICHD

In July 2021, we entered into a CRADA with the U.S. Department of Health and Human Services, as represented by NICHD, part of the National Institutes of Health, or NIH, for the conduct of a pivotal Phase 3 clinical study of Ovaprene. See also "Our Pipeline: Clinical Stage Programs – Ovaprene" above. Pursuant to the terms of the CRADA, we are responsible for providing a total of $5.5 million in four payments to NICHD to be applied toward the costs of conducting the Phase 3 study, a total of $1.5 million of which we paid in two installments 2021 and $3.5 million of which we paid in the first quarter of 2022 in accordance with the payment schedule under the CRADA. The final payment, due in the second quarter of 2023, is $500,000. NICHD will be responsible for the other costs related to the conduct of the Phase 3 study and will manage the payment of expenses to other parties involved with the study. Either we or NICHD may terminate the CRADA for any reason upon 30 days' prior written notice to the other party. If the CRADA is terminated before completion of the Phase 3 study, NICHD will cooperate with us to transfer the data and the conduct of the study to us or our designee and will continue to conduct the study for so long as necessary to enable such transfer to be completed without interrupting the study. If we terminate the CRADA before the completion of any active study protocol, we generally will be responsible for providing sufficient clinical supplies of Ovaprene to NICHD in order to complete the study. NICHD may retain and use payments we make under the CRADA for up to one year after expiration or termination to cover costs associated with the conduct of activities described under the research plan in the CRADA that were initiated prior to expiration or termination, and any unused funds will be returned to us. Under the CRADA, each party granted the other party rights to use their respective background inventions solely to the extent necessary to conduct the activities described in the research plan in the CRADA. Subject to the U.S. government's nonexclusive, nontransferable, irrevocable, paid-up right to practice any CRADA invention for research or other government purposes, each party will own inventions, data and materials produced by its employees, and both parties will jointly own inventions jointly invented by their employees in performing the research plan. Under the CRADA, we were granted an exclusive option to negotiate an exclusive or nonexclusive development and commercialization license with a field of use that does not exceed the scope of the research plan to rights that the U.S. government may have in inventions jointly or independently invented by NICHD employees for which a patent application is filed. The CRADA also contains customary representations, warranties, and indemnification and confidentiality obligations. The CRADA expires five years from its effective date.

SST License and Collaboration Agreement

In February 2018, we entered into a license and collaboration agreement with Strategic Science and Technologies-D, LLC and Strategic Science Technologies, LLC, referred to collectively as SST, under which we received an exclusive, royalty-bearing, sublicensable license to develop and commercialize, in all countries and geographic territories of the world, for all indications for women related to female sexual dysfunction and/or female reproductive health, including treatment of female sexual arousal disorder, or the Field of Use, SST's topical formulation of Sildenafil Cream, 3.6% as it existed as of the effective date of this agreement, or any other topically applied pharmaceutical product containing sildenafil or a salt thereof as a pharmaceutically active ingredient, alone or with other active ingredients, but specifically excluding any product containing ibuprofen or any salt derivative of ibuprofen, or the Licensed Products.

The following is a summary of other terms of the SST license agreement:

Invention Ownership. We retain rights to inventions made by our employees, SST retains rights to inventions made by its employees, and each party owns a 50% undivided interest in all joint inventions.

Joint Development Committee. The parties will collaborate through a joint development committee that will determine the strategic objectives for, and generally oversee, the development efforts of both parties under the agreement.

Development. We must use commercially reasonable efforts to develop the Licensed Products in the Field of Use in accordance with a development plan in the agreement, and to commercialize the Licensed Products in the Field of Use. We are responsible for all reasonable internal and external costs and expenses incurred by SST in its performance of the development activities it must perform under the agreement.

Royalty Payments. SST will be eligible to receive tiered royalties based on percentages of annual net sales of Licensed Products in the single digits to the mid double digits, subject to customary royalty reductions and offsets, and a percentage of sublicense revenue.

Milestone Payments. SST will be eligible to receive payments (1) ranging from $0.5 million to $18.0 million in the aggregate upon achieving certain clinical and regulatory milestones in the U.S. and worldwide, and (2) between $10.0 million to $100 million in the aggregate upon achieving certain commercial sales milestones. If we enter into strategic development or distribution partnerships related to the Licensed Products, additional milestone payments would be due to SST.

License Term. Our license continues on a country-by-country basis until the later of 10 years from the date of the first commercial sale of such Licensed Product or the expiration of the last valid claim of patent rights covering the Licensed Product in the Field of Use. Upon expiration (but not termination) of the agreement in a particular country, we will have a fully paid-up license under the licensed intellectual property to develop and commercialize the applicable Licensed Products in the applicable country on a non-exclusive basis.

Termination. In addition to customary termination rights for both parties: (1) prior to receipt of approval by a regulatory authority necessary for commercialization of a Licensed Product in the corresponding jurisdiction, including NDA approval, we may terminate the agreement without cause upon 90 days prior written notice; (2) following receipt of approval by a regulatory authority necessary for commercialization of a Licensed Product in the corresponding jurisdiction, including NDA approval, we may terminate the agreement without cause upon 180 days prior written notice; and (3) SST may terminate the agreement with respect to the applicable Licensed Product(s) in the applicable country(ies) upon 30 days' notice if we fail to use commercially reasonable efforts to perform development activities in substantial accordance with the development plan and do not cure such failure within 60 days of receipt of SST's notice thereof.

Catalent JNP License Agreement

In April 2018, we entered into an exclusive license agreement with Catalent JNP, Inc. (formerly known as Juniper Pharmaceuticals, Inc., and which we refer to as Catalent in this report), under which Catalent granted us (a) an exclusive, royalty-bearing worldwide license under certain patent rights, either owned by or exclusively licensed to Catalent, to make, have made, use, have used, sell, have sold, import and have imported products and processes; and (b) a non-exclusive, royalty-bearing worldwide license to use certain technological information owned by Catalent to make, have made, use, have used, sell, have sold, import and have imported products and processes. We are entitled to sublicense the rights granted to us under this agreement.

The following is a summary of other terms of the Catalent license agreement:

Upfront Fee. We paid a $250,000 non-creditable upfront license fee to Catalent in connection with the execution of the agreement.

Annual Maintenance Fee. We will pay an annual license maintenance fee to Catalent on each anniversary of the date of the agreement, the amount of which will be $50,000 for the first two years, and $100,000 thereafter, and which will be creditable against royalties and other payments due to Catalent in the same calendar year but may not be carried forward to any other year. We made the first of these payments in April 2019.

Milestone Payments. We must make potential future development and sales milestone payments of (1) up to $13.5 million in the aggregate upon achieving certain clinical and regulatory milestones, $1.0 million of which became payable in the third quarter of 2021, and in accordance with the license agreement, the amount was offset by the $100,000 annual maintenance fee, resulting in a net amount of $900,000 paid during the third quarter of 2021, and (2) up to $30.3 million in the aggregate upon achieving certain commercial sales milestones for each product or process covered by the licenses granted under the agreement.

Royalty Payments. During the royalty term, we will pay Catalent mid-single-digit to low double-digit royalties based on worldwide net sales of products and processes covered by the licenses granted under the agreement. In lieu of such royalty payments, we will pay Catalent a low double-digit percentage of all sublicense income we receive for the sublicense of rights under the agreement to a third party. The royalty term, which is determined on a country-by-country basis and product-by-product basis (or process-by-process basis), begins with the first commercial sale of a product or process in a country and terminates on the latest of (1) the expiration date of the last valid claim within the licensed patent rights with respect to such product or process in such country, (2) 10 years following the first commercial sale of such product or process in such country, and (3) when one or more generic products for such product or process are commercially available in such country, except that if there is no such generic product by the 10th year following the first commercial sale in such country, then the royalty term will terminate on the 10-year anniversary of the first commercial sale in such country.

Efforts. We must use commercially reasonable efforts to develop and make at least one product or process available to the public, which efforts include achieving specific diligence requirements by specific dates specified in the agreement.

Term. Unless earlier terminated, the term of the agreement will continue on a country-by-country basis until the later of (1) the expiration date of the last valid claim within such country, or (2) 10 years from the date of first commercial sale of a product or process in such country. Upon expiration (but not early termination) of the agreement, the licenses granted thereunder will convert automatically to fully-paid irrevocable licenses. Catalent may terminate the agreement (1) upon 30 days' notice for our uncured breach of any payment obligation under the agreement, (2) if we fail to maintain required insurance, (3) immediately upon our insolvency or the making of an assignment for the benefit of our creditors or if a bankruptcy petition is filed for or against us, which petition is not dismissed within 90 days, or (4) upon 60 days' notice for any uncured material breach by us of any of our other obligations under the agreement. We may terminate the agreement on a country-by-country basis for any reason by giving 180 days' notice (or 90 days' notice if such termination occurs prior to receipt of marketing approval in the United States). If Catalent terminates the agreement for the reason described in clause (4) above or if we terminate the agreement, Catalent will have full access including the right to use and reference all product data generated during the term of the agreement that is owned by us.

Pear Tree Acquisition

In May 2018, we completed our acquisition of Pear Tree Pharmaceuticals, Inc., or Pear Tree. We acquired Pear Tree to secure the rights to develop a proprietary vaginal formulation of tamoxifen, now known as DARE-VVA1, as a potential treatment for vulvar and vaginal atrophy.

Milestone Payments. Contingent payments to the Pear Tree former stockholders or their representatives that become payable upon achievement of specified clinical, regulatory and commercial milestones, may be paid, in our sole discretion, in cash or shares of our common stock.

Royalty Payments. The former stockholders of Pear Tree will be eligible to receive, subject to certain offsets, tiered royalties, including customary provisions permitting royalty reductions and offset, based on percentages of annual net sales of certain products subject to license agreements we assumed and a percentage of sublicense revenue.

MBI Acquisition

In November 2019, we acquired Dare MB Inc. (formerly, Microchips Biotech, Inc.), or MBI, to secure the rights to develop a long-acting reversible contraception method that a woman can turn on or off herself, according to her own needs. This candidate is now known as DARE-LARC1.

At the closing of the merger, we issued an aggregate of approximately 3.0 million shares of our common stock to the holders of shares of MBI's capital stock outstanding immediately prior to the effective time of the merger. The transaction was valued at $2.4 million, based on the fair value of the approximately 3.0 million shares issued at $0.79 per share, which was the closing price per share of our common stock on the date of closing. The shares were issued in consideration of MBI's cash and cash equivalents of $6.1 million, less net liabilities of $3.5 million and transaction costs of $202,000, which was allocated based on the relative fair value of the assets acquired and liabilities assumed.

We agreed to pay the following additional consideration to the former MBI stockholders: (a) up to $46.5 million contingent upon the achievement of specified funding, product development and regulatory milestones; (b) up to $55.0 million contingent upon the achievement of specified amounts of aggregate net sales of products incorporating the intellectual property we acquired in the merger; (c) tiered royalty payments ranging from low single-digit to low double-digit percentages of annual net sales of such products, subject to customary provisions permitting royalty reductions and offset; and (d) a percentage of sublicense revenue related to such products. We agreed to use commercially reasonable efforts to achieve specified development and regulatory objectives relating to DARE-LARC1. In June 2021, a total of $1.25 million of that potential additional consideration became payable upon the achievement of certain of the funding and product development milestone events, $1.0 million of which was recorded as contingent consideration on our consolidated balance sheets upon the completion of the MBI acquisition and $250,000 of which was expensed in 2021. In July 2021, our board of directors elected to make these milestone payments in shares of our common stock, to the extent permissible under the terms of the merger agreement with MBI, and, in September 2021, we issued approximately 700,000 shares of our common stock to former stockholders of MBI and paid $75,000 in cash to the stockholders' representative in accordance with the terms of the merger agreement in satisfaction of the $1.25 million in milestone payments associated with milestones achieved in June 2021.

Adare Development and Option Agreement

In March 2018, we entered into an exclusive development and option agreement with Adare Pharmaceuticals (formerly known as Orbis Biosciences, and which we refer to as Adare), for the development of long-acting injectable etonogestrel contraceptive with 6- and 12-month durations (now known as ADARE-204 and ADARE-214, respectively). The agreement provides us with an option to negotiate an exclusive license agreement for the programs if we fund the conduct of specified development work by Adare.

Intellectual Property

We actively seek to protect the proprietary technology that we consider important to our business in the United States and other jurisdictions internationally. We also rely upon trade secrets and contracts to protect our proprietary information.

Patents

The medical device and pharmaceutical industries are characterized by the existence of a large number of patents and frequent litigation based on allegations of patent infringement. Patent litigation can involve complex factual and legal questions, and its outcome is uncertain. Any claim relating to infringement of third party patents that is successfully asserted against us or our licensors may require us to pay substantial damages or may limit our or our licensors' ability to rely on such patent protection. Any third party claim successfully alleging the invalidity or unenforceability of the patents may also limit our or our licensors' ability to rely on such patent protection. Even if we, or our licensors were to prevail in any such action, any litigation could be costly and time-consuming and would divert the attention of management and key personnel from our business operations. Also, if our product candidates or any future products are found to infringe the patents of others, our development, manufacture, and sale of these potential products could be severely restricted or prohibited. In addition, there can be no assurance that any patent applications filed by us or our licensors will result in the grant of a patent either in the United States or elsewhere, or that any patents granted will be valid and enforceable, or that any patents will provide a competitive advantage or afford protection against competitors with similar technologies. Because of the importance of the patents underlying our product candidates, our business and our prospects may be harmed if we fail to maintain existing or obtain new patent rights or if we and our licensors fail to protect key intellectual property rights.

Under the terms of the Assignment Agreement with Hammock Pharmaceuticals, Inc. and the License Amendment with TriLogic Pharma, LLC and MilanaPharm, LLC, regarding the thermosetting hydrogel platform which includes XACIATO, we are the exclusive licensee of three issued U.S. patents, two of which are set to expire in December 2028 and one of which is set to expire in September 2036, subject to any extensions or disclaimers, and three foreign patents, including one European Patent Office, or EPO, patent validated in four countries, that expire in December 2028, subject to any extensions or disclaimers. One of the three issued U.S. patents is listed in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," known as the Orange Book, under the Patent Exclusivity Information for XACIATO. In addition, we have rights to three pending foreign patent applications and one pending U.S. patent application. If issued, the patent term for these patents issuing from these pending applications would be expected to expire in 2036, subject to any extensions or disclaimers.

Under the terms of the ADVA-Tec license agreement, regarding Ovaprene, we are the exclusive licensee of nine granted U.S. patents, one pending U.S. patent application, eight granted foreign patents, including four EPO patents validated in a total of 55 countries, and seven pending foreign patent applications. Two of the patents that are particularly important to the protection of Ovaprene have terms until August 2028, which includes days added to the term by patent term adjustment, and a third patent has a term that expires in July 2027, including patent term adjustment, each of such terms being subject to any future extensions or disclaimers.

Under the terms of the SST license agreement, regarding Sildenafil Cream, 3.6%, we are the exclusive licensee in the Field of Use of 22 issued patents worldwide (nine U.S. patents and 13 foreign patents, including two EPO patents validated in a total of 24 countries). Additionally, there is one patent application pending in the US, one in Europe, and two in other international markets. The issued U.S. patents have a patent term that expires in June 2029, including any patent term adjustment, and may be eligible for regulatory exclusivity under the Hatch-Waxman Act, while several foreign patents have a term through that is set to expire in late 2031, each of such terms being subject to any future extensions of disclaimers.

Under the terms of the Catalent license agreement, regarding our intravaginal ring platform which includes DARE-HRT1, we are the exclusive licensee of four issued U.S. patents with patent terms set to expire in April 2024, November 2024, February 2025, and September 2027, including patent term adjustment, four issued foreign patents with patent terms until April 2024, including one European patent validated in three countries, as well as one pending U.S. application and two pending foreign applications that if granted are expected to have patent terms that expire in May 2038, subject to any extensions or disclaimers.

When we acquired Pear Tree Pharmaceuticals, Inc. in 2018, regarding DARE-VVA1, we obtained the rights to three U.S. patents and one Japanese patent. The patent term for the U.S. patents are expected to expire in June 2027, June 2028, and May 2035 including any patent term adjustment, extensions or disclaimers. The Japanese patent has a term that is set to expire in June 2027.

When we acquired MBI in 2019, we obtained the rights to over 100 patents and applications. The key technology underlying the platform is supported by 16 U.S. patents and 45 foreign patents, including six EPO patents validated in various European countries, and six pending patent applications, including two U.S. applications and one Patent Cooperation Treaty (PCT) international application. We believe that three of the most recently granted patent families are most directly applicable to our DARE-LARC1 program. Those patent families have patent terms that are set to expire 2032, 2033, and 2034 respectively, subject to any extensions or disclaimers. Those patent families include patents granted in the U.S., E.U. and other key international markets. One pending U.S. patent application, which has a pending PCT international counterpart, related to DARE-LARC1, if granted, would have a patent term that would be expected to expire in 2040, subject to any extensions or disclaimers.

We also rely upon trade secret rights to protect our product candidates as well as other technologies that may be used to discover, validate and commercialize our current or any future product candidates. We presently seek protection, in part, through confidentiality and proprietary information agreements.

Trademarks

We hold a domestic registration for the trademark Daré Bioscience and our registration for the XACIATO trademark in the U.S. is pending. In accordance with the terms of the ADVA-Tec license agreement, we are the exclusive licensee of the Ovaprene registered trademark.

Competition

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and medical device) are highly competitive and subject to rapid and significant change. Our success is highly dependent upon our

ability to acquire or in-license, develop and obtain regulatory approval for innovative medical products on a cost-effective basis and to market them successfully, either on our own or together with strategic partners. We face and will continue to face intense competition from a variety of businesses, including large, fully integrated, well-established pharmaceutical companies that already possess a significant share of the women's health market. Many of our potential competitors have greater clinical, regulatory, manufacturing, marketing, distribution, compliance and financial resources and experience than we do. See ITEM 1A. "RISK FACTORS—Risks Related to Commercialization of XACIATO and Our Product Candidates— Our product candidates, if approved, and XACIATO will face intense competition and our business and operating results will suffer if we, or our commercial collaborators, fail to compete effectively" and "— The women's health market includes many generic products and growth in generics is expected to continue, which could make the successful introduction of our branded products difficult and expensive" below.

XACIATO will compete directly with the multiple generic and branded prescription drug products currently approved in the U.S. for the treatment of bacterial vaginosis, including oral and vaginal gel formulations of metronidazole and vaginal cream formulations of clindamycin. Branded, single-dose FDA-approved products for bacterial vaginosis include Solosec® (secnidazole) oral granules manufactured for and distributed by Lupin Pharmaceuticals, Inc., Clindesse® (clindamycin phosphate) vaginal cream, 2% manufactured and distributed by Padagis, and Nuvessa™ (metronidazole vaginal gel 1.3%) distributed by Exeltis USA, Inc. Based on the XACIATO product profile reflected in the FDA-approved prescribing information, including the consistent cure rates demonstrated among the subsets of patients defined by prior episodes of bacterial vaginosis (≤ 3 and >3 episodes in the previous 12 months), and the labeling for special populations such as pregnant and lactating women, we expect that the product may to be used by health care providers as a first line option for treating bacterial vaginosis.

Our investigational contraceptive products, including Ovaprene, if approved, will compete with a wide range of prescription and over-the-counter contraceptive options, including hormone-free options such as condoms, diaphragms, cervical caps, sponges, copper IUDs, spermicides and vaginal gels, as well as hormonal products such as pills, patches, vaginal rings and injectables. In addition, multiple new methods of pregnancy prevention are in development, including hormone-free options, and some may be marketed in the U.S. before Ovaprene, potentially adding to the level of market competition Ovaprene will face, if approved.

Currently, there are no FDA-approved therapies for FSAD. Sildenafil Cream, 3.6% has the potential to be the first FDA-approved product for the treatment of FSAD.

Over the longer term, our ability, independently or otherwise, to successfully develop, manufacture, market, distribute and sell any approved products, expand their usage or bring additional new products to the marketplace will depend on many factors, including, but not limited to, FDA and foreign regulatory agency approval of new products and of new indications for existing products, the efficacy and safety of our products (alone and relative to other treatment options), the degree of patent or other protection afforded to particular products, and reimbursement for use of those products.

Many other organizations are developing drug products and other therapies intended to treat the same diseases and conditions for which our product candidates are in development, and the success of others may render potential application of our product candidates obsolete or noncompetitive, even prior to completion of its development.

Government Regulation

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate the research, development, testing, manufacturing, labeling and packaging, storage, recordkeeping, advertising, promotion, import, export, marketing, and distribution, among other things, of pharmaceutical, medical device, and drug-device combination products. The process of obtaining regulatory approvals in the U.S. and in foreign countries and jurisdictions, and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, require the expenditure of substantial time and financial resources.

We and our third-party manufacturers, distributors and contract research organizations, or CROs, may also be subject to government regulation under other federal, state, and local laws, including the U.S. Foreign Corrupt Practices Act, the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, the Health Insurance Portability and Accountability Act, privacy laws and import, export and customs regulations, as well as comparable laws and regulations of other countries.

U*.S. Government Regulation*

In the U.S., the FDA, under the authorities granted to the agency by the Federal Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations, subjects pharmaceutical and other regulated medical products to rigorous premarket review as well as post-marketing oversight and potential enforcement actions. Failure to comply with applicable U.S. requirements at any time during the product development or approval process, or after approval, may subject a company to a variety of administrative or judicial sanctions brought by the FDA and the Department of Justice, or DOJ, or other governmental entities, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending or future marketing applications;
- warning or untitled letters;
- withdrawal of an approval;
- imposition of a clinical hold;
- voluntary product recalls;
- seizures or administrative detention of product;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, civil penalties or criminal prosecution.

FDA Approval Process for Prescription Drugs

To obtain approval of a new drug product from the FDA, we must, among other requirements, submit extensive data supporting its safety and efficacy, as well as detailed information on the manufacture and composition of the drug and proposed product labeling and packaging. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our product candidates.

The process required by the FDA before a new drug may be marketed in the U.S. generally involves some or all of the following key steps:

- completion of nonclinical studies, such as laboratory tests, animal studies, and formulation studies, performed in compliance with FDA regulations for good laboratory practices, or GLPs, and other applicable regulations;
- design of a clinical protocol and its submission to the FDA as part of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to good clinical practices, or GCPs, to establish the safety and efficacy of the product candidate for its intended use;
- submission of a NDA to the FDA along with payment of the application user fee and FDA acceptance of that NDA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the active pharmaceutical ingredient, or API, and finished drug product are produced and tested to assess readiness for commercial manufacturing and conformance to the manufacturing-related elements of the application, to conduct a data integrity audit, and to assess compliance with current good manufacturing practices, or cGMP, in order to assure that the facilities, methods and controls are adequate to preserve the drug candidate's identity, strength, quality and purity;
- possible inspection of selected clinical study sites to confirm compliance with GCP requirements and data integrity; and
- FDA review and approval of the NDA, including satisfactory completion of an FDA advisory committee review of the product candidate, if applicable, which must occur prior to any commercial marketing or sale of the drug product in the U.S.

Preclinical Studies

After a therapeutic candidate is identified for development, it enters the preclinical or nonclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with GLP regulations and the United States Department of Agriculture's Animal Welfare Act, if applicable. A drug sponsor must submit the results of the preclinical

tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some nonclinical testing may continue after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will include one or more clinical protocols detailing, among other things, the objectives of the clinical trial and the safety and effectiveness criteria to be evaluated.

An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND. Occasionally, clinical holds are imposed due to manufacturing issues that may present safety issues for the clinical study subjects.

Human Clinical Trials in Support of an NDA

The clinical investigation of an investigational new drug is divided into three phases that typically are conducted sequentially but may overlap or be combined. The three phases are as follows:

Phase 1. Phase 1 includes initial clinical trials introducing an investigational new drug into humans and may be conducted in subjects with the target disease or healthy volunteers. These trials are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

Phase 2. Phase 2 includes the controlled clinical trials conducted to evaluate the effectiveness of the drug candidate for a particular indication or indications in subjects with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 trials are typically well controlled, closely monitored, and conducted in a relatively small number of subjects.

Phase 3. Phase 3 trials are typically large trials performed after preliminary evidence suggesting effectiveness of the drug candidate has been obtained. They are intended to gather additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling and product marketing approval. Phase 3 trials usually are conducted at geographically dispersed clinical study sites.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed.

A pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with the FDA's GCP requirements. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must report to the FDA serious and unexpected adverse reactions in a timely manner, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure or any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product or therapeutic candidate. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time, via a clinical hold, or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or that the subjects are being exposed to an unacceptable health risk. An institutional review board, or IRB, is responsible for ensuring that human subjects in clinical studies are protected from inappropriate study risks. An IRB at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, monitor the

trial until completed and otherwise comply with IRB regulations. The IRB also may halt a study, either temporarily or permanently, for failure to comply with GCP or the IRB's requirements, or if the investigational new drug has been associated with unexpected serious harm to patients.

During the development of a new drug product candidate, sponsors are given opportunities to meet with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new therapeutic.

Post-approval trials, sometimes referred to as "Phase 4" clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of "Phase 4" clinical trials.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, and purity of the finished drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Marketing Application Submission and FDA Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the product candidate is submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more indications. An NDA includes all relevant data available from pertinent nonclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information on the product candidate's chemistry, manufacturing, and controls, or CMC, and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the product candidate for its intended use to the satisfaction of the FDA.

Under the Prescription Drug User Fee Act, or PDUFA, each NDA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for prescription drug products. Fee waivers or reductions are available in certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from receipt in which to complete its initial review of a standard NDA for a drug that is not a new molecular entity, and six months from the receipt date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification and the sponsor's process to respond to such inquiries. As a result, the NDA review process can be very lengthy. Most innovative drug products (other than biological products) obtain FDA marketing approval pursuant to an NDA submitted under Section 505(b)(1) of the FDCA, commonly referred to as a traditional or "full NDA." In 1984, with passage of the Drug Price Competition and Patent Term Restoration Act, informally known as the Hatch-Waxman Act, that established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs based on an innovator or "reference" product, Congress also enacted Section 505(b)(2) of the FDCA, which provides a hybrid pathway combining features of a traditional NDA and a generic drug application. Section 505(b)(2) enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy data for an existing product, or published literature, in support of its application. Section 505(b)(2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products; for example, an applicant may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness. Section 505(b)(2) permits the filing of an NDA in which the applicant relies, at least in part, on information from studies made to show whether a drug is safe or effective that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. A Section 505(b)(2) applicant may eliminate or reduce the need to conduct certain pre-clinical or clinical studies, if it can establish that reliance on studies conducted for a previously-approved product is scientifically appropriate. The FDA may also require companies to perform additional studies or measurements, including nonclinical and clinical studies,

to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication for which the Section 505(b)(2) NDA applicant has submitted data.

The FDA conducts a preliminary review of all NDAs it receives, whether submitted under Section 505(b)(1) or Section 505(b)(2), to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission, and may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA has 60 days after submission of an NDA to conduct an initial review to determine whether it is sufficient to accept for filing. If the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA. The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, whether it has an acceptable purity profile and whether the product is being manufactured in accordance with cGMP. During its review of an NDA, the FDA may refer the application to an advisory committee of independent experts for a recommendation as to whether the application should be approved. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical trials are not always conclusive, and the FDA or its advisory committee may interpret data differently than the NDA sponsor interprets the same data. The FDA may also re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process.

Before approving an NDA, the FDA will typically inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving the NDA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements and to assure the integrity of the clinical data submitted to the FDA. To ensure cGMP and GCP compliance by its employees and third-party contractors, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

The FDA also may require the submission of a risk evaluation and mitigation strategy, or REMS, plan if it determines that a REMS is necessary to ensure that the benefits of the drug outweigh its risks and to assure the safe use of the product. The REMS plan could include medication guides, physician communication plans, assessment plans and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS plan. The FDA will not approve an NDA without a REMS plan, if required.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities where the drug product or its API will be produced and the clinical trial sites, the FDA will either issue an approval letter or, in some cases, a complete response letter, or CRL, that describes all of the specific deficiencies in the NDA identified by the agency. An approval letter authorizes commercial marketing of the drug product with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application will not be approved in its present form. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the CRL may include recommended actions that the applicant might take to place the application in a condition for approval. If a CRL is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter to the applicant. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, the FDA nevertheless may ultimately decide that the NDA does not satisfy the regulatory criteria for approval.

Even if a drug product receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a product's safety and effectiveness, and/or testing and surveillance programs to monitor the safety of approved products that

have been commercialized. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Programs to Facilitate and Expedite Development and Review of Certain New Drugs

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include, but are not limited to, fast track designation, QIDP designation, and priority review designation. The purpose of these programs is to provide important new drugs to patients earlier than could occur under standard FDA procedures for interacting with and responding to product sponsors during development and regulatory review.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. A drug that is designated as a qualified infectious disease product ("QIDP") is also eligible for fast track status. Fast track designation provides opportunities for more frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the NDA. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply. In addition, fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process.

The Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, included the Generating Antibiotics Incentives Now Act, or the GAIN Act, which directed FDA to implement QIDP designation program. The GAIN Act created incentives for the development of antibacterial and antifungal drug products for the treatment of serious or life-threatening infections. A therapeutic candidate designated as a QIDP is eligible for fast track designation, and the first marketing application submitted for a specific drug product and indication for which QIDP designation was granted will be granted priority review. A subsequent application from the same sponsor for the same product and indication will receive priority review designation only if it otherwise meets the criteria for priority review. As discussed further below under "New Drug Marketing Exclusivity under the Hatch-Waxman Act Amendments & GAIN Exclusivity Extension - Qualified Infectious Disease Product Exclusivity," the GAIN Act also provides the possibility of a five-year exclusivity extension that is added to any other marketing exclusivity for which a QIDP-designated drug qualifies upon FDA approval.

Finally, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, QIDP designation, and priority review do not change the standards for marketing approval and may not ultimately expedite the development or approval process.

From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Post-Approval Requirements for Prescription Drugs

Following approval of a new drug product, the manufacturer and the approved drug are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Moreover, if there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or an NDA supplement, which may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials. In particular, securing FDA approval for new indications is similar to the process for approval of the original indication and requires, among other things, submitting data from adequate and well-controlled clinical trials to demonstrate the product's safety and efficacy in the new indication. Even if such trials are conducted, the FDA may not approve any expansion of the labeled indications for use in a timely fashion, or at all. There also are continuing, annual user fee requirements for that are now assessed as program fees for certain NDA-approved drugs.

In addition, FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and some state agencies, and are subject to periodic unannounced inspections by the FDA for compliance with cGMP and other requirements. Changes to the manufacturing process, specifications or container closure system for an approved drug product are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the NDA sponsor and any third-party manufacturers involved in producing the approved drug product. Accordingly, both sponsors and manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance and other aspects of quality control and quality assurance, and to ensure ongoing compliance with other statutory requirements of the FDCA, such as the requirements for making manufacturing changes to an approved NDA.

Accordingly, even after a new drug approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or the imposition of distribution or other restrictions under a REMS plan. Other potential consequences of regulatory non-compliance include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs; or
- mandated modification of promotional materials and labeling and the issuance of corrective information.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased in to the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act of 1987, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose

requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act, or DSCSA, which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability. The comprehensive system envisioned by this law is being implemented both by the FDA and those various stakeholders towards the shared goal of building an interoperable electronic system to identify and trace prescription drugs distributed in the United States for enhanced supply chain security. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, repackagers, wholesale distributors, and dispensers (primarily pharmacies) over a 10-year period that is expected to culminate in November 2023.

FDA Review and Approval of Medical Devices

Medical devices also are strictly regulated by the FDA in the United States. Under the FDCA, a medical device is defined as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component, part or accessory which is, among other things: intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes." This definition provides a clear distinction between a medical device and other FDA-regulated products such as drugs. If the primary intended use of a medical product is achieved through chemical action or by being metabolized by the body, the product is usually a drug or biologic. If not, it is generally a medical device.

Unless an exemption applies, a new medical device may not be marketed in the United States unless and until it has been cleared through the premarket notification, or 510(k), process, or approved by the FDA pursuant to a PMA. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. As electronic and digital medical devices have become increasingly connected to the Internet, hospital networks, and other medical devices to provide features that improve health care and patient accessibility, FDA and other regulatory authorities have recognized that those same features also increase the risk of potential cybersecurity threats. These types of medical devices may be vulnerable to security breaches, potentially impacting the safety and effectiveness of the device, and accordingly device manufacturers are responsible for identifying cybersecurity risks and hazards associated with their products. In recent years, the FDA has increased its scrutiny of this issue as part of the review and marketing authorization process for new medical devices; the agency also monitors reports of cybersecurity risks as part of its post-marketing device surveillance activities.

Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably assure their safety and effectiveness. Class I devices are those low risk devices for which reasonable assurance of safety and effectiveness can be provided by adherence to the FDA's general controls for medical devices, which include applicable portions of the FDA's Quality System Regulation, or QSR; facility registration and product listing; reporting of adverse medical events and malfunctions; and appropriate, truthful and non-misleading labeling, advertising and promotional materials. Most Class I devices are exempt from premarket regulation; however, some Class I devices require premarket clearance by the FDA through the 510(k) process.

Class II devices are moderate risk devices and are subject to the FDA's general controls, and any other special controls, such as performance standards, post-market surveillance, and FDA guidelines, deemed necessary by the FDA to provide reasonable assurance of the devices' safety and effectiveness. Premarket review and clearance by the FDA for most Class II devices is accomplished through the 510(k) process, although some Class II devices are exempt from the 510(k) requirements. To obtain 510(k) clearance, a sponsor must submit to the FDA a premarket notification demonstrating that the device is substantially equivalent to a device that is already legally marketed in the United States and for which a PMA was not required (i.e., a Class II device). The device to which the sponsor's device is compared for the purpose of determining substantial equivalence is called a "predicate device." The FDA's goal is to make a substantial equivalence determination within 90 days of FDA's receipt of the 510(k) application, but it often takes longer if the FDA requests additional information. Most 510(k)s do not require supporting data from clinical trials, but such data is typically required if the predicate device relied in part on clinical trial data to obtain clearance. After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, will require a new clearance or possibly a pre-market approval. Premarket notifications are subject to user fees, unless a specific exemption applies.

Class III devices are deemed by the FDA to pose the greatest risk to patients, such as life-sustaining or life-supporting devices, devices that present a potential unreasonable risk of illness or injury, or, more generally, devices whose safety and effectiveness cannot be assured solely by the general controls and special controls described above. All Class III devices must be reviewed and approved by the FDA through the PMA process. A PMA must be supported by extensive data including, but not limited to, technical data, nonclinical studies, clinical trials, manufacturing and labeling to demonstrate to the FDA's satisfaction the safety and effectiveness of the device for its intended use. After a PMA is submitted and the FDA determines the application is sufficiently complete, the agency will accept it for filing and begin an in-depth review of the submitted information. By statute, the FDA has 180 days to review the accepted application, although review of the application generally can take between one and three years. During this review period, the FDA may request additional information or clarification of information already provided. Also during the review period, an advisory panel of experts from outside the FDA may be convened to review and evaluate the application and provide recommendations to the FDA as to the approvability of the device. Although the FDA is not bound by the advisory panel decision, it considers such recommendations when making final decisions on approval. In addition, the FDA will conduct a preapproval inspection of the manufacturing facility to ensure compliance with the QSR. New PMA applications or supplements are also required for product modifications that affect the safety and efficacy of the device. PMA (and supplemental PMAs) are subject to significantly higher user fees than are 510(k) premarket notifications.

Novel medical device types that the FDA has not previously classified as Class I, II or III are automatically classified into Class III regardless of the level of risk they ultimately pose to patients and/or users. The Food and Drug Administration Modernization Act of 1997 established a new route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the *De Novo* classification procedure. This procedure allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II based on a benefit-risk analysis demonstrating the device actually presents low or moderate risk, rather than requiring the submission and approval of a PMA application. Prior to the enactment of FDASIA, a medical device could only be eligible for *De Novo* classification if the manufacturer first submitted a 510(k) premarket notification and received a determination from the FDA that the device was not substantially equivalent. FDASIA streamlined the *De Novo* classification pathway by permitting manufacturers to request *De Novo* classification directly without first submitting a 510(k) premarket notification to the FDA and receiving a not substantially equivalent determination. Under the provisions enacted under FDASIA, the FDA is required to classify the device within 120 days following receipt of the *De Novo* application however, the most recent FDA premarket review goals state that in fiscal year 2022, FDA will attempt to issue a decision on 70% of all *De Novo* classification requests received within 150 days of receipt. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. In addition, the FDA may reject the reclassification petition if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk or that general controls would be inadequate to control the risks and special controls cannot be developed. *De Novo* classification requests are also subject to user fees, unless a specific exemption applies.

Clinical trials are almost always required to support a PMA application and are sometimes required for a *De Novo* classification request or 510(k) premarket notification. In order to conduct a clinical investigation involving human subjects for the purpose of demonstrating the safety and effectiveness of a medical device, an investigator acting on behalf of the company must, among other things, apply for and obtain IRB approval of the proposed investigation. In addition, if the clinical study involves a "significant risk" (as defined by the FDA) to human health, the company sponsoring the investigation must also submit and obtain FDA approval of an IDE. An IDE must be supported by appropriate data, such as animal and laboratory testing results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE must be approved in advance by the FDA for a specified number of study participants, unless the product is deemed a non-significant risk device and eligible for abbreviated IDE requirements. Generally, clinical trials for a significant risk device may begin once the IDE is approved by the FDA and the study protocol and informed consent form are approved by a duly-appointed IRB at each clinical trial site.

FDA's IDE regulations govern investigational device labeling, prohibit promotion, and specify an array of GCP requirements, which include, among other things, recordkeeping, reporting and monitoring responsibilities of study sponsors and study investigators. Clinical trials must further comply with the FDA's regulations for IRB approval and for informed consent and other human subject protections. Required records and reports are subject to inspection by the FDA. The results of clinical testing may be unfavorable or, even if the intended safety and efficacy success criteria are achieved, may not be considered sufficient for the FDA to grant approval or clearance of a product.

Post-Marketing Requirements for Medical Devices

After a medical device is placed on the market, numerous regulatory requirements apply that in some ways mirror the post-approval requirements for prescription drugs. These include, but are not limited to:

- submitting and updating establishment registration and device listings with the FDA;
- compliance with the QSR, which requires manufacturers to follow stringent design, testing, control, documentation, record maintenance, including maintenance of complaint and related investigation files, and other quality assurance controls during the manufacturing process;
- pre-scheduled or unannounced device facility inspections by the FDA;
- labeling regulations, which prohibit the promotion of devices for uncleared or unapproved (or "off-label") uses and impose other restrictions relating to promotional activities;
- corrections and removal reporting regulations, which require that manufacturers report to the FDA field corrections or removals if undertaken to reduce a risk to health posed by a device or to remedy a violation of the FDCA that may present a risk to health; and
- post-market surveillance regulations, which apply to certain Class II or III devices when necessary to protect the public health or to provide additional safety and effectiveness data for the device.

Under the FDA medical device reporting, or MDR, regulations, medical device manufacturers are required to report to the FDA information that a device has or may have caused or contributed to a death or serious injury or has malfunctioned in a way that would likely cause or contribute to death or serious injury if the malfunction of the device or a similar device of such manufacturer were to recur. The decision to file an MDR involves a judgment by the manufacturer. If the FDA disagrees with the manufacturer's determination, the FDA can take enforcement action.

Additionally, the FDA has the authority to require the recall of commercialized products in the event of material deficiencies or defects in design or manufacture. The authority to require a recall must be based on an FDA finding that there is reasonable probability that the device would cause serious adverse health consequences or death. Manufacturers may, under their own initiative, recall a product if any distributed devices fail to meet established specifications, are otherwise misbranded or adulterated, or if any other material deficiency is found. The FDA requires that certain classifications of recalls be reported to the FDA within ten working days after the recall is initiated.

As with prescription drugs, the failure to comply with applicable device regulatory requirements can result in enforcement action by the FDA, which may include any of the following sanctions:

- warning letters, fines, injunctions or civil penalties;
- recalls, detentions or seizures of products;
- operating restrictions;
- delays in the introduction of products into the market;
- total or partial suspension of production;
- delay or refusal of the FDA or other regulators to grant 510(k) clearance or PMA approvals of new or modified devices;
- withdrawals of marketing authorization; or
- in the most serious cases, criminal prosecution.

To ensure compliance with regulatory requirements, medical device manufacturers are subject to market surveillance and periodic, prescheduled or unannounced inspections by the FDA, and these inspections may include the manufacturing facilities of subcontractors and third-party component suppliers.

FDA Review and Approval Process for Combination Products

A combination product is a product composed of a combination of two or more FDA-regulated product constituent parts or products, e.g., drug-device or biologic-device. Such products often raise regulatory, policy and review management challenges because they integrate constituent parts that are regulated under different types of regulatory requirements and by different FDA Centers, namely, the Center for Drug Evaluation and Research, or CDER, the Center for Devices and Radiological Health, or CDRH, or the Center for Biologics Evaluation and Research, or CBER. Differences in regulatory pathways for each constituent part can impact the regulatory processes for all aspects of product development and management, including preclinical testing, clinical investigation, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, and post-approval modifications. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated constituent parts that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;
- a drug or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug or device where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- any investigational drug or device packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA's Office of Combination Products, or OCP, was established to provide prompt determination of the FDA Center with primary jurisdiction over the review and regulation of a combination product; ensure timely and effective premarket review by overseeing the timeliness of and coordinating reviews involving more than one center; ensure consistent and appropriate post-market regulation; resolve disputes regarding review timeliness; and review/revise agreements, guidance and practices specific to the assignment of combination products.

OCP determines which Center will have primary jurisdiction for the combination product, referred to as the Lead Center, based on the combination product's "primary mode of action," or PMOA. A mode of action is the means by which a product achieves an intended therapeutic effect or action. The PMOA is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product. The Lead Center has primary responsibility for the review and regulation of a combination product; however a second Center is often involved in the review process, especially to provide input regarding the "secondary" component(s). In most instances, the Lead Center applies its usual regulatory pathway. For example, a drug-device combination product assigned to CDER will typically be reviewed under an NDA, while a drug-device combination product assigned to CDRH is typically reviewed under through a 510(k), PMA, or *De Novo* classification request.

Often it is difficult for OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which Center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product. A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which Center will regulate the combination product. If the sponsor objects to that decision, the sponsor may request that OCP reconsider its decision.

Combination products are subject to FDA user fees based on the type of application submitted for the product's premarket approval or clearance. For example, a combination product for which an NDA is submitted is subject to the NDA fee under PDUFA. Likewise, a combination product for which a PMA is submitted is subject to the PMA fee under the Medical Device User Fee and Modernization Act.

Since a combination product incorporates two or more constituent parts that have different regulatory requirements, a combination product manufacturer must comply with all cGMP and QSR requirements that apply to each constituent part. The FDA has issued a combination product cGMP regulation, along with final guidance, describing two approaches a combination product manufacturer may follow to demonstrate compliance. Under these two options, the manufacturer demonstrates compliance with: (1) All cGMP regulations applicable to each separate

regulated constituent part included in the combination product; or (2) either the drug cGMP or the QSR, as well as with specified provisions from the other of these two sets of requirements (also called the “streamlined approach”). In addition, The 21st Century Cures Act, or the Cures Act, which became law in December 2016 and, among other things, amended provisions of the FDCA, clarified that for drug-device combination products with a device PMOA and an FDA-approved drug constituent part, Hatch-Waxman Act requirements apply. Accordingly, a potential patent dispute regarding the listed drug that is being referenced by the combination product sponsor may delay the marketing authorization of the combination product. Furthermore, the Cures Act amendments applied Hatch-Waxman Act exclusivity provisions (e.g., new chemical entity and new clinical investigation) to the device clearance and approval process for combination products with a device PMOA.

New Drug Marketing Exclusivity under the Hatch-Waxman Act Amendments & GAIN Exclusivity Extension

Orange Book Listing & Patent Certification

As noted above, Congress created the 505(b)(2) NDA pathway in 1984 as part of the Hatch-Waxman Act amendments to the FDCA. At the same time, it also established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are “abbreviated” because they cannot include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer must rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD. Unlike the ANDA pathway, which does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data, the 505(b)(2) regulatory pathway does not preclude the possibility that a follow-on applicant would need to conduct additional clinical trials or nonclinical studies to demonstrate safety or effectiveness of the proposed change(s) being made to a previously approved drug.

In order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug.” Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in the Orange Book. Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

As part of the NDA review and approval process, applicants are required to list with the FDA each patent that has claims that cover the applicant’s product or method of therapeutic use. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential follow-on competitors in support of approval of an ANDA or a 505(b)(2) NDA that relies in full or in part on the reference product.

When an ANDA applicant submits its application to the FDA, it is required to certify to the FDA concerning any patents listed for the reference product in the FDA’s Orange Book. Specifically, the ANDA applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA applicant would.

If the follow-on applicant does not challenge the innovator’s listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product’s listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the follow-on applicant has provided a Paragraph IV certification to the FDA, the applicant

must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA/505(b)(2) applicant.

Non-Patent Exclusivity

An ANDA or 505(b)(2) NDA also will not be approved until any applicable non-patent exclusivities listed in the Orange Book for the referenced product have expired. The Hatch-Waxman Act amendments to the FDCA provided a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) NDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of data exclusivity if an NDA or NDA supplement includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. This three-year exclusivity period often protects changes to a previously approved drug product, such as new indications, dosage forms, route of administration or combination of ingredients. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; rather, this three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving follow-on applications for drugs containing the original active ingredient.

Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDCA; however, an applicant submitting a traditional NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Qualified Infectious Disease Product Exclusivity

Under the GAIN Act amendments to the FDCA, the FDA may designate a product as a QIDP for a specific use for which it is being studied, upon the written request of a sponsor at any time prior to submission of a marketing application. In order to qualify for designation as a QIDP, the drug product candidate must qualify as an antibiotic or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (i) an antibiotic or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (ii) a so-called “qualifying pathogen” found on a list of potentially dangerous, drug-resistant organisms established and maintained by the FDA. In addition to the expedited review benefits that a QIDP-designated drug candidate may be eligible for (described above under “Special FDA Programs to Facilitate and Expedite Development and Review of Certain New Drugs”), such a drug that is approved for the use for which the QIDP designation was granted will receive a five-year extension to any non-patent marketing exclusivity period for which the drug qualified upon approval, such as a five-year NCE exclusivity or three-year new clinical data exclusivity. This so-called GAIN exclusivity extension is not available to a QIDP-designated drug that has previously received the five-year extension period, such as when an applicant is seeking approval for a new indication or new strength for a marketed infectious disease product.

Patent Term Extension

A patent claiming a prescription drug or medical device for which FDA approval is granted may be eligible for a limited patent term extension under the FDCA, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review provided that certain statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug or medical device is under regulatory review while the patent is in force. The restoration period granted on a patent covering a new FDA-regulated medical product is typically one-half the time between the date a clinical investigation on human beings is begun and the submission date of an application for premarket approval of the product, plus the time

between the submission date of an application for approval of the product and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the marketing approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs and medical devices, are required to register and disclose certain clinical trial information on a public registry maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and both NIH and the FDA have recently begun enforcing those requirements against non-compliant clinical trial sponsors.

Other U.S. Health Care Laws and Compliance Requirements

In addition to FDA requirements, several other types of state and federal laws apply and will apply to our operations. These laws include, among others, health care information and data privacy protection laws, transparency laws, and fraud and abuse laws, such as:

- The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, providing, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal health care programs such as the Medicare and Medicaid programs. The federal Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the federal Anti-Kickback Statute to reach large settlements with health care companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under these laws may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. The federal government uses these laws, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other allegedly unlawful sales and marketing practices;
- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal, civil and criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- The Physician Payments Sunshine Act, enacted as part of the ACA (defined below), among other things, imposes reporting requirements on manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report, on an annual basis, to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and, beginning in 2022 for payments and other transfers of value provided in the previous year, certain advanced non-physician health care practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members in such manufacturers;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations impose specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain health care providers, health plans, and health care clearinghouses, that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions; and
- State and local laws which require the registration of pharmaceutical sales representatives.

The majority of states also have statutes or regulations similar to the aforementioned federal anti-kickback and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. We may be subject to state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to health care providers and entities.

Moreover, in November 2020, the U.S. Department of Health and Human Services finalized significant changes to the regulations implementing the Anti-Kickback Statute and the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the health care industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants.

To the extent we commercialize or co-promote our products, if approved, and because such products could be reimbursed under federal and other governmental health care programs, we expect to develop a compliance program that establishes internal controls to facilitate adherence to the rules and health care program requirements. Although compliance programs and adherence thereto may mitigate the risk of violation of and subsequent investigation and prosecution for violations of the laws described above, the risks cannot be eliminated entirely. Ensuring that our current and future business arrangements with third parties comply with applicable health care laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other health care laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal and administrative penalties, including monetary damages, fines, individual imprisonment, disgorgement, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, health care reimbursement or other government programs, including Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with any of these laws, and/or the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

Coverage, Pricing, and Reimbursement

Sales of our drug and drug-device combination products, if approved, will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health care programs,

private health insurers, managed health care providers, and other organizations. These third-party payors are increasingly challenging drug prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, even if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

Significant uncertainty exists as to the reimbursement status for newly approved prescription products, including coding, coverage and payment. Sales of any products for which we obtain marketing approval will depend in part on coverage and adequate payment from third-party payors. There is no uniform policy requirement for coverage and reimbursement for prescription products among third-party payors in the United States; therefore coverage and reimbursement for prescription products can differ significantly from payor to payor.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by third-party payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Accordingly, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product.

Accordingly, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or granted at all. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for health care providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use.

Additionally, the containment of health care costs has become a priority of federal and state governments and the prices of drug products have been a focus in this effort. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of health care. Individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers, or PBMs, and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had and is expected to continue to have a significant impact on the health care industry. The ACA, among other things, imposes a significant annual fee on certain companies that manufacture or import branded prescription drug products. The ACA also increased the Medicaid rebate rate and the volume of rebated drugs has been expanded to include beneficiaries in Medicaid managed care organizations. The ACA also expanded the 340B drug discount program (excluding orphan drugs), including a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, and revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of the Medicaid

drug rebates paid to states. It also contains substantial provisions intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against health care fraud and abuse, add new transparency requirements for the health care industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business.

Since enactment of the ACA, there have been judicial and Congressional challenges to certain aspects of the ACA, and as a result certain sections of the ACA have not been fully implemented or have been effectively repealed through Executive Orders and/or executive agency actions. However, following several years of litigation in the federal courts, in June 2021, the U.S. Supreme Court upheld the ACA when it dismissed a legal challenge to the ACA's constitutionality. Further legislative and regulatory changes under the ACA remain possible, although the new federal administration under President Biden has signaled that it plans to build on the ACA and expand the number of people who are eligible for health insurance subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect the biopharmaceutical industry as a whole or our business in the future. We expect that changes or additions to the ACA, the Medicare and Medicaid programs, such as changes allowing the federal government to directly negotiate drug prices, and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the health care industry in the United States.

Other legislative changes have also been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, which was signed into law on March 27, 2020 and was designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020 (the suspension was subsequently extended through March 31, 2022, with a reduction of the suspension to 1% sequester through June 30, 2022), and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation. The 2021 Consolidated Appropriations Act was subsequently signed into law on December 27, 2020 and extends the CARES Act suspension period to March 31, 2021.

The Biden Administration, which assumed control of the Executive Branch on January 20, 2021, has indicated that lowering prescription drug prices is a priority. For example, in July 2021, President Biden issued a sweeping executive order on promoting competition in the American economy that includes several mandates pertaining to the pharmaceutical and health care insurance industries. Among other things, the executive order directs the FDA to work towards implementing a system for importing drugs from Canada (following on a Trump administration notice-and-comment rulemaking on Canadian drug importation that was finalized in October 2020). The Biden order also called on HHS to release a comprehensive plan to combat high prescription drug prices, and it includes several directives regarding the Federal Trade Commission's oversight of potentially anticompetitive practices within the pharmaceutical industry. The drug pricing plan released by HHS in September 2021 in response to the executive order makes clear that the Biden Administration supports aggressive action to address rising drug prices, including allowing HHS to negotiate the cost of Medicare Part B and D drugs, but such significant changes will require either new legislation to be passed by Congress or time-consuming administrative actions.

It is uncertain whether and how future legislation or regulatory changes could affect prospects for our product candidates or what actions federal, state, or commercial payors for pharmaceutical products may take in response to any such health care reform proposals or legislation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Data Privacy and the Protection of Personal Information

We are subject to laws and regulations governing data privacy and the protection of personal information including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which will continue to affect our business. In the United States, we may be subject to state security breach notification laws, state laws protecting the privacy of health and personal information and federal and state consumer protections laws that regulate the collection, use, disclosure and transmission of personal information. These laws overlap and often conflict and each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties. Our customers and research partners must comply with laws governing the privacy and security of health information, including HIPAA, HITECH and state health information privacy laws. If we knowingly obtain health information that is protected under HIPAA, called "protected health information," our customers or

research collaborators may be subject to enforcement and we may have direct liability for the unlawful receipt of protected health information or for aiding and abetting a HIPAA violation.

State laws protecting health and personal information are becoming increasingly stringent. For example, California has implemented the California Confidentiality of Medical Information Act that imposes restrictive requirements regulating the use and disclosure of health information and other personally identifiable information, and California has recently adopted the California Consumer Privacy Act of 2018, or CCPA. The CCPA mirrors a number of the key provisions of the European General Data Protection Regulation, or GDPR, described below. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. Additionally, a new privacy law, the California Privacy Rights Act, or CPRA, was approved by California voters in the election on November 3, 2020. The CPRA will modify the CCPA significantly, potentially resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply. Other states in the U.S. are considering privacy laws similar to CCPA. In February 2021, the Virginia legislature became the second to enact a state-specific law called the Consumer Data Protection Act, which includes key differences from California's law, further complicating compliance by industry and other stakeholders.

Health Care Reform and Potential Changes to Laws and Regulations

FDA and other regulatory authority policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in August 2017, the FDA Reauthorization Act was signed into law, which reauthorized the FDA's user fee programs and included additional drug and device provisions that build on the Cures Act enacted in December 2016. Furthermore, the next FDA Reauthorization Act is currently being negotiated and is due to be submitted to Congress in 2022. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in health care systems with the stated goals of containing health care costs, improving quality and/or expanding access. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other health care funding and applying new payment methodologies. In addition to the sweeping reforms contained in the ACA (summarized above in the section entitled "Coverage, Pricing, and Reimbursement"), other legislative changes have been proposed and adopted in the United States that may affect health care expenditures. For example, the 2020 Consolidated Appropriations Act (P.L. 116-94) included a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act, or the CREATES Act. The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS program for certain products, to deny generic product developers access to samples of brand products. Because generic product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

Other new laws may result in additional reductions in Medicare and other health care funding, which could have an adverse effect on customers for our approved product and, accordingly, our financial operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services. Moreover, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our therapeutic candidates may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Government Regulation Outside the U.S.

In addition to regulations in the U.S., we may be subject to a variety of regulations in foreign jurisdictions that govern, among other things, clinical trials and any commercial sales and distribution of our products, if approved, either directly or through our distribution partners. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical trials or marketing and sale of the product in those countries. The foreign regulatory approval process includes all of the risks associated with the FDA approval described above, and the time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Some foreign jurisdictions have a drug product approval process similar to that in the U.S., which requires the submission of a clinical trial application much like the IND prior to the commencement of clinical studies. In Europe, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed. To obtain regulatory approval of a therapeutic product candidate under European Union, or EU, regulatory systems, we would be required to submit a Marketing Authorisation Application, which is similar to the NDA, except that, among other things, there are country-specific document requirements. For countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, and recently the United Kingdom, the requirements governing the conduct of clinical trials, product approval, pricing and reimbursement vary from country to country. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Moreover, some nations may not accept clinical studies performed for U.S. approval to support approval in their countries or require that additional studies be performed on natives of their countries. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or any future partner of ours. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

International marketing and distribution of medical devices are also subject to foreign government regulations, which may vary substantially from country to country. There is a trend towards harmonization of quality system standards for medical device products among the European Union, United States, Canada and various other industrialized countries.

As of January 31, 2020, the United Kingdom is no longer a member state of the EU, and therefore a separate marketing authorization application and approval will be required to market a medicinal product in the U.K. The Medicines and Healthcare products Regulatory Agency is the U.K.'s standalone pharmaceutical and medical devices regulator.

Review and Approval of Medicinal Products in the European Union

As in the United States, medicinal products can be marketed in the EU only if a marketing authorization from the competent regulatory agencies has been obtained. Similar to the United States, the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. Also similar to the United States, when a drug-device combination product's principal intended action is accomplished by the drug constituent part, the EU regulates the combination product as a medicinal product.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. Clinical trial applications must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents. In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted and became effective on January 31, 2022. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

To obtain marketing approval of a drug in the EU, an applicant must submit an marketing authorization application ("MAA") either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states, Iceland, Lichtenstein and Norway. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products (such as gene-therapy, somatic cell-therapy or tissue-engineered medicines) and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of certain diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the European Medicines Agency ("EMA") is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use ("CHMP"). Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

The decentralized procedure is available to applicants who wish to market a product in specific EU member states where such product has not received marketing approval in any EU member states before. The decentralized procedure provides for an applicant to apply to one-member state to assess the application (the reference member state) and specifically list other member states in which it wishes to obtain approval (concerned member states). Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labelling and package leaflet, to the reference member state and each concerned member state. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application which is then reviewed and approved commented on by the concerned member states. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

In the EU, only products for which marketing authorizations have been granted may be promoted. A marketing authorization is valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Moreover, even if authorized to be marketed in the EU, prescription-only medicines may only be promoted to health care professionals, not the general public. All promotion should be in accordance with the particulars listed in the summary of product characteristics. Promotional materials must also comply with various laws, and codes of conduct developed by pharmaceutical industry bodies in the EU which govern (among other things) the training of sales staff, promotional claims and their justification, comparative advertising, misleading advertising, endorsements, and (where permitted) advertising to the general public. Failure to comply with these requirements could lead to the imposition of penalties by the competent authorities of the EU member states. The penalties could include warnings, orders to discontinue the promotion of the drug product, seizure of promotional materials, fines and possible imprisonment.

Prior to May 26, 2021, the date on which the new Medical Device Regulation ("MDR") became effective, medical devices marketed in Europe were required to comply with the Essential Requirements defined in Annex I to the EU Medical Devices Directive, or MDD, a coordinated system for the authorization of medical devices. The MDD regulated the design, manufacture, clinical trials, labeling and adverse event reporting for medical devices. Devices that comply with the requirements of a relevant directive are entitled to bear the CE conformity marking, indicating that the device conforms to the essential requirements of the applicable directives. The method of assessing conformity depended on the class of the product, but normally involved a combination of self-assessment by the manufacturer and a third-party assessment by a “Notified Body.” This third-party assessment may consist of an audit of the manufacturer’s quality system and specific testing of the manufacturer’s product.

In 2017, European Union regulatory bodies finalized a new Medical Device Regulation (“MDR”), which replaced the existing MDD framework and provided three years for transition and compliance, for a final effective date of May 26, 2020. As a result of the COVID-19 pandemic, however, the European Parliament voted in April 2020 to postpone implementation of the MDR by one year, giving the medical device industry and Notified Bodies until May 26, 2021 to come into compliance. The MDR changes several aspects of the existing regulatory framework for medical device marketing in Europe and is expected to result in increased regulatory oversight of all medical devices marketed in the EU, which may, in turn, increase the costs, time and requirements that need to be met in order to place an innovative or high-risk medical device on the European market. Specifically, the MDR will require changes in the clinical evidence required for medical devices, post-market clinical follow-up evidence, annual reporting of safety information for Class III products, and bi-annual reporting for Class II products, unique device identification, or UDI, for all products, submission of core data elements to a European UDI database prior to placement of a device on the market, reclassification of medical devices, and multiple other labeling changes. An assessment by a Notified Body of one country within the European Union and designated under the MDR is required in order for a manufacturer to commercially distribute the product throughout the EU. A CE certificate issued under the MDD before May 26, 2021 may remain valid until May 25, 2024 under certain conditions. However, we must acquire approvals under the MDR for new products and renew our existing CE mark certificates once our current certifications expire, which could be challenging and costly.

Review and Approval of Medicinal Products in Canada

Health Canada is the Canadian federal authority that regulates, evaluates and monitors the safety, effectiveness, and quality of drugs, medical devices, and other therapeutic products available to Canadians. Health Canada’s regulatory process for review, approval and regulatory oversight of products is similar to the regulatory process conducted by the FDA. To initiate clinical testing of a drug candidate in human subjects in Canada, a CTA must be filed with and approved by Health Canada. In addition, all federally regulated trials must be approved and monitored by research ethics boards. The review boards study and approve study-related documents and monitor trial data.

Prior to being given market authorization for a drug product, a manufacturer must present substantive scientific evidence of a product’s safety, efficacy and quality as required by the Food and Drugs Act (Canada) and its associated regulations, including the Food and Drug Regulations. This information is usually submitted in the form of a New Drug Submission, or NDS. Health Canada reviews the submitted information, sometimes using external consultants and advisory committees, to evaluate the potential benefits and risks of a drug. If after of the review, the conclusion is that the patient benefits outweigh the risks associated with the drug, the drug is issued a Drug Identification Number (“DIN”), followed by a Notice of Compliance (“NOC"), which permits the market authorization holder (i.e., the NOC and DIN holder) to market the drug in Canada. Drugs granted an NOC may be subject to additional postmarket surveillance and reporting requirements.

All establishments engaged in the fabrication, packaging/labeling, importation, distribution, and wholesale of drugs and operation of a testing laboratory relating to drugs are required to hold a Drug Establishment License to conduct one or more of the licensed activities unless expressly exempted under the Food and Drug Regulations. The basis for the issuance of a Drug Establishment License is to ensure the facility complies with cGMP as stipulated in the Food and Drug Regulations and as determined by cGMP inspection conducted by Health Canada. An importer of pharmaceutical products manufactured at foreign sites must also be able to demonstrate that the foreign sites comply with cGMP, and such foreign sites are included on the importer’s Drug Establishment License.

Regulatory obligations and oversight continue following the initial market approval of a pharmaceutical product. For example, every market authorization holder must report any new information received concerning adverse drug reactions, including timely reporting of serious adverse drug reactions that occur in Canada and any

serious unexpected adverse drug reactions that occur outside of Canada. The market authorization holder must also notify Health Canada of any new safety and efficacy issues that it becomes aware of after the launch of a product.

The Canadian regulatory approval requirements for new drugs outlined above are similar to those of other major pharmaceutical markets. While the testing carried out in Canada is often acceptable for the purposes of regulatory submissions in other countries, individual regulatory authorities may request supplementary testing during their assessment of any submission. Therefore, the clinical testing conducted under Health Canada authorization or the approval of regulatory authorities of other countries may not be accepted by regulatory authorities outside Canada or other countries.

Health Canada has also implemented a similar process as the FDA for regulating combination products comprising both drug and device constituent parts. The agency considers the principal mechanism of action by which the claimed effect or purpose of the product is achieved, and then subjects the entire product to regulation under either the Food and Drug Regulations or the Medical Devices Regulations.

Rest of the World Regulation

In addition to regulations in the United States and Australia, EU, and Canada, we may become subject to a variety of regulations governing clinical studies and commercial sales and distribution of prescription drug and drug-device combination products in other jurisdictions around the world. These laws and regulations typically require the licensing of manufacturing and contract research facilities, carefully controlled research and testing of product candidates and governmental review and approval of results prior to marketing therapeutic product candidates. Additionally, they may require adherence to the FDA's GLPs, GCPs, and GMPs during manufacturing. The process of new drug approvals by regulators in the United States, Canada and the European Union are generally considered to be among the most rigorous in the world.

Whether or not FDA, EMA, or Health Canada approval is obtained for a product, we must obtain approval from the comparable regulatory authorities of other countries before we can commence clinical studies or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for the FDA, EMA, or Health Canada approval. The requirements governing the conduct of clinical studies, product licensing, pricing and reimbursement vary greatly from country to country. In some international markets, additional clinical trials may be required prior to the filing or approval of marketing applications within the country.

Moreover, outside of the United States, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed to. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. In some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

Europe – Data Privacy

On May 25, 2018, the GDPR went into effect, implementing a broad data protection framework that expanded the scope of EU data protection law, including to non-EU entities that process, or control the processing of, personal data relating to individuals located in the EU, including clinical trial data. The GDPR sets out a number of requirements that must be complied with when handling the personal data of European Union-based data subjects including: providing expanded disclosures about how their personal data will be used; higher standards for organizations to demonstrate that they have obtained valid consent or have another legal basis in place to justify their data processing activities; the obligation to appoint data protection officers in certain circumstances; new rights for individuals to be "forgotten" and rights to data portability, as well as enhanced current rights (e.g. access requests); the principal of accountability and demonstrating compliance through policies, procedures, training and audit; and a new mandatory data breach regime. In particular, medical or health data, genetic data and biometric data where the latter is used to uniquely identify an individual are all classified as "special category" data under the GDPR and afforded greater protection and require additional compliance obligations. Further, EU member states have a broad right to impose additional conditions – including restrictions – on these data categories. This is because the GDPR allows EU member states to derogate from the requirements of the GDPR mainly in regard to specific processing situations (including special category data and processing for scientific or statistical purposes). As the EU states

continue to reframe their national legislation to harmonize with the GDPR, we will need to monitor compliance with all relevant EU member states' laws and regulations, including where permitted derogations from the GDPR are introduced.

We will also be subject to evolving EU laws on data export, if we transfer data outside the EU to ourselves or third parties outside of the EU. The GDPR only permits exports of data outside the EU where there is a suitable data transfer solution in place to safeguard personal data (e.g. the European Union Commission approved Standard Contractual Clauses). On July 16, 2020, the Court of Justice of the European Union or the CJEU, issued a landmark opinion in the case *Maximilian Schrems vs. Facebook* (Case C-311/18), called *Schrems II*. This decision calls into question certain data transfer mechanisms as between the EU member states and the U.S. The CJEU is the highest court in Europe and the *Schrems II* decision heightens the burden on data importers to assess U.S. national security laws on their business and future actions of EU data protection authorities are difficult to predict. Consequently, there is some risk of any data transfers from the European Union being halted. If we have to rely on third parties to carry out services for us, including processing personal data on our behalf, we are required under the GDPR to enter into contractual arrangements to help ensure that these third parties only process such data according to our instructions and have sufficient security measures in place. Any security breach or non-compliance with our contractual terms or breach of applicable law by such third parties could result in enforcement actions, litigation, fines and penalties or adverse publicity and could cause customers to lose trust in us, which would have an adverse impact on our reputation and business. Any contractual arrangements requiring the transfer of personal data from the EU to us in the United States will require greater scrutiny and assessments as required under *Schrems II* and may have an adverse impact on cross-border transfers of personal data, or increase costs of compliance. The GDPR provides an enforcement authority to impose large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. We will be subject to the GDPR when we have a European Union presence or "establishment" (e.g., EU based subsidiary or operations), when conducting clinical trials with EU based data subjects, whether the trials are conducted directly by us or through a vendor or partner, or offering approved products or services to EU-based data subjects, regardless of whether involving a EU based subsidiary or operations.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, or FCPA, prohibits U.S. corporations and their representatives from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA would include interactions with certain health care professionals in many countries, either directly or through third parties. Our present and future business has been and will continue to be subject to various other U.S. and foreign laws, rules and/or regulations.

Environmental, Health and Safety Regulation

We are subject to numerous federal, state and local environmental, health and safety, or EHS, laws and regulations relating to, among other matters, safe working conditions, product stewardship, environmental protection, and handling or disposition of products, including those governing the generation, storage, handling, use, transportation, release, and disposal of hazardous or potentially hazardous materials, medical waste, and infectious materials that may be handled by our research laboratories. Some of these laws and regulations also require us to obtain licenses or permits to conduct our operations. If we fail to comply with such laws or obtain and comply with the applicable permits, we could face substantial fines or possible revocation of our permits or limitations on our ability to conduct our operations. Certain of our development and manufacturing activities involve use of hazardous materials, and we believe we are in compliance with the applicable environmental laws, regulations, permits, and licenses. However, we cannot ensure that EHS liabilities will not develop in the future. EHS laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Employees

As of March 30, 2022, we had 28 employees. Twenty of our employees are full-time and eight are part-time, 17 are in research and development and 11 are in general and administrative. Given the differing characteristics of our product candidates, our approach is to engage consultants with experience in varying specialties to help us develop such candidates. Our numerous consultants serve as an extension to our employee base. We believe this approach enables us to access the expertise needed in a cost-efficient manner and without the need to rapidly increase the number of full-time employees and their associated costs. In the future, if we select a commercialization strategy for a

product or product candidate that requires us to establish marketing, sales or distribution infrastructure and capabilities, we may need to rapidly increase our employee base.

Company Information

We were incorporated in Delaware in December 2005. Until July 2017, our corporate name was Cerulean Pharma Inc., or Cerulean. In July 2017, Cerulean completed a business combination with Daré Bioscience Operations, Inc., at which time we changed our name to "Daré Bioscience, Inc." and began to focus on development of innovative, investigational products in women's health. We and our wholly-owned subsidiaries operate in one business segment.

Available Information

Our website is located at *http://www.darebioscience.com*. Information found on our website is not incorporated by reference into this report. We make our filings with the U.S. Securities and Exchange Commission, or SEC, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments and exhibits to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, available free of charge on or through our website, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings at *http://www.sec.gov*.

ITEM 1A. RISK FACTORS

Summary of Risk Factors

Below is a summary of the principal factors that make an investment in our securities speculative or risky. This summary does not address all of the risks that we face. We urge investors to carefully review and consider the additional discussion of the risks summarized in this risk factor summary, and other risks that we face, which can be found below under the heading "Risk Factors," together with other information in this report, before making investment decisions regarding our securities.

- We will need to raise additional capital to continue our operations, execute our business strategy and remain a going concern, and our ability to do so may be limited. If we fail to obtain additional capital, we may be unable to complete development or obtain regulatory approval to commercialize for our product candidates.
- We have a limited operating history, have incurred significant losses since our inception and expect to continue to incur losses for the foreseeable future, which, together with our limited financial resources and substantial capital requirements, make it difficult to assess our prospects.
- Our business depends on obtaining the approval of regulatory authorities, and in particular, FDA approval, to market products that we develop. XACIATO is our first and only FDA-approved product. Our other products are investigational, require the conduct and successful completion of clinical studies and nonclinical work, and may never complete development or be submitted for or receive regulatory approval.
- Clinical development is a lengthy and expensive process with an inherently uncertain outcome. Failure to successfully complete clinical trials and nonclinical activities and obtain regulatory approval to market and sell our product candidates on our anticipated timelines at reasonable costs to us, or at all, particularly Ovaprene and Sildenafil Cream, 3.6%, could have a material adverse effect on our business, operating results and financial condition.
- The regulatory approval processes of the FDA and comparable foreign authorities are expensive, lengthy, time-consuming, and inherently unpredictable. If we are not able to obtain regulatory approvals for our product candidates, our ability to generate product revenue will be materially impaired.
- Drug products and drug/device combination products are complex to manufacture. Manufacturing and supply delays and disruptions may significantly delay our clinical studies, disrupt commercial supply of any approved product, and be expensive for us to resolve.
- Strategic collaborations are a key part of our strategy and our existing strategic collaborations are important to our business. If we are unable to establish and maintain strategic collaborations, or if they are not successful, we may require substantial additional capital to develop and commercialize our products and product candidates and our business and prospects may be materially harmed.
- We have no manufacturing, sales, marketing or distribution infrastructure. We depend heavily on, and expect to continue to rely on, the performance of third parties, including our strategic collaborators, contract manufacturers and suppliers, CROs, medical institutions, and scientific, medical, regulatory and other consultants and advisors to develop our product candidates and commercialize any approved products. Failure of these third parties to perform as expected could result in substantial delays, increased costs or failures of our product development programs, delayed or unsuccessful commercialization of any approved products, and the need for significant additional capital.
- Due in part to our limited financial and human resources, we may fail to effectively execute our product development, regulatory submission and commercialization plans in accordance with communicated timelines, or at all.

- The loss or impairment of our rights under our license agreements for XACIATO or any of our product candidates could prevent us from developing or commercializing them, which could have a material adverse effect on our business prospects, operations and viability.
- The commercial success of XACIATO will depend on Organon's efforts and capabilities, as well as a variety of factors, many of which currently are unknown or uncertain, and if commercialization of XACIATO is not successful, our business and prospects may suffer.
- XACIATO and any future products will face intense competition, including from generic products, and our business, operating results and financial condition will suffer if we, or our commercial collaborators, fail to compete effectively.
- XACIATO and any future products may fail to achieve the degree of market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success, which would negatively impact our business.
- Failure to successfully obtain coverage and reimbursement for XACIATO and any future products from government health care programs and private commercial health insurance companies, or the availability of coverage only at limited levels, would diminish our ability, or that of a commercial collaborator, to generate net product revenue. If out-of-pocket costs for our products are deemed by women to be unaffordable, a commercial market may never develop.
- We have a relatively small number of employees, and if we fail to attract and retain key personnel or experience significant increases in our compensation costs to attract and retain key personnel, our business may materially suffer.
- We may not be successful in our efforts to identify and acquire or in-license additional product candidates or technologies, which may limit our growth potential.
- Our failure to adequately protect or enforce our intellectual property rights, and those of our licensors, could materially harm our proprietary position in the marketplace or prevent or impede the commercialization of XACIATO and any future products.
- Lack of patent protection for the active ingredients in certain of our products and product candidates, including XACIATO and Sildenafil Cream, 3.6%, may limit the commercial opportunity for those products if competitors are able to develop and commercialize safe and effective alternative formulations or methods of delivery of the active ingredients.
- The COVID-19 pandemic, escalating geopolitical events and macroeconomic factors may negatively impact our business, financial condition and results and our stock price, including by increasing the cost and timelines for our clinical development programs or negatively impacting our ability to raise additional capital.
- Product liability lawsuits against us could cause us to incur substantial liabilities.
- The price of our common stock has been and may continue to be highly volatile and such volatility may be related or unrelated to our performance and operating results. Volatility in our stock price may subject us to increased risk of securities litigation, including class-action lawsuits, which could be expensive and divert management attention.
- There is no assurance that we will continue satisfying the listing requirements of the Nasdaq Capital Market, and failure to do so could result in the suspension or delisting of our common stock, which could, among other things, limit demand for our common stock, substantially impair our ability to raise additional capital and have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock.

- Future dilution to our existing stockholders from sales and issuances of our common stock through at-the-market, or ATM, offerings, other types of public or private offerings of our equity securities and upon the exercise of stock options and warrants, or the expectation that such sales of equity may occur, could adversely affect the market price of our common stock, even if our business is doing well.
- Cyber-attacks, security breaches, loss of data and other disruptions to our information technology systems or those of our strategic collaborators or third-party service providers could compromise sensitive information related to our business, delay or prevent us from accessing critical information or expose us to liability, any of which could adversely affect our business and our reputation.

Risk Factors

Investment in our securities involves a high degree of risk and uncertainty. Our business, operating results, growth prospects and financial condition are subject to various risks, many of which are not exclusively within our control, that may cause actual performance to differ materially from historical or projected future performance. We urge investors to consider carefully the risks described below, together with all of the information in this report and our other public filings, before making investment decisions regarding our securities. Each of these risk factors, as well as additional risks not presently known to us or that we currently deem immaterial, could adversely affect our business, operating results, growth prospects or financial condition, as well as the trading price of our common stock, in which case you may lose all or part of your investment.

Risks Related to Our Financial Position and Capital Needs

We will need to raise additional capital to continue our operations and execute our business strategy.

We expect that our net losses will continue for the foreseeable future as we develop and seek to bring to market our existing product candidates and any product candidates we may add to our portfolio in the future. Advancing our investigational women's health products through clinical development and pursuing regulatory approval will require substantial additional investment. We currently do not have the capital necessary to advance all of our product candidates through research and clinical development and regulatory approval. XACIATO is our first and only product approved for marketing and sale and we do not anticipate the potential upfront, milestone and royalty payments to us under our exclusive license agreement for XACIATO will be sufficient to cover all of our operating expenses. Accordingly, our ability to continue as a going concern and execute our business strategy depends on our ability to raise additional capital through equity, debt or structured financings, government or other grant funding, collaborations and strategic alliances or other similar types of arrangements. This report includes disclosures and an opinion from our independent registered public accounting firm stating that our recurring losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. Our financial statements as of December 31, 2021 were prepared under the assumption that we will continue as a going concern and do not include any adjustments that might result from the outcome of this uncertainty.

Our capital needs have depended on, and will continue to depend on, many factors that are highly variable and difficult to predict, including:

- the product development programs we choose to pursue;
- the cost and pace of preclinical and clinical development;
- clinical trial results;
- the cost and timing of obtaining clinical and commercial supplies of products and product candidates;
- the cost and timing of regulatory submissions and decisions by the FDA and other regulatory authorities on our applications to commence clinical development and market our product candidates;
- the costs involved in acquiring or in-licensing product candidates or technologies; and
- our commercialization plans and the timing and terms of our agreements with third parties relating to commercialization of any approved product.

Should we add product candidates to our portfolio, should our existing product candidates require testing or other capital-intensive development activities that we do not anticipate, should the duration of our clinical trials be longer than anticipated, should manufacturing and supply be disrupted, or should regulatory approvals be delayed, our cash resources will be further strained. Should our product development efforts succeed, we will need to develop a commercialization plan for each product, which may also require significant resources to create and implement. In addition, the terms of any collaboration agreements for development and/or commercialization of our product and product candidates may significantly impact our need for additional capital.

At December 31, 2021, our cash and cash equivalents were approximately $51.7 million and our accumulated deficit was approximately $110.1 million. We incurred a net loss of approximately $38.7 million for the year ended December 31, 2021. We may never become profitable. We expect negative cash flows from our operations to continue for the foreseeable future. Based on our current operating plan estimates, we do not have sufficient cash to satisfy our working capital needs and other liquidity requirements over the next 12 months from the date of issuance of the accompanying consolidated financial statements. We will need to raise additional capital or significantly curtail our planned operations to remain a going concern.

Additional capital may not be available to us, or even if it is, the cost of such capital may be high. We may be forced to obtain additional capital before reaching clinical, regulatory and/or sales milestones, when our stock price or trading volume or both are low, or when the general market for life sciences companies is weak. Raising capital under any of these or similar scenarios, if we can raise any at all, may lead to significant dilution to our existing stockholders. See also "Our ability to raise capital may be limited by laws and regulations," and “We are heavily reliant on our ability to raise capital through capital market transactions. A low trading volume, price and market capitalization together with our lack of revenue, net losses, limited operating history and limited amount of unissued authorized common stock may make it difficult and expensive for us to raise additional capital” below.

If we raise capital through collaborations, strategic alliances or other similar types of arrangements, we may be required to relinquish, on terms that are not favorable to us, rights to some of our technologies or product candidates that we would otherwise seek to develop or commercialize. In addition, our current and future commercial license agreements may not provide a level of funding sufficient to satisfy our working capital needs or liquidity requirements, thus requiring that we continue to seek to raise additional capital to fund product development through other means. See also “If a commercial counterparty terminates its exclusive license agreement with us or fails to perform as expected, our need for additional capital may significantly increase,” below. Further, operational disruptions, resource constraints or shifts in business strategy of potential collaborators as a result of the COVID-19 pandemic, macroeconomic factors or escalating geopolitical events may adversely affect collaboration terms and opportunities for our product candidates. See also “Risks Related to Our Business Operations and Industry- The COVID-19 pandemic has negatively impacted our business and, in the future, may materially and adversely affect our business, financial condition and results and stock price, including by increasing the cost and timelines for our clinical development programs,” and “- Our business may be adversely affected by unfavorable or unanticipated macroeconomic conditions and geopolitical events,” below.

There can be no assurance that we can raise capital when needed or on terms favorable to us and our stockholders. The COVID-19 pandemic, macroeconomic conditions, and heightened global uncertainties may adversely affect general commercial activity and the U.S. and global economies and financial markets, which increases uncertainty around our ability to access the capital markets when needed and on acceptable terms. If we cannot raise capital when needed on acceptable terms, or at all, we will not be able to advance our product candidates as currently planned or grow our product portfolio, we will need to reevaluate our planned operations, we may relinquish rights under our license agreements with third parties relating to our product candidates, and we may need to delay, scale back or eliminate some or all of our development programs, reduce expenses or cease operations, any of which would have a significant negative impact on our prospects and financial condition, as well as the trading price of our common stock. Moreover, if we are unable to obtain additional funds on a timely basis, there will be an increased risk of insolvency and up to a total loss of investment by our stockholders.

We have a limited operating history, have incurred significant losses since our inception and expect to continue to incur losses for the foreseeable future, which, together with our limited financial resources and substantial capital requirements, make it difficult to assess our prospects.

We have a limited operating history upon which to evaluate our business and prospects. The development of drug and drug/device combination products in order to obtain regulatory approval is a highly speculative, lengthy and expensive undertaking and involves substantial risk. Other than XACIATO, which received FDA approval in December 2021 and has not yet been commercially launched, we have not obtained any regulatory approvals for any of our product candidates, commercialized any of our product candidates or generated any product revenue. We have not been profitable since we commenced operations and may never achieve profitability. We have devoted significant resources to acquiring XACIATO and our product candidates and to research and development, or R&D, activities for them. Since inception, we have incurred significant operating losses. As discussed above, we must raise additional capital to finance our operations and remain a going concern.

If a commercial counterparty terminates its exclusive license agreement with us or fails to perform as expected, our need for additional capital may significantly increase.

We have entered into an exclusive license agreement with Organon for the commercialization of XACIATO and an exclusive license agreement with Bayer for the commercialization of Ovaprene, if approved. Each of these license agreements may be terminated by the licensee for convenience upon the completion of a specified notice period, subject to limited restrictions. Furthermore, under our agreement with Organon, we will not receive any payments unless the agreement becomes fully effective, and the effective date of the agreement is subject to the satisfaction of closing conditions, including antitrust law clearance which is outside of our control. Moreover, under our agreement with Bayer, Bayer has no future payment obligations to us, unless, after reviewing the results of our pivotal clinical trial of Ovaprene, it elects, in its sole discretion, to make the license grant under our agreement effective by making a $20.0 million payment to us. If we do not successfully complete a pivotal clinical trial of Ovaprene in a timely manner, the license grant may never become effective, and we may not receive any additional payments from Bayer. Bayer may elect not to make the license grant effective regardless of the outcome of the pivotal clinical trial. If an exclusive license agreement is terminated early or does not become fully effective, we may realize none or only a small fraction of the potential value of the agreement to us, and we may need to raise significant additional capital to pursue further development and commercialization of XACIATO or Ovaprene, as applicable.

If these license agreements are not terminated and the license grants become effective, we expect XACIATO's and Ovaprene's value to us to be generated primarily through royalties based on net sales and achievement of commercial milestones. The successful or timely achievement of these milestones is largely outside of our control because the relevant activities will be conducted by the licensee. Accordingly, if the licensee is not successful or has limited commercialization success, our ability to monetize XACIATO and, if approved, Ovaprene, may be significantly impaired and our need for additional capital could significantly increase.

In the future, we may depend to a large degree on payments from third-party licensees to fund our operations, and failure to receive such payments may cause us to, among other things:

- pursue raising additional funds through equity or debt financings that could be dilutive to our stockholders or involve restrictive covenants, operational restrictions and security interests in our assets;
- enter into new strategic collaborations that may be less favorable than those we would have obtained under different circumstances;
- delay, reduce or terminate one or more development programs;
- reduce headcount;
- forgo opportunities to expand our product portfolio; or
- consider strategic transactions with a third party.

Our ability to raise capital may be limited by laws and regulations.

During the year ended December 31, 2021 and through March 30, 2022, we raised approximately $70.9 million in gross proceeds through the sale of equity securities under a Form S-3 "shelf" registration statement. Using a shelf registration statement to raise capital generally takes less time and is less expensive than other means, such as conducting an offering under a Form S-1 registration statement. We currently have a shelf registration statement effective, however, our ability to raise capital under this registration statement was in the past, and may again be in the future, limited by, among other things, current and future SEC rules and regulations impacting the eligibility of smaller companies to use Form S-3 for primary offerings of securities. For example, in fiscal year 2020, we were subject to the "baby shelf rule" because the market value of our outstanding shares of common stock held by non-affiliates, or public float, was less than $75.0 million at the time we filed our shelf registration statement on Form S-3 and remained below $75.0 million during the year. As a result, that we were able to use our shelf registration statement to raise additional funds only to the extent that the aggregate market value of securities sold by us or on our behalf pursuant to Instruction I.B.6. of Form S-3 during the 12 calendar months immediately prior to, and including, any intended sale did not exceed one-third of the aggregate market value of our public float, calculated in accordance with the instructions to Form S-3. In the future, if our public float were to decline below $75.0 million at the time we file our next annual report on Form 10-K, which will be due in March of 2023, we could again become subject to the baby shelf rule. If our ability to offer securities under an effective shelf registration statement is limited, including by the baby shelf rule, we may choose to conduct an offering of our securities under an exemption from registration under the

Securities Act or under a Form S-1 registration statement. We would expect either of these alternatives to take more time and be a more expensive method of raising additional capital relative to using our shelf registration statement.

In addition, under SEC rules and regulations, our common stock must be listed and registered on a national securities exchange in order to use a Form S-3 registration statement (1) for a primary offering, if our public float is not at least $75.0 million as of a date within 60 days prior to the date of filing the Form S-3 or a re-evaluation date, whichever is later, and (2) to register the resale of our securities by persons other than us (i.e., a resale offering). While our common stock is currently listed on the Nasdaq Capital Market, there can be no assurance that we can maintain such listing. See, “Risks Related to Our Securities-There is no assurance that we will continue satisfying the listing requirements of the Nasdaq Capital Market,” below.

Our ability to raise capital on a timely basis through the issuance and sale of equity securities may also be limited by Nasdaq’s stockholder approval requirement for any transaction that is not a public offering (as defined in Nasdaq listing rules). For transactions other than public offerings, Nasdaq requires stockholder approval prior to the issuance or potential issuance of common stock (or securities convertible into or exercisable for common stock) at a price per share that is less than the "Minimum Price" if the issuance (together with sales by our officers, directors and substantial shareholders (as defined in Nasdaq listing rules)) would equal 20% or more of our common stock outstanding before the issuance. Under Nasdaq rules, the "Minimum Price" means a price that is the lower of (i) the Nasdaq official closing price immediately preceding the signing of the binding agreement; or (ii) the average Nasdaq official closing price of the common stock for the five trading days immediately preceding the signing of the binding agreement. In addition, certain prior sales of securities by us may be aggregated with any offering we may propose at a price that is less than the Minimum Price and which is not considered a public offering by Nasdaq, further limiting the amount we could raise in the offering. Under Nasdaq rules, stockholder approval is also required prior to the issuance of securities when the issuance or potential issuance will result in a change of control of our company. Even if a public offering under Nasdaq rules is not subject to the 20% limitation described above, it may involve publicly announcing the proposed transaction before it is completed, which often has the effect of depressing a company's stock price. Accordingly, our existing investors may suffer greater dilution if we seek to raise additional capital through such a public offering of our securities.

Furthermore, our ability to raise capital through the issuance and sale of equity securities is limited by the number of shares of our common stock that we are authorized to issue, and increasing the number of authorized shares of our common stock requires stockholder approval. Currently, we are authorized to issue up to 120,000,000 shares of our common stock and, as of March 30, 2022, 92,244,591 shares of our common stock were outstanding or reserved for issuance upon exercise of outstanding warrants or stock options or for future equity awards under our stock incentive plan, which leaves only 27,755,409 shares of our authorized common stock unreserved and available for issuance.

Obtaining stockholder approval is a costly and time-consuming process. If we must obtain stockholder approval to increase the amount of common stock we are authorized to issue or for a potential transaction, we would expect to spend substantial additional money and resources. In addition, seeking stockholder approval would delay our receipt of otherwise available capital, which may materially and adversely affect our ability to execute our business plan, and there is no guarantee our stockholders ultimately would approve a proposed increase in our authorized common stock or a proposed transaction.

We are heavily reliant on our ability to raise capital through capital market transactions. A low trading volume, price and market capitalization together with our lack of revenue, net losses, limited operating history and limited amount of unissued authorized common stock may make it difficult and expensive for us to raise additional capital.

We are heavily reliant on our ability to raise additional capital by selling shares of our common stock or securities linked to our common stock. Our ability to raise capital through capital market transactions will depend on several factors, many of which may not be in our favor, including the trading volume and volatile trading price of our common stock, our relatively low public float and market capitalization, our potential inability to continue to satisfy the listing requirements of the Nasdaq Capital Market, unfavorable market conditions or other market factors outside of our control, and the risk factors described elsewhere in this report. In addition, our ability to raise additional capital by selling shares of our common stock or securities linked to our common stock is limited by the amount of our unissued authorized common stock. See also “Our ability to raise capital may be limited by laws and regulations,” above, and the risk factors under “Risks Related to Ownership of Our Common Stock,” below.

Even if we are able to raise additional capital, it will likely be dilutive to existing stockholders and the cost of such capital may be substantial and may be more expensive than the cost of capital for larger public companies. The terms of any funding we obtain may not be favorable to us and may be highly dilutive to our stockholders, and debt financing, if available, may involve restrictive covenants, operational restrictions and security interests in our assets

that may have negative consequences for us, including, among other things, by increasing our vulnerability to adverse economic and industry conditions, limiting our ability to obtain additional funding and enter into partnership and other strategic agreements, and requiring the dedication of a portion of our cash flow to service our indebtedness. There can be no assurance that we can raise additional capital when needed. Failing to raise additional capital when needed would have a material adverse effect on our business.

Due in part to our limited financial resources, we may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable indications or therapeutic areas for our product candidates, we may be unable to pursue and complete the clinical trials we would like to pursue and complete, and we may be unable to commence or complete clinical trials and pursue regulatory approvals in accordance with our current timeline expectations.

Our current financial and technical resources are limited and not sufficient to develop all of the product candidates to which we hold licenses or options to license. This may affect our efforts to develop and bring to market the product candidates currently in our portfolio and any candidates we may add to our portfolio in the future. Due to our limited resources, we may be required to curtail our development programs and clinical and nonclinical development activities that might otherwise have led to more rapid progress of our product candidates, or product candidates that we may in the future choose to develop, through the regulatory and development processes. We may make determinations with regard to the indications and clinical trials on which to focus our resources that result in our realization of less than the full potential value of a product candidate. The decisions to allocate our research, management and financial resources toward particular indications may not lead to positive clinical milestones or to the development of viable commercial products and may divert resources from better opportunities. Similarly, our decisions to delay or terminate development programs may also cause us to miss valuable opportunities, including the potential for some of our product candidates to be first-in-category products.

As a result of financial and other resource constraints, we may be unable to commence or complete our planned clinical trials or prepare and submit applications for marketing approval of our product candidates in accordance with our currently anticipated timelines. See also “Risks Related to Product Research & Development, and Regulatory Approval – Delays in the commencement or completion of clinical testing of product candidates we are developing or may develop in the future may occur due to any of a number of factors and could result in significantly increased costs and longer timelines and could impact our ability to ever become profitable” below.

Risks Related to Product Research & Development and Regulatory Approval

XACIATO is our first and only FDA-approved product. The FDA’s approval of XACIATO does not provide any assurance or predict that we will be successful in developing or achieving regulatory approval of any other product candidate. If we are unable to successfully conduct and complete development of and obtain regulatory approvals for our investigational products, which may never occur, our business may fail and you could lose all or part of your investment.

Historical success in clinical development of and obtaining regulatory approval for a product candidate does not guarantee or predict future successful outcomes for other investigational products. Each of our development programs is unique and subject to substantial uncertainty of success inherent in pharmaceutical and biopharmaceutical development.

Except for XACIATO, which was approved by the FDA for U.S. marketing in December 2021 but has not yet been commercially launched, our pipeline consists entirely of investigational products, which we also refer to as product candidates, which means that they must successfully complete one or more clinical studies to be considered for marketing approval by the FDA, or similar regulatory authorities for jurisdictions outside of the U.S., and will require submission of an application to and approval of that application by the FDA to be marketed in the U.S., and will need to undergo a submission, review and approval process with other regulatory authorities to be marketed outside of the U.S. FDA or other regulatory authority approval may never be obtained. XACIATO has not been approved for marketing anywhere outside of the U.S., and cannot be marketed outside of the U.S. unless and until marketing applications for other jurisdictions are submitted and approved by the applicable regulatory authorities, which may require additional clinical and nonclinical development, and may never occur. If we are unable to successfully complete development of and obtain regulatory approvals for our product candidates, our business may fail and you could lose all or part of your investment.

We depend heavily on the successful development of our lead product candidates, Ovaprene and Sildenafil Cream, 3.6%. Clinical development is a lengthy and expensive process with an inherently uncertain outcome. Failure to successfully develop and obtain regulatory approval to market and sell either of these product candidates would likely adversely affect our business.

Our business depends on the successful clinical development and regulatory approval of our lead product candidates, which may never occur. The product candidates we develop require substantial clinical testing to demonstrate that they are safe and effective for their proposed uses. Clinical testing is expensive, difficult to design and implement, can take many years to complete and its outcome is inherently uncertain. A failure of one or more clinical trials could occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of success of later clinical trials, and interim results of a particular clinical trial do not necessarily predict final results of that trial. Accordingly, while some of our product candidates have undergone clinical trials and demonstrated positive results, including Ovaprene and Sildenafil Cream, 3.6%, there is no guarantee of successful outcomes in future clinical studies of these product candidates or of obtaining marketing approval for any of them. The fact that the active pharmaceutical ingredients in certain of our product candidates, including Sildenafil Cream, 3.6%, have received regulatory approval in other formulations and/or for other indications does not guarantee successful development of our product candidates for their proposed intended uses. Clinical trials may never demonstrate sufficient safety and effectiveness to obtain the requisite regulatory approvals for our product candidates.

Even if we conduct and complete clinical trials for our product candidates, we may not obtain regulatory approval to market and sell any of them on the timelines we anticipate, or at all, which would have a material adverse effect on our business and operations.

Delays in the commencement or completion of clinical testing of our product candidates may occur due to any of a number of factors and could result in significantly increased costs and longer timelines and could impact our ability to ever become profitable.

Clinical trials of our product candidates may not commence, progress or be completed as expected. Delays could significantly impact our product development costs and timelines, as well as a product candidate's market potential, if ultimately approved. The timing of initiation, conduct and completion of clinical trials and other development activities for our product candidates may vary dramatically due to factors within and outside of our control and is difficult to predict accurately. We may make statements regarding anticipated timing for commencement, completion of enrollment, and/or availability of results from our clinical studies, but those statements are predictions based on significant assumptions and the actual timing of achievement of development milestones may differ materially from our predictions for a variety of reasons.

The commencement of clinical trials of our product candidates can be delayed for many reasons, including:

- lack of adequate capital and the need to obtain additional funding;
- delays in obtaining guidance or authorizations from the FDA or foreign regulatory authorities;
- delays in obtaining approval from the institutional review boards, or IRBs, of prospective clinical study sites;
- delays in finalizing the trial design as a result of discussions with the FDA, foreign regulatory authorities, prospective clinical trial investigators or IRBs;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites; or
- inability to obtain sufficient quantities of clinical product supplies from our contract manufacturers and suppliers.

Once a clinical trial has begun, it may be delayed, suspended or terminated by us, an IRB, the FDA or other regulatory authorities as a result of the occurrence of any of a number of events or circumstances, including the following:

- lack of adequate capital and the need to obtain additional funding;
- failure to conduct the clinical trial in accordance with regulatory or IRB requirements;
- slower than expected rates of participant recruitment and enrollment;
- higher than anticipated participant drop-out rates;
- failure of participants to use the investigational product as directed or to report data as per trial protocols;

- inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- failure to achieve certain efficacy and/or safety standards;
- participants experiencing severe undesirable side effects or other unexpected adverse events related to the investigational product;
- disruptions in or insufficient supply of clinical trial material or inadequate quality of such materials;
- failure of our CROs or other third-party service providers to meet their contractual obligations to us in a timely manner, or at all; or
- delays quality control/quality assurance procedures necessary for study database lock and analysis of unblinded data.

Unexpected serious adverse events or other undesirable side effects could arise during clinical development and interrupt, delay, or cause the termination of clinical trials, and require us to conduct additional clinical and nonclinical studies that were not part of our development plan, which could significantly increase the development costs and timeline for a program and adversely impact its value and our ability to continue product development. These events may also cause our reputation to suffer and subject us to lawsuits.

The COVID-19 pandemic and recent geopolitical events are evolving and uncertain additional risks to our development timelines, having the potential to cause or contribute to significant delays in commencement and completion of our clinical trials. Global supply chain disruptions may adversely affect the ability of contract manufacturers to manufacture and supply our clinical trial material. Our prospective or contracted clinical trial sites may temporarily suspend activities at their sites for the safety of their employees or to adhere to government recommendations or orders related to social distancing and limiting public gatherings, or they may experience resource constraints, including staffing shortages, stemming from the pandemic and become unable to allocate adequate resources to reach agreements necessary to commence our clinical trials at their facilities or, even if agreements are in place, to conduct our clinical trials. For clinical trials that we are able to initiate, we may experience lower than anticipated subject enrollment and completion rates, including because individuals may avoid medical settings due to concerns of contracting COVID-19 or may become subject to governmental orders or adhere to governmental guidelines intended to reduce the spread of COVID-19, or, during periods when COVID-19 case rates are low, prospective participants may be less inclined to participate in or complete clinical studies that require multiple clinic visits when they have more freedom to travel and participate in other activities that were not available or considered too risky during other stages of the pandemic. In addition, increased rates of employee absences due to worker or family member illness and work-from-home and restricted travel policies implemented in response to the COVID-19 pandemic may delay any regulatory authority and/or IRB approvals necessary for our clinical trials and/or prevent our CROs and other third-party contractors who are necessary for the conduct of our clinical trials from meeting their contractual obligations to us in a timely manner, any of which could delay commencement and completion of our clinical trials.

Significant clinical trial delays could adversely impact on financial condition and results of operations by substantially increasing the costs of our development programs. Significant clinical trial delays also could jeopardize our ability to meet obligations under agreements under which we license our rights to our product candidates, allow other companies to bring competitive products to market before we do, shorten any period of market exclusivity we may otherwise have under our patent rights, and weaken our negotiating position in discussions with potential collaborators, any of which could impair our ability to successfully commercialize our product candidates, if ultimately approved. Any significant delays in commencement or completion of clinical trials of our product candidates, or the suspension or termination of a clinical trial, could materially harm our business, financial condition and results of operations.

Manufacturing and supply delays and disruptions may significantly delay our clinical studies and be expensive for us to resolve.

Our product and product candidates are complex to manufacture and we rely on single source contract manufacturers and suppliers. Manufacturing disruptions may occur that may be difficult and expensive to resolve and may cause substantial delays in development of our product candidates. To date, our clinical-stage product candidates have been tested only in a relatively small number of clinical study participants. A significant scale-up of manufacturing by our contract manufacturers and suppliers may be necessary to meet our supply requirements for Phase 2 or Phase 3 clinical studies, which may take longer and be more expensive than anticipated, potentially resulting in a significant negative impact our development timelines and costs.

For example, the pivotal clinical study of Ovaprene will require far more clinical product supplies than were manufactured for prior clinical and nonclinical studies combined, and the quantity of Ovaprene clinical supplies needed to support the pivotal clinical study has not yet been produced. A substantial scale up in production is necessary to meet the study's requirements, which may not occur on projected timelines and may be more expensive for us than anticipated. Manufacturing disruptions may delay commencement of the pivotal clinical study or disrupt the conduct of the study after commencement. Under our agreement with ADVA-Tec, we are dependent on ADVA-Tec and its contract manufacturers for all Ovaprene clinical and commercial product supplies and we have limited ability to influence or control the efforts and resources they expend to meet our supply requirements. Furthermore, some of the key raw materials and components of Ovaprene have only a single source of supply. Global supply chain disruptions related to the COVID-19 pandemic or recent geopolitical events may contribute to delays in and increased costs for the manufacture and supply of sufficient quantities of Ovaprene to meet the pivotal clinical study's requirements.

See also "Risks Related to Our Dependence on Third Parties- We rely on third-party suppliers and manufacturers for clinical and commercial supplies of XACIATO and our product candidates, including multiple single source suppliers and manufacturers, and we currently have no plans to build or acquire our own manufacturing capabilities. If these third parties do not perform as we expect, do not maintain their regulatory approvals or become subject to negative circumstances, it could delay, prevent or impair our product development or commercialization efforts, or those of our collaborators," and "- In some cases, we may be contractually required to obtain clinical or commercial product supplies from specific third parties or there may be a limited number of third-party suppliers of raw materials and other components of our product and product candidates, which may heighten our dependence on those third parties and the risk of manufacturing disruptions" below.

Ovaprene is a drug/device combination and the process for obtaining regulatory approval in the United States will require compliance with complex procedures because concordance between two centers of the FDA (CDRH and CDER) is necessary for approval of this combination product. A change in the FDA's prior determination that CDER would lead the review of a marketing application for Ovaprene would adversely impact Ovaprene's development timeline and significantly raise our costs to complete clinical development and obtain regulatory approval for Ovaprene.

Ovaprene is composed of both device and drug components and is considered a combination product by the FDA. Ovaprene previously underwent a request for designation, or RFD, process with the FDA that determined that CDRH would lead the review of a PMA for potential marketing approval of this product candidate. If the designation were to be changed to CDER, or if either center were to institute additional requirements for the approval of Ovaprene, we could be required to complete clinical studies with more patients and over longer periods of time than is currently anticipated. This would significantly increase the anticipated cost and timeline to completion of Ovaprene's development and require us to raise additional funds. Based on discussions with the FDA, we believe that if our planned pivotal clinical study of Ovaprene is successful, the FDA will not require additional clinical studies to support the PMA for Ovaprene. However, the FDA may determine that the results of the study are not sufficiently robust or convincing and require additional clinical and/or nonclinical studies prior to approval of Ovaprene. In addition, our ability to commence the pivotal clinical study of Ovaprene is subject to the FDA's review and approval of an IDE, the timing of which will be later than we anticipated when we initiated the process based feedback from the FDA, and could delay or contribute to a delay in the commencement of the pivotal clinical study. Because Ovaprene is one of our lead product candidates, the impact of either a change in the lead FDA review center or the imposition of additional, currently unplanned requirements for approval could be significant to us and have a material adverse effect on the prospects for developing Ovaprene, as well as on our business and our financial condition. See also "The commercial success of Ovaprene will depend on market acceptance of a hormone-free monthly, intravaginal product, availability and effectiveness of alternative contraceptive products and women's preferences, as well as the success of Bayer's marketing and sales efforts" below.

The factors contributing to female sexual dysfunction disorders, including FSAD, are complex and there is limited clinical trial precedent from which to draw experience, making the design and execution of a clinical trial that demonstrates effectiveness of Sildenafil Cream, 3.6% in treating FSAD more inherently challenging and uncertain compared with investigational products for many other conditions.

There are currently no FDA-approved treatments for female sexual arousal disorder, or FSAD, and there is no precedent program to reference in the design of our clinical trials for Sildenafil Cream, 3.6%. Female sexual dysfunction disorders in women vary in nature and may be the result of a variety of physiological and psychological factors. Given the variability of factors contributing to the underlying condition, and the product candidates attributes, clinical studies to evaluate effectiveness in any subset of the condition under the umbrella of Sexual Dysfunction, such as FSAD, are complex. While we worked with experts to develop novel patient reported outcome, or PRO, instruments for our ongoing Phase 2b study of Sildenafil Cream, 3.6%, tested the proposed PRO instruments in a

content validity study, reviewed the results of that study with the FDA and aligned with the FDA on the Phase 2b study design, the Phase 2b study may nevertheless prove difficult to enroll on the anticipated timeline or fail to demonstrate effectiveness of Sildenafil Cream, 3.6% in treating FSAD. For example, Sildenafil Cream, 3.6% is designed to work primarily by increasing blood flow to the genital tissue. Therefore, it will be critical for us to identify and enroll patients in our clinical trials of Sildenafil Cream, 3.6% for whom inadequate blood flow to the genital tissue is the primary contributor to their arousal disorder. If we fail to screen properly, and instead enroll patients with different contributing factors, the results of our clinical trials are unlikely to demonstrate effectiveness of Sildenafil Cream, 3.6%. Conversely, trying to screen out patients with different contributing factors may slow enrollment in a study, delay its completion and increase its costs. The pace of enrollment of participants in the study during 2021 was slower than expected. We identified a number of contributing factors and implemented mitigation strategies to increase study subject recruitment, however, the initial slower pace of enrollment lengthened our original estimated timeline for the study. We may experience additional delays in enrollment relative to what we currently anticipate, which may further lengthen the study timeline and increase its overall cost.

Even if we can identify and enroll a sufficient number of women for whom inadequate blood flow to the genital tissue is the primary contributing factor to their arousal disorder, there is no guaranty that the use of Sildenafil Cream, 3.6% will improve their general feelings of arousal or that the PRO instruments we utilize to measure the effectiveness of Sildenafil Cream, 3.6% in the study will adequately capture their genital arousal response. Given the factors contributing to arousal disorders, we may be required to conduct clinical trials in large patient populations, extending the timeline and increasing the cost of development for Sildenafil Cream, 3.6%. For example, the total number of participants that the Phase 2b study will seek to randomize has not yet been determined and the high end of the range is almost 200 more participants than the low end. The final size of the study will be determined by a single interim analysis for unblinded sample size re-estimation, which analysis has not yet occurred. If the study requires a number of randomized participants on the high end of the range, then the study could take significantly longer and be significantly more expensive to complete than if the final size of the study need only be on the low end of the range. If we are unable to efficiently and successfully complete our Phase 2b clinical trial of Sildenafil Cream, 3.6%, product development costs for the program would increase significantly, and such failure could negatively impact the perception of the program's potential for future clinical and regulatory success, either of which could have a material adverse effect on our business, results of operations and financial condition, as well as our stock price.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data, and others, including regulatory authorities, may not agree with our interpretation of study data.

From time to time, we may publicly disclose interim, preliminary or topline data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analysis of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results of clinical trials we report may differ from final results reported for those studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final, complete data are available.

Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. There can be no guarantee that a favorable interim analysis will result in a favorable final result at the completion of the clinical trial.

Further, others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of study data differently than we do, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically an extensive set of data and analyses, and investors and others may disagree with the information we determine is the material or otherwise appropriate information to include in our public disclosure. Information we determine not to publicly disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate, product or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Our business depends on obtaining regulatory approval to market our product candidates in a timely manner, in particular, FDA approval. The regulatory approval processes of the FDA and comparable foreign authorities are expensive, lengthy, time-consuming, and inherently unpredictable. If we are not able to obtain regulatory approvals for our product candidates, our ability to generate product revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, release, safety, efficacy, regulatory filings, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA, other regulatory authorities in the U.S., and comparable authorities in other countries or jurisdictions where we seek to test or market our product candidates. The process of obtaining marketing approvals in the U.S. and elsewhere is expensive, may take many years and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. In addition, requirements for approval may change over time and our current development plans may not accurately anticipate all applicable requirements for marketing approval by the FDA or comparable regulatory authorities for jurisdictions outside the U.S.

Our success depends on our ability to obtain regulatory approvals for our product candidates in a timely and cost-efficient manner. Even if we successfully complete nonclinical studies, clinical studies, manufacturing and other required activities, we may still experience delays in our efforts to obtain marketing approvals for any of our product candidates. Marketing approval applications require the submission of extensive clinical and nonclinical data and supporting information to establish the safety and efficacy of our product candidates for the specified indication. The process of responding to the FDA or other regulatory authorities' information requests in the review process, potentially preparing for and appearing at a public advisory committee or oral hearing, and preparing our third-party manufacturers and clinical investigators to successfully complete inspections by the FDA or other regulatory authorities during the approval process requires significant human and financial resources.

We may change the development plan for a product candidate as a result of changes during the development period in the FDA's marketing approval policies or the amendment or enactment of additional statutes or regulations, updated interpretations of applicable policies, statutes or regulations, or upon review of outcomes of other similar product candidates under development. This could significantly lengthen our development timelines and cost.

The FDA and comparable regulatory authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that the data are insufficient for approval and require additional clinical or nonclinical studies or changes in the manufacturing process or facilities, even if we had previously aligned with the FDA on such data and other requirements. We cannot assure you that we will obtain any additional marketing approvals for our product or product candidates in any jurisdiction.

The announcement of new requirements by the FDA, the failure of a competitive product to receive regulatory approval, or the receipt of a complete response letter from the FDA by another company pursuing the FDA's 505(b)(2) pathway that may have implications for our proposed regulatory approval pathway could impact how investors and potential strategic collaborators view the development risks associated with our product candidates. Changing testing or manufacturing requirements for our product candidates or for product candidates deemed to be comparable to ours may adversely impact our financial resources, our development timelines and may harm the perception held by others of our business.

We expect to utilize the FDA's Section 505(b)(2) pathway for most of our current product candidates and if that pathway is not available, the development of our product candidates will likely take significantly longer, cost significantly more and entail significantly greater complexity and risk than currently anticipated, and, in any case, may not be successful.

We intend to develop and seek approval for many of our product candidates, including Sildenafil Cream, 3.6%, DARE-HRT1, DARE-VVA1, DARE-FRT1, DARE-PTB1, DARE-LARC1 and other candidates we may develop, including ADARE-204 and ADARE-214, pursuant to the FDA's 505(b)(2) pathway. If the FDA determines that we may not use this regulatory pathway, then we would need to seek regulatory approval via a "full" or "stand-alone" NDA under Section 505(b)(1) of the FDCA. This would require us to conduct additional clinical trials, provide additional safety and efficacy data and other information, and meet additional standards for regulatory approval including possibly nonclinical data. If this were to occur, the time and financial resources required to obtain FDA approval, as well as the development complexity and risk associated with these programs, would likely substantially increase, which could have a material adverse effect on our business and financial condition.

The Drug Price Competition and Patent Term Restoration Act of 1984, informally known as the Hatch-Waxman Act, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies and information that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Section 505(b)(2), if applicable to us under the FDCA, would allow an NDA we submit to the FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved compounds, which could expedite the

development programs for Sildenafil Cream, 3.6%, our current IVR product candidates, DARE-VVA1, DARE-LARC1, ADARE-204 and ADARE-214.

Notwithstanding the approval of an increasing number of products by the FDA under Section 505(b)(2) over the last few years, certain brand-name pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, or Congress were to amend the statute to alter the currently available regulatory pathway, the FDA may change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive, and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs referenced in a Section 505(b)(2) NDA. Even if we are able to utilize the Section 505(b)(2) regulatory pathway for one or more of our candidates, there is no guarantee this would ultimately lead to faster product development or earlier approval.

Moreover, any delay resulting from our inability to pursue the FDA's 505(b)(2) pathway could result in new competitive products reaching the market more quickly than our product candidates, which may have a material adverse impact our competitive position and prospects. Even if we are allowed to pursue the FDA's 505(b)(2) pathway, we cannot assure you that our product candidates will receive the requisite approvals for commercialization.

Our clinical-stage product candidates have only been tested in a small number of women over short periods of use and no data exists regarding a potential increase in fetal abnormalities in pregnant women.

If our clinical-stage product candidates, including Ovaprene and Sildenafil Cream, 3.6%, are successful in their clinical development, we expect that women of child-bearing age will use them, and potentially for many months or years. To date, human clinical studies of these product candidates have been for relatively short periods of time and these product candidates lack safety data over longer periods of use. For example, while we believe the risk of adverse fetal development from using these product candidates is low, the impact of these product candidates on fetal development has not been studied and there are no adequate or well-controlled studies of these product candidates in pregnant women. Thus, the risk of adverse fetal development from any one or more of these product candidates may be greater than expected. Should any of these product candidates be shown to increase the risk of adverse fetal development, our ability to develop those or other product candidates would be substantially impaired, our business prospects and operations would be materially harmed, and we could also be subject to potential claims and lawsuits.

Pre-clinical product candidates may not be valued by investors and may be difficult to fund.

Given their early stage of development and the lack of data, many pre-clinical assets are often perceived as having low valuations by investors and potential strategic collaborators, such as pharmaceutical companies. Our investment of time and resources in such assets may not be appreciated or valued. As a result, it may be difficult for us to fund such programs. Additionally, past receipt of grant funding may not be predictive of our ability to secure additional grants to fund further development of a program. If DARE-VVA1, DARE-LARC1, DARE-FRT1, DARE-PTB1, DARE-RH1 or the injectable etonogestrel product candidates we may license from Adare fail to be valued, our stock price may be adversely affected.

Several of our product candidates are in pre-clinical stages of development and may never advance to clinical development.

Pre-clinical studies refer to a stage of research that begins before clinical trials (testing in humans) can begin, and during which important feasibility, iterative testing and drug safety data are collected. Because of their early nature, pre-clinical product candidates tend to carry a higher risk of failure as compared with clinical-stage assets. Pre-clinical candidates must generate sufficient safety and efficacy data through in vitro studies, animal studies and a variety of tests before they can be considered appropriate for testing in humans. The development risks, timeline and cost of pre-clinical assets can be high because of the unknowns and absence of data. It can be difficult to identify relevant tests and animal models for pre-clinical studies. Even if the results from our pre-clinical studies are favorable, we still may not be able to advance the candidates into clinical trials. If pre-clinical studies of product candidates do not generate strong data, our pre-clinical stage programs may never progress to clinical development and may prove to be worthless.

The grants supporting the DARE-LARC1 program do not guarantee that its pre-clinical development will be successful or that we will be able to fund its clinical development in the future.

The grants supporting pre-clinical development of DARE-LARC1, including the grant agreement under which we were awarded up to $48.95 million in non-dilutive funding for pre-clinical development of DARE-LARC1, do not guarantee that its pre-clinical development will be successful, or, even if we are successful with all specified pre-clinical activities, that we will be able to fund its future clinical development. Further, while we received an initial

payment of $11.45 million under the grant agreement in 2021, additional payments are contingent upon the DARE-LARC1 program's achievement of specified development and reporting milestones during the grant period and our compliance with other obligations under the agreement, and there is no assurance those milestones will be achieved or that we will receive additional payments or the full potential amount of the grant.

Risks Related to Our Dependence on Third Parties

Our existing product development and commercialization collaborations are important to our business, and future collaborations may also be important to us. If we are unable to maintain any of these collaborations, if these collaborations are not successful, or if we are unable to establish additional strategic collaborations, our business and prospects may be materially harmed.

We have limited resources and no internal sales, marketing or distribution capabilities. A key aspect of our strategy is to establish collaborations with third parties, such as large and mid-size pharmaceutical companies and other third parties with the relevant R&D and/or commercial expertise and infrastructure to help bring our product candidates to market. We currently do not expect to directly market, sell or distribute any of our products that receive regulatory approval, and instead intend to enter into agreements with third parties to market, sell and distribute and provide related support services for those products. For example, we have entered into out-license agreements with third parties for the commercialization of XACIATO and, if approved, Ovaprene. We also have a CRADA for the conduct of a pivotal clinical study of Ovaprene with NICHD. We intend to seek additional strategic collaborations. However, these collaborations make the successful development and commercialization of our products and product candidates dependent upon the performance of third parties. By entering into strategic collaborations, we may relinquish control over important elements of product development and commercialization, and the collaborator may fail to develop or effectively commercialize the applicable products or product candidates. In addition, in the case of commercial collaborations, our product revenues, may be lower than if we were to sell and distribute products that we develop ourselves.

Our existing collaborations, and any future strategic collaborations we establish, may involve a number of significant risks to the success of the product, including that:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development or commercialization of a product or product candidate or elect not to continue or renew a collaboration based on clinical or nonclinical study results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition or a pandemic, that divert its resources or create competing priorities;
- collaborators may refuse to perform clinical studies or other development work required for approval in a particular jurisdiction outside the United States;
- collaborators may delay or stop clinical studies, provide insufficient funding for or abandon a clinical program, repeat or conduct new clinical studies or require a new formulation of a product or product candidate for clinical testing;
- collaborators could independently, or together with third parties, develop and commercialize products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more of our products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation, or product development or commercialization strategy, might cause delays or termination of the research, development or commercialization of our products or product candidates, might lead to additional responsibilities for us with respect to products or product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

- collaborators may violate, or be investigated for potentially violating, health care compliance and related laws and regulations, which may expose us to litigation, enforcement actions or inquiries, or other potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, could significantly delay product development and commercial launch and increase the cost to us to pursue further development or commercialization of the applicable product or product candidate. For example, our out-license agreements for XACIATO and Ovaprene and the CRADA with NICHD may be terminated by the counterparty for convenience upon the completion of a specified notice period, subject to limited restrictions.

If one of our collaborators terminates its agreement with us or our strategic collaborations otherwise do not result in the successful development of our product candidates and/or commercialization of any approved products, we may not receive any future payments under the collaboration, our development programs may not be funded as we expect, and our ability to establish another collaboration for the applicable product or product candidate may be negatively impacted. We may be unable to replace any commercial collaborator with an alternate third party on a timely or commercially reasonable basis, or at all. See also, "Risks Related to Our Financial Position and Capital Needs- If a commercial counterparty terminates its exclusive license agreement with us or fails to perform as expected, our need for additional capital may significantly increase," above and "We rely on, and intend to continue to rely on, third parties for the execution of significant aspects of our product development programs. Failure of these third parties to successfully carry out their contractual duties, comply with regulatory requirements and applicable law, or meet expected deadlines may cause significant delays in our development timelines and/or failure of our programs," below. Moreover, the risks relating to product development, regulatory approval and commercialization and compliance with health care related laws and regulations described in this report also apply to the activities of our collaborators.

Except to the extent of any license fees or milestone payments under our current and any future collaboration agreements, because we currently have only one FDA-approved product, our ability to generate revenue over the next several years will largely be dependent on royalties and other net sales-based payments under our exclusive license agreement with Organon. Accordingly, our revenues may be dependent on Organon's ability to successfully market, sell and distribute XACIATO and to perform its contractual obligations. There is no assurance that the commercial launch of XACIATO will occur when expected or be successful and the timing and amount of potential payments to us under the license agreement is uncertain. Apart from Organon's diligence obligation under our license agreement, we have no control over the efforts and resources Organon devotes to the marketing and sale of XACIATO. In addition, the effective date of the license agreement is subject to the satisfaction of closing conditions, including antitrust law clearance which is outside of our control. The occurrence of any of the risks described above could negatively impact the commercial success of XACIATO and have a material adverse effect on our business, financial condition and results of operations.

Termination of the CRADA by NICHD or by us could significantly delay the commencement, conduct and/or completion of the Phase 3 study of Ovaprene and significantly increase the overall timeline and costs for development of Ovaprene. Though the CRADA has a five-year term, either party may terminate it for any reason or for no reason upon 30 days' prior written notice to the other party. If the CRADA is terminated before completion of the Phase 3 study of Ovaprene, NICHD will cooperate with us to transfer the data and the conduct of the study to us or our designee and will continue to conduct the study for so long as necessary to enable such transfer to be completed without interrupting the study. If we terminate the CRADA before the completion of any active study protocol, we generally will be responsible for providing sufficient clinical supplies of Ovaprene to NICHD in order to complete the study. NICHD may retain and use payments we make under the CRADA for up to one year after expiration or termination to cover costs associated with the conduct of activities described under the research plan in the CRADA that were initiated prior to expiration or termination. If we fail to make any scheduled payment to NICHD under the CRADA, the final one of which is due in the second quarter of 2023, NICHD is not obligated to carry out research and development activities until it receives the funds. Suspension by NICHD of activities under the CRADA or termination by NICHD or by us of the CRADA could have a material adverse effect on the Phase 3 study of Ovaprene and on our business, results of operations and financial condition, and may cause the market price of our common stock to decline.

We face significant competition in seeking strategic collaborations. Collaborations can also be complex and time-consuming arrangements to negotiate and document. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product or product candidate, reduce or delay one or more of our other development programs, delay or reduce the scope of any commercial readiness activities, delay commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. Our success in entering into a definitive agreement for any

collaboration will depend upon, among other things, our assessment of the prospective collaborator's resources and expertise, the terms of the proposed collaboration and the proposed collaborator's evaluation of several factors. Those factors may include the design and outcomes of our clinical studies, the likelihood of approval by regulatory authorities, the potential market for the product, the costs and complexities of manufacturing and delivering such product to customers, the potential of competing products, the strength of the intellectual property and other potential sources of market exclusivity for such product, the market performance of other products we developed, and industry and market conditions generally. The prospective collaborator may also have opportunities to collaborate with third parties on products or technologies that would compete with our products or product candidates and will evaluate whether those opportunities are more attractive than a collaboration with us. We also face competition in our search for collaborators from other biotechnology and pharmaceutical companies worldwide, many of which are larger and able to offer more attractive deals in terms of financial commitments, contribution of human resources, or development, manufacturing, regulatory or commercial expertise and support. Inadequate capitalization of our company, or the perception thereof, could negatively affect our negotiating leverage in transactions.

We may also be restricted under existing collaboration agreements from entering into other collaborations on certain terms with other potential collaborators. For example, the terms of our exclusive license agreement also provide Organon exclusive worldwide rights of first negotiation for specified potential future products of ours, which may increase the complexity and time required, or otherwise inhibit our ability to transfer, license, sublicense, assign, grant or otherwise dispose of any rights in those potential future products to a third party, and lead to delays in their development and commercialization.

If we are not successful in attracting collaborators, entering into collaborations on acceptable terms and maintaining our collaborations for the products we develop, we may not complete development of or obtain regulatory approval for such products and product candidates, or if we obtain regulatory approval, commercial launch may be delayed and market penetration could be limited. In such event, our ability to generate revenues from such products and achieve or sustain profitability would be significantly hindered which would materially harm our business and financial condition.

We rely on third-party suppliers and manufacturers for clinical and commercial supplies of XACIATO and our product candidates, including multiple single source suppliers and manufacturers, and we currently have no plans to build or acquire our own manufacturing capabilities. If these third parties do not perform as we expect, do not maintain their regulatory approvals or become subject to negative circumstances, it could delay, prevent or impair our product development or commercialization efforts, or those of our collaborators.

XACIATO and our product candidates (including their respective components) must be manufactured, packaged, tested, and labeled in conformity with cGMP and other applicable regulatory requirements. We do not own or operate, nor do we expect to own or operate, facilities for manufacturing, storage and distribution, or testing of our product or product candidates. We rely on third parties to supply and manufacture our product candidates and other materials necessary to commence and complete pre-clinical testing, clinical trials and other activities required for regulatory approval of our product candidates, and expect to continue to do so in the future. In addition, we expect to rely on third parties to manufacture the commercial supplies of XACIATO and any future products. This reliance on contract manufacturers and suppliers subjects us to inherent uncertainties related to product safety, availability, security and cost. Holders of NDAs, or other forms of FDA approvals, or those distributing a regulated product under their own name, are ultimately responsible for compliance with manufacturing obligations even if the manufacturing is conducted by a third party.

Because we currently rely, and expect to continue to rely, on third parties to supply and manufacture our product and product candidates and their respective components (including the active pharmaceutical ingredients), we do not expect to control the manufacturing processes for their production, all of which must be made in accordance with relevant regulations, which include, among other things, quality control, quality assurance, compliance with cGMP and the maintenance of records and documentation. Continuous compliance with cGMP and other applicable requirements, requires significant expenditure of time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, recordkeeping and other requirements. In the future, it is possible that we or our third-party suppliers or manufacturers, or those of our commercial partners, may fail to comply with cGMP requirements, other applicable FDA regulations, the requirements of other regulatory bodies or our own requirements, any of which could result in suspension or prevention of commercialization and/or manufacturing of our products or product candidates, delay or suspension of ongoing research, including clinical trials, disqualification of data or other enforcement actions such as product recall, injunctions, civil penalties or criminal prosecutions against us. Furthermore, we or a commercial collaborator, as applicable, may be unable to replace any third-party supplier or manufacturer with an alternate supplier or manufacturer on a commercially reasonable or timely basis, or at all. Inability to obtain product quantities needed for

our clinical trials and to meet commercial demand, as applicable, could have a material adverse effect on our business, financial condition and results of operations.

If we were to experience an unexpected loss of supply, or if any supplier or manufacturer were unable to meet our demand for our products or product candidates, including due to geopolitical events, natural disasters or public health emergencies or pandemics, such as the COVID-19 pandemic, we could experience delays in research, planned or ongoing clinical trials or commercialization. We might not find alternative suppliers or manufacturers with FDA approval, of acceptable quality, or able to provide the appropriate volumes and at an acceptable cost. The long transition periods that may be necessary to switch manufacturers and suppliers could significantly increase our development costs and result in delays in clinical trials, regulatory submissions and approvals, and, if approved, commercial launch, and, for commercial products, could result in significant loss of sales and associated revenue.

Third-party suppliers, manufacturers, distributors or regulatory service providers may not perform as agreed or may terminate their agreements with us, including due to the effects related to geopolitical events, natural disasters, public health emergencies or pandemics, such as the COVID-19 pandemic, or force majeure events that affect their facilities or ability to perform. Any significant problem that our suppliers, manufacturers, distributors or regulatory service providers experience could delay or interrupt supply of materials necessary to produce our products and product candidates or the finished product, as applicable, until the supplier, manufacturer, distributor or regulatory service provider cures the problem, until the event that resulted in the delay or interruption is adequately addressed, or until we locate, negotiate for, validate and receive FDA approval for an alternative provider (when necessary), if one is available, and we may not have recourse against the party who did not perform or terminated their agreement with us if such non-performance or termination is excused under our agreements with such party. Failure to obtain the needed quantities of products and product candidates could have a material and adverse effect on our business, financial condition, results of operations and prospects.

In some cases, we may be contractually required to obtain clinical or commercial product supplies from specific third parties or there may be a limited number of third-party suppliers of raw materials and other components of our product and product candidates, which may heighten our dependence on those third parties and the risk of manufacturing disruptions.

Under our license agreement with Organon, we will be responsible for providing product supply of XACIATO on an interim basis. We have entered into a long-term supply and manufacturing agreement for commercial supply of XACIATO with the same CMO that provided clinical supplies for our Phase 3 DARE-BVFREE clinical study. Under our supply and manufacturing agreement, we agreed to purchase at least 80% of our XACIATO requirements from the CMO, subject to limited exceptions. Currently, this CMO is our sole supplier of XACIATO. As a result, XACIATO's commercial success will depend in part on the CMO's ability to manufacture and deliver adequate commercial quantities of the product on agreed upon timelines in accordance with our specifications and in compliance with cGMP and other applicable requirements. In addition, the CMO relies on other third parties, for supply of raw materials required to produce XACIATO and those supplies may become more difficult and costly to obtain. For example, the current single source supplier of clindamycin is located in China. Should this supplier slow production, shut down its factory or increase its prices for any reason, including due to factors related to the COVID-19 pandemic, recent geopolitical events, poor political relations between the U.S. and China and increased taxes or imposition of sanctions, our CMO may not be able to obtain adequate supplies of clindamycin to manufacture sufficient commercial quantities of XACIATO, which could impede XACIATO's commercial success. If these circumstances were to occur, the CMO could be forced to source clindamycin from a different supplier, which could lead to higher costs to us and disruption in commercial supply of XACIATO. After Organon assumes the manufacturing and supply responsibilities for XACIATO, we will have no control over the production and supply of the product. Our failure, or after the transfer of manufacturing responsibilities, Organon's failure, to produce, or cause to be produced, sufficient quantities of XACIATO for commercial sale could have a significant negative effect on commercialization efforts and the payments we receive under our license agreement.

Our agreement with ADVA-Tec restricts our ability to engage a manufacturing source for Ovaprene other than ADVA-Tec during Ovaprene's development period as well as following regulatory approval, subject to limited exceptions. If ADVA-Tec fails to provide sufficient clinical supply of Ovaprene on anticipated timelines, our ability to complete clinical development and seek regulatory approval of Ovaprene could be significantly delayed. A substantial scale up in production of Ovaprene clinical supplies is necessary to support the planned pivotal Phase 3 clinical study of Ovaprene, which may not occur on projected timelines and may be more expensive for us than anticipated. If Ovaprene receives marketing approval, failure by ADVA-Tec to provide sufficient commercial product quantities at reasonable costs could have a significant adverse effect on our revenue and ability to become profitable. Furthermore, for some key raw materials and components of Ovaprene, there currently is only a single source of supply, and alternate sources of supply may not be readily available.

Under the terms of the SST license agreement, SST will be responsible for obtaining supplies of Sildenafil Cream, 3.6% for Phase 2 clinical trials expected to be conducted in the United States, which includes the ongoing Phase 2b clinical study. Thereafter, we will be responsible for obtaining pre-clinical, clinical and commercial supplies of Sildenafil Cream, 3.6%. Future supplies of raw materials required to produce Sildenafil Cream, 3.6% may be more difficult and costly to obtain. For example, the current supplier of sildenafil is located in India. Should this supplier slow production, shut down its factory or increase its prices for any reason, including due to factors related to the COVID-19 pandemic and recent geopolitical events, we may not be able to obtain adequate supplies of sildenafil to satisfy our clinical supply requirements.

We rely on, and intend to continue to rely on, third parties for the execution of significant aspects of our product development programs. Failure of these third parties to successfully carry out their contractual duties, comply with regulatory requirements and applicable law, or meet expected deadlines may cause significant delays in our development timelines and/or failure of our programs.

Our business model relies on the outsourcing of important product development functions, tests and services to CROs, medical institutions and other specialist providers, vendors and consultants. We rely on these third parties to conduct our clinical trials and perform related activities, including quality assurance, clinical monitoring and clinical data management, as well as to assist us in preparing, submitting and supporting the applications necessary to gain marketing approvals for our product candidates. For example, we engaged CROs to run all aspects of the pivotal Phase 3 clinical trial of XACIATO and the PCT clinical trial for Ovaprene. We similarly expect to rely on CROs and other third parties to perform all clinical and nonclinical testing and many other important development and regulatory affairs activities needed to support applications for regulatory approvals of all product candidates we develop. We do not control these third parties and they may not devote sufficient time and resources to our projects, or their performance may be substandard, resulting in clinical trial delays or suspensions, delays in submission of our marketing applications or failure of a regulatory authority to accept our applications for filing. There is no assurance that the third parties we engage will be able to provide the functions, tests, activities or services as agreed upon, or provide them at the agreed upon price and timeline or to our requisite quality standards, including due to geopolitical events, natural disasters, public health emergencies or pandemics, such as the COVID-19 pandemic, or poor workforce relations or human capital management. We rely on the efforts of these third parties and if they fail to perform as expected, we could suffer significant delays and additional costs in, and potentially failure of, the development of one or more of our product candidates.

There is also no assurance these third parties will not make errors in the design, management or retention of our data or data systems. Any failures by such third parties could lead to a loss of data, which in turn could lead to delays in clinical development and obtaining regulatory approval. Third parties may not pass FDA or other regulatory audits, which could delay or prohibit regulatory approval. In addition, the cost of such services could significantly increase over time. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, regulatory approval of current and future product candidates may be delayed, prevented or cost significantly more than expected, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In particular, as a result of the CRADA, we are highly dependent on NICHD and the third parties it engages for the commencement, conduct and completion of our pivotal Phase 3 clinical trial of Ovaprene. Pursuant to the terms of the CRADA, the study will be conducted within NICHD's Contraceptive Clinical Trial Network, or the CCTN, with NICHD contractor Health Decisions Inc. providing clinical coordination and data collection and management services for the study. NICHD is responsible for selecting participating clinical sites from the pool of CCTN sites and, together with Health Decisions Inc., overseeing the clinical investigators in the conduct of the study, providing clinical site monitoring and quality assurance along with establishing the electronic data capture database for the study and performing data analysis, which are key factors to the successful completion of a clinical trial. We do not control these third parties and, accordingly, our control over the commencement, conduct and completion of the study is limited. If NICHD or the third parties it engages for the study prioritize other projects over the study or otherwise do not devote adequate time and resources to the study, or their performance is substandard, commencement and completion of the study may be delayed or suspended or the study may be unsuccessful, any of which could significantly harm our business, operating results and financial condition, as well as our relationship with Bayer, and cause the price of our common stock to decline.

Our ability to develop and commercialize XACIATO and our product candidates depends upon maintaining rights granted to us under license agreements with third parties. The loss or impairment of our rights under any of these agreements could have a material adverse effect on our business prospects, operations and viability.

Our rights to XACIATO and our product candidates arise from license agreements between us and third-party licensors. The loss or impairment of our licensed rights to develop and commercialize XACIATO or our product candidates, including as a result of our inability or other failure (or that of our licensors, in the case of sublicenses) to meet our obligations under any one of such license agreements, including, without limitation, our payment obligations, could have a substantial negative effect on our company's prospects.

In December 2018, we entered into definitive agreements with Hammock Pharmaceuticals, Inc., TriLogic Pharma LLC and MilanaPharm LLC under which we acquired exclusive global rights to XACIATO for the treatment of bacterial vaginosis, as well as the rights to utilize the underlying proprietary hydrogel drug delivery technology for any vaginal or urological application in humans. Under the license agreement with TriLogic Pharma and MilanaPharm, we must use commercially reasonable efforts and resources consistent with those we undertake in pursuing development and commercialization of other pharmaceutical products, taking into account program-specific factors, (a) to develop and commercialize at least one licensed product or process in the United States and at least one licensed product or process in at least one of Canada, the United Kingdom, France, Germany, Italy or Spain, and (b) following the first commercial sale of a licensed product or process in any jurisdiction, to continue to commercialize that product or process in that jurisdiction. MilanaPharm may terminate our license if, after having launched such product or process in such country, we, or our affiliates or sublicensees, as applicable, discontinue the sale of, or commercially reasonable marketing efforts to sell, such product or process in such country, and fail to resume such efforts or to reasonably demonstrate a strategic justification for the discontinuation and failure. See ITEM 1. "BUSINESS-Strategic Agreements for Pipeline Development-Hammock/MilanaPharm Assignment and License Agreement," above.

We entered into a license agreement with ADVA-Tec for the exclusive worldwide rights to develop and commercialize Ovaprene that became effective in July 2017. In addition to standard termination rights, ADVA-Tec may terminate the license agreement if we (1) fail to make significant scheduled investments in product development activities over the course of the agreement, (2) fail to commercialize Ovaprene within six months of obtaining a pre-market approval from the FDA, (3) with respect to the license in any particular country, fail to commercialize Ovaprene in that particular country within three years of the first commercial sale, (4) develop or commercialize a non-hormonal ring-based vaginal contraceptive device other than Ovaprene, (5) fail to conduct certain clinical trials, or (6) fail to make certain milestone, sublicense and/or royalty payments to ADVA-Tec, including a milestone payment due upon the FDA's approval to commence a pivotal human clinical trial of Ovaprene. See ITEM 1. "BUSINESS-Strategic Agreements for Pipeline Development-ADVA-Tec License Agreement," above.

In February 2018, we entered into a world-wide license and collaboration agreement with SST for the exclusive worldwide rights to develop and commercialize Sildenafil Cream, 3.6% for all indications for women related to female sexual dysfunction and/or female reproductive health, including treatment of the female sexual arousal disorder, or FSAD. The SST license agreement provides that each party will have customary rights to terminate the agreement in the event of material uncured breach by the other party and under certain other circumstances. The SST license agreement provides SST with the right to terminate it with respect to the applicable SST licensed products in specified countries upon 30 days' notice if we fail to use commercially reasonable efforts to perform development activities in substantial accordance with the development plan contained in the SST license agreement, or any updated development plan approved by the joint development committee, and do not cure such failure within 60 days of receipt of SST's notice thereof. See ITEM 1. "BUSINESS-Strategic Agreements for Pipeline Development-SST License and Collaboration Agreement," above.

In April 2018, we entered into the Catalent license agreement under which we acquired exclusive global rights to Catalent's IVR technology platform, including the product candidates we now call DARE-HRT1, DARE-FRT1, DARE-PTB1 and DARE-OAB1. Under this agreement, we must use commercially reasonable efforts to develop and make at least one product or process available to the public, which efforts include achieving specific diligence requirements by specific dates specified in the agreement, and Catalent may terminate the agreement upon 60 days' notice for any uncured material breach by us of any of our other obligations under the agreement. See ITEM 1. "BUSINESS-Strategic Agreements for Pipeline Development-Catalent JNP License Agreement," above.

If we do not meet our obligations under our license agreements in a timely manner, some of which require the expenditure or payment to the licensor of significant amounts of cash, or if we are unable to obtain an extension of deadlines for satisfying our obligations, we could lose our rights under these agreements. Moreover, because some of our rights to XACIATO and our product candidates are sublicensed to us, our license agreements may be terminated or we may otherwise lose rights to intellectual property underlying our product or product candidates in the event of termination or loss of rights by our licensors, which may be outside of our control. There is no assurance that we would be able to renew or renegotiate license agreements on acceptable terms, or at all, if our existing license agreements (or the underlying agreements in the case of sublicenses) are terminated. Furthermore, we cannot guarantee that any license agreement will be enforceable. The termination of these license agreements or our inability to enforce our rights under these license agreements could result in the loss of our ability to develop, manufacture,

market or sell XACIATO or the product candidate covered by the agreement, as well as our ability to grant rights to other third parties to collaborate with us in the development and commercialization of our product or product candidate, which could have a material adverse effect on our business prospects and operations.

Disputes may arise regarding intellectual property subject to, and any of our rights and obligations under, any license or other strategic agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe, misappropriate or violate the intellectual property of the licensor that is not subject to the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the sublicensing of patent and other rights to third parties under any such agreement or collaborative relationships;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product or product candidate.

We may seek to license the product and technology rights to additional product candidates in accordance with our business strategy, but there can be no assurance we will be able to do so on favorable terms or at all. There are risks, uncertainties and costs associated with identifying, licensing and advancing product candidates through successful clinical development. Even if we obtained the rights to additional product candidates, there can be no assurance those candidates would ever be advanced successfully through clinical development.

Risks Related to Commercialization of XACIATO and Our Product Candidates

The commercial success of XACIATO will depend on Organon's efforts and capabilities, as well as a variety of factors, many of which currently are unknown or uncertain, and if commercialization of XACIATO is not successful, our business and prospects may suffer.

If commercialization of XACIATO is not successful, or is perceived to be unsuccessful, our business, financial condition, results of operations and prospects may suffer, particularly because XACIATO is the first and only product for which we have received regulatory approval. XACIATO's commercial success will depend on many factors, including:

- the capabilities of Organon and its commitment of sufficient resources to market, distribute and sell the product;
- timely and adequate commercial supply of the finished product and its components;
- perceived superiority of its cure rates compared to other available treatments;
- the extent to which the approved product labeling contains features or expected benefits that differentiate it from other available treatments;
- preferences by health care providers and women for a vaginally administered therapy;
- the prevalence and severity of any adverse side effects;
- patient satisfaction and willingness to use it again and refer it to others;
- price pressure given the high level of generic treatments;
- adequate coverage, pricing and reimbursement from third-party payors;
- the willingness of patients, without third-party insurance coverage or adequate reimbursement, to pay for the product;
- the success or failure of other branded therapies;
- market exclusivity provided by our intellectual property rights or conferred by regulatory authorities; and

- approval of new entrants, including alternative, non-antibiotic treatment options.

There is no assurance that the commercial launch of XACIATO in the U.S. will occur when expected. There is no assurance that Organon's efforts with respect to XACIATO will be successful or that product sales will be able to generate revenue at the levels or within the timing we expect or at the levels or within the timing necessary to support our goals. See also the risks and uncertainties described under "Risks Related to Our Dependence on Third Parties," above.

If we are unable to establish or maintain commercial collaborations on favorable terms, on a timely basis, or at all, we may need to establish a commercial infrastructure, which would be costly, could delay product launch, and may not be successful.

We have no internal sales, marketing or distribution capabilities. We currently do not intend to directly sell or distribute our products into the market and instead intend to enter into agreements with third parties to market, sell and distribute and provide related support services for our product candidates that receive regulatory approval. If we are unable to establish and maintain commercial collaborations on favorable terms, on a timely basis, or at all, to generate revenue from our products, we would need to establish a sales organization. There are significant risks involved with establishing our own commercial infrastructure. For example, recruiting and training a sales force is expensive and time-consuming and could delay product launch. If we recruit and train a sales force and the commercial launch of the product is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred significant commercialization expenses. This may be costly, and our investment would be lost if we could not retain or reposition our sales and marketing personnel. Both the launch and ongoing commercial support of our products would require significant capital, which may not be available to us when needed or on acceptable terms or at all. All of these factors could strain our cash resources and require us to raise additional capital. In addition, there is no guarantee that our efforts to generate product revenue would be successful.

Factors that may hinder efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or educate an adequate number of physicians as to the benefits of our products;
- the lack of complementary products our sales personnel could offer, which may put us at a competitive disadvantage compared to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

The risks described above may also apply if our commercial collaborations do not involve an exclusive license of substantially all commercialization rights to a third party and we instead enter into co-promotion arrangements with a third party.

Failure to timely enter into or maintain a commercialization arrangement with a third party or establish our own commercialization capabilities, could significantly delay commercial launch of our products or require us to reduce the scope of any sales and marketing activities, which could have a material adverse effect on our business, financial condition and results of operations.

Our product candidates, if approved, and XACIATO will face intense competition and our business and operating results will suffer if we, or our commercial collaborators, fail to compete effectively.

The biopharmaceutical industry is intensely competitive and characterized by rapid technological developments. Our competitors and potential competitors include large, well-established pharmaceutical and biotechnology companies, many of which have robust product portfolios and strong franchises in women's health. Many of our competitors or potential competitors, either alone or with strategic collaborators, have:

- much greater financial, research, technical and human resources than we have at every stage of the product development and commercialization life cycle;
- more extensive experience in designing and conducting clinical trials, nonclinical studies, obtaining regulatory approvals, and in manufacturing, marketing and selling prescription medical products; and
- approved products or product candidates in late stages of development for one or more of our target indications.

Competitive products may be equally safe and as effective as our products, but sold at a substantially lower price. Alternatively, competitive products may be safer or more effective, more convenient to use, have better insurance coverage or reimbursement levels or be more effectively marketed and sold than our products.

Our products will compete with products that have already been accepted by the medical community and patients. If our product candidates fail to generate compelling clinical results or if patients and health care providers fail to adopt our products for their respective indications, their commercial potential could be adversely impacted or severely diminished. It is possible that the potential advantages of our product candidates do not materialize or that the approved prescribing information for our products does not describe expected features or benefits. We also expect to face competition from new products that enter the market over time. We are aware of products currently under development intended for the same indications as our product candidates. These competitive product candidates may prove safer, more tolerable and more effective and may be less expensive, introduced to market earlier, or produced, marketed and sold more effectively or on a more cost-effective basis, than our product candidates. The success of competitive products may render potential application of our product candidates noncompetitive or obsolete, even prior to completion of their development.

With respect to XACIATO, there are many FDA-approved products for treating bacterial vaginosis, and many are generic. XACIATO will compete with those products. Current therapies for the treatment of bacterial vaginosis primarily consist of oral and vaginal formulations of antibiotics delivered as a single dose or through multiple doses over consecutive days. Two of the most common antibiotics used today are generic clindamycin and metronidazole. In particular, XACIATO will likely be compared with Clindesse® (clindamycin phosphate) Vaginal Cream, 2% as this treatment is a vaginally administered, single dose cream formulation of clindamycin. If health care providers do not view the prescribing information for XACIATO, including the cure rates that XACIATO demonstrated in the Phase 3 DARE-BVFREE clinical study, as compelling compared with other products available for the treatment of bacterial vaginosis, or if competitive products have better insurance coverage or reimbursement levels than XACIATO, health care providers may opt to continue to prescribe existing treatments rather than recommend or prescribe XACIATO to their patients. In addition, women may prefer orally delivered options to vaginally administered XACIATO unless they view XACIATO as providing significantly superior efficacy, safety and/or convenience.

The women's health market includes many generic products and growth in generics is expected to continue, which could make the successful introduction of our branded products difficult and expensive.

The proportion of the U.S. market made up of generic products has been increasing. If this trend continues, it may be more difficult for us or a commercial collaborator to introduce a new branded medical product, if approved, at a price that will allow us to achieve acceptable levels of revenue and net income from product sales. Generic competition is particularly strong in contraception, hormone therapy and the treatment of bacterial vaginosis, which are areas in which our product candidates, if approved, and XACIATO will compete. In order for our branded products to develop commercial markets and for third-party payors to cover these higher cost products, our products must demonstrate better patient compliance and clinical benefit in their clinical trials compared to other available products.

Additional marketing and educational efforts may be required to introduce a new branded prescription medical product in order to overcome the trend towards generics and gain access to reimbursement by payors. If we or a commercial collaborator cannot introduce a product at the desired price or gain reimbursement from payors for the product, or if patients opt for a lower cost generic product rather than pay out-of-pocket or a higher co-pay for our product, our revenues or royalties and other license fees, as applicable, will be limited.

XACIATO and any future products may fail to achieve the degree of market acceptance by physicians, patients third-party payors or others in the medical community necessary for commercial success, which would negatively impact our business.

XACIATO and any future products may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our products do not achieve an adequate level of market acceptance, they may not generate significant net product revenues, we may not become profitable and we may suffer reputational harm. The degree of market acceptance of XACIATO and any future products will depend on several factors, including:

- the timing of our receipt of any marketing approvals;
- the terms of any approvals and the countries in which marketing approvals are obtained, such as any restrictions on the use of our products together with other medications;
- the indications for which the products are approved;
- demonstrated evidence of efficacy and safety;
- availability of alternative treatments and products;
- the approval of other products for the same indications as our products;
- convenience and ease of administration for patients compared to alternative treatments and products, or other potential advantages and disadvantages compared to the alternatives;

- adverse publicity about our products or favorable publicity about competing products;
- our ability to offer our products for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the success of any physician education programs that we or our commercial collaborators may create for the products;
- the availability of third-party coverage and adequate reimbursement, including patient cost-sharing programs such as co-pays and deductibles;
- the willingness of uninsured patients to pay for the product;
- the willingness of pharmacy chains to stock the products;
- effectiveness of our or our collaborators' sales and marketing strategy and efforts; and
- the prevalence and severity of any adverse side effects associated with the product.

If XACIATO or any future product does not achieve an adequate level of market acceptance, it could have a material and adverse effect on our business, financial condition, results of operation and prospects.

The commercial success of Ovaprene, if approved, will depend on market acceptance of a hormone-free, monthly intravaginal product, availability and effectiveness of alternative contraceptive products and women's preferences, as well as the success of Bayer's marketing and sales efforts.

Today, there are a variety of hormonal and non-hormonal contraceptive options available to women, including oral contraceptive pills and intrauterine devices, newer hormonal contraceptive products including implants, injectables, vaginal rings, patches, and hormonal intrauterine systems, and non-hormonal methods such as female condoms, novel diaphragms, and new methods of female sterilization. In surveys, women have said that the features they consider most important when selecting a contraceptive method are efficacy, ease-of-use and side effects. To have significant revenue potential as a new contraceptive product option, Ovaprene may need to have a typical use efficacy outcome (which is the expected rate of pregnancy protection once the product is used widely under everyday circumstances) comparable to current non-implanted hormonal contraceptive methods (pills, patches and vaginal rings), which is approximately 86%-91% typical use efficacy. Clinical testing will also need to demonstrate that the product can be safely worn for multiple weeks.

If we receive regulatory approval to market Ovaprene, its commercial success, or the success of any other future contraceptive product candidate we may seek to develop, including our current pre-clinical candidates, will depend upon the contraceptive market and market acceptance of an alternative method. Risks related to market acceptance include:

- minimum acceptable contraceptive efficacy rates;
- perceived safety differences of hormonal and/or non-hormonal contraceptive options;
- changes in health care laws and regulations, including the ACA, and its effect on pharmaceutical coverage, reimbursement and pricing, and the birth control mandate;
- competition from new lower dose hormonal contraceptives with more favorable side effect profiles; and
- new generic contraceptive options including a generic version of the hormone-containing intravaginal product NuvaRing®.

If one or more of these risks occur, it could reduce the market potential for Ovaprene, or any future contraceptive product we may seek to develop, and place pressure on our business, financial condition, results of operations and prospects.

Under our license agreement with Bayer, provided the license grant becomes effective, Bayer will have exclusive rights to market and sell Ovaprene in the U.S. Accordingly, the potential value of Ovaprene to our company is highly dependent on the efforts and activities of Bayer. Should Ovaprene fail to generate compelling clinical safety and efficacy data, the license grant under our agreement with Bayer may never become effective. Even if Bayer elects to make the license agreement effective, Bayer has significant discretion in determining the resources that it will allocate to commercialization of Ovaprene and Ovaprene's commercial success may be limited, in which case our business, financial condition, results of operations and prospects could suffer significantly.

The commercial success of Sildenafil Cream, 3.6%, if approved, will depend on the availability of alternative products for female sexual dysfunction disorders, the age group for which our product is indicated and women's preferences, in addition to the market's acceptance of our topical cream.

Today, there are no FDA-approved products to treat FSAD. While our goal is for Sildenafil Cream, 3.6% to be the first product to receive such approval, one or more competitive products may be approved before our product. Even if we achieve our goal of being first-to-market for FSAD, the costs associated with introducing a new product into the sexual dysfunctions market would likely be significant, and regardless of the amount spent, there is no guarantee that our new product will be broadly adopted. Women may be hesitant to use Sildenafil Cream, 3.6% for many reasons, including the lack of experience with any product designed to treat FSAD, the lack or perceived lack of clinical evidence supporting its benefits, and the out-of-pocket cost of Sildenafil Cream, 3.6%, particularly if it is not covered by insurance.

In addition, FSAD is a condition that impacts women of many ages, including older and elderly populations. We have not yet thoroughly studied the topical or clinical pharmacology of Sildenafil Cream, 3.6% in different patient populations, and sildenafil, the active ingredient in our drug candidate, has not been tested over long periods of time in older or elderly women. Older or elderly women may react differently and adversely to Sildenafil Cream, 3.6% than younger populations. Should Sildenafil Cream, 3.6% show increased risk of adverse reactions, or signs thereof, in older or elderly women during clinical development, the potential market for Sildenafil Cream, 3.6% could be significantly limited, which could have a material adverse impact on the value of this program.

If we receive marketing approval in the future, our commercial success with Sildenafil Cream, 3.6% will depend, in large part, on the ability of the product candidate to demonstrate safety and effectiveness in treating FSAD in clinical trials, as well as our ability to educate doctors and women about the need to diagnose and treat FSAD and the potential benefits of using of Sildenafil Cream, 3.6%, at which we or any third party with which we may collaborate to commercialize Sildenafil Cream, 3.6% may not prove successful. Sexual arousal can be influenced by many emotional and physiological factors. To be successful, our clinical trials of Sildenafil Cream, 3.6% must anticipate such factors. Sildenafil Cream, 3.6% is designed to increase local blood flow to the genital tissue. Even if Sildenafil Cream, 3.6% demonstrates success in increasing blood flow, the product candidate may not demonstrate a significant, or any, increase in arousal or improvement in the overall sexual experience in some women in our clinical trials. If we fail to generate compelling clinical results, we may not receive regulatory approval to market Sildenafil Cream, 3.6%, or, if approved, many physicians may not prescribe and/or many women diagnosed with sexual arousal disorder may opt not to try Sildenafil Cream, 3.6%. If we fail to produce strong clinical outcomes, our ability to build a commercial market for Sildenafil Cream, 3.6% will be materially adversely impacted.

The commercial success of DARE-HRT1, if approved, will depend on the availability of alternative products for managing the vasomotor and vaginal symptoms of menopause and women's preferences, in addition to the market's acceptance of our IVR.

Treatments to address the symptoms associated with menopause, including the vasomotor symptoms, also known as hot flashes, include combinations of prescription hormones, some of which are FDA-approved and others which are prepared in compounding pharmacies. Numerous products already exist, and this number is likely to expand with time. In addition, there has been an emerging preference among some women and providers for bio-identical hormones that are chemically identical to those the body produces. DARE-HRT1 is designed to offer a convenient vaginal ring that continuously delivers a combination of bio-identical estradiol and progesterone over 28 days. Until relatively recently, no FDA-approved bio-identical hormone treatments existed. In 2018, Bijuva® estradiol and progesterone capsules, which are to be taken daily, received the first such approval. Studies have failed to demonstrate that bio-identical hormones are safer than other hormones, so DARE-HRT1 will need to compete with many types of hormone therapy options in terms of convenience, safety and efficacy in managing symptoms of menopause.

Risks related to market acceptance of DARE-HRT1, if approved for hormone therapy, include:

- preference for a vaginal ring delivery of hormone therapy over pills, patches and creams by menopausal women;
- data regarding symptom relief of DARE-HRT1 over other hormonal treatments for vasomotor symptoms associated with menopause;
- preference for bio-identical hormones by women and health care providers;
- positive or negative news and research regarding bio-identicals;
- the success or failure of Bijuva®, the first FDA-approved bio-identical product;
- new information supportive or against the use of hormones in menopause; and
- availability of insurance reimbursement for DARE-HRT1.

Depending upon the direction of the factors above, a commercial market for DARE-HRT1 may develop more slowly than expected, or not at all, and our business, financial condition, results of operation and prospects could be hurt as a result.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses for prescription medical products. If we or any commercial collaborator is found or alleged to have improperly promoted any of our products for off-label uses, we may become subject to significant liability, including fines, penalties or injunctions, and reputational harm.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription medical products such as XACIATO. In particular, a product may not be promoted for uses that are not approved by the FDA (i.e., off-label uses), as reflected in the product's approved or cleared labeling. Promotional labeling and advertising for XACIATO, and for any other of our drug products that receive marketing approval, must be submitted to FDA at the time of first use and the agency actively solicits reports from health care professionals about improper promotional claims or activities by the drug manufacturer or distributor. Medical device promotion and advertising are subject to similar off-label restrictions, although without the same requirement to submit promotional materials to FDA at the time of first use. Both prescription drug and medical device promotional materials must present a fair balance between the product's effectiveness and the risks associated with its use, and must be truthful and not misleading.

If we or a commercial collaborator is alleged or found to have promoted XACIATO or any other future commercial product for any off-label use, we may become subject to significant liability and reputational harm. The federal government has levied large civil and criminal fines against companies for alleged improper medical product promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. Other enforcement authorities may also take action against a company for promoting an off-label use of a prescription medical product, which could result in penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. See also "Risks Related to Our Business Operations and Industry- The pharmaceutical and medical device industries are highly regulated and subject to various fraud and abuse laws, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act and the U.S. Foreign Corrupt Practices Act" below.

If we or our commercial collaborators, as applicable, cannot successfully manage the promotion of XACIATO or our product candidates, if approved in the future, to ensure compliance with these legal and regulatory requirements, we could become subject to significant liability, our reputation could be damaged, and adoption of our products could be considerably impaired.

Unexpected safety, efficacy or quality concerns relating to XACIATO could develop, which could have significant negative consequences for us.

XACIATO was approved by the FDA based on prior findings of safety or effectiveness of previously approved clindamycin products and on clinical data from the Phase 3 DARE-BVFREE clinical trial, in which 307 patients were randomized. Following its commercial launch, XACIATO will be used by larger numbers of patients, potentially for longer periods of time. New data may emerge from market surveillance or clinical trials of XACIATO that we or a third party may conduct in the future that give rise to safety, efficacy or quality concerns and result in negative consequences, including:

- modification to the product's prescribing information, such as the addition of boxed or other warnings, contraindications, or limitations of use;
- restrictions on the promotion or marketing of the product;
- issuance of "Dear Doctor Letters" or similar communications to health care professionals or the public regarding safety or efficacy concerns;
- imposition of post-marketing clinical trial requirements or other post-marketing studies;
- product distribution restrictions or other risk management measures, such as a risk evaluation and mitigation strategy, or REMS, which could include elements to assure safe use;
- warning or untitled letters;
- suspension or withdrawal of marketing approvals;
- withdrawal of the product from the market;
- suspension or termination of ongoing clinical trials, if any;

- refusal by regulators to approve pending marketing applications or supplements to approved applications that we submit;
- suspension of, or imposition of restrictions on, our operations or those of our commercial collaborator or CMO, including costly new manufacturing requirements;
- costly and time-consuming corrective actions;
- voluntary or mandatory product recalls or withdrawals from the market;
- significant reputational harm; and
- product liability claims and lawsuits.

Furthermore, the discovery of significant problems with another intravaginally administered or clindamycin-containing product that implicates XACIATO, or is perceived to implicate XACIATO, could have an adverse impact on commercialization of XACIATO and our business, including as a result of occurrence of the events described above. For example, XACIATO has not been studied in pregnant or breastfeeding women. Should increased risk of miscarriage or other adverse effects on maternal or fetal outcomes or breastfed infants be observed in future data from market surveillance or clinical trials of XACIATO, or products that implicate or are perceived to implicate XACIATO, XACIATO's commercial potential may be limited and we could become subject to product liability claims and lawsuits.

The occurrence of any of the circumstances described above could reduce XACIATO's market acceptance, inhibit or delay its commercialization within or outside of the U.S. and adversely affect sales of XACIATO, which could have a material adverse impact on our financial condition, operating results and stock price.

If we suffer negative publicity concerning the safety or efficacy of XACIATO or the product candidates we develop, our reputation could be harmed, product sales could be adversely affected or we may be forced to cease or curtail product development efforts.

If concerns should arise about the actual or anticipated clinical outcomes regarding the safety of XACIATO or any of our product candidates, including as a result of safety concerns related to third-party products containing the same or similar active or excipient substances, such concerns could adversely affect the market's perception of our product and product candidates. Negative publicity could be time consuming and expensive to address and could adversely affect potential opportunities with strategic partners or collaborators, lead to a decline in product sales, and negatively impact investor sentiment toward a product or product candidate or our company as a whole, which could lead to a decline in the price of our common stock.

We are and will remain subject to ongoing regulatory requirements even after obtaining regulatory approval for a product candidate.

Even though XACIATO has been approved by the FDA for the treatment of bacterial vaginosis and even if any other product candidates we develop are approved, we are and will be subject to ongoing regulatory requirements with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing clinical trials and submission of safety, efficacy and other post-approval information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

In addition, manufacturers and manufacturers' facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring quality control and manufacturing procedures conform to cGMP regulations and corresponding foreign regulatory manufacturing requirements. Accordingly, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in our NDA or PMA submissions to the FDA.

Any marketing approvals we receive for our other product candidates in the future may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, we will be required to report adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities (when products are approved in foreign markets). Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance.

If a regulatory agency discovers previously unknown problems with XACIATO or a future product, such as problems with the facility where the product is manufactured, or it disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or on us or our commercial collaborator,

including requiring withdrawal of the product from the market. If we are unable to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- require a product recall.

Any government investigation of alleged violations of law would require us to expend significant time and resources in response and could generate adverse publicity. Any inability to comply with ongoing regulatory requirements may significantly and adversely affect our ability to develop and commercialize our products and the value of our business, and our operating results would be adversely affected.

Failure to successfully obtain coverage and reimbursement for XACIATO and any future products in the United States, or the availability of coverage only at limited levels, would diminish our ability, or that of a commercial collaborator, to generate net product revenue.

Coverage from government health care programs and private commercial health insurance companies is critical to the commercial success of XACIATO and any future products. Market acceptance and sales of XACIATO and any future products that we or a commercial collaborator may seek to commercialize will depend in part on the extent to which reimbursement for these products will be available from third-party payors. Third-party payors, such as government health care programs, private health insurers, managed health care providers, and other organizations, are increasingly challenging medical product prices and examining the medical necessity and cost-effectiveness of medical products, in addition to their safety and efficacy. If these third-party payors do not consider XACIATO or any future product to be cost-effective compared to other available therapies and medical products, they may not cover our products as a benefit under their plans or, even if they do, the level of payment may not be sufficient to allow us, or a commercial collaborator, to sell our products on a profitable basis. Coverage decisions can depend upon clinical and economic standards that disfavor new prescription medical products when more established or lower cost alternatives are already available or subsequently become available. Third-party payor coverage may not be available to patients for XACIATO or any future product. If third-party payors do not provide adequate coverage and reimbursement, health care providers may not prescribe our products or patients may ask their health care providers to prescribe competing products with more favorable reimbursement.

Significant uncertainty exists as to the reimbursement status for newly approved prescription medical products, including coverage and payment. There is no uniform policy requirement for coverage and reimbursement for prescription medical products among third-party payors in the United States; therefore, coverage and reimbursement for our products could differ significantly from payor to payor. In the U.S., the principal decisions about reimbursement for new medical products are typically made by the Centers for Medicare and Medicaid Services, or CMS, as CMS decides whether and to what extent a new medical product will be covered and reimbursed under Medicare. Third-party payors often rely upon Medicare coverage policy and payment limitations to a substantial degree in setting their own reimbursement policies, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. It is difficult to predict what CMS will decide with respect to reimbursement. Decisions regarding the extent of coverage and amount of reimbursement to be provided for XACIATO and any future products will be made on a payor-by-payor basis. Accordingly, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and adequate reimbursement for the product. Moreover, reimbursement agencies in Europe may be more conservative than CMS, should XACIATO or any of our product candidates be approved for marketing in Europe.

In addition to CMS and private payors, professional organizations can influence decisions about reimbursement for new medical products by determining standards of care. In addition, many private payors contract with commercial vendors who sell software that provides guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit as compared to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of any of our commercialized products.

To secure coverage and reimbursement for XACIATO and any future product, we or a commercial collaborator may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product to third-party payors, which costs would be in addition to those required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Managed care organizations and other private

insurers frequently adopt their own payment or reimbursement reductions. Consolidation among managed care organizations has increased the negotiating power of these entities. Third-party payors increasingly employ formularies to control costs by negotiating discounted prices in exchange for formulary inclusion. Failure to obtain timely or adequate pricing or formulary placement for XACIATO or any future product, or obtaining such pricing or placement at unfavorable pricing levels, could materially adversely affect our business, financial conditions, results of operations and prospects. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, or those of a commercial collaborator. Interim payments for new products, if applicable, also may not be sufficient to cover our costs, or those of a commercial collaborator, and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by third-party payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States.

Accordingly, the coverage determination process is often a time-consuming and costly process that will require us or our commercial collaborator to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or obtained. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be cost prohibitive for health care providers or their patients, or less profitable than alternative treatments or products, or if administrative burdens make our products less desirable to use. Our inability, or that of our commercial collaborator, to obtain coverage and profitable payment rates from both government-funded and private payors for XACIATO or any future product could have a material adverse effect on our operating results, our ability to raise capital needed to execute our business strategy and our overall financial condition.

Additionally, the containment of health care costs has become a priority of federal and state governments and the prices of drug products have been a focus of this effort. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of health care and prescription drugs. Individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

The Biden Administration has also indicated that lowering prescription drug prices is a priority, and the Department of Health and Human Services, or DHHS, released a drug pricing plan in September 2021 that indicates the Administration supports aggressive actions such as allowing DHHS to negotiate the cost of Medicare Part B and D drugs. Such significant changes will require either new legislation to be passed by Congress or time-consuming administrative actions. It is uncertain whether and how future legislation or regulatory changes could affect prospects for XACIATO or our product candidates or what actions third-party payors may take in response to any such health care reform proposals or legislation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms, may prevent or limit our ability, or the ability of a commercial collaborator, to commercialize XACIATO or any future products as well as our ability to generate revenue and attain profitability.

Failure by us or a commercial collaborator to obtain timely and adequate coverage and pricing for XACIATO and any future products, or obtaining such coverage and pricing at unfavorable levels, could materially adversely affect our business, financial condition, results of operations and prospects.

Even seemingly small copayments or other cost-sharing requirements could dramatically reduce the market potential for XACIATO and our product candidates.

If the out-of-pocket costs for XACIATO or any of our product candidates, if approved, are deemed by women to be unaffordable, a commercial market may never develop or the market potential for that product may be significantly reduced, which could have a material adverse effect on our business, financial condition, and prospects.

With regard to contraceptive products, the ACA and subsequent regulations enacted by DHHS, require health plans to provide coverage for women's preventive care, including all forms of FDA-cleared or approved contraception, without imposing any cost sharing on the plan beneficiary. These regulations ensure that women in the U.S. who wish to use an approved form of contraception may request it from their doctors and their health insurance plan must cover all costs associated with such contraceptive products. In January 2022, the DHHS, Department of Labor, and Treasury Department jointly issued guidance on implementation of this ACA mandate, among other things. The recently issued federal guidance makes clear that all FDA-approved or cleared contraceptive products that are determined by an individual's medical provider to be medically appropriate for such individual must be covered without-cost sharing, regardless of whether the product is specifically identified in a Birth Control Guide published by the FDA. Any future repeal or elimination of the ACA's preventive care coverage rules would mean that women seeking to use prescribed forms of contraceptives may have to pay some portion of the cost for such products out-of-pocket, which could deter some women from using prescription contraceptive products or branded prescription contraceptive products, including Ovaprene and our other investigational contraceptive products, if and when approved by the FDA.

As no FDA-approved treatments for FSAD currently exist, there is little precedent to help assess whether health insurance plans will cover Sildenafil Cream, 3.6% if approved.

Sildenafil Cream, 3.6%, is being developed for female sexual arousal disorder, a life altering, but not a life threatening, condition, Hence, there is no assurance that third-party reimbursement will be available for Sildenafil Cream, 3.6%, if approved. Even if reimbursement becomes available, the amount of such reimbursement may not make our product affordable to women and profitable to us. Insurers may deem Sildenafil Cream, 3.6% to be a life-style drug and decide not to provide reimbursement. Today, many health insurance plans provide reimbursement for male sexual arousal medications. However, we cannot predict whether they will continue to do so or whether they will do so for FSAD treatments as well. The safety and efficacy data from our clinical trials may impact whether Sildenafil Cream, 3.6% will become eligible for insurance coverage, and if it does, the level of such reimbursement. In an environment of rapidly rising health care costs, insurers have been looking for ways to reduce costs, which could make it difficult for new therapies to gain coverage if they are not deemed medically critical or essential. If Sildenafil Cream, 3.6% fails to obtain insurance coverage, or if the patient's share of the cost is deemed to be expensive, a market may never develop for Sildenafil Cream, 3.6%, which would have a material adverse effect on our financial condition and prospects.

The commercial success of products we develop, if approved, will be impacted by the prescribing information approved by the FDA and comparable regulatory authorities outside the United States.

The commercial success of any products we develop will significantly depend upon our ability, or that of our commercial collaborator, to obtain approval from the FDA and other regulatory authorities of prescribing information for the product that adequately describes expected features or benefits. Failure to achieve such approval will prevent or substantially limit our or our collaborators' ability to advertise and promote such features and benefits in order to differentiate our products from competing products. This failure could have a material adverse effect on our business, financial condition, results of operations and prospects.

Drug products and drug/device combination products are complex to manufacture, and manufacturing disruptions may occur that could cause significant delays and disruption in the supply of XACIATO and any future product.

Our product and product candidates are complex to manufacture and we are dependent on, and expect to continue to rely on, contract manufacturers and other third parties to supply our products and their components. Manufacturing disruptions may occur, including as a result of scaling up production to meet commercial requirements or due to global supply chain disruptions. Such problems may prevent the production of lots that meet the specifications required for sale of our product and may be difficult and expensive to resolve. In particular because we rely on single source contract manufacturers and suppliers, if disruptions occur in the operations of one those third parties, we may experience immediate shortages of our products. If any such issues were to arise with respect to XACIATO or future products, we could lose sales and associated revenue, incur additional costs, delay commercial launch of new products or suffer harm to our reputation.

See also ""Risks Related to Our Dependence on Third Parties- We rely on third-party suppliers and manufacturers for clinical and commercial supplies of XACIATO and our product candidates, including multiple single source suppliers and manufacturers, and we currently have no plans to build or acquire our own manufacturing capabilities. If these third parties do not perform as we expect, do not maintain their regulatory approvals or become subject to negative circumstances, it could delay, prevent or impair our product development or commercialization efforts, or those of our collaborators," and "- In some cases, we may be contractually required to obtain clinical or

commercial product supplies from specific third parties or there may be a limited number of third-party suppliers of raw materials and other components of our product and product candidates, which may heighten our dependence on those third parties and the risk of manufacturing disruptions" above.

If competitors obtain approval for generic versions of XACIATO or any future products, our business may suffer.

Although XACIATO is FDA-approved for commercialization in the United States, it and any future product may face direct competition from generic products earlier or more aggressively than anticipated, depending upon how well such approved products perform in the United States prescription drug market. In addition to creating the 505(b)(2) NDA pathway, the Hatch-Waxman Act amendments to the FDCA authorized the FDA to approve generic drugs that are the same as drugs previously approved for marketing under the NDA provisions of the statute pursuant to abbreviated new drug applications, or ANDAs. An ANDA relies on the nonclinical and clinical testing conducted for a previously approved reference listed drug, or RLD, and must demonstrate to the FDA that the generic drug product is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug and also that it is "bioequivalent" to the RLD. The FDA is prohibited by statute from approving an ANDA when certain marketing or data exclusivity protections apply to the RLD. If a third party is able to demonstrate bioequivalence without infringing our patents, that third party may then be able to introduce a competing generic product onto the market.

The FDA granted XACIATO for the treatment of bacterial vaginosis in female patients 12 years of age and older three years of data exclusivity, which was extended by five years under the GAIN Act, such that the period is set to expire on December 7, 2029. XACIATO has also been designated as an RLD by the FDA for purposes of future generic drug development. Accordingly, the data exclusivity period should block the FDA from approving either a subsequent ANDA or 505(b)(2) NDA that relies in whole or in part on our protected clinical data. We cannot predict the interest of potential follow-on competitors in the future XACIATO market, whether a third party will attempt to invalidate our period of exclusivity or otherwise force the FDA to take other actions, or how quickly others may seek to come to market with competing products after the FDA-granted data exclusivity period ends. Other products candidates we develop, if approved, may also receive marketing exclusivity under the FDCA that may similarly be subject to challenge or uncertainty.

We will need to obtain FDA approval of any proposed prescription medical product name, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our current or future product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the United States Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed new prescription medical product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a proposed product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt alternative names for our product candidates. If we adopt alternative names, we would lose any goodwill or brand recognition developed for previously used names and marks as well as the benefit of any existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. We or a commercial collaborator may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our or our collaborator's ability to commercialize our product candidates.

Even if we receive marketing approval from the FDA, we may fail to receive similar approvals outside the United States, which could substantially limit the value of our products.

To market XACIATO or any future product outside the United States, we, or our commercial collaborators, must obtain separate marketing approvals from comparable regulatory authorities for each jurisdiction and comply with numerous and varying regulatory requirements of other countries, including clinical trials, commercial sales, pricing, manufacturing, distribution and safety requirements. The time required to obtain approval in other countries might differ from, and be longer than, that required to obtain FDA approval. Approval by the FDA or a comparable foreign authority does not ensure approval by regulatory authorities in any other countries or jurisdictions, but a failure to obtain marketing approval in one jurisdiction may adversely impact the likelihood of approval in other jurisdictions. The marketing approval process in other countries may include all of the risks associated with obtaining FDA approval in the United States, as well as other risks. Further, for approval in foreign jurisdictions, we may not have rights to reference the necessary clinical and nonclinical data that we do not own or have licensed rights to use, as we anticipate doing under the 505(b)(2) regulatory pathway in the United States, and we, or our commercial collaborator,

may have to develop our own additional data to seek approvals in other jurisdictions. In addition, in many countries outside the United States, a new product must receive pricing and reimbursement approval prior to commercialization. This can result in substantial delays in these countries. Additionally, the product labeling requirements outside the United States may be different and inconsistent with the United States labeling requirements, negatively affecting our ability to market our products in countries outside the United States.

In addition, we may be subject to fines, suspension or withdrawal of marketing approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we, or our commercial collaborator, fail to comply with applicable foreign regulatory requirements. In such an event, our ability, or our commercial collaborator's ability, to market to the full target market for our products will be reduced and our ability to realize the full market potential of our products will be harmed, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Employee Matters and Managing Our Growth

We have a relatively small number of employees to manage and operate our business.

As of March 30, 2022, we had 28 employees, of which 20 were full-time and eight were part-time. Our focus on limiting cash utilization requires us to manage and operate our business in a highly efficient manner, relying on consultants and other third-party service providers for product development and operational expertise we require, and to limit full-time personnel resources. With a small number of employees, our ability to supervise the service providers we engage may be constrained, which may impact the timing and quality of services we receive. No assurance can be given that we will be able to run our operations or accomplish all of the objectives we otherwise would seek to accomplish with the limited personnel resources we currently have.

In response to the COVID-19 pandemic, in March 2020, we implemented work-from-home and restricted travel policies. Since March 2020, the governors of California and Massachusetts, states in which we have operations, have issued, rescinded and reinstated statewide or regional stay-at-home orders and individual isolation and quarantine requirements to help combat the spread of COVID-19 that have impacted our ability to require or allow our employees to work in our facilities. In addition, many, if not all, of our consultants, collaborators and vendors on which we rely heavily have implemented similar policies, are or may be subject to similar orders, and/or may re-allocate resources otherwise intended for our activities to activities intended to address the COVID-19 pandemic. We have modified, and we may further modify, our work-from-home and restricted travel policies during the course of the pandemic. When and if we and our collaborators and service providers revert to pre-pandemic policies is indeterminable currently. Prolonged and indefinite remote working arrangements and travel restrictions may adversely affect our ability to effectively manage and operate our business, materially increase our expenses and may result in delays in our anticipated development program timelines.

In addition, we and our collaborators and service providers may be adversely affected by worker shortages directly or indirectly related to the COVID-19 pandemic that are difficult to predict, plan for or mitigate. For example, in late 2021, companies across many industries began experiencing severe staffing shortages reportedly caused by work absences due to a surge in COVID-19 cases and an economic trend known as the Great Resignation in which employees are voluntarily quitting their jobs in large numbers. Due to our small workforce, if multiple employees become unable to work or were to resign at roughly the same time, our ability to effectively manage and operate our business could become significantly impaired and our expenses could increase materially, including as a result of expenditures related to recruiting, hiring and training qualified new employees and engaging additional consultants and service providers to perform the job responsibilities of the employees on leave or who resign. If we or our collaborators or service providers experience staffing shortages, it may result in significant delays in our anticipated development program timelines.

If we fail to attract and retain management and other key personnel, we may not successfully complete development of, obtain regulatory approval for or commercialize our product candidates, or otherwise implement our business plan.

Our ability to compete in the highly competitive pharmaceutical, biotechnology and medical device industries depends upon our ability to attract and retain highly qualified managerial and key personnel. We depend highly on our senior management. Losing the services of our senior management could impede, delay or prevent the development and commercialization of our product candidates, hurt our ability to raise additional funds and negatively impact our ability to implement our business plan. If we lose the services of any of our senior management team, we might not find suitable replacements on a timely basis or at all, and our business could be materially harmed. We do not maintain "key man" insurance policies on the lives of any of our senior management employees.

We might not attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biopharmaceutical and biotechnology companies and other life sciences R&D organizations, particularly in the San Diego area where we are headquartered. In addition, our limited personnel and financial resources may result in greater workloads for our employees compared to those at companies with which we compete for personnel, which may lead to higher levels of employee burnout and turnover. As a result, we may have to expend significant financial resources in our employee recruitment and retention efforts. Many of the other companies within the women's health products industry with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better opportunities for career advancement. If we cannot attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will harm our ability to implement our business strategy and achieve our business objectives.

New legal precedent, laws and regulations could make it costlier or more difficult for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract or retain qualified persons to serve as our senior management or on our board of directors.

We may not be successful in our efforts to identify and acquire or in-license additional product candidates or technologies, which may limit our growth potential.

Our business development strategy involves identifying and acquiring or in-licensing potential product candidates or technologies. We assembled our current portfolio of product candidates through the acquisition of companies and assets and in-licensing transactions beginning in 2017. We may engage in strategic transactions that could cause us to incur additional liabilities, commitments or significant expense.

These efforts may not be successful, including for reasons discussed in elsewhere in these risk factors and also:

- we may fail to appropriately evaluate the potential risks and uncertainties associated with a transaction;
- there may be intense competition to acquire or in-license promising product candidates and technologies and many of our competitors have considerably more financial, development and commercialization resources than we have;
- we may not effectively integrate the acquired or in-licensed assets, businesses, personnel, intellectual property or business relationships; and
- we may underestimate the development costs, timelines, regulatory approval challenges and overestimate the market opportunity for the potential product candidates and technologies; and
- the acquired or in-licensed product candidates may prove during development to be unsafe or not effective in their targeted indications.

We may fail to realize the anticipated value of any strategic transaction and the costs of a transaction may outweigh the benefits we realize from it. Any strategic transaction we pursue may not produce the outcomes and benefits we originally anticipated and may adversely impact our financial condition and be detrimental to our company in general.

Risks Related to Our Intellectual Property

Our failure to adequately protect or enforce our and our licensors' intellectual property rights could materially harm our proprietary position in the marketplace or prevent or impede the commercialization of our current and potential future products.

Our success depends in part on our ability, and the ability of our licensors, to obtain and maintain protection in the United States and other countries for the intellectual property covering or incorporated into our technologies and products. Many of the patents and patent applications relied upon by us are licensed to us by third parties. Our ability, or the ability of our licensors, to protect our product candidates from unauthorized use or infringement by third parties depends substantially on our abilities and the abilities of such licensors to obtain and maintain, or license, valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability, and that of our licensors, to obtain or enforce patents is uncertain and involves complex legal and factual questions for which important legal principles are unresolved. As a result, the validity and enforceability of patents cannot be predicted with certainty. In addition, we do not know whether we or our licensors were the first to make the inventions covered

by each of our issued patents and pending patent applications. We or our licensors may not have been the first to file patent applications for these inventions.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We cannot be certain if any of the patents that cover our product candidates will be eligible to be listed in the Orange Book following a drug product marketing approval. The advantage of being listed in the Orange Book is that, under the Hatch-Waxman Act, any future generic applicant for any of our approved products needs to include a patent certification in their generic application with respect to each patent listed in the Orange Book for an approved product (referred to as the “listed drug”) for which they are seeking approval. If the generic applicant believes that any of the patents in the Orange Book on the listed drug is invalid, unenforceable, or not infringed by their product, the generic applicant usually will file a “Paragraph IV” certification on that patent if they plan to challenge the patent. When a generic applicant files a Paragraph IV certification, they must provide the listed drug applicant (and the patent owner if different) a notice that they filed a generic application with the Paragraph IV certification. If, in reply to that notice, the listed drug holder files a patent lawsuit against the generic applicant within 45 days of the Paragraph IV notice, a 30-month automatic stay is imposed by the Hatch-Waxman Act on FDA during which FDA may not approve the generic application (unless the patent litigation is resolved in the generic applicant’s favor). These 30-month stays are major protection available in the Hatch-Waxman Act for innovative drug makers. However, if our products are approved, but one or more of our patents are not listed in the Orange Book, generic firms that might seek approval of a generic version of our product would not have to “certify” in their generic drug applications as to any such unlisted patent. This could result in the absence of a 30-month stay and thus faster approval of some generic applications for our products.

Other companies or individuals may independently develop similar or alternative technologies or duplicate our technologies. This could enable our competitors to develop a competing product that avoids infringing our patents. In such an event, our competitors might be able to enter the market, which could significantly harm the commercial opportunity for our product candidates.

The laws of some foreign countries do not protect our proprietary rights to the same extent or in the same manner as U.S. laws, and we may encounter significant problems in protecting and defending our proprietary rights in these countries. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies, products and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets.

Our patent strategy for protecting Ovaprene includes in-licensing a patent family from ADVA-Tec, whose last claim expires in August 2028, but which could be extended to August 2033 in the United States and Europe. Patent prosecution for the intellectual property incorporated into Ovaprene is entirely controlled by ADVA-Tec and we have little, if any, influence or control over such patent prosecution.

Our patent strategy for protecting Sildenafil Cream, 3.6% includes in-licensing a patent family from SST, whose last U.S. claim expires in June 2029, but which could be eligible for three-year market exclusivity under the Hatch-Waxman Act in the United States. However, if granted 3-year exclusivity, generic applicants can still submit an abbreviated application during the 3-year period and the FDA is required to review the application, but will defer any approval until the end of the 3-year period. Three-year exclusivity differs from 5-year exclusivity under the Hatch-Waxman Act, which bars the submission of a generic application during the 5-year period, with the exception that a generic application can be filed after 4 years if it contains a Paragraph IV certification challenging an Orange Book-listed patent for the brand drug.

With respect to patents related to Sildenafil Cream, 3.6%, SST has the sole right, but not the obligation, to prepare, file, prosecute and maintain such patents. We will be responsible for the costs incurred to maintain and prosecute all such patents and we will be kept informed of all strategies. However, we will have little if any, influence or control over implementing the patent strategy.

With respect to patent rights related to our IVR product candidates, including DARE-HRT1 and DARE-FRT1, The General Hospital Corporation (also known as Massachusetts General Hospital or MGH) has the sole right to prosecute and maintain its patent rights, and we have the right to prosecute and maintain Catalent's patent rights. We

will be responsible for the costs incurred by MGH to maintain and prosecute such patents and we will be kept informed of all strategies. However, we will have little, if any, influence or control over MGH's implementation of the patent strategy.

With respect to patents related to DARE-VVA1, we have the right and obligation, at our expense, to prosecute and maintain the in-licensed patent rights in certain major markets, if possible.

There is a substantial backlog of patent applications at the USPTO that may lead to delays in having patent applications examined by the USPTO. There can be no assurance that any patent applications relating to our products or methods will be issued as patents or, if issued, that the patents will not be challenged, invalidated or circumvented or that the rights granted thereunder will provide a competitive advantage. We and our licensors may not obtain patent rights on products, treatment methods or manufacturing processes that we may develop or to which we may obtain license or other rights. Even if patents are issued to us and our licensors, rights under any issued patents may not provide us with sufficient protection for our product candidates or provide sufficient protection to afford us a commercial advantage against our competitors or their competitive products or processes. It is possible that no patents will be issued from any pending or future patent applications owned by us or licensed to us. Others may challenge, seek to invalidate, infringe or circumvent any patents we own or license, including the patents we have licensed to date and any other patents we may license in the future. Conversely, in the future we may have to initiate litigation against third parties to enforce our intellectual property rights. The defense and enforcement of patent and intellectual property claims are both costly and time consuming, even if the outcome is favorable to us. Any adverse outcome could subject us to significant liabilities, require us to license disputed rights from others or require us to cease selling our future products.

In addition, many other organizations are engaged in research and product development efforts that may overlap with our products. Such organizations may currently have, or may obtain in the future, legally blocking proprietary rights, including patent rights, in one or more products or methods we are developing or considering for development. These rights may prevent us from commercializing technology, or they may require us to obtain a license from the organizations to use the technology. We may not obtain any such licenses that may be required on reasonable financial terms, if at all, and there can be no assurance that the patents underlying any such licenses will be valid or enforceable. As with other companies in the pharmaceutical industry, we are subject to the risks that persons located in other countries will engage in development, marketing or sales activities of products that would infringe our intellectual property rights if such activities were conducted in the United States and enforcing our intellectual property rights against such persons may be difficult or not possible.

Our patents and other intellectual property also may not afford protection against competitors with similar technology. We may not have identified all patents, published applications or published literature that affect our business either by blocking our ability to commercialize our product candidates, by preventing the patentability of our products or by covering the same or similar technologies that may affect our ability to market or license our product candidates. Many companies have encountered difficulties in protecting and defending their intellectual property rights in foreign jurisdictions. If we encounter such difficulties or are otherwise precluded from effectively protecting our intellectual property rights in either the United States or foreign jurisdictions, our business prospects could be substantially harmed.

In addition, because of funding limitations and our limited cash resources, we may not be able to devote the resources that we might otherwise desire to prepare or pursue patent applications, either at all or in all jurisdictions in which we might desire to obtain patents, or to maintain already-issued patents.

The patents and the patent applications covering Sildenafil Cream, 3.6% and XACIATO are limited to specific formulations, processes and uses of sildenafil and clindamycin, and our market opportunity may be limited by the lack of patent protection for the active ingredient itself and other formulations and delivery technology and systems that may be developed by competitors.

The active ingredient in our product candidate for FSAD, Sildenafil Cream, 3.6%, is sildenafil and the active ingredient in our FDA-approved product for the treatment of bacterial vaginosis, XACIATO, is clindamycin. Patent protection for these ingredients has expired and generic products are available. As a result, a competitor that obtains the requisite regulatory approvals could offer products with the same active ingredient in a different formulation so long as the competitor does not infringe any process, use or formulation patents that we have developed, or that may not be barred by any three-year Waxman-Hatch Act exclusivity, or any GAIN Act extension thereof, we might enjoy upon approval of our products.

Competitors may seek to develop and market competing formulations that may not be covered by our patents and patent applications. The commercial opportunity for Sildenafil Cream, 3.6% and XACIATO could be significantly harmed if competitors are able to develop and commercialize alternative formulations using these ingredients.

The patents and the patent applications covering our IVR product candidates cover the method of delivery and the device and our market opportunity may be limited by the lack of patent protection for the active ingredients themselves and other formulations, delivery technology and systems that may be developed by competitors.

The active ingredients in our IVR product candidates include bio-identical progesterone, estrogen and oxybutynin, and none of those ingredients are proprietary to us. As a result, we must compete with currently available products and any future products developed by competitors using same active ingredients in a different formulation or via a different delivery system. The commercial opportunity for our IVR product candidates, including DARE-HRT1 for hormone therapy, could be significantly harmed if competitors develop and commercialize alternative formulations or better delivery approaches.

The patents and the patent applications covering the use and delivery of DARE-VVA1 and our market opportunity may be limited by the lack of patent protection for the active ingredient itself and other formulations, delivery technology and systems that may be developed by competitors.

The active ingredient in DARE-VVA1, tamoxifen, is not proprietary to us. As a result, we must compete with currently available products and any future products developed by competitors using the same active ingredient in a different formulation or via a different delivery system. The commercial opportunity for our product candidate for the treatment of vulvar and vaginal atrophy could be significantly harmed if competitors develop and commercialize alternative formulations or better delivery approaches.

We may become involved in patent litigation or other intellectual property proceedings relating to our future product approvals, which could result in liability for damages or delay or stop our development and commercialization efforts.

The pharmaceutical industry has been characterized by significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights. The situations in which we may become party to such litigation or proceedings may include any third parties initiating litigation claiming that our products infringe their patent or other intellectual property rights, or that one of our trademarks or trade names infringes the third party's trademark rights; in such case, we would need to defend against such proceedings. The costs of resolving any patent litigation or other intellectual property proceeding, even if resolved in our favor, could be substantial. Many of our potential competitors will be able to sustain the cost of such litigation and proceedings more effectively than us because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property proceedings could have a material adverse effect on our ability to compete in the marketplace, our financial condition and our stock price. Patent litigation and other intellectual property proceedings may also consume significant management time.

If a competitor infringes upon our patent or other intellectual property rights, including any rights licensed by us, enforcing those rights may be costly, difficult and time-consuming. Even if successful, litigation to enforce our intellectual property rights or to defend our patents against challenge could be expensive and time-consuming and could divert our management's attention. We may not have sufficient resources to enforce our intellectual property rights or to defend our patent or other intellectual property rights against a challenge. If we were unsuccessful in enforcing and protecting our intellectual property rights and protecting our products, it could materially harm our business.

With respect to XACIATO, we have the initial right to enforce patents we license from TriLogic and MilanaPharm against third parties whose activities infringe such patents in a manner that could affect our exercise of the licenses granted to us, and TriLogic and MilanaPharm must reasonably cooperate with in any such suit, including, if necessary, by being joined as a party to any such suit. In some cases, MilanaPharm may assume the defense of a claim initiated by a third-party alleging infringement of a third party's intellectual property rights as a result of the manufacture or sale of a product we develop under our license agreement with TriLogic/MilanaPharm. While our license agreement would require MilanaPharm to indemnify us for certain losses arising from these third-party claims, this indemnification may not be sufficient to adequately compensate us for any related losses or the potential loss of our ability to manufacture and sell XACIATO.

With respect to Ovaprene, ADVA-Tec has the right, in certain instances, to control the defense against any infringement litigation arising from the manufacture or development (but not the sale) of Ovaprene. While our license agreement with ADVA-Tec requires ADVA-Tec to indemnify us for certain losses arising from these claims, this indemnification may not be sufficient to adequately compensate us for any related losses or the potential loss of our ability to manufacture and develop Ovaprene. Additionally, our license agreement with Bayer requires that we indemnify Bayer from and against all liabilities, damages, losses and expenses arising from or occurring as a result of development, manufacture, use or commercialization of Ovaprene by us or any licensee of ours, including without

limitation, product liability claims, except in limited circumstances. As a result of our indemnification obligations to Bayer and limitations on ADVA-Tec's obligations to indemnify us, any patent infringement litigation relating to Ovaprene could subject us to significant liabilities that may have a material adverse effect on our business, results of operations and financial condition.

With respect to Sildenafil Cream, 3.6%, we have the initial right to enforce the applicable licensed patents against infringers in the field of use where a third party is exploiting a topically applied pharmaceutical product that contains at least one of the same active pharmaceutical ingredients as a licensed product, and SST will provide us with reasonable assistance (excluding financial assistance), at our expense. We also have the initial right to defend any claim initiated by any third-party alleging that a licensed product developed or commercialized under the SST license agreement has infringed any third-party intellectual property rights. While the SST license agreement requires SST to indemnify us for certain losses arising from these claims, this indemnification may not be sufficient to adequately compensate us for any related losses or the potential loss of our ability to manufacture and develop Sildenafil Cream, 3.6%.

With respect to our IVR product candidates, including DARE-HRT1, DARE-FRT1, and DARE-PTB1 we have the first right to enforce the applicable licensed patents against third party infringers in the fields of pharmaceutical, therapeutic, preventative, diagnostic and palliative uses.

With respect to DARE-VVA1, we have the first right to enforce the applicable licensed patents against third-party infringers in all fields.

We cannot guarantee that we or any of our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our future product candidates, or their manufacture or use may currently be unpublished. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our or our licensors' interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We our licensors may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our or our licensors' determination of the expiration date of any patent in the United States, the EU or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our licensors' failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

From time to time, we or our licensors may identify patents or applications in the same general area as our products and product candidates. We or our licensors may determine these third-party patents are irrelevant to our business based on various factors including our or our licensors' interpretation of the scope of the patent claims and our or our licensors' interpretation of when the patent expires. If the patents are asserted against us, however, a court may disagree with our or our licensors' determinations. Further, while we or our licensors' may determine that the scope of claims that will issue from a patent application does not present a risk, it is difficult to accurately predict the scope of claims that will issue from a patent application, our determination may be incorrect, and the issuing patent may be asserted against us or our licensors. We cannot guarantee that we or our licensors will be able to successfully settle or otherwise resolve such infringement claims. If we or our licensors fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing our product candidates. We or our licensors' might, if possible, also be forced to redesign our product candidates so that we or our licensors' no longer infringe on the third-party intellectual property rights. Any of these events, even if we or our licensors' were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

We also rely upon trade secrets to protect our technology, product and product candidates, and trade secrets can be difficult to maintain and enforce.

In addition to patent and trademark protection, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to derive a competitive advantage for products we develop, especially

where we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to maintain. While we use reasonable efforts to protect our trade secrets, monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. Moreover, we or any of our collaborators' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors and we may not have adequate remedies in respect of that disclosure. Enforcement of claims that a party illegally disclosed or obtained and is using trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, foreign courts are sometimes less willing than U.S. courts to protect trade secrets. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secrets against them and our business could be harmed.

Our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors may be able to legally obtain products of ours and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position could be harmed.

Confidentiality agreements with employees and others may not adequately prevent disclosure of our know-how, trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.

We enter into confidentiality, nondisclosure, and intellectual property assignment agreements with our employees, consultants, collaborators, sponsored researchers, and scientific and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party on our behalf or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. We also have not entered into any non-compete agreements with any of our employees. We cannot guarantee that the confidential nature of our proprietary information will be maintained by our employees and others in the course of their future employment with or provision of services to a competitor. Enforcing a claim that a party illegally disclosed or obtained and is using our know-how, trade secrets or other proprietary information is difficult, expensive and time consuming and the outcome is unpredictable. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage for the products we develop, which could materially adversely affect our business, operating results and financial condition.

Provisions in our agreements with governmental agencies and non-profit organizations may affect our intellectual property rights and the value of our development programs to our company.

Certain of our product development activities have been funded, are being funded and may in the future be funded, by the U.S. government and not-for-profit organizations. Our agreements for these sources of funding include, and may in the future include, terms and conditions that affect our intellectual property rights. For example, under our CRADA with NICHD for the Phase 3 clinical study of Ovaprene, the U.S. government has a nonexclusive, nontransferable, irrevocable, paid-up right to practice for research or other government purposes any invention of either party conceived or first actually reduced to practice in the party's performance of the CRADA and both parties will jointly own inventions jointly invented by their employees in performing the research plan. Under the CRADA, we were granted an exclusive option to negotiate an exclusive or nonexclusive development and commercialization license with a field of use that does not exceed the scope of the research plan to rights that the U.S. government may have in inventions jointly or independently invented by NICHD employees for which a patent application is filed.

Under the grant agreement supporting development of DARE-LARC1, we agreed to make DARE-LARC1, and any other products, services, processes, technologies, materials, software, data, other innovations, and intellectual property resulting from the project funded by the grant (referred to as Funded Developments), available and accessible at an affordable price to people most in need within developing countries, and to promptly and broadly disseminate the knowledge and information gained from the project funded by the grant (referred to as the Global Access Commitment). In connection with the Global Access Commitment, under the agreement, we also granted the foundation that awarded the grant a nonexclusive, perpetual, irrevocable, worldwide, royalty-free, fully paid up, sublicensable license to make, use, sell, offer to sell, import, distribute, copy, create derivative works, publicly perform, and display Funded Developments and essential background technology (referred to as the Humanitarian License). We are required to ensure that the Humanitarian License survives the assignment or transfer of Funded

Developments and essential background technology. Our obligations under the Global Access Commitment and the Humanitarian License may limit the value of our rights in DARE-LARC1 and other Funded Developments.

Risks Related to Our Business Operations and Industry

The COVID-19 pandemic has negatively impacted our business and, in the future, may materially and adversely affect our business, financial condition and results and stock price, including by increasing the cost and timelines for our clinical development programs.

The ultimate impact of the COVID-19 pandemic on our operations and, financial condition is unknown and will depend on future developments that are highly uncertain, beyond our control and cannot be predicted with confidence, including, but not limited to, the duration and severity of the pandemic, governmental and individual organization actions and policies implemented to reduce transmission of the disease, governmental actions and programs implemented to mitigate and alleviate the economic impact of the pandemic, and the speed with which and degree to which normal economic and operating conditions resume.

The longer the pandemic persists, the greater the potential for significant adverse impact to our business operations and those of the CROs, CMOs, commercial collaborators, and other third-party service providers and vendors on which we depend to, among other things, conduct our clinical and nonclinical studies, supply our clinical trial materials, assist with regulatory affairs necessary to advance and seek regulatory approval for our programs, and market, sell and distribute our products, if approved. Employee and family member illness, increased childcare and elder care responsibilities, and quarantines, travel restrictions, prohibitions on non-essential gatherings, shelter-in-place orders and other similar directives and policies intended to reduce the spread of the disease, may reduce our productivity and that of the third parties on which we rely and may disrupt and delay many aspects of our business, including R&D activities, production and supply of clinical trial materials and commercial product, and regulatory affairs activities. As a result of resource constraints, third parties on which we rely may not meet their contractual obligations to us or may allocate constrained resources to projects other than ours, any of which could significantly increase the cost and timelines for our development programs. In addition, the significant amount of personnel continuing to work remotely, both ours and those of the third parties on which we rely, could increase our cybersecurity risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could significantly adversely impact our business operations or significantly delay necessary interactions with the FDA and other regulatory agencies, our CROs and CMOs, clinical trial sites, current and potential collaborators, and other third parties. Conversely, as more personnel return to work, travel and non-essential gatherings, there is increased risk of transmission of the disease and other communicable illnesses, potentially leading to resource constraints while personnel are unable to work due to illness and caring for family members who become ill. In addition, vaccination mandates may lead to human resource constraints at our strategic collaborators, CROs, CMOs and other third parties on which we rely if substantial proportions of their workforce quit or are terminated for refusing to comply with vaccine mandates.

The COVID-19 pandemic could cause delays in the current timelines for our ongoing and planned clinical studies, our regulatory submissions, potential marketing approvals and, ultimately, commercial launch of any approved product, including XACIATO. The clinical and regulatory milestones we are targeting to occur in 2022 and 2023 may be delayed or otherwise adversely impacted as a result of the pandemic. For example, clinical trial site initiation and/or patient enrollment may be significantly delayed or suspended as a result of personnel and other resource constraints of health care providers, as well as adherence to governmental orders and internal policies intended to reduce the spread of COVID-19. In addition, we may experience lower than anticipated subject enrollment and completion rates, including because individuals may avoid medical settings, particularly for non-critical conditions, due to concerns of contracting COVID-19 or due to shelter-in-place and social distancing orders, or conversely, as pandemic-related restrictions ease and there are increased opportunities to travel and participate in other activities again, individuals may be less inclined to participate in or complete clinical trials such as ours that require multiple clinic visits. Commencement and completion of our clinical trials may also be significantly delayed by disruptions to production by our contract manufacturers of clinical supplies needed for those studies. The COVID-19 pandemic contributed to a slower than anticipated pace of enrollment of participants in our Phase 2b clinical study of Sildenafil Cream, 3.6% as a result of operational restrictions or closure of certain study sites due to their adherence to governmental guidelines intended to reduce the spread of COVID-19. The commencement of clinical trials and nonclinical testing for our programs may be delayed due to the failure to obtain clinical and other supplies on a timely basis as a result of supply chain disruptions and human resources constraints.

In addition, the pandemic has resulted in disruption and volatility in the global capital markets, and while the longer-term economic impact is difficult to assess and predict at this time, it could negatively impact our ability to access additional capital when needed or on terms favorable to us and our stockholders. If we cannot raise capital when needed on acceptable terms, or at all, we may not be able to continue development of our product candidates

as currently planned or at all, will need to reevaluate our planned operations and may need to delay, scale back or eliminate some or all of our development programs, reduce expenses or cease operations, any of which could have a significant negative impact on our prospects and financial condition, as well as the trading price of our common stock.

A key aspect of our business strategy is to seek collaborations with third parties, such as large pharmaceutical companies, that are willing to conduct later-stage clinical trials and further develop and commercialize our product candidates. As a result of the pandemic, potential and current collaborators may experience operational disruptions and financial and other resource constraints and implement new strategic plans that delay or reduce their efforts in the women's health in general or in our programs in particular, which could adversely affect our ability to enter into or maintain collaborations, strategic alliances or other similar types of arrangements and may result in or contribute to disruption and delays in later-stage clinical development and, if approved, commercial launch of our product candidates.

The plans we implement to help mitigate negative impacts on our business from the COVID-19 pandemic, including those designed to protect the safety, health and well-being of our employees while maintaining employee productivity, may not be effective.

The extent to which the pandemic, efforts to reduce the spread of COVID-19 and efforts to return to pre-pandemic economic conditions impact our business, financial condition and results of operations is uncertain and cannot be predicted with reasonable accuracy at this time and will depend on future developments that are also uncertain and cannot be predicted with reasonable accuracy at this time including emergence of new and more contagious or deadly variants of the virus that causes COVID-19, new information regarding the long-term health impacts of COVID-19, the rate and efficacy of vaccinations against COVID-19, the effect of actions taken in the United States and other countries to contain and treat COVID-19 and to address the pandemic's impact on economic health, and further actions implemented to contain and treat the disease and its impact, among others.

The COVID-19 pandemic may also have the effect of heightening many of the other risks and uncertainties described in this "Risk Factors" section.

Product liability lawsuits against us could cause us to incur substantial liabilities.

We face an inherent risk of product liability exposure as a result of testing of our product candidates in human clinical trials and will face an even greater risk following commercial launch of XACIATO and any future product we develop. If we cannot successfully defend ourselves against claims that our products or product candidates caused injuries, we will incur substantial liabilities or be required to limit commercialization of our products. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any marketed product;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- termination of product development or commercial collaborations;
- loss of revenue;
- withdrawal of clinical study participants and delays in commencement or completion of clinical studies;
- injury to our reputation and significant negative media attention;
- significant costs to defend the related litigation;
- substantial monetary awards to patients or clinical study participants;
- diversion of our management's time and other resources from pursuing our business strategy; and
- a decline in our stock price.

We carry product liability insurance that we believe to be adequate for our clinical testing and product development programs and in connection with our commercial-stage asset, XACIATO. However, insurance coverage is increasingly expensive, and it may be difficult to obtain adequate product liability insurance in the future. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of XACIATO or any of our product candidates, if approved. We also have indemnification obligations to our commercial and other collaborators. Although we will endeavor to obtain and maintain such insurance in coverage amounts we deem adequate, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our current or future employees, clinical investigators, consultants and commercial collaborators may engage in misconduct or other improper activities, including non-compliance with regulatory standards.

We may become exposed to the risk of employees, independent contractors, clinical investigators, consultants, suppliers, commercial collaborators or vendors engaging in fraud or other misconduct. Misconduct by employees, independent contractors, clinical investigators, consultants, suppliers, commercial collaborators and vendors could include intentional failures, such as failures to: (1) comply with FDA or other regulators' requirements, (2) provide accurate information to such regulators, (3) comply with clinical and nonclinical research standards and manufacturing standards established by us and/or required by law, or (4) comply with SEC rules and regulations. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws, regulations and industry guidance intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by current or future employees, independent contractors, clinical investigators, consultants, suppliers, commercial collaborators and vendors could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory or civil sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees, independent contractors, clinical investigators, consultants, suppliers, commercial collaborators and vendors, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses, or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending or asserting our rights, those actions could have a significant adverse effect on our business, including the imposition of significant fines or other sanctions, and our reputation.

The pharmaceutical and medical device industries are highly regulated and subject to various fraud and abuse laws, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act and the U.S. Foreign Corrupt Practices Act.

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products and medical devices that are granted marketing approval. Our arrangements with health care providers, commercial collaborators, principal investigators, consultants, third-party payors, customers and other organizations may expose us to broadly applicable fraud and abuse and other health care laws and regulations in the United States. Health care fraud and abuse regulations are complex, and even minor irregularities can give rise to claims that a statute or prohibition has been violated. The laws that may affect our operations include:

- the federal Anti-Kickback Statute (and comparable state laws), which prohibits, among other things, any person from knowingly and willfully offering, providing, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal health care programs such as the Medicare and Medicaid programs. The federal Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the federal Anti-Kickback Statute to reach large settlements with health care companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- federal and state civil and criminal false claims laws, including the civil False Claims Act which prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under these laws may be brought by the U.S. Attorney General or as a qui tam action by a private individual in the name of the government. The federal government uses these laws, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other allegedly unlawful sales and marketing practices;
- federal, civil and criminal statues created under HIPAA (and similar state laws), which prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially

false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the Physician Payments Sunshine Act, enacted as part of the ACA, which, among other things, imposes reporting requirements on manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare or Medicaid to report to CMS, on an annual basis, information related to payments and other transfers of value to physicians (defined broadly to include doctors, dentists, optometrists, podiatrists, chiropractors, and certain advanced non-physician health care practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members in such manufacturers;
- HIPAA, as amended by HITECH, and their respective implementing regulations, which impose specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain health care providers, health plans, and health care clearinghouses, that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions; and
- the U.S. Foreign Corrupt Practices Act, which prohibits U.S. organizations and their representatives from offering, promising, authorizing or making corrupt payments, gifts or transfers of value to non-U.S. officials, which in many countries, could include interactions with certain health care professionals.

The scope and enforcement of these laws is uncertain and subject to rapid change in the current environment of health care reform, especially in light of the lack of applicable precedent and regulations.

The risk of violation of, and subsequent investigation and prosecution for violations of, the laws described above may be mitigated through the implementation and maintenance of compliance programs by us and our commercial collaborators and other third parties on which we rely for important aspects of development or commercialization of our products and product candidates, but these risks cannot be eliminated entirely. Ensuring that our current and future business operations and arrangements with third parties comply with applicable health care laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other health care laws and regulations. If we or our operations, or those of a commercial collaborator or other third party on which we rely for development or commercialization of our products and product candidates, are found to be in violation of any of the laws described above or any other governmental regulations that apply to us or that third party, we may be subject to significant civil, criminal and administrative penalties, including monetary damages, fines, individual imprisonment, disgorgement, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, health care reimbursement or other government programs, including Medicare and Medicaid, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with any of these laws, and/or the curtailment or restructuring of our operations. If any of the physicians or other health care providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

If regulatory authorities challenge our activities, or those of a commercial collaborator or other third party on which we rely, under these laws, any such challenge could have a material adverse effect on our reputation, business, results of operations and financial condition. Any investigation of us or the third parties with whom we contract, including a commercial collaborator, regardless of the outcome, would be costly and time consuming, and may negatively affect our results of operations and financial condition.

Cyber-attacks, security breaches, loss of data and other disruptions to our information technology systems or those of our collaborators and third-party service providers could compromise sensitive information related to our business, delay or prevent us from accessing critical information or expose us to liability, any of which could adversely affect our business and our reputation.

We utilize information technology systems and networks to process, transmit and store electronic information in connection with our business activities. As the use of digital technologies has increased, cyber incidents, including deliberate attacks, the deployment of harmful malware or ransomware, denial of service, and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and those of our collaborators and third-party service providers, and could compromise the confidentiality, availability and integrity of our data, confidential information, or other intellectual property, all of which are vital to our operations and business strategy. Organizations and governmental bodies with far greater resources than ours dedicated to cyber security have proven vulnerable to cyber-attacks. There can be no assurance we will succeed in preventing cyber security breaches or successfully mitigate their effects.

Despite implementing security measures, any of the computer systems belonging to us or our collaborators and third-party service providers are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failure. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches. Any system failure, accident, security breach or data breach that causes interruptions in our own or in third-party service vendors' operations could result in a material disruption of our product development programs. For example, losing clinical study data from future clinical studies could result in delays in our or our collaborators' regulatory approval efforts and significantly increase our costs in order to recover or reproduce the lost data. In addition, a security breach or privacy violation that leads to disclosure of personally identifiable information or protected health information could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and subject us to litigation or other liability under laws and regulations that protect personal data. Further, our information technology and other internal infrastructure systems, including firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure, which could disrupt our operations. If any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur resulting liability, our product development programs and competitive position may be adversely affected, the further development of our product candidates may be delayed, and the manufacture and sale of any approved products may be impaired. Furthermore, we may incur additional costs to remedy the damage caused by these disruptions or security breaches.

Our business may be adversely affected by unfavorable or unanticipated macroeconomic conditions and geopolitical events.

Various macroeconomic factors could adversely affect our business, our results of operations and financial condition, including changes in inflation, interest rates and overall economic conditions and uncertainties, including those resulting from geopolitical events, international economic sanctions or a global health emergency.

Interest rates and the ability to access credit markets could also adversely affect the ability of patients, payors and distributors to purchase, pay for and effectively distribute our products, if and when approved. Similarly, these macroeconomic factors could affect the ability of our current or potential future third-party manufacturers, sole source or single source suppliers, licensors or licensees to remain in business, or otherwise manufacture or supply our clinical trial material and products or commercialize our products, if and when approved. Failure by any of them to remain in business could have a material adverse effect on our ability to develop and obtain regulatory approvals for our product candidates, and, if approved, market and sell our products or provide sufficient quantities of our products to meet market demand.

We expect to continue to incur increased costs as a result of operating as a public company, and our management will have to devote substantial time to compliance initiatives and corporate governance practices.

We incur and expect to continue to incur significant legal, accounting and other expenses as a public reporting company. We expect that these expenses will increase if and when we become an "accelerated filer," as defined in rules adopted by the SEC under the Securities Exchange Act of 1934. Generally, we will become an accelerated filer if our public float as of the last business day of June is $75 million or more and we reported annual revenues of $100 million or more for our most recently completed fiscal year. Regardless of whether we become an accelerated filer, we may need to hire additional accounting, finance and other personnel in connection with our continuing efforts to comply with the requirements of being a public company. Even while we have non-accelerated filer status, our management and other personnel will need to continue to devote substantial time towards maintaining compliance with the requirements of being a public company. The Sarbanes-Oxley Act of 2002 and rules and regulations subsequently implemented by the SEC and Nasdaq imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance

practices. Our management and other personnel, of whom we have a small number, devote substantial time to these compliance initiatives. Moreover, if and when we become an accelerated filer, our compliance costs will increase.

For example, pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we must furnish a report annually by our management on the effectiveness of our internal control over financial reporting, and performing the system and process documentation and evaluation necessary to issue that report requires us to incur substantial expense and expend significant management time. If and when we are an accelerated filer, we will also have to obtain an attestation report on our internal control over financial reporting by our independent registered public accounting firm, which may substantially increase compliance costs.

We are a smaller reporting company and a non-accelerated filer and the reduced disclosure requirements available to us may make our common stock less attractive to investors.

The SEC established the smaller reporting company, or SRC, category of companies in 2008, and expanded it in 2018, in an effort to provide general regulatory relief for smaller companies. SRCs may choose to comply with scaled financial and non-financial disclosure requirements in their annual and quarterly reports and registration statements relative to non-SRCs. In addition, companies that are not “accelerated filers” can take advantage of additional regulatory relief. Whether a company is an accelerated filer or a SRC is determined on an annual basis. For so long as we qualify as a non-accelerated filer and/or a SRC, we will be permitted to and we intend to rely on some or all of the accommodations available to such companies. These accommodations include:

- not being required to provide an auditor’s attestation of management’s assessment of internal control over financial reporting required by Section 404(b) of the Sarbanes-Oxley Act of 2002;
- reduced financial disclosure obligations, including that SRCs need only provide two years of financial statements rather than three years; a maximum of two years of acquiree financial statements are required rather than three years; fewer circumstances under which pro forma financial statements are required; and less stringent age of financial statements requirements;
- reduced non-financial disclosure obligations, including regarding the description of their business, management’s discussion and analysis of financial condition and results of operations, market risk, executive compensation, transactions with related persons, and corporate governance; and
- later deadlines for the filing of annual and quarterly reports compared to accelerated filers.

We will continue to qualify as a SRC and non-accelerated filer for so long as (a) our public float is less than $75 million as of the last day of our most recently completed second fiscal quarter or (b) our public float is $75 million or more but less than $700 million and we reported annual revenues of less than $100 million for our most recently completed fiscal year.

We may choose to take advantage of some, but not all, of the available accommodations. We cannot predict whether investors will find our common stock less attractive if we rely on these accommodations. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and the price of our common stock may be more volatile.

Risks Related to Ownership of Our Common Stock

The price of our common stock may rise and fall rapidly, substantial price fluctuations may occur regardless of developments in our business or our operating performance, and you could lose all or part of your investment as a result.

The stock market in general, and the market for biopharmaceutical companies in particular, have experienced volatility that has often been unrelated to the operating performance of particular companies. The stocks of small cap and microcap companies in the life sciences sector like ours tend to be highly volatile. Our common stock has experienced extreme trading price and volume fluctuations in the past, including fluctuations that have been unrelated or disproportionate to developments in our business and our operating performance, and we expect that our stock price will continue to experience high volatility. The market price for our common stock may be influenced by a variety of factors, some of which are beyond our control or are related in complex ways, including:

- failure or discontinuation of any of our product development programs;
- actual or anticipated changes to our product development and approval timelines, results from any clinical trial, and communications or decisions from regulatory authorities relating to a review of or decisions on applications we submit for our product candidates, in each case particularly those related to our clinical-stage product candidates;

- announcements of capital raising transactions, including sales of our common stock or securities convertible into or exercisable for shares of our common stock by us, or expectation of additional financing efforts;
- the amount of our unrestricted cash;
- the level of expenses related to development of product candidates we develop, and in particular our clinical-stage development programs;
- commencement or termination of any collaboration or licensing arrangement;
- the results of our efforts to discover, develop, acquire or in-license product candidates or products, if any;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures and capital commitments;
- additions or departures of key management or scientific personnel;
- variations in our financial results or those of companies perceived to be similar to us;
- new products, product candidates or new uses for existing products introduced or announced by our competitors, and the timing of these introductions or announcements;
- results of clinical trials of product candidates of our competitors;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies and effects from geopolitical events, including military conflicts, war, terrorism and economic conflicts, or natural disasters such as earthquakes, typhoons, floods and fires or public health emergencies or pandemics, such as the COVID-19 pandemic;
- regulatory or legal developments in the United States and other countries;
- changes in the structure of health care payment systems;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- recommendations or reports issued by securities research analysts;
- sales of common stock by our stockholders, as well as the overall trading volume of our common stock; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in companies’ stock prices, securities class-action litigation has often been instituted against such companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management’s attention and resources, which could materially and adversely affect our business and financial condition.

There is no assurance that we will continue satisfying the listing requirements of the Nasdaq Capital Market.

Our common stock is listed on the Nasdaq Capital Market. To maintain our listing we are required to satisfy continued listing requirements, including the requirements commonly referred to as the minimum bid price rule and with either the stockholders’ equity rule or the market value of listed securities rule. The minimum bid price rule requires that the closing bid price of our common stock be at least $1.00 per share, and the stockholders’ equity rule requires that our stockholders' equity be at least $2.5 million, or, alternatively, that the market value of our listed securities be at least $35 million or that we have net income from continuing operations of $500,000 in the most recently completed fiscal year or in two of the three most recently completed fiscal years. There can be no assurance we will continue to satisfy applicable continued listing requirements. For example, in 2018 and 2019, we were not in compliance with the minimum bid price rule and the stockholders' equity rule. We subsequently regained compliance with both rules, but there can be no assurance that we will continue to satisfy these or other continued listing standards and maintain the listing of our common stock with Nasdaq.

The suspension or delisting of our common stock, or the commencement of delisting proceedings, for whatever reason could, among other things, substantially impair our ability to raise additional capital; result in the loss of interest from institutional investors, the loss of confidence in our company by investors and employees, and in fewer financing, strategic and business development opportunities; and result in potential breaches of agreements under which we made representations or covenants relating to our compliance with applicable listing requirements. Claims related to any such breaches, with or without merit, could result in costly litigation, significant liabilities and diversion of our management’s time and attention and could have a material adverse effect on our financial condition, business and results of operations. In addition, the suspension or delisting of our common stock, or the

commencement of delisting proceedings, for whatever reason may materially impair our stockholders' ability to buy and sell shares of our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock.

A significant portion of our total outstanding shares of common stock may be sold into the public market at any point, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, either by us or our stockholders. For example, in 2021, we sold an aggregate of 41.1 million shares of our common stock in at-the-market, or ATM offerings and under our equity line arrangement. Actual sales of our common stock, or the perception in the market that we or holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates.

As of December 31, 2021, there were 4.7 million shares of our common stock subject to outstanding options, almost all of which have been registered under the Securities Act on Form S-8. The shares so registered can be freely sold in the public market after being issued to the option holder upon exercise, except to the extent they are held by an affiliate of ours, in which case such shares will become eligible for sale in the public market as permitted by Rule 144 under the Securities Act. Furthermore, as of March 30, 2022, there were approximately 1.4 million shares of our common stock subject to outstanding warrants to purchase common stock, virtually all of which currently have an exercise price of $0.96 per share. To the extent these warrants are exercised, the shares underlying these warrants may be immediately sold in the public market.

The sale of our common stock in ATM offerings may cause substantial dilution to our existing stockholders, and such sales, or the anticipation of such sales, may cause the price of our common stock to decline.

Since 2020, we have used ATM offerings to fund a significant portion of our operations, and we may continue to use ATM offerings to fund our operations in the future. While sales of shares of our common stock in ATM offerings may enable us to raise capital at a lower cost compared with other types of equity financing transactions; such sales may result in substantial dilution to our existing stockholders, and such sales, or the anticipation of such sales, may cause the trading price of our common stock to decline.

The exercise of our outstanding options and warrants may result in significant dilution to our stockholders.

As of December 31, 2021, we had outstanding options to purchase up to 4.7 million shares of our common stock and, and as of March 30, 2022, we had outstanding warrants to purchase up to approximately 1.4 million shares of our common stock. The exercise of a significant portion of our outstanding options and warrants may result in significant dilution to our stockholders.

We may issue preferred stock with terms that could dilute the voting power or reduce the value of our common stock.

Our certificate of incorporation authorizes us to issue, without stockholder approval, one or more series of preferred stock having such designation, powers, privileges, preferences, including preferences over our common stock respecting dividends and distributions, terms of redemption and relative participation, optional, or other rights, if any, of the shares of each such series of preferred stock and any qualifications, limitations or restrictions thereof, as our board of directors may determine. The terms of one or more series of preferred stock could dilute the voting power or reduce the value of our common stock. For example, the repurchase or redemption rights or liquidation preferences we could assign to holders of preferred stock could affect the residual value of our common stock.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future; capital appreciation, if any, will be your sole source of gain as a holder of our shares.

We have never declared or paid cash dividends on any shares of our capital stock. We currently plan to retain all of our future earnings, if any, and all cash received from the sale of securities, the sale of assets or a strategic

transaction to finance the growth and development of our business. Accordingly, capital appreciation, if any, of our common stock will be the sole source of gain for our common stockholders for the foreseeable future.

Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our Restated Certificate of Incorporation, as amended, our Second Amended and Restated By-Laws, as amended, or Delaware law may discourage, delay or prevent a merger, acquisition or other change in control that our stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions might frustrate or prevent any attempts by our stockholders to replace or remove the current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of directors to be changed only by resolution of the board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize the board to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by the board; and
- require the approval of the holders of at least 75% of the votes that all stockholders would be entitled to cast to amend or repeal certain provisions of the charter or bylaws.

In addition, we are governed by Section 203 of the Delaware General Corporate Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of its voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

Provisions in our by-laws could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Second Amended and Restated By-Laws, as amended, provide that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by stockholders; provided that, the exclusive forum provision will not apply to actions or suits brought to enforce any liability or duty created by the Securities Act, the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. In addition, our by-laws provide that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States of America shall be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and to have consented to these provisions.

Under the Securities Act, federal and state courts have concurrent jurisdiction over all suits brought to enforce any duty or liability created by the Securities Act. There is uncertainty as to whether a court (other than state courts in the State of Delaware, where the Supreme Court of the State of Delaware recently decided that exclusive forum provisions for causes of action arising under the Securities Act are facially valid under Delaware law) would enforce forum selection provisions and whether investors can waive compliance with the federal securities laws and the rules and regulations thereunder. We believe the forum selection provisions in our by-laws may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However,

these provisions may have the effect of discouraging lawsuits against us and/or our directors, officers and employees as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers or employees. The enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a future court could find the choice of forum provisions contained in our by-laws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our by-laws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

If we fail to attract or maintain securities analysts to publish research on our business or if they publish or convey negative evaluations of our business, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our common stock could decline. As of the date of this report, to our knowledge, six analysts cover our company. If one or more of these analysts cease coverage or fail to regularly publish reports on our business, we could lose visibility in the financial markets, which in turn could cause our common stock price or trading volume to decline.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease real property to support our business. The office space for our corporate headquarters, which is in good operating condition, is in San Diego, California. We believe that the real property we lease meets our current needs and that we will be able to renew our lease when needed on acceptable terms or find alternative facilities.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become involved in various claims and legal proceedings. Regardless of outcome, litigation and other legal proceedings can have an adverse impact on us because of defense and settlement costs, diversions of management resources and other factors. As of the date of filing this report, there is no material pending legal proceeding to which we are a party or to which any of our property is subject, and management is not aware of any contemplated proceeding by any governmental authority against us.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is listed on the Nasdaq Capital Market under the symbol “DARE.”

Holders of Common Stock

As of March 30, 2022, we had approximately 35 stockholders of record.

The number of stockholders of record is based upon the actual number of holders registered on our books at such date. A substantially greater number of holders of our common stock are "street name" or beneficial holders, whose shares are held by banks, brokers and other financial institutions.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws and contractual limitations, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Recent Sales of Unregistered Securities

We did not sell any unregistered securities during the period covered by this report that were not previously reported in a Quarterly Report on Form 10-Q or Current Report on Form 8-K.

Issuer Purchases of Equity Securities

None.

ITEM 6. [REMOVED AND RESERVED.]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion should be read in conjunction with our consolidated financial statements and the notes thereto included in Part II, Item 8 of this report. This following discussion includes forward-looking statements. See PART I "CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS,” above. Forward-looking statements are not guarantees of future performance and our actual results may differ materially from those currently anticipated and from historical results depending upon a variety of factors, including, but not limited to, those discussed in Part I, Item 1A of this report under the heading “Risk Factors,” which are incorporated herein by reference.

Business Overview

We are a biopharmaceutical company committed to advancing innovative products for women’s health. We are driven by a mission 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. Our business strategy is to in-license or otherwise acquire the rights to differentiated product candidates in our areas of focus, some of which have existing clinical proof-of-concept data, to take those candidates through mid to late-stage clinical development or regulatory approval, and to establish and leverage strategic collaborations to achieve commercialization. We and our wholly owned subsidiaries operate in one business segment.

Our first product, XACIATO, which was approved by the FDA in December 2021, is a single-dose vaginal gel prescription product for the treatment of bacterial vaginosis in females 12 years of age and older. In March 2022, we entered into an exclusive global license agreement with Organon to commercialize XACIATO. XACIATO is expected to be available commercially in the United States in the fourth quarter of 2022.

Our product pipeline includes diverse programs that target unmet needs in women's health in the areas of contraception, fertility and vaginal and sexual health and aim to expand treatment options, enhance outcomes and improve ease of use for women. Our portfolio includes two product candidates in advanced clinical development:

- **Ovaprene®**, a hormone-free, monthly contraceptive; and
- **Sildenafil Cream, 3.6%**, a proprietary cream formulation of sildenafil for topical administration to the vulva and vagina for treatment of female sexual arousal disorder.

Our portfolio also includes four product candidates in Phase 1 clinical development or that we believe are Phase 1-ready:

- **DARE-HRT1**, a combination bio-identical estradiol and progesterone intravaginal ring, for the treatment of menopausal symptoms, including vasomotor symptoms, as part of hormone therapy following menopause;
- **DARE-VVA1**, a vaginally delivered formulation of tamoxifen to treat vulvar vaginal atrophy as an option for women with hormone-receptor positive breast cancer;
- **DARE-FRT1**, an intravaginal ring containing bio-identical progesterone for broader luteal phase support as part of an in vitro fertilization treatment plan; and
- **DARE-PTB1**, an intravaginal ring containing bio-identical progesterone for the prevention of preterm birth.

In addition, our portfolio includes these pre-clinical stage potential product candidates:

- **DARE-LARC1**, a contraceptive implant delivering levonorgestrel with a woman-centered design that has the potential to be a long-acting, yet convenient and user-controlled contraceptive option;
- **ADARE-204 and ADARE-214**, injectable formulations of etonogestrel designed to provide contraception over 6-month and 12-month periods, respectively; and
- **DARE-RH1**, a novel approach to non-hormonal contraception for both men and women by targeting the CatSper ion channel.

See ITEM 1. "BUSINESS," in Part I of this report for additional information regarding our product and product candidates.

Our primary operations have consisted of research and development activities to advance our portfolio of product candidates through clinical development and regulatory approval. We expect our research and development expenses will continue to represent the majority of our operating expenses for at least the next twelve months. In 2022, we expect to focus our resources on advancement of Ovaprene and Sildenafil Cream, 3.6%, and our other product candidates that have reached the human clinical study development phase. In addition, we expect to incur significant research and development expenses for the DARE-LARC1 program for the next several years, but we also expect such expenses will be supported by non-dilutive funding provided under a grant agreement we entered into in June 2021.

To date, we have not generated any revenue**.** We are subject to several risks common to biopharmaceutical companies, including dependence on key employees, dependence on third-party collaborators and service providers, competition from other companies, the need to develop commercially viable products in a timely and cost-effective manner, and the need to obtain adequate additional capital to fund the development of product candidates. We are also subject to several risks common to other companies in the industry, including rapid technology change, regulatory approval of products, uncertainty of market acceptance of products, success of third parties in the marketing, sale and distribution of our products, competition from substitute products and larger companies, compliance with government regulations, protection of proprietary technology, and product liability.

The COVID-19 pandemic remains an evolving and uncertain risk to our business, operating results, financial condition and stock price. To date, we believe the pandemic contributed to a slower than expected initial pace of enrollment in our Phase 2b clinical study of Sildenafil Cream, 3.6% and delays in commencement of clinical studies and nonclinical testing for more than one of our earlier stage clinical programs, but has not had a material adverse effect on our business as a whole. Continued uncertainty regarding the duration and impact of the pandemic on the U.S. and global economies, healthcare systems, workplace environments and capital markets, preclude any prediction as to the ultimate effect of the pandemic on our business. See the risk factor in Part I, Item 1A of this report

titled, *The COVID-19 pandemic has negatively impacted our business and, in the future, may materially and adversely affect our business, financial condition and results and stock price, including by increasing the cost and timelines for our clinical development programs.*

Recent Events

Global License Agreement with Organon to Commercialize XACIATO

On March 31, 2022, we entered into an exclusive license agreement with Organon, pursuant to which Organon will obtain exclusive worldwide rights to develop, manufacture and commercialize XACIATO. See ITEM 1. "BUSINESS," in Part I of this report under “Strategic Agreements for Product Commercialization – Organon License Agreement,” for a description of the terms of the license agreement.

We will receive a $10.0 million non-refundable and non-creditable payment from Organon following the effective date of the agreement, which is expected in the second quarter of 2022, and we are entitled to receive a $2.5 million milestone payment following the first commercial sale of a licensed product in the United States, which is expected to occur in the fourth quarter of 2022. We currently cannot predict with any reasonable certainty the timing or amount of other potential payments from Organon under the license agreement in future periods.

Under the license agreement, we will be responsible for regulatory interactions and for providing product supply on an interim basis until Organon assumes such responsibilities. Until such time, Organon will purchase all of its product requirements of XACIATO from us at a transfer price equal to our manufacturing costs plus a single-digit percentage markup. We will not be responsible for other costs of commercializing XACIATO.

FDA Approval of XACIATO

On December 7, 2021, the FDA approved our new drug application for XACIATO for the treatment of bacterial vaginosis in female patients 12 years of age and older.

October 2021 ATM Sales Agreement

On October 13, 2021, we entered into a new sales agreement with SVB Leerink LLC to sell shares of our common stock from time to time through an “at-the-market,” or ATM, equity offering program under which SVB Leerink acts as our agent. SVB Leerink also acts as our sales agent under an ATM sales agreement we entered into in April 2021. As with the April 2021 sales agreement with SVB Leerink, under the October 2021 sales agreement, we set the parameters for the sale of shares of our common stock, including the maximum number or amount of shares to be sold, the time period during which sales may be made, any limitation on the number or amount of shares that may be sold in any one trading day, and any minimum price below which sales may not be made. Subject to the terms and conditions of the October 2021 sales agreement, the sales agent could sell shares of our common stock by any method permitted by law deemed to be an "at the market offering” as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including, without limitation, including sales made directly on or through the Nasdaq Capital Market, on or through any other existing trading market for our common stock or to or through a market maker. The sales agent must use commercially reasonable efforts in conducting such sales activities consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and applicable Nasdaq rules. If expressly authorized by us, the sales agent could also sell shares in privately negotiated transactions. We made certain customary representations, warranties and covenants to the sales agent in the October 2021 sales agreement, and we agreed to customary indemnification and contribution obligations, including with respect to liabilities under the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act. The October 2021 sales agreement may be terminated by us for any or no reason at any time upon five days' prior notice to the sales agent or by the sales agent for any or no reason at any time upon five days' prior notice to us. We have no obligation to sell any shares under the October 2021 sales agreement, and we may suspend solicitation and offers under the agreement for any reason in our sole discretion. We agreed to pay the sales agent a commission equal to 3.0% of the gross proceeds from the sales of shares pursuant to the agreement. Shares of our common stock sold under the October 2021 sales agreement will be issued pursuant to our shelf registration statement on Form S-3 (File No. 333-254862) and the base prospectus included therein, originally filed with the SEC on March 30, 2021 and declared effective by the SEC on April 7, 2021, and the prospectus supplement, dated October 13, 2021, relating to the offering of up to $50.0 million in shares of our common stock under the October 2021 sales agreement and any subsequent prospectus supplement related to the offering of shares of our common stock under the October 2021 sales agreement.

Financial Overview

Revenue

To date we have not generated any revenue. In the future, we may generate revenue from royalties and commercial milestones based on the net sales of XACIATO, from product sales of other approved products, if any, and from license fees, milestone payments, research and development payments in connection with strategic collaborations. Our ability to generate such revenue, with respect to XACIATO, will depend on the extent to which its commercialization is successful, and with respect to our product candidates, will depend on their successful clinical development, the receipt of regulatory approvals to market such product candidates and the eventual successful commercialization of products. If the commercialization of XACIATO is not successful or we fail to complete the development of product candidates in a timely manner, or to receive regulatory approval for such product candidates, our ability to generate future revenue and our results of operations would be materially adversely affected.

Research and Development Expenses

Research and development expenses include research and development costs for our product candidates and transaction costs related to our acquisitions. We recognize all research and development expenses as they are incurred. Research and development expenses consist primarily of:

- expenses incurred under agreements with clinical trial sites and consultants that conduct research and development and regulatory affairs activities on our behalf;
- laboratory and vendor expenses related to the execution of nonclinical studies and clinical trials;
- contract manufacturing expenses, primarily for the production of clinical supplies;
- transaction costs related to acquisitions of companies, technologies and related intellectual property, and other assets;
- milestone payments under our in-licensing arrangements and under our merger agreement with MBI that we incur, or the incurrence of which we deem probable; and
- internal costs that are associated with activities performed by our research and development organization and generally benefit multiple programs.

In 2021, our research and development expenses consisted primarily of costs associated with the continued development of XACIATO, Ovaprene and Sildenafil Cream 3.6%. We expect research and development expenses to increase in the future as we continue to invest in the development of and seek regulatory approval for our clinical-stage and Phase 1-ready product candidates and as any other potential product candidates we may develop are advanced into and through clinical trials in the pursuit of regulatory approvals. Such activities will require a significant increase in investment in regulatory support, clinical supplies, inventory build-up related costs, and the payment of success-based milestones to licensors. In addition, we continue to evaluate opportunities to acquire or in-license other product candidates and technologies, which may result in higher research and development expenses due to, among other factors, license fee and/or milestone payments.

Conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We may not obtain regulatory approval for any product candidate on a timely or cost-effective basis, or at all. The probability of success of our product candidates may be affected by numerous factors, including clinical results and data, competition, intellectual property rights, manufacturing capability and commercial viability. As a result, we cannot accurately determine the duration and completion costs of development projects or when and to what extent we will generate revenue from the commercialization of any of our product candidates.

License Fees

License fees consist of up-front license fees and annual license fees due under our in-licensing arrangements.

General and Administrative Expense

General and administrative expenses consist of personnel costs, facility expenses, expenses for outside professional services, including legal, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. Facility expenses consist of rent and other related costs.

Recently Issued Accounting Standards

From time to time, the Financial Accounting Standards board, or FASB, or other standard setting bodies issue new accounting pronouncements. Updates to the FASB Accounting Standards Codification are communicated through issuance of an Accounting Standards Update. We have implemented all new accounting pronouncements that are in effect and that may impact our financial statements. We have evaluated recently issued accounting pronouncements and determined that there is no material impact on our financial position or results of operations.

Critical Accounting Policies and Estimates

Management's discussion and analysis of financial condition and results of operations is based on our financial statements that we prepared in accordance with accounting principles generally accepted in the United States. Preparing these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses, and related disclosures. On an ongoing basis, we evaluate these estimates and judgments. We base our estimates on historical experience and on various assumptions we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially from these estimates. Historically, revisions to our estimates have not resulted in a material change to the financial statements. While our significant account policies are described in more detail in Note 2 to our consolidated financial statements included herein, we believe that the following accounting policies are most important to the portrayal of our financial condition and results of operations and require management's most difficult, subjective and complex judgments.

Stock-Based Compensation

The compensation cost for all stock-based awards is measured at the grant date, based on the fair value of the award (determined using a Black-Scholes option pricing model), and is recognized as an expense over the requisite service period (generally the vesting period of the award). Determining the fair value of stock-based awards at the grant date requires significant estimates and judgments, including estimating the market price volatility of our common stock, future stock option exercise behavior and requisite service periods. Due to our limited history of stock option exercises we applied the simplified method prescribed by SEC Staff Accounting Bulletin 110, Share-Based Payment: Certain Assumptions Used in Valuation Methods - Expected Term, to estimate expected life.

The fair value of non-employee stock options or stock awards are remeasured as the awards vest, and the resulting increase or decrease in fair value, if any, is recognized as an increase or decrease to compensation expense in the period the related services are rendered. Stock options or stock awards with performance conditions issued to non-employees who are not directors are measured and recognized when the performance is complete or is expected to be met. Refer to Note 10 to our consolidated financial statements included in this report for more information.

Grant Funding

We receive certain research and development funding from the U.S. government and not-for-profit organizations. In accordance with a policy we adopted in 2018, we recognize grant funding in the statements of operations as a reduction to research and development expense as the related costs are incurred to meet those obligations over the grant period. Grant funding payments received in advance of research and development expenses incurred are recorded as deferred grant funding liability in our consolidated balance sheets. For the years ended December 31, 2021 and December 31, 2020, there were no material adjustments to our prior period estimates of grant funded research and development expenses. Refer to Note 13 to our consolidated financial statements included in this report for more information.

Clinical Trial Expense Accruals

We estimate expenses resulting from our obligations under contracts with vendors, CROs and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts vary and may result in payment flows that do not match the periods over which materials or services are provided.

We record clinical trial expenses in the period in which services are performed and efforts are expended. We accrue for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We estimate accruals through financial models taking into account discussion with applicable personnel and outside service providers as to the progress of trials. During the course of a clinical trial, we may adjust our clinical accruals if actual results differ from our estimates. We estimate accrued expenses as of each balance sheet date based on the facts and circumstances known at that time. Our clinical trial accruals are dependent

upon accurate reporting by CROs and other third-party vendors. Although we do not expect our estimates to differ materially from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2021 and 2020 there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Results of Operations

Comparison of the Years ended December 31, 2021 and 2020

The following table summarizes our consolidated results of operations for the years ended December 31, 2021 and 2020, and the change in the applicable category in terms of dollars and percentage:

	Years Ended December 31,		Change	
	2021	2020	$	%
Operating expenses:				
General and administrative	$ 8,350,945	$ 6,549,508	$ 1,801,437	28 %
Research and development	30,617,567	20,769,416	9,848,151	47 %
License fees	100,000	83,333	16,667	20 %
Loss from operations	(39,068,512)	(27,402,257)	(11,666,255)	(43)%
Other income	2,520	1,514	1,006	66 %
Gain on extinguishment of note payable	369,887	—	369,887	—
Net loss	$ (38,696,105)	$ (27,400,743)	$ (11,295,362)	41 %

Revenues

We did not recognize any revenue for the years ended December 31, 2021 or 2020.

General and administrative expenses

The increase of approximately $1.8 million in general and administrative expenses from 2020 to 2021 was primarily attributable to increases in (i) personnel costs of approximately $688,000, (ii) commercial-readiness expenses of approximately $635,000, (iii) stock-based compensation expense of approximately $559,000, and (iv) expenses for legal, professional, and accounting services of approximately $112,000. Such increases were partially offset by a decrease in rent and facilities expenses of approximately $264,000 attributable to the allocation of a portion of rent and facilities expense included in general and administrative expenses in 2020 to research and development in 2021.

We expect an increase in general and administrative expenses of approximately 15% to 20% in 2022 compared to 2021 primarily due to increased personnel expenses and other general corporate overhead. Our 2022 general and administrative expenses will include costs related to commercial-readiness activities and obtaining commercial supplies of XACIATO from our contract manufacturer. Following commercial launch of XACIATO, we expect our general and administrative expenses will include payments by us to a third-party licensor, including royalty payments at rates in the high single-digit to low double-digits based on annual net sales of XACIATO. In 2022, in connection with commercialization of XACIATO in the U.S., these payments may include a milestone payment in the mid six-figures and royalty payments on net sales at a high single digit royalty rate.

Research and development expenses

The increase of approximately $9.8 million in research and development expenses from 2020 to 2021 was primarily attributable to increased research and development spend for Sildenafil Cream, 3.6% related to the ongoing Sildenafil Cream, 3.6% Phase 2b RESPOND clinical trial of approximately $7.7 million. Also contributing to the increase were increases in (a) costs related to manufacturing and regulatory affairs activities for Ovaprene and development activities for our Phase 1 and Phase 1-ready programs of approximately $5.6 million, (b) personnel costs of approximately $553,000, and (c) stock-based compensation expense of approximately $298,000. Such increases were partially offset by a decrease in development costs of approximately $5.0 million as a result of the completion of the Phase 3 clinical trial for XACIATO in December 2020.

We expect research and development expenses to increase significantly in 2022 as we continue to develop our product candidates. If we advance our programs as currently planned, our research and development expenses for 2022 could be more than double our research and development expenses for 2021. Our 2022 research and development expenses could include up to $4.0 million in milestone payments due under license agreements related to certain of our product candidates payable by us to our third-party licensors. As discussed below in the section titled “Liquidity and Capital Resources,” we will need to raise substantial additional capital to continue to fund our operations and successfully execute our current operating plan. The pace and extent of our research and development activities and, therefore, our research and development spend, will depend on our cash resources. We expect our research and development spend to vary across our fiscal quarters. In regard to Sildenafil Cream, 3.6%, we anticipate that the costs of the Phase 2b RESPOND clinical trial will be approximately $20.0 million, approximately $8.8 million of which was recorded in fiscal 2021 and approximately $0.7 million of which was recorded in fiscal 2020.

License fees

The $16,667 increase in license expenses from 2020 to 2021 was attributable to an increase in license fees accrued or paid under our license agreement related to DARE-HRT1. During 2020 and 2021, we accrued or paid $83,333 and $100,000, respectively, of license fees under such license agreement.

See Note 3 "Strategic Agreements— Strategic Agreements for Pipeline Development" to the accompanying consolidated financial statements for more information about our license agreements.

Other income and gain on extinguishment of note payable

The increase of $1,006 in other income from 2020 to 2021 was primarily due to an increase in interest earned on cash balances in 2021.

The $369,887 recorded as a gain on extinguishment of note payable and debt forgiveness income represents the forgiveness of all the principal and accrued interest of the loan we obtained under the Paycheck Protection Program, or the PPP, of the Coronavirus Aid, Relief, and Economic Security Act, administered by the U.S. Small Business Administration, which forgiveness occurred during the first quarter of 2021.

Liquidity and Capital Resources

Plan of Operations and Future Funding Requirements

We prepared the accompanying consolidated financial statements on a going concern basis, which assumes that we will realize our assets and satisfy our liabilities in the normal course of business. We have a history of losses from operations, we expect negative cash flows from our operations to continue for the foreseeable future, and we expect that our net losses will continue for at least the next several years as we develop and seek to bring to market our existing product candidates and potentially acquire, license and develop additional product candidates. These circumstances raise substantial doubt about our ability to continue as a going concern. The accompanying financial statements do not include any adjustments to reflect the possible future effects on the recoverability and reclassification of assets or the amounts and classifications of liabilities that may result from the outcome of the uncertainty of our ability to remain a going concern.

At December 31, 2021, our accumulated deficit was approximately $110.1 million, our cash and cash equivalents were approximately $51.7 million, and our working capital was approximately $39.2 million. For the year ended December 31, 2021, we incurred a net loss of $38.7 million and had negative cash flow from operations of approximately $28.8 million.

We expect our primary uses of capital to be staff-related expenses, the cost of clinical trials and regulatory activities related to our product candidates, costs associated with contract manufacturing services and third-party clinical research and development services, payments to third-party licensors upon the occurrence of commercial milestones for XACIATO and development milestones for our product candidates, legal expenses, other regulatory expenses and general overhead costs. Our future funding requirements could also include significant costs related to commercialization of our product candidates, if approved, depending on the type, nature and terms of commercial collaborations we establish.

As discussed above, we expect our expenses, and in particular our research and development expenses, to increase significantly in 2022 compared to 2021 as we continue to develop and seek to bring to market our product candidates, with a focus on our product candidates that have reached the human clinical study development phase. Under the terms of our license agreement, Organon will purchase all of its product requirements of XACIATO from us

at a price equal to our manufacturing costs plus a single digit percentage markup. As a result, we do not anticipate our costs of providing XACIATO commercial supplies will have a material impact on our cash resources and requirements.

Based on our current operating plan estimates, we do not have sufficient cash to satisfy our working capital needs and other liquidity requirements over at least the next 12 months from the date of issuance of the accompanying financial statements. Historically, the cash used to fund our operations has come from a variety of sources and predominantly from sales of our common stock. During 2021, we received (1) approximately $68.5 million in net proceeds from ATM sales of shares of our common stock; (2) approximately $11.5 million in non-dilutive grant funding to advance DARE-LARC1 in non-clinical proof of principle studies; (3) approximately $6.8 million in net proceeds from sales of shares of our common stock under our equity line; and (4) approximately $0.5 million upon the exercise of warrants.

We will need to raise substantial additional capital to continue to fund our operations and to successfully execute our current business strategy. During 2022, we may receive up to $12.5 million under our license agreement for XACIATO, and we will continue to seek to raise capital through the sale of shares of our common stock under our ATM sales agreements, however, when we can effect such sales and the amount of shares we can sell depends on a variety of factors to be determined by us from time to time, including, among others, market conditions, the trading price of our common stock and our determination as to the appropriate sources of funding for our operations. For the foreseeable future, we will evaluate and may pursue a variety of capital raising options on an on-going basis, including equity and debt financings, government or other grant funding, collaborations and strategic alliances or other similar types of arrangements, to cover our operating expenses, and the cost of any license or other acquisition of new product candidates or technologies. The amount and timing of our capital needs have been and will continue to depend highly on many factors, including the product development programs we choose to pursue, the pace and results of our clinical development efforts, and the nature and extent of expansion of our product candidate portfolio, if any. If we raise capital through collaborations, strategic alliances or other similar types of arrangements, we may have to relinquish, on terms that are not favorable to us, rights to some of our technologies or product candidates we would otherwise seek to develop or commercialize. There can be no assurance that capital will be available when needed or that, if available, it will be obtained on terms favorable to us and our stockholders. In addition, equity or debt financings may have a dilutive effect on the holdings of our existing stockholders, and debt financings may subject us to restrictive covenants, operational restrictions and security interests in our assets. If we cannot raise capital when needed, on favorable terms or at all, we will not be able to continue development of our product candidates, will need to reevaluate our planned operations and may need to delay, scale back or eliminate some or all of our development programs, reduce expenses file for bankruptcy, reorganize, merge with another entity, or cease operations. If we become unable to continue as a going concern, we may have to liquidate our assets, and might realize significantly less than the values at which they are carried on our financial statements, and stockholders may lose all or part of their investment in our common stock. See ITEM 1A. "RISK FACTORS—Risks Related to Our Financial Position and Capital Needs —*We will need to raise additional capital to continue our operations and execute our business strategy*," above.

Cash Flows

The following table shows a summary of our cash flows for the periods indicated:

	Years Ended December 31,	
	2021	2020
Net cash used in operating activities	$ (28,764,037)	$ (25,234,924)
Net cash used in investing activities	(14,524)	(17,625)
Net cash provided by financing activities	75,846,766	25,130,672
Effect of exchange rate changes on cash and cash equivalents	(63,585)	11,237
Net increase (decrease) in cash	$ 47,004,620	$ (110,640)

Net cash used in operating activities

Cash used in operating activities during the year ended December 31, 2021 included the net loss of $38.7 million, decreased by non-cash stock-based compensation expense of approximately $1.6 million, and increased by the non-cash gain on extinguishment of the note payable and accrued interest of approximately $370,000 related to our PPP loan. Components providing operating cash were an increase in deferred grant funding of approximately $9.0 million, and an increase in accounts payable of approximately $1.1 million. Components reducing operating cash were

an increase in other receivables of approximately $685,000, an increase in prepaid expenses of approximately $622,000, and a decrease in accrued expenses of approximately $46,000.

Cash used in operating activities during the year ended December 31, 2020 included the net loss of $27.4 million, decreased by non-cash stock-based compensation expense of approximately $742,000. Components providing operating cash were an increase in accrued expenses of approximately $1.3 million, an increase in deferred license revenue of $1.0 million, an increase in other non-current assets and deferred charges of approximately $158,000, and an increase in other receivables of approximately $95,000. Components reducing operating cash were an increase in prepaid expenses of approximately $454,000, a decrease in deferred grant funding of approximately $455,000, and a decrease in accounts payable of approximately $62,000.

Net cash used in investing activities

Cash used in investing activities during the years ended December 31, 2021 and December 31, 2020 was related to purchases of property and equipment of approximately $15,000 and $18,000, respectively.

Net cash provided by financing activities

Net cash provided by financing activities during the years ended December 31, 2021 and December 31, 2020 was approximately $75.8 million and $25.1 million, respectively, consisting primarily of net proceeds from sales of our common stock under our ATM sales agreements and our equity line.

License and Royalty Agreements

We agreed to make royalty and milestone payments under the license and development agreements related to XACIATO, Ovaprene, and Sildenafil Cream, 3.6%, and under other agreements related to our other clinical and preclinical candidates. For further discussion of these potential payments, see Note 3 "Strategic Agreements—Strategic Agreements for Pipeline Development" to the accompanying consolidated financial statements for more information about our license agreements.

Other Contracts

We enter into contracts in the normal course of business with various third parties for research studies, clinical trials, testing and other services. These contracts generally provide for termination upon notice, and we do not believe that our non-cancelable obligations under these agreements are material.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Under SEC rules and regulations, as a smaller reporting company we are not required to provide the information required by this item.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements required to be included in this Item 8 are set forth in a separate section of this report commencing on page F-1.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rule 13a-15(e) of the Exchange Act) designed to provide reasonable assurance that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such

information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on an evaluation, performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures (as defined in Rule 13a-15(e) of the Exchange Act) were effective as of December 31, 2021 at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as such term is defined in Rule 13a-15(f) of the Exchange Act). Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. Because of its inherent limitations, internal controls over financial reporting may not prevent or detect misstatements. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on our assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2021 to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles in the United States.

Under SEC rules, because we are a non-accelerated filer, we are not required to provide an auditor attestation report on internal control over financial reporting, nor did we engage our independent registered public accounting firm to perform an audit of our internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fourth quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item will be included in the Company's 2022 Proxy Statement and is incorporated in this report by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be included in the Company's 2022 Proxy Statement and is incorporated in this report by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item will be included in the Company's 2022 Proxy Statement and is incorporated in this report by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item will be included in the Company's 2022 Proxy Statement and is incorporated in this report by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item will be included in the Company's 2022 Proxy Statement and is incorporated in this report by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this annual report on Form 10-K:

(1) Financial Statements

See “Index to Consolidated Financial Statements” on page F-1.

(2) Financial Statement Schedules

All financial statement schedules have been omitted, since the required information is not applicable or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the consolidated financial statements and notes thereto included in this report.

(3) Exhibits

Exhibits not filed or furnished herewith are incorporated by reference to exhibits previously filed with the SEC, as reflected in the table below. We will furnish a copy of any exhibit to stockholders, without charge upon written request to Daré Bioscience, Inc., 3655 Nobel Drive, Suite 260, San Diego, CA 92122, or by calling 858-926-7655.

		Incorporated by Reference				
Exhibit Number	**Description of Exhibit**	**Form**	**File No.**	**Filing Date**	**Exhibit No.**	**Filed Herewith**
2.1§ Δ	Agreement and Plan of Merger, dated as of April 30, 2018, by and among Daré Bioscience, Inc., Daré Merger Sub, Inc., Pear Tree Pharmaceuticals, Inc., and Fred Mermelstein and Stephen C. Rocamboli, as Holders' Representatives	10-Q	001-36395	8/13/2018	10.10	
2.2+	Agreement and Plan of Merger, dated November 10, 2019, Dare Bioscience, Inc., MC Merger Sub, Inc., Microchips Biotech, Inc., and Shareholder Representative Services LLC, as the stockholders' representative	8-K	001-36395	11/12/2019	2.1	
3.1	Restated Certificate of Incorporation, as amended by Certificate of Amendment dated July 19, 2017 to effect the Reverse Stock Split effective July 20, 2017, and by Certificate of Amendment dated July 19, 2017 stating the name change effective July 20, 2017	10-Q	001-36395	08/14/2017	3.1	
3.2	Second Amended and Restated By-Laws (as amended through June 1, 2020)	8-K	001-36395	6/3/2020	3.1	
4.1	Specimen stock certificate evidencing the shares of common stock	10-K	001-36395	03/28/2018	4.1	
4.2	Warrant Agreement to purchase shares of common stock of the registrant with Aquilo Partners, L.P., entered into as of October 16, 2016.					X

4.3(a)	Form of Warrant to Purchase Shares of Common Stock (February 2018 Underwritten Offering)	8-K	001-36395	02/13/2018	4.1
4.3(b)	Form of Amendment to Warrant to Purchase Common Stock entered into as of June 27, 2018	10-Q	001-36395-181175221	11/13/2018	4.1
4.4	Description of securities of the registrant	10-K	001-36395	03/27/2020	4.6
10.1Δ	License and Collaboration Agreement dated February 11, 2018 between Daré Bioscience, Inc., Strategic Science and Technologies-D, LLC and Strategic Science Technologies, LLC	10-K/A	001-36395	04/30/2018	10.1
10.2Δ	License Agreement dated March 19, 2017, between Daré Bioscience Operations, Inc. and ADVA-Tec, Inc.	10-Q	001-36395	11/13/2017	10.1
10.3(a)*	Daré Bioscience, Inc. Amended and Restated 2014 Stock Incentive Plan	8-K	001-36395-18949535	7/12/2018	10.1
10.3(b)*	Form of Incentive Stock Option Agreement for grants under the Daré Bioscience, Inc. Amended and Restated 2014 Stock Incentive Plan	10-Q	001-36395	08/13/2018	10.3
10.3(c)*	Form of Nonstatutory Stock Option Agreement for grants under the Daré Bioscience, Inc. Amended and Restated 2014 Stock Incentive Plan	10-Q	001-36395	08/13/2018	10.4
10.4	Form of indemnification agreement between the registrant and each of its executive officers and directors	S-1	333-194442	03/10/2014	10.16
10.5*	Non-Employee Director Compensation Policy (as amended through April 9, 2018)	10-Q	001-36395	8/13/2018	10.2
10.6Δ	Exclusive License Agreement made as April 24, 2018 by and between Catalent JNP, Inc. (fka Juniper Pharmaceuticals, Inc.), and Daré Bioscience, Inc.	10-Q	001-36395	8/13/2018	10.1
10.7(a)Δ	Amended and Restated Exclusive License Agreement, dated as of July 14, 2006, by and between Fred Mermelstein, Ph.D. and Janet Chollet, M.D., and Pear Tree Women's Health Care, Inc.	10-Q	001-36395	8/13/2018	10.5

10.7(b)Δ	Amendment No. 1 to the Amended and Restated Exclusive License Agreement, dated as of October 10, 2007, by and among Fred Mermelstein, Ph.D. and Janet Chollet, M.D., and Pear Tree Pharmaceuticals, Inc.	10-Q	001-36395	8/13/2018	10.6
10.7(c)Δ	Amendment No. 2 to the Amended and Restated Exclusive License Agreement, dated as of February 13, 2017, by and among Fred Mermelstein, Ph.D., and Janet Chollet, M.D., Pear Tree Pharmaceuticals, Inc. and Bernadette Klamerus	10-Q	001-36395	8/13/2018	10.7
10.7(d)Δ	Exclusive License Agreement, dated as of February 13, 2017, by and between GYN Holdings, Inc., a wholly owned subsidiary of Pear Tree Pharmaceuticals, Inc. and Bernadette Klamerus	10-Q	001-36395	8/13/2018	10.8
10.7(e)Δ	Exclusive License Agreement, dated as of September 15, 2017, by and between Fred Mermelstein, Ph.D., Janet Chollet, M.D., Pear Tree Pharmaceuticals, Inc., and Stephen C. Rocamboli	10-Q	001-36395	8/13/2018	10.9
10.8	2014 Employee Stock Purchase Plan	S-1/A	333-194442	03/31/2014	10.26
10.9(a)Δ	Assignment Agreement by and between Daré Bioscience, Inc. and Hammock Pharmaceuticals, Inc. effective as of December 5, 2018	10-K	001-36395	04/01/2019	10.10(a)
10.9(b)Δ	First Amendment to the License Agreement effective as of December 5, 2018 by and among Daré Bioscience, Inc., TriLogic Pharma, LLC and MilanaPharm LLC	10-K	001-36395	04/01/2019	10.10(b)
10.9(c)	Amendment No. 1 to Assignment Agreement entered into as of December 4, 2019 between Daré Bioscience, Inc. and Hammock Pharmaceuticals, Inc.	10-K	001-36395	03/27/2020	10.10(c)
10.9(d)	Amendment No. 2 to the License Agreement entered into as of December 3, 2019 between Daré Bioscience, Inc., TriLogic Pharma, LLC and MilanaPharm LLC	10-K	001-36395	03/27/2020	10.10(d)
10.9(e)	Amendment to License Agreement effective as of September 21, 2021 by and among Daré Bioscience, Inc., TriLogic Pharma, LLC and MilanaPharm LLC	10-Q	001-36395	11/10/2021	10.1

10.10(a)*	2007 Stock Incentive Plan	S-1	333-194442	03/10/2014	10.1
10.10(b)	Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan	S-1	333-194442	03/10/2014	10.2
10.10(c)*	Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan	S-1	333-194442	03/10/2014	10.3
10.10(d)	Stock Option Agreement and Contingent Consideration Award Agreement, dated March 31, 2013, between Cerulean Pharma, Inc. and Alan Crane	S-1	333-194442	03/10/2014	10.24
10.10(e)	Amendment to the Stock Option Agreement and Termination of Contingent Consideration Award dated September 16, 2014, by and between Cerulean Pharma, Inc. and Alan Crane	10-Q	001-36395	11/13/2014	10.4
10.11(a)*	Employment Agreement by and between Daré Bioscience, Inc. and Sabrina Martucci Johnson dated as of August 15, 2017	8-K	001-36395	08/18/2017	10.1
10.11(b)*	Amendment No. 1 to Employment Agreement between Daré Bioscience, Inc. and Sabrina Martucci Johnson dated as of March 9, 2020	10-Q	001-36395	05/14/2020	10.13(b)
10.12(a)*	Employment Agreement by and between Daré Bioscience, Inc. and Lisa Walters-Hoffert dated as of August 15, 2017	8-K	001-36395	08/18/2017	10.2
10.12(b)*	Amendment No. 1 to Employment Agreement between Daré Bioscience, Inc. and Lisa Walters-Hoffert dated as of March 9, 2020	10-Q	001-36395	05/14/2020	10.14(b)
10.13*	Daré Bioscience, Inc. Performance Bonus Plan	10-Q	001-36395	11/12/2019	10.1
10.14+	License Agreement dated as of January 10, 2020 between Bayer HealthCare LLC and Daré Bioscience, Inc.	10-K	001-36395	03/27/2020	10.16
10.15*	Daré Bioscience, Inc. Employment Offer Letter to John Fair, dated April 24, 2018	S-1	333-251599	01/05/2021	10.19
10.16*	Daré Bioscience, Inc. Change in Control Policy (effective October 15, 2019)	S-1	333-251599	01/05/2021	10.20
10.17+	Grant Agreement between Daré Bioscience, Inc. and the Bill & Melinda Gates Foundation effective as of June 30, 2021	10-Q	001-36395	08/12/2021	10.1

10.18+	Cooperative Research and Development Agreement entered into as of July 8, 2021 between Daré Bioscience, Inc. and the Eunice Kennedy Shriver National Institutes of Child Health and Human Development Institute	10-Q	001-36395	11/10/2021	10.2	
21.1	Subsidiaries of the registrant					X
23.1	Consent of Mayer Hoffman McCann P.C.					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1#	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2#	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101)					X

§ All schedules (or similar attachments) have been omitted from this filing pursuant to Item 601(b)(2) of Regulation S-K. The registrant will furnish copies of any schedules to the Securities and Exchange Commission upon request.

Δ Confidential treatment has been requested or granted to certain confidential information contained in this exhibit.

+	Portions of this exhibit have been redacted in compliance with Regulation S-K Item 601(b)(10). The omitted information is not material and would likely cause competitive harm to the Company if publicly disclosed.
*	Management contract or compensatory plan or arrangement
#	Furnished herewith. This certification is being furnished solely to accompany this report pursuant to U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated herein by reference into any filing of the registrant whether made before or after the date hereof, regardless of any general incorporation language in such filing.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Daré Bioscience, Inc.

By: /s/ SABRINA MARTUCCI JOHNSON

President and Chief Executive Officer

Date: March 31, 2022

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ SABRINA MARTUCCI JOHNSON Sabrina Martucci Johnson	President and Chief Executive Officer (Principal Executive Officer) and Director	March 31, 2022
/s/ LISA WALTERS-HOFFERT Lisa Walters-Hoffert	Chief Financial Officer and Secretary (Principal Financial and Accounting Officer)	March 31, 2022
/s/ WILLIAM H. RASTETTER William H. Rastetter, Ph.D.	Chairman of the Board and Director	March 31, 2022
/s/ CHERYL R. BLANCHARD Cheryl R. Blanchard, Ph.D.	Director	March 31, 2022
/s/ JESSICA D. GROSSMAN Jessica D. Grossman, M.D.	Director	March 31, 2022
/s/ SUSAN L. KELLEY Susan L. Kelley, M.D.	Director	March 31, 2022
/s/ GREGORY W. MATZ Gregory W. Matz, CPA	Director	March 31, 2022
/s/ SOPHIA ONONYE-ONYIA Sophia Ononye-Onyia, Ph.D.	Director	March 31, 2022
/s/ ROBIN STEELE Robin Steele, J.D., L.L.M.	Director	March 31, 2022

DARÉ BIOSCIENCE, INC. AND SUBSIDIARIES
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
of Daré Bioscience, Inc. and Subsidiaries

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of **Daré Bioscience, Inc.** and Subsidiaries ("the Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of their operations and their cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

The Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company had recurring losses from operations, negative cash flow from operations and is dependent on additional financing to fund operations. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are described in Note 2 to the financial statements. The financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there were no critical audit matters.

We have served as the Company's auditor since 2017.

/s/ Mayer Hoffman McCann P.C.

March 31, 2022
San Diego, California

Daré Bioscience, Inc. and Subsidiaries
Consolidated Balance Sheets

	December 31, 2021	December 31, 2020
Assets		
Current Assets		
Cash and cash equivalents	$ 51,674,087	$ 4,669,467
Other receivables	1,145,317	460,168
Prepaid expenses	2,476,612	1,854,277
Total current assets	55,296,016	6,983,912
Property and equipment, net	26,041	37,930
Other non-current assets	485,120	528,870
Total assets	$ 55,807,177	$ 7,550,712
Liabilities and stockholders' equity (deficit)		
Current Liabilities		
Accounts payable	$ 2,103,083	$ 1,021,333
Accrued expenses	3,136,244	3,359,718
Deferred grant funding	10,542,983	1,564,553
Note payable	—	367,285
Contingent consideration	—	1,000,000
Current portion of lease liabilities	270,546	347,712
Total current liabilities	16,052,856	7,660,601
Deferred license revenue	1,000,000	1,000,000
Lease liabilities long-term	—	41,844
Total liabilities	17,052,856	8,702,445
Commitments and contingencies (Note 12)		
Stockholders' equity (deficit)		
Preferred stock, $0.01 par value, 5,000,000 shares authorized		
None issued and outstanding	—	—
Common stock: $0.0001 par value, 120,000,000 shares authorized, 83,944,119 and 41,596,253 shares issued and outstanding at December 31, 2021 and December 31, 2020, respectively	8,394	4,159
Accumulated other comprehensive loss	(154,973)	(91,388)
Additional paid-in capital	149,027,802	70,366,293
Accumulated deficit	(110,126,902)	(71,430,797)
Total stockholders' equity (deficit)	38,754,321	(1,151,733)
Total liabilities and stockholders' equity (deficit)	$ 55,807,177	$ 7,550,712

See accompanying notes.

Daré Bioscience, Inc. and Subsidiaries
Consolidated Statements of Operations and Comprehensive Loss

	Years Ended December 31,	
	2021	**2020**
Operating expenses		
General and administrative	$ 8,350,945	$ 6,549,508
Research and development	30,617,567	20,769,416
License fees	100,000	83,333
Total operating expenses	39,068,512	27,402,257
Loss from operations	(39,068,512)	(27,402,257)
Other income	2,520	1,514
Gain on extinguishment of note payable	369,887	—
Net loss	$ (38,696,105)	$ (27,400,743)
Deemed dividend from trigger of round down provision feature	—	(6,863)
Net loss to common shareholders	$ (38,696,105)	$ (27,407,606)
Foreign currency translation adjustments	(63,585)	11,237
Comprehensive loss	$ (38,759,690)	$ (27,396,369)
Loss per common share - basic and diluted	$ (0.63)	$ (0.91)
Weighted average number of common shares outstanding:		
Basic and diluted	61,154,157	30,091,469

See accompanying notes.

Daré Bioscience, Inc. and Subsidiaries
Consolidated Statements of Stockholders' Equity (Deficit)

	Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount				
Balance at December 31, 2019	**19,683,401**	**$ 1,968**	**$ 44,564,674**	**$ (102,625)**	**$ (44,023,191)**	**$ 440,826**
Stock-based compensation	—	—	742,031	—	—	742,031
Issuance of common stock, net of issuance costs	19,791,989	1,979	22,975,428	—	—	22,977,407
Issuance of common stock from the exercise of warrants	1,825,000	182	1,785,797	—	—	1,785,979
Issuance cost on equity paid in common stock	285,714	29	291,500	—	—	291,529
Stock options exercised	10,149	1	—	—	—	1
Deemed dividend from trigger of down round provision	—	—	6,863	—	(6,863)	—
Net loss	—	—	—	—	(27,400,743)	(27,400,743)
Foreign currency translation adjustments	—	—	—	11,237	—	11,237
Balance at December 31, 2020	**41,596,253**	**$ 4,159**	**$ 70,366,293**	**$ (91,388)**	**$ (71,430,797)**	**$ (1,151,733)**
Stock-based compensation	—	—	1,599,692	—	—	1,599,692
Issuance of common stock, net of issuance costs	41,094,657	4,109	75,309,982	—	—	75,314,091
Issuance of common stock from the exercise of warrants	520,985	52	500,094	—	—	500,146
Stock options exercised	35,500	4	32,525	—	—	32,529
Issuance of common stock in connection with milestone payment	696,724	70	1,219,216	—	—	1,219,286
Net loss	—	—	—	—	(38,696,105)	(38,696,105)
Foreign currency translation adjustments	—	—	—	(63,585)	—	(63,585)
Balance at December 31, 2021	**83,944,119**	**$ 8,394**	**$ 149,027,802**	**$ (154,973)**	**$ (110,126,902)**	**$ 38,754,321**

See accompanying notes.

Daré Bioscience, Inc. and Subsidiaries
Consolidated Statements of Cash Flows

	Years Ended December 31,	
	2021	**2020**
Operating activities:		
Net loss	$ (38,696,105)	$ (27,400,743)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	26,413	43,227
Stock-based compensation	1,599,692	742,031
Non-cash operating lease cost	(96,132)	(162,167)
Non-cash loss on settlement of contingent liability	44,286	—
Gain on extinguishment of note payable and accrued interest	(369,887)	—
Changes in operating assets and liabilities:		
Other receivables	(685,149)	95,042
Prepaid expenses	(622,336)	(454,133)
Other non-current assets	20,873	157,725
Accounts payable	1,081,749	(61,850)
Accrued expenses	(45,871)	1,261,065
Deferred grant funding	8,978,430	(455,121)
Deferred license revenue	—	1,000,000
Net cash used in operating activities	(28,764,037)	(25,234,924)
Investing activities:		
Purchases of property and equipment	(14,524)	(17,625)
Net cash used in investing activities	(14,524)	(17,625)
Financing activities:		
Net proceeds from issuance of common stock	75,314,091	22,977,407
Proceeds from the exercise of common stock warrants	500,146	1,785,979
Proceeds from the exercise of stock options	32,529	1
Proceeds from issuance of note payable	—	367,285
Net cash provided by financing activities	75,846,766	25,130,672
Effect of exchange rate changes on cash and cash equivalents	(63,585)	11,237
Net change in cash and cash equivalents	47,004,620	(110,640)
Cash and cash equivalents, beginning of year	4,669,467	4,780,107
Cash and cash equivalents, end of year	$ 51,674,087	$ 4,669,467
Supplemental disclosure of non-cash investing and financing activities:		
Operating right-of-use assets obtained in exchange for new operating lease liabilities	$ 308,533	$ —
Settlement of contingent closing consideration liability with stock issuance in connection with acquisition of business	$ 925,000	$ —
Milestone payment paid in common stock	$ 250,000	$ —
Issuance cost on equity paid in common stock	$ —	$ 291,428
Deemed dividend from trigger of down round provision	$ —	$ 6,863

See accompanying notes.

1. ORGANIZATION AND DESCRIPTION OF BUSINESS

Organization and business

Daré Bioscience, Inc. is a biopharmaceutical company committed to advancing innovative products for women's health. Daré Bioscience, Inc. and its wholly owned subsidiaries operate one segment. In this report, the "Company" refers collectively to Daré Bioscience, Inc. and its wholly owned subsidiaries, unless otherwise stated or the context otherwise requires.

The Company is driven by a mission 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. The Company's business strategy is to in-license or otherwise acquire the rights to differentiated product candidates in the Company's areas of focus, some of which have existing clinical proof-of-concept data, to take those candidates through mid to late-stage clinical development, and to establish and leverage strategic collaborations to achieve commercialization.

The Company's first product, XACIATO™, which was approved by the FDA in December 2021, is a single-dose vaginal gel prescription product for the treatment of bacterial vaginosis in females 12 years of age and older. In March 2022, the Company entered into an exclusive global license agreement with an affiliate of Organon & Co., Organon International GmbH, or Organon, to commercialize XACIATO. XACIATO is expected to be available commercially in the United States in the fourth quarter of 2022.

The Company began assembling its diverse portfolio of clinical-stage product candidates and pre-clinical programs in 2017 through acquisitions, exclusive in-licenses and other collaborations. The Company's programs target unmet needs in women's health in the areas of contraception, fertility, and vaginal and sexual health, and aim to expand treatment options, enhance outcomes and improve ease of use for women.

The Company's portfolio includes two product candidates in advanced clinical development:

- **Ovaprene®**, a hormone-free, monthly contraceptive; and
- **Sildenafil Cream, 3.6%**, a proprietary cream formulation of sildenafil for topical administration to the vulva and vagina for treatment of female sexual arousal disorder.

The Company's portfolio also includes four product candidates in Phase 1 clinical development or that the Company believes are Phase 1-ready:

- **DARE-HRT1**, a combination bio-identical estradiol and progesterone intravaginal ring for the treatment of menopausal symptoms, including vasomotor symptoms, as part of hormone therapy following menopause;
- **DARE-VVA1**, a vaginally delivered formulation of tamoxifen to treat vulvar vaginal atrophy as an option for women with hormone- receptor positive breast cancer;
- **DARE-FRT1**, an intravaginal ring containing bio-identical progesterone for broader luteal phase support as part of an in vitro fertilization treatment plan; and
- **DARE-PTB1**, an intravaginal ring containing bio-identical progesterone for the prevention of preterm birth;

In addition, the Company's portfolio includes these pre-clinical stage potential product candidates:

- **DARE-LARC1**, a contraceptive implant delivering levonorgestrel with a woman-centered design that has the potential to be a long-acting, yet convenient and user-controlled contraceptive option;
- **ADARE-204 and ADARE-214**, injectable formulations of etonogestrel designed to provide contraception over 6-month and 12-month periods, respectively; and

- **DARE-RH1**, a novel approach to non-hormonal contraception for both men and women by targeting the CatSper ion channel.

The Company's primary operations have consisted of, and are expected to continue to consist primarily of, research and development activities to advance its portfolio of product candidates through clinical development and regulatory approval.

The Company has one FDA-approved product, XACIATO, which has not yet been commercially launched. To date, the Company has not obtained any other regulatory approvals for any of its product candidates, commercialized any of its product candidates or generated any revenue.

The Company is subject to several risks common to biopharmaceutical companies, including dependence on key employees, dependence on third-party collaborators and service providers, competition from other companies, the need to develop commercially viable products in a timely and cost-effective manner, and the need to obtain adequate additional capital to fund the development of product candidates. The Company is also subject to several risks common to other companies in the industry, including rapid technology change, regulatory approval of products, uncertainty of market acceptance of products, success of third parties in the marketing, sale and distribution of the Company's products, competition from substitute products and larger companies, compliance with government regulations, protection of proprietary technology, and product liability.

The COVID-19 pandemic remains an evolving and uncertain risk to the Company's business, operating results, financial condition and stock price. To date, the Company believes the pandemic contributed to a slower than expected initial pace of enrollment in its Phase 2b clinical study of Sildenafil Cream, 3.6% and delays in commencement of clinical studies and nonclinical testing for more than one of its earlier stage clinical programs, but has not had a material adverse effect on its business as a whole. Continued uncertainty regarding the duration and impact of the pandemic on the U.S. and global economies, healthcare systems, workplace environments and capital markets, preclude any prediction as to the ultimate effect of the pandemic on the Company's business. For further discussion of risks and uncertainties related to the pandemic, see the risk factor in Part I, Item 1A of this report titled, The COVID-19 pandemic has negatively impacted our business and, in the future, may materially and adversely affect our business, financial condition and results and stock price, including by increasing the cost and timelines for our clinical development programs.

2. BASIS OF PRESENTATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of presentation

The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States, or U.S. GAAP, as defined by the Financial Accounting Standards Board, or FASB.

Going Concern

The Company prepared its consolidated financial statements on a going concern basis, which assumes that the Company will realize its assets and satisfy its liabilities in the normal course of business. The Company has a history of losses from operations, expects negative cash flows from its operations to continue for the foreseeable future, and expects that its net losses will continue for at least the next several years as it develops and seeks to bring to market its existing product candidates and potentially acquire, license and develop additional product candidates. These circumstances raise substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements do not include any adjustments to reflect the possible future effects on the recoverability and reclassification of assets or the amounts and classifications of liabilities that may result from the outcome of the uncertainty of the Company's ability to continue as a going concern.

At December 31, 2021, the Company had an accumulated deficit of approximately $110.1 million, cash and cash equivalents of approximately $51.7 million, and working capital of approximately $39.2 million. For the year ended December 31, 2021, the Company incurred a net loss of $38.7 million and had negative cash flow from operations of approximately $28.8 million.

The Company expects its primary uses of capital to be staff-related expenses, the cost of clinical trials and regulatory activities related to its product candidates, costs associated with contract manufacturing services and third-party clinical research and development services, payments due to third-party licensors upon the occurrence of commercial milestones for XACIATO and development milestones for the Company's product candidates, legal expenses, other regulatory expenses and general overhead costs. The Company's future funding requirements could

also include significant costs related to commercialization of its product candidates, if approved, depending on the type, nature and terms of commercial collaborations the Company establishes.

The Company expects its expenses, and in particular its research and development expenses, to increase significantly in 2022 compared to 2021 as the Company continues to develop and seek to bring to market its product candidates, with a focus on its product candidates that have reached the human clinical study development phase.

To date, the Company has one FDA-approved product, XACIATO, which has not yet been commercially launched. The Company has not obtained any other regulatory approvals for any of its product candidates, commercialized any of its product candidates or generated any revenue. Commercial launch of XACIATO in the U.S. by the Company's licensee, Organon, is expected in the fourth quarter of 2022. Under the terms of its license agreement with Organon, the Company will receive a $10.0 million non-refundable and non-creditable payment following the effective date of the license agreement and will be entitled to receive tiered double-digit royalties based on net sales and up to $182.5 million in milestone payments as follows: $2.5 million following the first commercial sale of a licensed product in the United States; and up to $180.0 million in tiered commercial sales milestones and regulatory milestones. The Company has devoted significant resources to building its portfolio of product candidates and to research and development activities related to these product candidates. The Company or its licensees must obtain regulatory approvals to market and sell any of its product candidates in the future and to market and sell XACIATO anywhere outside the U.S. The Company will need to generate sufficient safety and efficacy data on each of its product candidates in order to apply for regulatory approvals and for such assets to be attractive assets to potential strategic collaborators to license or to acquire, and for the Company to generate revenue through license fees, royalties on net revenues and commercial milestones related to such product candidates.

Based on the Company's current operating plan estimates, the Company does not have sufficient cash to satisfy its working capital needs and other liquidity requirements over at least the next 12 months from the date of issuance of the accompanying financial statements. The Company will need to raise substantial additional capital to continue to fund its operations and to successfully execute its current strategy. The Company will continue to seek to raise capital through the sale of shares of its common stock under its ATM sales agreements, however, when the Company can effect such sales and the amount of shares the Company can sell depends on a variety of factors to be determined by the Company from time to time, including, among others, market conditions, the trading price of its common stock and its determination as to the appropriate sources of funding for its operations. For the foreseeable future, the Company will evaluate and may pursue a variety of capital raising options on an on-going basis, including equity and debt financings, government or other grant funding, collaborations and strategic alliances or other similar types of arrangements, to cover its operating expenses, and the cost of any license or other acquisition of new product candidates or technologies. The amount and timing of the Company's capital needs have been and will continue to depend highly on many factors, including the product development programs the Company chooses to pursue, the pace and results of its clinical development efforts, and the nature and extent of expansion of its product candidate portfolio, if any. If the Company raises capital through collaborations, strategic alliances or other similar types of arrangements, it may have to relinquish, on terms that are not favorable to the Company, rights to some of its technologies or product candidates the Company would otherwise seek to develop or commercialize.

There can be no assurance that capital will be available when needed or that, if available, it will be obtained on terms favorable to the Company and its stockholders. In addition, equity or debt financings may have a dilutive effect on the holdings of the Company's existing stockholders, and debt financings may subject the Company to restrictive covenants, operational restrictions and security interests in its assets. If the Company cannot raise capital when needed, on favorable terms or at all, the Company will not be able to continue development of its product candidates, will need to reevaluate its planned operations and may need to delay, scale back or eliminate some or all of its development programs, reduce expenses, file for bankruptcy, reorganize, merge with another entity, or cease operations. If the Company becomes unable to continue as a going concern, the Company may have to liquidate its assets, and might realize significantly less than the values at which they are carried on its condensed consolidated financial statements, and stockholders may lose all or part of their investment in the Company's common stock. The Company's condensed consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Principles of Consolidation

The consolidated financial statements of the Company are stated in U.S. dollars. These consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. One wholly owned subsidiary, Daré Bioscience Australia Pty LTD, operates primarily in Australia. The financial statements of the Company’s wholly owned subsidiaries are recorded in their functional currency and translated into the reporting currency. The cumulative effect of changes in exchange rates between the foreign entity’s functional currency and the reporting currency is

reported in Accumulated Other Comprehensive Loss. All intercompany transactions and accounts have been eliminated in consolidation.

Grant Funding

The Company receives certain research and development funding through grants issued by a division of the National Institutes of Health and the Bill & Melinda Gates Foundation, or the Foundation. Under the Foundation grant, which the Company considers to be a research and development contract under FASB Accounting Standards Codification, or ASC, Topic 730 *Research and Development*, the Company granted the Foundation a Humanitarian License which gives the Foundation the right to make the funded developments accessible at an affordable price to people within developing countries. The Company recognizes grant funding in the statements of operations as a reduction to research and development expense as the related costs are incurred to meet those obligations over the grant period. The Company adopted this policy in 2018. For the years ended December 31, 2021 and December 31, 2020, the Company recognized approximately $2.5 million and $3.7 million, respectively, in the statements of operations as a reduction to research and development expense. Grant funding payments received in advance of research and development expenses incurred are recorded as deferred grant funding liability in the Company's consolidated balance sheets.

Use of Estimates

The preparation of the consolidated financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Significant estimates include the fair value of stock-based compensation. Actual results could differ from those estimates and could materially affect the reported amounts of assets, liabilities and future operating results.

Risks and Uncertainties

The Company will require approvals from the U.S. Food and Drug Administration, or FDA, or foreign regulatory agencies prior to being able to sell any products. The Company received approval from the FDA for its first product, XACIATO™, in December 2021. There can be no assurance that the Company’s current or future product candidates will receive the necessary approvals. If the Company is denied regulatory approval of its product candidates, or if approval is delayed, it may have a material adverse impact on the Company’s business, results of operations and its financial position.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, risks related to the ability to license product candidates, successfully develop product candidates, successfully commercialize approved products or enter into strategic relationships with third parties who are able to successfully commercialize approved products, raise additional capital, compete with other products, and protect proprietary technology. As a result of these and other factors and the related uncertainties, there can be no assurance of the Company’s future success.

Cash and Cash Equivalents

The Company considers cash and all highly liquid investments with an original maturity of three months or less to be cash and cash equivalents. The Company’s wholly owned subsidiary, Dare MB Inc., has a $35,903 letter of credit related to the lease of real property that serves as security for future default of lease payments. The letter of credit is collateralized by cash which is unavailable for withdrawal or for usage for general obligations and is included in cash and cash equivalents on the Company's consolidated balance sheets.

Concentration of Credit Risk

The Company maintains cash balances at various financial institutions and such balances commonly exceed the $250,000 amount insured by the Federal Deposit Insurance Corporation. The Company also maintains money market funds at various financial institutions which are not federally insured although are invested primarily in the U.S. The Company has not experienced any losses in such accounts and management believes that the Company does not have significant risk with respect to such cash and cash equivalents.

Fair Value of Financial Instruments

GAAP defines fair value as the price that would be received for an asset or the exit price that would be paid to transfer a liability in the principal or most advantageous market in an orderly transaction between market participants on the measurement date, and also establishes a fair value hierarchy which requires an entity to maximize the use of observable inputs, where available. The three-level hierarchy of valuation techniques established to measure fair value is defined as follows:

- Level 1: inputs are unadjusted quoted prices in active markets for identical assets or liabilities.
- Level 2: inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices in active markets for similar assets and liabilities, quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of assets or liabilities.
- Level 3: unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The following tables present the classification within the fair value hierarchy of financial assets and liabilities that are remeasured on a recurring basis as of December 31, 2021 and December 31, 2020. There were no financial assets or liabilities that were remeasured using a quoted price in active markets for identical assets (Level 2) as of December 31, 2021.

	Fair Value Measurements			
	Level 1	Level 2	Level 3	Total
Balance at December 31, 2021				
Current assets:				
Cash equivalents [1]	$ 49,666,064	$ —	$ —	$ 49,666,064
Balance at December 31, 2020				
Current assets:				
Cash equivalents [1]	$ 2,823,099	$ —	$ —	$ 2,823,099
Other non-current liabilities:				
Current portion of contingent consideration [2]	$ —	$ —	$ 1,000,000	$ 1,000,000

[1] Represents cash held in money market funds.

[2] Represented the estimated fair value of the contingent consideration payable by the Company related to an acquisition completed in November 2019, and which was paid in September 2021, as described in Note 3.

The following table presents a reconciliation of contingent consideration, which was measured at fair value on a recurring basis using significant unobservable inputs (Level 3):

	Year Ended December 31,	
	2021	2020
Balance at beginning of period	$ 1,000,000	$ 1,000,000
Satisfaction of contingent consideration [1]	(1,000,000)	—
Balance at end of period	$ —	$ 1,000,000

[1] In June 2021, the contingent consideration payable by the Company related to an acquisition completed in November 2019 became due. In September 2021, the Company issued approximately 700,000 shares of its common stock in satisfaction of the milestone payments associated with milestones achieved, as described in Note 3.

Revenue Recognition

The Company recognizes revenue in accordance with FASB ASC Topic 606, *Revenue from Contracts with Customers*, which applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments.

The Company recognizes revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which it expects to be entitled in exchange for those goods or services. To determine

revenue recognition for contracts with customers, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligations. At contract inception, the Company assesses the goods or services agreed upon within each contract and assesses whether each good or service is distinct, and determines those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

In a contract with multiple performance obligations, the Company develops estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation, which determines how the transaction price is allocated among the performance obligations. The estimation of the stand-alone selling price(s) may include estimates regarding forecasted revenues or costs, development timelines, discount rates, and probabilities of technical and regulatory success. The Company evaluates each performance obligation to determine if it can be satisfied at a point in time or over time. Any change made to estimated progress towards completion of a performance obligation and, therefore, revenue recognized will be recorded as a change in estimate. In addition, variable consideration must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

License Fees. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in a contract, the Company recognizes revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. To date, the Company has not recognized any license fee revenue resulting from any of its collaborative arrangements.

Royalties and Commercial Milestones. For arrangements that include sales-based royalties and milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties and milestones relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue or any commercial milestones resulting from any of its collaborative arrangements.

Bayer License. In January 2020, the Company entered into a license agreement with Bayer HealthCare LLC, or Bayer, regarding the further development and commercialization of Ovaprene in the U.S. Upon execution of the agreement, the Company received a $1.0 million upfront non-refundable license fee payment from Bayer. Bayer, in its sole discretion, has the right to make the license effective by paying the Company an additional $20.0 million. The Company concluded that there was one significant performance obligation related to the $1.0 million upfront payment: a distinct license to commercialize Ovaprene effective upon the receipt of the $20.0 million fee. The $1.0 million upfront payment will be recorded as license revenue at the earlier of (1) the point in time the Company receives the $20.0 million fee, the license is transferred to Bayer and Bayer is able to use and benefit from the license and (2) the termination of the agreement. As of December 31, 2021, neither of the foregoing had occurred. The $1.0 million payment is recorded as deferred license revenue in the Company's consolidated balance sheets at December 31, 2021 and December 31, 2020.

The Company will also be entitled to receive (a) milestone payments totaling up to $310.0 million related to the commercial sales of Ovaprene, if all such milestones are achieved, (b) tiered royalties starting in the low double digits based on annual net sales of Ovaprene during a calendar year, subject to customary royalty reductions and offsets, and (c) a percentage of sublicense revenue.

Potential future payments for variable consideration, such as commercial milestones, will be recognized when it is probable that, if recorded, a significant reversal will not take place. Potential future royalty payments will be recorded as revenue when the associated sales occur. (See Note 3, Strategic Agreements.)

Leases

The Company determines if an arrangement is a lease at inception. Operating leases are included in other non-current assets as right-of-use, or ROU, lease assets, current portion of lease liabilities, and long-term lease liabilities on the Company's consolidated balance sheets.

ROU lease assets represent the Company's right to use an underlying asset for the lease term and lease obligations represent the Company's obligation to make lease payments arising from the lease. Operating ROU lease assets and obligations are recognized at the commencement date based on the present value of lease payments over the lease term. If the lease does not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The ROU lease asset also includes any lease payments made and excludes lease incentives. The Company's lease terms may include options to extend or terminate the lease and the related payments are only included in the lease liability when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term. (See Note 11, Leased Properties.)

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. Its chief operating decision maker is the chief executive officer. The Company has one operating segment, women’s health.

Research and Development Costs

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses, manufacturing process-development and scale-up activities, fees paid to clinical and regulatory consultants, clinical trial and related clinical trial manufacturing expenses, fees paid to contract research organizations, or CROs, and investigative sites, transaction expenses incurred in connection with the expansion of the product portfolio through acquisitions and license and option agreements, milestone payments incurred or probable to be incurred for the Company's in-licensing arrangements, payments to universities under the Company’s license agreements and other outside expenses. Research and development costs are expensed as incurred. Nonrefundable advance payments, if any, for goods and services used in research and development are recognized as an expense as the related goods are delivered or services are performed.

Net Loss Per Share

Basic net loss attributable to common stockholders per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period without consideration of common stock equivalents. Since the Company was in a loss position for all periods presented, diluted net loss per share is the same as basic net loss per share for all periods presented as the inclusion of all potential dilutive securities would have been antidilutive.

There were stock options exercisable into 4,717,602 and 2,786,591 shares of common stock outstanding at December 31, 2021 and 2020, respectively. There were warrants exercisable into 1,381,015 and 1,908,643 shares of common stock outstanding at December 31, 2021 and 2020, respectively. These securities were not included in the computation of diluted loss per share because they are antidilutive, but they could potentially dilute earnings (loss) per share in future years.

Stock-Based Compensation

The Company records compensation expense for all stock-based awards granted based on the fair value of the award at the time of grant. The Company uses the Black-Scholes Pricing Model to determine the fair value of each of the awards which considers factors such as expected term, volatility, risk free interest rate and dividend yield. Due to the limited history of the Company, the simplified method was utilized in order to determine the expected term of the awards. Additionally, the Company considered comparable companies in the industry which have available share price history to calculate the volatility. The Company compared U.S. Treasury Bills in determining the risk-free interest rate appropriate given the expected term. The Company has not established and has no plans to establish, a dividend policy, and the Company has not declared, and has no plans to declare dividends in the foreseeable future and thus no dividend yield was determined necessary in the calculation of fair value.

Income Taxes

The Company accounts for income taxes using the asset and liability method in accordance with FASB ASC 740, *Income Taxes*. Under this method deferred income taxes are provided to reflect the tax consequences in future years of differences between the tax basis of assets and liabilities and their financial reporting amounts based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect

taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company follows the two-step approach to recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates it is more likely than not, that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount, which is more than 50% likely of being realized upon ultimate settlement. The Company considers many factors when evaluating and estimating the Company's tax positions and tax benefits, which may require periodic adjustments. At December 31, 2021, the Company did not record any liabilities for uncertain tax positions.

During each of 2021 and 2020, the Company recorded no provision for income taxes. Management evaluated the Company's tax positions and, as of December 31, 2021, the Company had approximately $1.9 million of unrecognized benefits. The tax years 2017 to 2021 remain open to examination by federal and state taxing authorities while the statute of limitations for U.S. net operating losses generated remain open beginning in the year of utilization.

Indemnification Obligations

As permitted under Delaware law, the Company has entered into indemnification agreements with its officers and directors that provide that the Company will indemnify its directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by such director or officer in any action or proceeding arising out of their service as a director and/or officer. The term of the indemnification is for the officer's or director's lifetime. During the year ended December 31, 2021, the Company did not experience any losses related to those indemnification obligations. The Company does not expect significant claims related to these indemnification obligations, and consequently, has concluded the fair value of the obligations is not material. Accordingly, as of December 31, 2021 and 2020, no amounts have been accrued related to such indemnification provisions.

3. STRATEGIC AGREEMENTS

Strategic Agreement for Product Commercialization

Bayer HealthCare License Agreement

In January 2020, the Company entered into a license agreement with Bayer, regarding the further development and commercialization of Ovaprene in the U.S. The Company received a $1.0 million upfront non-refundable license fee payment from Bayer and Bayer agreed to support the Company in development and regulatory activities by providing the equivalent of two experts to advise the Company in clinical, regulatory, preclinical, commercial, CMC and product supply matters. Bayer, in its sole discretion, has the right to make the license effective by paying the Company an additional $20.0 million, referred to as the Clinical Trial and Manufacturing Activities Fee. Such license would be exclusive with regard to the commercialization of Ovaprene for human contraception in the U.S. and co-exclusive with the Company with regard to development.

The following is a summary of the other terms of the Bayer license agreement:

Milestone & Royalty Payments. The Company will be entitled to receive (a) a milestone payment in the low double-digit millions upon the first commercial sale of Ovaprene in the U.S. and escalating milestone payments based on annual net sales of Ovaprene during a calendar year, totaling up to $310.0 million if all such milestones, including the first commercial sale, are achieved, (b) tiered royalties starting in the low double digits based on annual net sales of Ovaprene during a calendar year, subject to customary royalty reductions and offsets, and (c) a percentage of sublicense revenue.

Efforts. The Company is responsible for the pivotal trial for Ovaprene and for its development and regulatory activities and has product supply obligations. After payment of the Clinical Trial and Manufacturing Activities Fee, Bayer will be responsible for the commercialization of Ovaprene for human contraception in the U.S.

Term. The initial term of the agreement, which is subject to automatic renewal terms, continues until the later of (a) the expiration of any valid claim covering the manufacture, use, sale or import of Ovaprene in the U.S.; or (b) 15 years from the first commercial sale of Ovaprene in the U.S. In addition to customary termination rights for both parties, Bayer may terminate the agreement at any time on 90 days' notice and the agreement will automatically terminate if the Company does not receive the Clinical Trial and Manufacturing Activities Fee if and when due.

Strategic Agreements for Pipeline Development

Hammock/MilanaPharm Assignment and License Agreement

In December 2018, the Company entered into (a) an Assignment Agreement with Hammock Pharmaceuticals, Inc., or the Assignment Agreement, and (b) a First Amendment to License Agreement with TriLogic Pharma, LLC and MilanaPharm LLC, or the License Amendment. Both agreements relate to the Exclusive License Agreement among Hammock, TriLogic and MilanaPharm dated as of January 9, 2017, or the MilanaPharm License Agreement. Under the Assignment Agreement and the MilanaPharm License Agreement, as amended by the License Amendment, the Company acquired an exclusive, worldwide license under certain intellectual property to, among other things, develop and commercialize products for the diagnosis, treatment and prevention of human diseases or conditions in or through any intravaginal or urological applications. The licensed intellectual property relates to the hydrogel drug delivery platform of TriLogic and MilanaPharm known as TRI-726. In XACIATO, this proprietary technology is formulated with clindamycin for the treatment of bacterial vaginosis. In December 2019, the Company entered into amendments to each of the Assignment Agreement and License Amendment. In September 2021, the Company and Trilogic and MilanaPharm entered into another amendment to the License Agreement.

The following is a summary of other terms of the License Amendment, as amended:

License Fees. A total of $235,000 in license fees were payable to MilanaPharm, the final installment of which was $110,000 paid in 2020.

Milestone Payments. The Company paid MilanaPharm $300,000 in the aggregate upon achievement of certain clinical and regulatory development milestones; $50,000 of which was paid in 2020 and $250,000 of which was paid in 2021. The Company may also pay MilanaPharm up to $1.75 million in the aggregate upon achieving certain commercial sales milestones.

Foreign Sublicense Income. The Company will pay MilanaPharm a low double-digit percentage of all income received by the Company or its affiliates in connection with any sublicense granted to a third party for use outside of the United States, subject to certain exclusions.

Royalty Payments. During the royalty term, the Company will pay MilanaPharm high single-digit to low double-digit royalties based on annual worldwide net sales of licensed products and processes. The royalty term, which is determined on a country-by-country basis and licensed product-by-product basis (or process-by-process basis), begins with the first commercial sale of a licensed product or process in a country and terminates on the latest of (1) the expiration date of the last valid claim of the licensed patent rights that cover the method of use of such product or process in such country, or (2) 10 years following the first commercial sale of such product or process in such country. Royalty payments are subject to reduction in certain circumstances, including as a result of generic competition, patent prosecution expenses incurred by the Company, or payments to third parties for rights or know-how required for the Company to exercise the licenses granted to it under the MilanaPharm License Agreement or that are strategically important or could add value to a licensed product or process in a manner expected to materially generate or increase sales.

Efforts. The Company must use commercially reasonable efforts and resources to (1) develop and commercialize at least one licensed product or process in the United States and at least one licensed product or process in at least one of Canada, the United Kingdom, France, Germany, Italy or Spain, and (2) continue to commercialize that product or process following the first commercial sale of a licensed product or process in the applicable jurisdiction.

Term. Unless earlier terminated, the license term continues until (1) on a licensed product-by-product (or process-by-process basis) and country-by-country basis, the date of expiration of the royalty term with respect to such licensed product in such country, and (2) the expiration of all applicable royalty terms under the MilanaPharm License Agreement with respect to all licensed products and processes in all countries. Upon expiration of the term with respect to any licensed product or process in a country (but not upon earlier termination of the MilanaPharm License Agreement), the licenses granted to the Company under the MilanaPharm License Agreement will convert automatically to an exclusive, fully paid-up, royalty-free, perpetual, non-terminable and irrevocable right and license under the licensed intellectual property.

In addition to customary termination rights for all parties, MilanaPharm may terminate the license granted to the Company solely with respect to a licensed product or process in a country if, after having launched such product or process in such country, (1) the Company or its affiliates or sublicensees discontinue the sale of such product or

process in such country and MilanaPharm notifies the Company of such termination within 60 days of having first been notified by the Company of such discontinuation, or (2) the Company or its affiliates or sublicensees (A) discontinue all commercially reasonable marketing efforts to sell, and discontinue all sales of, such product or process in such country for nine months or more, (B) fail to resume such commercially reasonable marketing efforts within 120 days of having been notified of such failure by MilanaPharm, (C) fail to reasonably demonstrate a strategic justification for the discontinuation and failure to resume to MilanaPharm, and (D) MilanaPharm gives 90 days' notice to the Company.

The following is a summary of other terms of the Assignment Agreement, as amended:

Assignment; Technology Transfer. Hammock assigned and transferred to the Company all of its right, title and interest in and to the MilanaPharm License Agreement and agreed to cooperate to transfer to the Company all of the data, materials and the licensed technology in its possession pursuant to a technology transfer plan to be agreed upon by the parties, with a goal for the Company to independently practice the licensed intellectual property as soon as commercially practical in order to develop and commercialize the licensed products and processes.

Fees. A total of $512,500 in fees were payable to Hammock, the final installment of which was $137,500 paid in 2020.

Milestone Payments. The Company will pay Hammock up to $1.1 million in the aggregate upon achievement of certain clinical and regulatory development milestones, $100,000 of which was paid in 2020 and $750,000 of which was paid in 2021. The remaining milestone does not relate to a bacterial vaginosis product.

Term. The Assignment Agreement will terminate upon the later of (1) completion of the parties' technology transfer plan, and (2) payment to Hammock of the last of the milestone payments.

ADVA-Tec License Agreement

In March 2017, the Company entered into a license agreement with ADVA-Tec, Inc., under which the Company was granted the exclusive right to develop and commercialize Ovaprene for human contraceptive use worldwide. The Company must use commercially reasonable efforts to develop and commercialize Ovaprene and must meet certain minimum spending amounts per year, including $2.5 million per year to cover such activities until a final PMA is filed, or until the first commercial sale of Ovaprene, whichever occurs first. ADVA-Tec will conduct certain research and development work as necessary to allow the Company to seek a PMA from the FDA and will provide the Company with clinical trial and commercial supplies of Ovaprene, either directly or through a CMO, on commercially reasonable terms.

Under the license agreement, in addition to an exclusive license to ADVA-Tec's and its affiliates' intellectual property rights for all uses of Ovaprene as a human contraceptive device, the Company has a right of first refusal to license these patents and patent applications for additional indications.

The following is a summary of other terms of the ADVA-Tec license agreement:

Milestone Payments. The Company will pay to ADVA-Tec: (1) up to $14.6 million in the aggregate based on the achievement of specified development and regulatory milestones, $200,000 of which was paid in 2021; and (2) up to $20.0 million in the aggregate based on the achievement of certain worldwide net sales milestones. The remaining development and regulatory milestones include: the FDA's approval to commence a pivotal clinical trial; successful completion of such pivotal clinical trial; the FDA's acceptance of a PMA filing for Ovaprene; the FDA's approval of the PMA for Ovaprene; CE Marking of Ovaprene in at least three designated European countries; obtaining regulatory approval in at least three designated European countries; and obtaining regulatory approval in Japan.

Royalty Payments. After the commercial launch of Ovaprene, the Company will pay to ADVA-Tec royalties based on aggregate annual net sales of Ovaprene in specified regions, at a royalty rate that will vary between 1% and 10% and will increase based on various net sales thresholds.

Term. Unless earlier terminated, the license the Company received under the agreement continues on a country-by-country basis until the later of the life of the licensed patents or the Company's last commercial sale of Ovaprene. In addition to customary termination rights for both parties: (A) the Company may terminate the agreement with or without cause in whole or on a country-by-country basis upon 60 days prior written notice; and (B) ADVA-Tec may terminate the agreement if the Company develops or commercializes any non-hormonal ring-based vaginal contraceptive device competitive to Ovaprene or if the Company fails to: (1) in certain limited circumstances, commercialize Ovaprene in certain designated countries within three years of the first commercial sale of Ovaprene;

(2) satisfy the annual spending obligation described above, (3) use commercially reasonable efforts to complete all necessary pre-clinical and clinical studies required to support and submit a PMA, (4) conduct clinical trials as set forth in the development plan to which the Company and ADVA-Tec agree, and as may be modified by a joint research committee, unless such failure is caused by events outside of the Company's reasonable control, or (5) enroll a patient in the first non-significant risk medical device study or clinical trial as allowed by an institutional review board within six months of the production and release of Ovaprene, unless such failure is caused by events outside of the Company's reasonable control.

SST License and Collaboration Agreement

In February 2018, the Company entered into a license and collaboration agreement with Strategic Science & Technologies-D, LLC and Strategic Science & Technologies, LLC, referred to collectively as SST, under which the Company received an exclusive, royalty-bearing, sublicensable license to develop and commercialize, in all countries and geographic territories of the world, for all indications for women related to female sexual dysfunction and/or female reproductive health, including treatment of female sexual arousal disorder, or the Field of Use, SST's topical formulation of Sildenafil Cream, 3.6% as it existed as of the effective date of the agreement, or any other topically applied pharmaceutical product containing sildenafil or a salt thereof as a pharmaceutically active ingredient, alone or with other active ingredients, but specifically excluding any product containing ibuprofen or any salt derivative of ibuprofen, or the Licensed Products.

The following is a summary of other terms of the SST license agreement:

Invention Ownership. The Company retains rights to inventions made by its employees, SST retains rights to inventions made by its employees, and each party owns a 50% undivided interest in all joint inventions.

Joint Development Committee. The parties will collaborate through a joint development committee that will determine the strategic objectives for, and generally oversee, the development efforts of both parties under the agreement.

Development. The Company must use commercially reasonable efforts to develop the Licensed Products in the Field of Use in accordance with a development plan in the agreement, and to commercialize the Licensed Products in the Field of Use. The Company is responsible for all reasonable internal and external costs and expenses incurred by SST in its performance of the development activities it must perform under the agreement.

Royalty Payments. SST will be eligible to receive tiered royalties based on percentages of annual net sales of Licensed Products in the single digits to the mid double digits, subject to customary royalty reductions and offsets, and a percentage of sublicense revenue.

Milestone Payments. SST will be eligible to receive payments (1) ranging from $0.5 million to $18.0 million in the aggregate on achieving certain clinical and regulatory milestones in the U.S. and worldwide, and (2) between $10.0 million to $100.0 million in the aggregate upon achieving certain commercial sales milestones. If the Company enters into strategic development or distribution partnerships related to the Licensed Products, additional milestone payments would be due to SST.

Term. The Company's license continues on a country-by-country basis until the later of 10 years from the date of the first commercial sale of such Licensed Product or the expiration of the last valid claim of patent rights covering the Licensed Product in the Field of Use. Upon expiration (but not termination) of the agreement in a particular country, the Company will have a fully paid-up license under the licensed intellectual property to develop and commercialize the applicable Licensed Products in the applicable country on a non-exclusive basis.

Termination. In addition to customary termination rights for both parties: (1) prior to receipt of approval by a regulatory authority necessary for commercialization of a Licensed Product in the corresponding jurisdiction, including NDA approval, the Company may terminate the agreement without cause upon 90 days prior written notice; (2) following receipt of approval by a regulatory authority necessary for commercialization of a Licensed Product in the corresponding jurisdiction, including NDA approval, the Company may terminate the agreement without cause upon 180 days prior written notice; and (3) SST may terminate the agreement with respect to the applicable Licensed Product(s) in the applicable country(ies) upon 30 days' notice if the Company fails to use commercially reasonable efforts to perform development activities in substantial accordance with the development plan and do not cure such failure within 60 days of receipt of SST's notice thereof.

Catalent JNP License Agreement

In April 2018, the Company entered into an exclusive license agreement with Catalent JNP, Inc. (formerly known as Juniper Pharmaceuticals, Inc., and which the Company refers to as Catalent), under which Catalent granted the Company (a) an exclusive, royalty-bearing worldwide license under certain patent rights, either owned by or exclusively licensed to Catalent, to make, have made, use, have used, sell, have sold, import and have imported products and processes, and (b) a non-exclusive, royalty-bearing worldwide license to use certain technological information owned by Catalent to make, have made, use, have used, sell, have sold, import and have imported products and processes. The Company is entitled to sublicense the rights granted to it under this agreement.

Upfront Fee. The Company paid a $250,000 non-creditable upfront license fee to Catalent in connection with the execution of the agreement.

Annual Maintenance Fee. The Company will pay an annual license maintenance fee to Catalent on each anniversary of the date of the agreement, the amount of which will be $50,000 for the first two years and $100,000 thereafter, and which will be creditable against royalties and other payments due to Catalent in the same calendar year but may not be carried forward to any other year. The Company made the first payments in April 2019.

Milestone Payments. The Company must make potential future development and sales milestone payments of (1) up to $13.5 million in the aggregate upon achieving certain clinical and regulatory milestones, $1.0 million of which became payable in the third quarter of 2021, and in accordance with the license agreement, the amount was offset by the $100,000 annual maintenance fee, resulting in a net amount of $900,000 paid during the third quarter of 2021, and (2) up to $30.3 million in the aggregate upon achieving certain commercial sales milestones for each product or process covered by the licenses granted under the agreement.

Royalty Payments. During the royalty term, the Company will pay Catalent mid-single-digit to low double-digit royalties based on worldwide net sales of products and processes covered by the licenses granted under the agreement. In lieu of such royalty payments, the Company will pay Catalent a low double-digit percentage of all sublicense income the Company receives for the sublicense of rights under the agreement to a third party. The royalty term, which is determined on a country-by-country basis and product-by-product basis (or process-by-process basis), begins with the first commercial sale of a product or process in a country and terminates on the latest of (1) the expiration date of the last valid claim within the licensed patent rights with respect to such product or process in such country, (2) 10 years following the first commercial sale of such product or process in such country, and (3) when one or more generic products for such product or process are commercially available in such country, except that if there is no such generic product by the 10th year following the first commercial sale in such country, then the royalty term will terminate on the 10-year anniversary of the first commercial sale in such country.

Efforts. The Company must use commercially reasonable efforts to develop and make at least one product or process available to the public, which efforts include achieving specific diligence requirements by specific dates specified in the agreement.

Term. Unless earlier terminated, the term of the agreement will continue on a country-by-country basis until the later of (1) the expiration date of the last valid claim within such country, or (2) 10 years from the date of first commercial sale of a product or process in such country. Upon expiration (but not early termination) of the agreement, the licenses granted thereunder will convert automatically to fully-paid irrevocable licenses. Catalent may terminate the agreement (1) upon 30 days' notice for the Company's uncured breach of any payment obligation under the agreement, (2) if the Company fails to maintain required insurance, (3) immediately upon the Company's insolvency or the making of an assignment for the benefit of the Company's creditors or if a bankruptcy petition is filed for or against the Company, which petition is not dismissed within 90 days, or (4) upon 60 days' notice for any uncured material breach by the Company of any of the Company's other obligations under the agreement. The Company may terminate the agreement on a country-by-country basis for any reason by giving 180 days' notice (or 90 days' notice if such termination occurs prior to receipt of marketing approval in the United States). If Catalent terminates the agreement for the reason described in clause (4) above or if the Company terminates the agreement, Catalent will have full access including the right to use and reference all product data generated during the term of the agreement that is owned by the Company.

Adare Development and Option Agreement

In March 2018, the Company entered into an exclusive development and option agreement with Adare Pharmaceuticals (formerly known as Orbis Biosciences, and which the Company refers to as Adare), for the development of long-acting injectable etonogestrel contraceptive with 6- and 12-month durations (now known as

ADARE-204 and ADARE-214, respectively). The agreement provides the Company with an option to negotiate an exclusive license agreement for the programs if the Company funds the conduct of specified development work by Adare.

MBI Acquisition

In November 2019, the Company acquired Dare MB Inc. (formerly, Microchips Biotech, Inc.), or MBI, to secure the rights to develop a long-acting reversible contraception method, that a woman can turn on or off herself, according to her own needs. This candidate is now known as DARE-LARC1.

At the closing of the acquisition, the Company issued an aggregate of approximately 3.0 million shares of its common stock to the holders of shares of MBI's capital stock outstanding immediately prior to the effective time of the merger. The transaction was valued at $2.4 million, based on the fair value of the approximately 3.0 million shares issued at $0.79 per share, which was the closing price per share of the Company's common stock on the date of closing. The shares were issued in exchange for MBI's cash and cash equivalents of $6.1 million, less net liabilities of $3.5 million and transaction costs of $202,000, which was allocated based on the relative fair value of the assets acquired and the liabilities assumed.

The Company also agreed to pay the following additional consideration to the former MBI stockholders: (a) up to $46.5 million contingent upon the achievement of specified funding, product development and regulatory milestones; (b) up to $55.0 million contingent upon the achievement of specified amounts of aggregate net sales of products incorporating the intellectual property acquired by the Company in the merger; (c) tiered royalty payments ranging from low single-digit to low double-digit percentages of annual net sales of such products, subject to customary provisions permitting royalty reductions and offset; and (d) a percentage of sublicense revenue related to such products. The Company agreed to use commercially reasonable efforts to achieve specified development and regulatory objectives relating to DARE-LARC1. In June 2021, a total of $1.25 million of that potential additional consideration became payable upon the achievement of certain of the funding and product development milestone events, $1.0 million of which was recorded as contingent consideration on the Company's consolidated balance sheets upon the completion of the MBI acquisition and $250,000 of which was expensed in 2021. In July 2021, the Company's board of directors elected to make these milestone payments in shares of the Company's common stock, to the extent permissible under the terms of the merger agreement with MBI, and, in September 2021, the Company issued approximately 700,000 shares of its common stock to former stockholders of MBI and paid $75,000 in cash to the stockholders' representative in accordance with the terms of the merger agreement in satisfaction of the $1.25 million in milestone payments associated with milestones achieved in June 2021. See Note 12.

Pear Tree Acquisition

In May 2018, the Company completed its acquisition of Pear Tree Pharmaceuticals, Inc., or Pear Tree. The Company acquired Pear Tree to secure the rights to develop a proprietary vaginal formulation of tamoxifen, now known as DARE-VVA1, as a potential treatment for vulvar and vaginal atrophy.

Milestone Payments. The Company must make contingent payments to the Pear Tree former stockholders or their representatives, or the Holders, that become payable upon achievement of specified clinical, regulatory and commercial milestones, which may be paid, in the Company's sole discretion, in cash or shares of the Company's common stock.

Royalty Payments. The Holders will be eligible to receive, subject to certain offsets, tiered royalties, including customary provisions permitting royalty reductions and offset, based on percentages of annual net sales of certain products subject to license agreements the Company assumed and a percentage of sublicense revenue.

4. PREPAID EXPENSES

Prepaid expenses consisted of the following:

	As of December 31,	
	2021	2020
Prepaid clinical expense	$ 1,728,421	$ 1,288,341
Prepaid insurance expense	552,354	227,298
Prepaid legal and professional expenses	195,837	338,638
Total prepaid expenses	$ 2,476,612	$ 1,854,277

5. OTHER NON-CURRENT ASSETS

Other non-current assets consisted of the following:

	As of December 31,	
	2021	2020
Prepaid insurance, long-term portion	$ 87,891	$ 246,016
Deferred financing costs	143,002	—
Deposits	37,554	43,304
Operating lease assets	216,673	239,550
Total other non-current assets	$ 485,120	$ 528,870

6. ACCRUED EXPENSES

Accrued expenses consisted of the following:

	As of December 31,	
	2021	2020
Accrued compensation and benefits expenses	$ 1,533,475	$ 1,157,074
Accrued legal and professional expenses	293,688	297,395
Accrued license expense	66,667	66,667
Accrued clinical and related expenses	1,242,414	1,838,582
Total accrued expenses	$ 3,136,244	$ 3,359,718

7. VENDOR CONCENTRATION

The Company had a major vendor that accounted for approximately 23% and 20% of the research and development expenditures for one of the Company's late-stage product candidates for the years ended December 31, 2021 and 2020, respectively. The same vendor also accounted for approximately 4% and 23% of the total accounts payable and vendor-related accrued expenses as of December 31, 2021 and 2020, respectively. The Company continues to maintain this vendor relationship and anticipates incurring significant expenses with this vendor over the next 12 months.

8. INCOME TAXES

The components of loss from continuing operations before provision for income taxes consists of the following (in thousands):

	Years Ended December 31,	
	2021	2020
Domestic	$ 37,083	$ 27,249
Foreign	1,613	152
Loss before taxes	$ 38,696	$ 27,401

The difference between the provision for income taxes (benefit) and the amount computed by applying the U.S. federal income tax rate for the years ended December 31, 2021 and 2020 are as follows:

	Years Ended December 31,	
	2021	2020
Federal statutory rate	21.0 %	21.0 %
State income tax, net of federal benefit	9.64 %	8.86 %
Permanent differences	0.19 %	— %
Research and development credit	2.70 %	1.80 %
Stock compensation	(0.41)%	(0.34)%
Other	0.25 %	(0.4)%
Change in valuation allowance	(33.38)%	(30.93)%
Effective income tax rate	(0.01)%	(0.01)%

The major components of the Company's deferred tax assets as of December 31, 2021 and 2020 are shown below (in thousands).

	2021	2020
Net operating loss carryforwards	$ 81,817	$ 68,437
Research and development credit carryforwards	7,186	4,903
Capitalized research and development costs	7,417	9,398
Other	801	376
Stock compensation	2,540	2,183
Total deferred tax assets	99,761	85,297
Valuation allowance	(99,761)	(85,297)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Under applicable accounting standards, management has considered the Company's history of losses and concluded that it is more likely than not the Company will not recognize the benefits of federal and state deferred tax assets. Accordingly, a valuation allowance of $99.8 million and $85.3 million was established at December 31, 2021 and 2020, respectively, to offset the net deferred tax assets. When and if management determines that it is more likely than not that the Company will be able to utilize the deferred tax assets prior to their expiration, the valuation allowance may be reduced or eliminated.

The increase in valuation allowance of approximately $14.5 million and $22.1 million for the years ending December 31, 2021 and 2020, respectively, is primarily related to an increase in net operating losses generated during the year.

The Company has U.S. federal net operating loss, or NOL, carryforwards available at December 31, 2021 of approximately $295.2 million of which $0.2 million begin expiring in 2022 unless previously utilized and $117.6 million that do not expire. The Company has state NOL carryforwards of $292.6 million that begin expiring in 2031 unless previously utilized. The Company has U.S. federal research credit carryforwards available at December 31, 2021 of approximately $6.9 million that begin expiring in 2027 unless previously utilized. The Company has state research credit carryforwards of $2.7 million of which $0.1 million begin expiring in 2022 unless previously utilized. These federal and state research and development credits are subject to a 20% reserve under FASB ASC 740. The difference between federal and state NOL carryforwards is primarily due to previously expired state NOL carryforwards.

Utilization of the NOL and research and development credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986 due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company has not yet completed an evaluation of ownership changes. To the extent an ownership change occurs, the NOL and credit carryforwards and other deferred tax assets may be subject to limitations.

A reconciliation of the beginning and ending amount of uncertain tax benefits is as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Beginning uncertain tax benefits	$ 1,341	$ 935
Current year - increases	$ 426	$ 237
Prior year - additions (reductions)	$ 142	$ 169
Ending uncertain tax benefits	$ 1,909	$ 1,341

Included in the balance of uncertain tax benefits at December 31, 2021 are $1.9 million of tax benefits that, if recognized, would impact the effective tax rate. The Company anticipates that no material amounts of unrecognized tax benefits will be settled within 12 months of the reporting date.

The Company's policy is to record estimated interest and penalties related to uncertain tax benefits as income tax expense. As of December 31, 2021 and 2020, the Company had no accrued interest or penalties recorded related to uncertain tax positions.

The tax years 2017 through 2021 remain open to examination by major taxing jurisdictions to which the Company is subject, which are primarily in the U.S. The statute of limitations for U.S. net operating losses utilized in future years will remain open beginning in the year of utilization.

No additional provision has been made for U.S. income taxes related to undistributed foreign earnings of the Company's wholly owned Australian subsidiary or for unrecognized deferred tax liabilities for temporary differences related to investments in subsidiaries. As such, earnings are expected to be permanently reinvested, the investments are permanent in duration, or the Company has estimated that no additional tax liability will arise as a result of the distribution of such earnings. A liability could arise if amounts are distributed by the subsidiary or if the subsidiary is ultimately disposed. It is not practical to estimate the additional income taxes, if any, related to permanently reinvested earnings. There are no unremitted earnings as of December 31, 2021.

9. STOCKHOLDERS' EQUITY

October 2021 ATM Sales Agreement

In October 2021, the Company entered into a sales agreement with SVB Leerink LLC to sell shares of its common stock from time to time through an "at-the-market," or ATM, equity offering program under which SVB Leerink acts as the Company's agent. The Company agreed to pay a commission equal to 3% of the gross proceeds of any common stock sold under the agreement, plus certain legal expenses. Shares of the Company's common stock sold under the agreement will be issued pursuant to the Company's shelf registration statement on Form S-3 (File No. 333-254862) and the base prospectus included therein, originally filed with the SEC on March 30, 2021, and declared effective on April 7, 2021, and the prospectus supplement dated October 13, 2021 relating to the offering of up to $50.0 million in shares of the Company's common stock under this sales agreement, and any subsequent prospectus supplement filed with the SEC related to this ATM equity offering program.

During 2021, the Company sold approximately 7.1 million shares of common stock under this agreement for gross proceeds of approximately $16.3 million and incurred offering expenses of approximately $537,000.

April 2021 ATM Sales Agreement

In April 2021, the Company entered into a sales agreement with SVB Leerink to sell shares of its common stock from time to time through an ATM equity offering program under which SVB Leerink acts as the Company's agent. Under the sales agreement, the Company may issue and sell up to $50.0 million of shares of its common stock. The Company agreed to pay a commission equal to 3% of the gross proceeds of any common stock sold under the agreement, plus certain legal expenses. Any shares of the Company's common stock sold under the agreement will be issued pursuant to the Company's shelf registration statement on Form S-3 (File No. 333-254862) and the base prospectus included therein, originally filed with the SEC on March 30, 2021, and declared effective on April 7, 2021, and the prospectus supplement dated April 7, 2021 filed with the SEC on April 8, 2021.

During 2021, the Company sold approximately 26.0 million shares of common stock under this agreement for gross proceeds of approximately $46.9 million and incurred offering expenses of approximately $1.6 million.

2018 ATM Sales Agreement

In January 2018 the Company entered into a common stock sales agreement with H.C. Wainwright & Co., LLC, or Wainwright, relating to the offering and sale of shares of its common stock from time to time in an ATM equity offering program through Wainwright, acting as sales agent. In March 2021, the Company provided notice to Wainwright to terminate the agreement, and the agreement terminated in April 2021. Under the agreement, Wainwright was entitled to a commission at a fixed commission rate equal to 3% of the gross proceeds per share sold under the agreement.

During 2021, the Company sold approximately 3.3 million shares of common stock under this agreement for gross proceeds of approximately $7.7 million and incurred offering expenses of approximately $245,000. During 2020, the Company sold approximately 12.6 million shares of common stock under this agreement for gross proceeds of approximately $15.8 million and incurred offering expenses of approximately $594,000.

Equity Line

In April 2020, the Company entered into a purchase agreement, or the Purchase Agreement, and a registration rights agreement with Lincoln Park Capital Fund, LLC, or Lincoln Park. Under the terms and subject to the conditions of the Purchase Agreement, the Company had the right, but not the obligation, to sell to Lincoln Park, and Lincoln Park was obligated to purchase up to $15.0 million of the Company's common stock.

The Company incurred legal, accounting, and other fees related to the Purchase Agreement of approximately $374,000. Those costs were amortized and expensed as shares were sold under the Purchase Agreement, and as of December 31, 2021 there were no unamortized costs. During 2021, the Company sold, and Lincoln Park purchased, approximately 4.8 million shares under the Purchase Agreement for gross proceeds to the Company of approximately $7.0 million and recognized offering expenses of approximately $175,000. During 2020, the Company sold, and Lincoln Park purchased, approximately 7.2 million shares under the Purchase Agreement for gross proceeds to the Company of approximately $8.0 million and recognized offering expenses of approximately $236,000. As of December 31, 2021, the Company had sold and Lincoln Park had purchased a total of $15.0 million of the Company's common stock under the Purchase Agreement, and no more shares of common stock may be sold by the Company to Lincoln Park under the Purchase Agreement.

Common Stock Warrants

In February 2018, the Company closed an underwritten public offering in connection with which the Company issued to the investors in that offering warrants exercisable through February 2023 that initially had an exercise price of $3.00 per share. The warrants include a price-based anti-dilution provision, which provides that, subject to certain limited exceptions, the exercise price of the warrants will be reduced each time the Company issues or sells (or is deemed to issue or sell) securities for a net consideration per share less than the exercise price of those warrants in effect immediately prior to such issuance or sale. In addition, subject to certain exceptions, if the Company issues, sells or enters into any agreement to issue or sell securities at a price which varies or may vary with the market price of the shares of the Company's common stock, the warrant holders have the right to substitute such variable price for the exercise price of the warrant then in effect. These warrants are exercisable only for cash, unless a registration statement covering the shares issued upon exercise of the warrants is not effective, in which case the warrants may be exercised on a cashless basis. A registration statement covering the shares issued upon exercise of the warrants is currently effective. The Company estimated the fair value of the warrants as of February 15, 2018 to be approximately $3.0 million which was recorded in equity as of the grant date. The Company early adopted ASU 2017-11 as of January 1, 2018 and recorded the fair value of the warrants as equity.

In April 2019 and July 2020, in accordance with the price-based anti-dilution provision discussed above, the exercise price of these warrants was automatically reduced to $0.98 per share and to $0.96 per share, respectively, and as a result of the triggering of the anti-dilution provision, $0.8 million and $6,863, respectively, was recorded to additional paid-in capital.

During 2021, warrants to purchase an aggregate of 520,985 shares of common stock were exercised for gross proceeds of approximately $0.5 million. During 2020, warrants to purchase an aggregate of 1,825,000 shares of common stock were exercised for gross proceeds of approximately $1.8 million. As of December 31, 2021, the Company had the following warrants outstanding:

Shares Underlying Outstanding Warrants		Exercise Price	Expiration Date
6,500	$	10.00	04/04/2026
1,374,515	$	0.96	02/15/2023
1,381,015			

Common Stock

The authorized capital of the Company consists of 120,000,000 shares of common stock with a par value of $0.0001 and 5,000,000 shares of preferred stock with a par value of $0.01 per share. The issued and outstanding common stock of the Company consisted of 83,944,119 and 41,596,253 shares of common stock as of December 31, 2021 and 2020, respectively. There were no shares of preferred stock outstanding as of December 31, 2021 or 2020.

Common Stock Reserved for Future Issuance

The following table summarizes common stock reserved for future issuance at December 31, 2021:

Common stock reserved for issuance upon exercise of warrants outstanding	1,381,015
Common stock reserved for issuance upon exercise of options outstanding	4,717,602
Common stock reserved for future equity awards (under the Amended 2014 Plan)	201,855
Total	6,300,472

10. STOCK-BASED COMPENSATION

2014 Employee Stock Purchase Plan

The Company's 2014 Employee Stock Purchase Plan, or the ESPP, became effective in April 2014, but no offering period has been initiated thereunder since January 2017 and there was no stock-based compensation related to the ESPP for the years ended December 31, 2021 or December 31, 2020.

Amended and Restated 2014 Stock Incentive Plan

The Company maintains the Amended and Restated 2014 Stock Incentive Plan, or the Amended 2014 Plan. There were 2,046,885 shares of common stock authorized for issuance under the Amended 2014 Plan when it was approved by the Company's stockholders in July 2018. The number of authorized shares increases annually on the first day of each fiscal year until, and including, the fiscal year ending December 31, 2024 by the least of (i) 2,000,000, (ii) 4% of the number of outstanding shares of common stock on such date, or (iii) an amount determined by the Company's board of directors. As a result of the foregoing, the number of shares available under the Amended 2014 Plan increased by 1,663,850 to 2,168,366 on January 1, 2021, which increase represented 4% of the number of outstanding shares of common stock on such date.

Summary of Stock Option Activity

The table below summarizes stock option activity under the Amended 2014 Plan and related information for the years ended December 31, 2021 and 2020. The exercise price of all options granted during the years ended December 31, 2021 and 2020 was equal to the market value of the Company's common stock on the date of grant. As of December 31, 2021, unamortized stock-based compensation expense of approximately $3.7 million will be amortized over the weighted average period of 2.7 years. As of December 31, 2021, 201,855 shares of common stock were available for future award grants under the Amended 2014 Plan.

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2019 [1]	1,889,775	$ 1.21		
Granted	906,965	1.06		
Exercised	(10,149)	—		
Canceled/forfeited	—	—		
Expired	—	—		
Outstanding at December 31, 2020	2,786,591	$ 1.16		
Granted	2,052,075	2.31		
Exercised	(35,500)	0.92		
Canceled/forfeited	(85,564)	1.82		
Expired	—	—		
Outstanding at December 31, 2021	4,717,602	$ 1.65	8.11	$ 2,998,680
Options exercisable at December 31, 2021	2,319,775	$ 1.43	7.49	$ 1,993,377
Options vested and expected to vest at December 31, 2021	4,717,602	$ 1.65	8.11	$ 2,998,680

(1) Includes 10,149 shares subject to options granted under an equity incentive plan assumed in connection with an acquisition.

Compensation Expense

Total stock-based compensation expense related to stock options granted to employees and directors recognized in the consolidated statements of operations is as follows:

	Years Ended December 31,	
	2021	2020
Research and development	$ 524,071	$ 225,579
General and administrative	1,075,621	516,452
Total	$ 1,599,692	$ 742,031

The assumptions used in the Black-Scholes option-pricing model for stock options granted to employees and to directors in respect of board services during the years ended December 31, 2021 and 2020 is as follows:

	2021	2020
Expected life in years	6.0	10.0
Risk-free interest rate	0.67 %	0.82 %
Expected volatility	122 %	120 %
Forfeiture rate	0.0 %	0.0 %
Dividend yield	0.0 %	0.0 %
Weighted-average fair value of options granted	$ 2.01	$ 1.00

11. LEASED PROPERTIES

The Company's lease for its corporate headquarters (3,169 square feet of office space) commenced on July 1, 2018. In February 2022, the Company entered into an amendment to extend the term of the lease for two years such that the term now expires on August 31, 2024. (See Note 14, Subsequent Events.)

MBI, a wholly owned subsidiary the Company acquired in November 2019, leases general office space in Lexington, Massachusetts and warehouse space in Billerica, Massachusetts. The Lexington lease commenced on July 1, 2013. In February 2022, the Company entered into an amendment to extend the term of the lease for three years such that the term now expires on December 31, 2025. (See Note 14, Subsequent Events.) The Billerica lease commenced on October 1, 2016 and terminates on March 31, 2022.

Under the terms of each lease, the lessee pays base annual rent (subject to an annual fixed percentage increase), plus property taxes, and other normal and necessary expenses, such as utilities, repairs, and maintenance.

The Company evaluates renewal options at lease inception and on an ongoing basis and includes renewal options that it is reasonably certain to exercise in its expected lease terms when classifying leases and measuring lease liabilities. The leases do not require material variable lease payments, residual value guarantees or restrictive covenants.

The leases do not provide an implicit rate, and therefore the Company uses its incremental borrowing rate as the discount rate when measuring operating lease liabilities. The incremental borrowing rate represents an estimate of the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of the lease within a particular currency environment. The Company uses an incremental borrowing rate of 7% for operating leases that commenced prior to January 2019 (and all of the Company's operating leases commenced prior to such date). The depreciable lives of operating leases and leasehold improvements are limited by the expected lease term.

At December 31, 2021, the Company reported operating lease right of use assets of approximately $216,700 in other non-current assets and approximately $270,500 in current liabilities on the consolidated balance sheet.

Total operating lease costs were approximately $561,000 and $435,000 for the years ended December 31, 2021 and 2020, respectively. Operating lease costs consist of monthly lease payments expense, common area maintenance and other repair and maintenance costs and are included in general and administrative expenses in the consolidated statements of operations.

Cash paid for amounts included in the measurement of operating lease liabilities was approximately $462,000 for the year ended December 31, 2021, and these amounts are included in operating activities in the consolidated statements of cash flows. Further, at December 31, 2021, operating leases had a weighted average remaining lease term of 0.56 years.

At December 31, 2021, future minimum lease payments under the Company's operating leases are as follows:

Year ending December 31,	
2022	$ 277,700
Total future minimum lease payments	277,700
Less: accreted interest	7,200
Total operating lease liabilities	$ 270,500

12. COMMITMENTS AND CONTINGENCIES

CRADA with NICHD for the Pivotal Phase 3 Study of Ovaprene

In July 2021, the Company entered into a Cooperative Research and Development Agreement, or the CRADA, with the U.S. Department of Health and Human Services, as represented by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, or NICHD, for the conduct of a multi-center, non-comparative, pivotal Phase 3 clinical study of Ovaprene, or the Ovaprene Phase 3. The Ovaprene Phase 3 will be conducted within NICHD's Contraceptive Clinical Trial Network with NICHD contractor Health Decisions Inc., a contract research organization, providing clinical coordination and data collection and management services for the Ovaprene Phase 3. The Company and NICHD will each provide medical oversight and final data review and analysis for the Ovaprene Phase 3 and will work together to prepare the final report of the results of the Ovaprene Phase 3. The Company is responsible for providing clinical supplies of Ovaprene, coordinating interactions with the FDA, preparing and submitting supportive regulatory documentation, and providing a total of $5.5 million in payments to NICHD to be applied toward the costs of conducting the Ovaprene Phase 3. NICHD will be responsible for the other costs related to the conduct of the Ovaprene Phase 3. In 2021, in accordance with the payment schedule under the CRADA, the Company made aggregate payments of $1.5 million of the total amount payable to NICHD. The Company's remaining obligation under the CRADA at December 31, 2021 is $4.0 million.

Contingent Consideration

As discussed in Note 3 above, in connection with the acquisition of MBI, the Company agreed to pay additional consideration of up to $46.5 million to the former stockholders of MBI contingent upon the achievement of specified funding, product development and regulatory milestones. In June 2021, a total of $1.25 million of that potential additional consideration became payable upon the achievement of certain of the funding and product development milestone events, $1.0 million of which was previously recorded as contingent consideration on the Company's consolidated balance sheets upon the completion of the MBI acquisition and $250,000 of which was

expensed in 2021. In July 2021, the Company's board of directors elected to make these milestone payments in shares of the Company's common stock, to the extent permissible under the terms of the merger agreement with MBI, and, in September 2021, the Company issued approximately 700,000 shares of its common stock to former stockholders of MBI and paid $75,000 to the stockholders' representative in accordance with the terms of the merger agreement in satisfaction of the $1.25 million in milestone payments associated with milestones achieved in June 2021.

Note Payable

In April 2020, due to the economic uncertainty resulting from the impact of the COVID-19 pandemic on the Company's operations and to support its ongoing operations and retain all employees, the Company applied for and received a loan of $367,285 under the Paycheck Protection Program, or the PPP, of the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, administered by the U.S. Small Business Administration, or the SBA. Under the terms of the PPP, the loan proceeds could be used for "qualifying expenses" and, subject to specified limitations in the CARES Act and under the terms of the PPP, certain amounts of the loan, including accrued interest, may be forgiven if used for qualifying expenses. In January 2021, the Company was notified that the principal balance of its PPP loan and all accrued interest, which together totaled $369,887, were fully forgiven by the SBA. The Company recorded a gain on extinguishment of note payable and debt forgiveness income with respect to such loan forgiveness in the first quarter of 2021.

Legal Proceedings

From time to time, the Company may be involved in various claims arising in the normal course of business. Management is not aware of any material claims, disputes or unsettled matters that would have a material adverse effect on the Company's results of operations, liquidity or financial position that the Company has not adequately provided for in the accompanying consolidated financial statements.

Employment Agreements

Certain executive officers of the Company are entitled to payments if their employment is terminated by the Company without cause, if they resign for good reason, if their employment agreements are not renewed, or if their employment is terminated by the Company without cause or if they resign for good reason, in each case, within three months prior to or 12 months following a change in control of the Company. Upon termination by the Company without cause, if they resign for good reason, if their employment agreements are not renewed, such executives are entitled to receive a payment of an amount equal to either nine or twelve months of base salary and to receive continuing health benefits coverage for periods equal to either nine or twelve months following the termination of employment or until such officer is covered under a separate plan from another employer. If their employment is terminated by the Company without cause or if they resign for good reason, in each case, within three months prior to or 12 months following a change in control of the Company, such executives will be entitled to receive a payment of an amount equal to either twelve or eighteen months of base salary and target bonus and to receive continuing health benefits coverage for periods ranging between twelve and eighteen months following the termination of employment. In addition, upon a change in control of the Company, each officer's outstanding unvested options will fully vest and accelerate subject to the conditions outlined in such officer's employment agreement.

Employee Benefit – 401(k) Plan

The Company has a 401(k) retirement plan, or the 401(k) Plan, covering all qualified employees. The 401(k) Plan allows each participant to contribute a portion of their base wages up to an amount not to exceed an annual statutory maximum. The 401(k) Plan includes a Safe Harbor Plan that provides a Company match up to 4% of salary. The Company made matching contributions of approximately $160,000 and $136,000 during the years ended December 31, 2021 and 2020, respectively.

13. GRANT AWARDS

NICHD Non-Dilutive Grant Funding

The Company has received notices of awards and non-dilutive grant funding from NICHD to support the development of Ovaprene, DARE-PTB1 and DARE-LARC1. NICHD issues notices of awards to the Company for a specified amount, and the Company must incur and track expenses eligible for reimbursement under the award and submit a detailed accounting of such expenses to receive payment. If the Company receives payments under the

award, the amounts of such payments are recognized in the statements of operations as a reduction to research and development activities as the related costs are incurred to meet those obligations over the period.

Ovaprene

Since 2018, the Company has received approximately $1.9 million of non-dilutive grant funding from NICHD for clinical development efforts supporting Ovaprene. The final notice of award the Company received was for approximately $731,000 in April 2020, all of which has been funded to date.

The Company recorded credits to research and development expense for costs related to the NICHD award of an immaterial amount the year ended December 31, 2021, and approximately $595,000 for the year ended December 31, 2020.

DARE-PTB1

In August 2020, the Company received a notice of award of a grant from NICHD to support the development of DARE-PTB1. The award in the amount of $300,000 was for what is referred to as the "Phase I" segment of the project outlined in the Company's grant application, which is ongoing. Additional potential funding of up to approximately $2.0 million for the "Phase II" segment of the project outlined in the grant application is contingent upon satisfying specified requirements, including, assessment of the results of the Phase I segment, determination that the Phase I goals were achieved, and availability of funds. There is no guarantee the Company will receive any Phase II award.

The Company recorded credits to research and development expense for costs related to the NICHD award of approximately $65,000 for the year ended December 31, 2021. At December 31, 2021, the Company recorded a receivable of approximately $9,600 for expenses incurred through such date that it believes are eligible for reimbursement under the grant.

DARE-LARC1

In September 2021, the Company received a notice of award of a grant from NICHD to support the development of DARE-LARC1. The award in the amount of approximately $300,000 is to be used to explore device insertion and removal in nonclinical studies, which is to occur during the period of September 2021 through August 2022.

The Company recorded credits to research and development expense of approximately $7,400 for costs related to the NICHD award during the year ended December 31, 2021. At December 31, 2021, the Company recorded a receivable of approximately $7,400 for expenses incurred through such date that it believes is eligible for reimbursement under the grant.

DARE-LARC1 Non-Dilutive Grant Funding

MBI Grant Agreement

The Company's wholly-owned subsidiary, MBI, was awarded $5.4 million to support the development of DARE-LARC1 under a grant agreement with the Bill & Melinda Gates Foundation, or the Foundation. The funding period under this agreement ended June 30, 2021. Expenses eligible for funding were incurred, tracked and reported to the Foundation. MBI received payments under this agreement of approximately $2.5 million in 2020. At December 31, 2021, all payments under this agreement associated with research and development expenses for DARE-LARC1 had been incurred and reported to the Foundation and no future funding will be received under this agreement.

2021 DARE-LARC1 Grant Agreement

In June 2021, the Company entered into an agreement with the Foundation, or the 2021 DARE-LARC1 Grant Agreement, under which the Company was awarded up to $48.95 million to support the development of DARE-LARC1. The 2021 DARE-LARC1 Grant Agreement will support technology development and preclinical activities over the period of June 30, 2021 to November 1, 2026, to advance DARE-LARC1 in nonclinical proof of principle studies. The Company received an initial payment of $11.45 million in July 2021. Additional payments are contingent upon the DARE-LARC1 program’s achievement of specified development and reporting milestones. At December 31, 2021, approximately $10.5 million of deferred grant funding liability under this agreement was recorded in the Company's consolidated balance sheet.

14. SUBSEQUENT EVENTS

Exclusive License Agreement with Organon to Commercialize XACIATO

On March 31, 2022, the Company entered into an exclusive license agreement with Organon pursuant to which Organon will obtain exclusive worldwide rights to develop, manufacture and commercialize XACIATO and other future intravaginal or urological products for human use formulated with clindamycin that rely on intellectual property controlled by the Company. Under the agreement, the Company will receive a $10.0 million non-refundable and non-creditable payment following the effective date of the agreement and will be entitled to receive tiered double-digit royalties based on net sales and up to $182.5 million in milestone payments as follows: $2.5 million following the first commercial sale of a licensed product in the United States; and up to $180.0 million in tiered commercial sales milestones and regulatory milestones. Royalty payments will be subject to customary reductions and offsets. The royalty period for each licensed product will continue on a country-by-country basis from the first commercial sale of the licensed product in the country until the expiration of the later of (i) the date that no valid patent claim would be infringed in the absence of the license granted under the agreement by the sale of the licensed product in the country, (ii) 10 years after the end of the month in which the first commercial sale of the licensed product in the country occurred, and (iii) the expiration of regulatory market exclusivity for the licensed product in that country.

Under the agreement, the Company will be responsible for regulatory interactions and for providing product supply on an interim basis until Organon assumes such responsibilities. Until such time, Organon will purchase all of its product requirements of XACIATO from the Company at a transfer price equal to the Company's manufacturing costs plus a single-digit percentage markup.

The effective date of the agreement will occur following the satisfaction of closing conditions that include receipt of all applicable approvals, or the expiration or termination of all applicable waiting periods, required under applicable antitrust laws, including the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended. Unless terminated earlier, the agreement will expire on a product-by-product and country-by-country basis upon expiration of the applicable royalty period for each licensed product. In addition to customary termination rights for both parties, following the first anniversary of the effective date of the agreement, Organon may terminate the agreement in its entirety or on a country-by-country basis at any time in Organon's sole discretion on 120 days' advance written notice.

The agreement includes customary representations and warranties, covenants and indemnification obligations of each party.

In addition, the terms of the agreement provide Organon exclusive worldwide rights of first negotiation for specified potential future products of the Company.

Leased Properties

On February 4, 2022, the Company entered into an amendment to extend the term of the lease for its corporate headquarters in San Diego, California for two years. The extended term begins August 1, 2022 and expires August 31, 2024.

On February 14, 2022, the Company entered into an amendment to extend the term of the lease for its office space in Lexington, Massachusetts for three years. The extended term begins October 1, 2022 and expires December 31, 2025.

EXECUTION COPY

THIS WARRANT AND THE SHARES ISSUABLE UPON EXERCISE HEREOF HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR ANY STATE SECURITIES LAWS, AND MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED, OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR, SUBJECT TO SECTION 11 HEREOF, AN OPINION OF COUNSEL (WHICH MAY BE COMPANY COUNSEL) REASONABLY SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT, OR ANY APPLICABLE STATE SECURITIES LAWS.

WARRANT

To Purchase Shares of the Common Stock of

CERULEAN PHARMA INC.

Dated as of October 4, 2016 (the "Effective Date")

WHEREAS, Cerulean Pharma Inc., a Delaware corporation (the "Company"), has engaged Aquilo Partners, L.P. (the "Warrantholder") as a financial advisor pursuant to a letter agreement dated as of the Effective Date (the "Letter Agreement");

WHEREAS, pursuant to the Letter Agreement and as additional consideration to the Warrantholder for services to be rendered to the Company under the Letter Agreement, the Company has agreed to grant to the Warrantholder the right to purchase shares of the Company's Common Stock (as defined below) (this "Warrant");

NOW, THEREFORE, in consideration of the Warrantholder having executed and delivered the Letter Agreement and the services to be rendered to the Company under the Letter Agreement, the Company and the Warrantholder agree as follows:

SECTION 1. GRANT OF THE RIGHT TO PURCHASE COMMON STOCK.

For value received, the Company hereby grants to the Warrantholder, and the Warrantholder is entitled, upon the terms and subject to the conditions hereinafter set forth, to subscribe for and purchase, from the Company, up to 65,000 fully paid and non-assessable shares of Common Stock (the "Warrant Shares"), at a purchase price per share of $1.00 (the "Exercise Price"). The number of Warrant Shares and the Exercise Price are subject to adjustment as provided in Section 8. As used herein, the following terms shall have the following meanings:

"Charter" means the Company's Certificate of Incorporation or other constitutional document, as may be amended and in effect from time to time.

"Common Stock" means the Company's common stock, $0.0001 par value per share, as presently constituted under the Charter, and any class and/or series of Company capital stock for or into which such common stock may be

converted or exchanged in a reorganization, recapitalization or similar transaction.

"Exchange Act" means the Securities Exchange Act of 1934, as amended.

"Liquid Sale" means the closing of a Merger Event in which the consideration received by the Company and/or its stockholders, as applicable, consists solely of cash and/or Marketable Securities.

"Marketable Securities" in connection with a Merger Event means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Exchange Act, and is then current in its filing of all required reports and other information under the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by the Warrantholder in connection with the Merger Event were the Warrantholder to exercise this Warrant on or prior to the closing thereof is then traded on a national securities exchange or over-the-counter market, and (iii) following the closing of such Merger Event, Warrantholder would not be restricted from publicly re-selling all of the issuer's shares and/or other securities that would be received by Warrantholder in such Merger Event were Warrantholder to exercise this Warrant in full on or prior to the closing of such Merger Event, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Merger Event.

"Merger Event" means any of the following: (i) a sale, lease or other transfer of all or substantially all assets of the Company, (ii) any merger or consolidation involving the Company in which the Company is not the surviving entity or in which the outstanding shares of the Company's capital stock are otherwise converted into or exchanged for shares of capital stock or other securities or property of another entity and in which the holders of a majority of the outstanding shares of capital stock of the Company immediately prior to such merger or consolidation do not hold a majority of the surviving entity or other entity immediately following such merger or consolidation, or (ii) any sale by holders of the outstanding voting equity securities of the Company in a single transaction or series of related transactions of shares constituting a majority of the outstanding combined voting power of the Company.

"Purchase Price" means, with respect to any exercise of this Warrant, an amount equal to the Exercise Price multiplied by the number of shares of Common Stock as to which this Warrant is then exercised.

"Rule 144" means Rule 144 under the Securities Act, as amended.

"Securities Act" means the Securities Act of 1933, as amended.

SECTION 2. TERM OF THE WARRANT.

The term of this Warrant and the right to purchase Common Stock as granted herein shall commence on the Effective Date and, subject to Section 8(a) below, shall be exercisable for a period ending upon the tenth (10^{th}) anniversary of the Effective Date.

SECTION 3. EXERCISE OF THE PURCHASE RIGHTS.

The purchase rights set forth in this Warrant are exercisable by the Warrantholder, in whole or in part, at any time, or from time to time, prior to the expiration of the term set forth in Section 2, by tendering to the Company at its principal office a notice of exercise in the form attached hereto as Exhibit I (the "Notice of Exercise"), duly completed and executed, accompanied by payment of the Purchase Price in cash, check or wire transfer of immediately available funds. Promptly upon receipt of the Notice of Exercise and the payment of the Purchase Price, the Company shall issue to the Warrantholder book entry units/shares representing the number of shares of Common Stock purchased. Upon partial exercise of this Warrant prior to the expiration or earlier termination hereof, the Company shall promptly issue an amended Warrant representing the remaining number of shares purchasable hereunder. All other terms and conditions of such amended Warrant shall be identical to those contained herein, including, but not limited to the Effective Date hereof.

SECTION 4. RESERVATION OF SHARES.

During the term of this Warrant, the Company will at all times have authorized and reserved a sufficient number of shares of its Common Stock to provide for the exercise of the rights to purchase Common Stock as provided for herein.

SECTION 5. NO FRACTIONAL SHARES OR SCRIP.

No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant, but in lieu of such fractional shares the Company shall make a cash payment therefor upon the basis of the Exercise Price then in effect.

SECTION 6. NO RIGHTS AS STOCKHOLDER.

Without limitation of any provision hereof, Warrantholder agrees that this Warrant does not entitle the Warrantholder to any voting rights or other rights as a stockholder of the Company prior to the exercise of any of the purchase rights set forth in this Warrant.

SECTION 7. WARRANTHOLDER REGISTRY.

The Company shall maintain a registry showing the name and address of the registered holder of this Warrant. Warrantholder's initial address, for purposes of such registry, is set forth in Section 12(g) below. Warrantholder may change such address by giving written notice of such changed address to the Company.

SECTION 8. ADJUSTMENT RIGHTS.

The number of Warrant Shares and the Exercise Price are subject to adjustment from time to time, as follows:

(a) Merger Event. In connection with a Merger Event that is a Liquid Sale, this Warrant shall, on and after the closing thereof, automatically and without further action on the part of

any party or other person, represent the right to receive the consideration payable on or in respect of all shares of Common Stock that are issuable hereunder as of immediately prior to the closing of such Merger Event less the Purchase Price for all such shares of Common Stock (such consideration to include both the consideration payable at the closing of such Merger Event and all deferred consideration payable thereafter, if any, including, but not limited to, payments of amounts deposited at such closing into escrow and payments in the nature of earn-outs, milestone payments or other performance-based payments), and such Merger Event consideration shall be paid to Warrantholder, in exchange for this Warrant, as and when it is paid to the holders of the outstanding shares of Common Stock. In connection with a Merger Event that is not a Liquid Sale, the Company shall cause the successor or surviving entity to assume this Warrant and the obligations of the Company hereunder on the closing thereof, and thereafter this Warrant shall be exercisable for the same number and type of securities or other property as the Warrantholder would have received in consideration for the shares of Common Stock issuable hereunder had it exercised this Warrant in full as of immediately prior to such closing, at an aggregate Exercise Price no greater than the aggregate Exercise Price in effect as of immediately prior to such closing, and subject to further adjustment from time to time in accordance with the provisions of this Warrant. The provisions of this Section 8(a) shall similarly apply to successive Merger Events.

(b) Reclassification of Shares. Except for Merger Events subject to Section 8(a), if the Company at any time shall, by combination, reclassification, exchange or subdivision of securities or otherwise, change any of the securities as to which purchase rights under this Warrant exist into the same or a different number of securities of any other class or classes of securities, this Warrant shall thereafter represent the right to acquire such number and kind of securities as would have been issuable as the result of such change with respect to the securities which were subject to the purchase rights under this Warrant immediately prior to such combination, reclassification, exchange, subdivision or other change. The provisions of this Section 8(b) shall similarly apply to successive combination, reclassification, exchange, subdivision or other change.

(c) Subdivision or Combination of Shares. If the Company at any time shall combine or subdivide its Common Stock, (i) in the case of a subdivision, the Exercise Price shall be proportionately decreased and the number of Warrant Shares shall be proportionately increased, or (ii) in the case of a combination, the Exercise Price shall be proportionately increased and the number of Warrant Shares shall be proportionately decreased.

(d) Dividends. If the Company at any time while this Warrant is outstanding and unexpired shall:

(i) pay a dividend with respect to the outstanding shares of Common Stock payable in additional shares of Common Stock, then the Exercise Price shall be adjusted, from and after the payment date for such dividend, to that price determined by multiplying the Exercise Price in effect immediately prior to such date of determination by a fraction (A) the numerator of which shall be the total number of shares of Common Stock outstanding immediately prior to such dividend or distribution, and (B) the denominator of which shall be the total number of shares of Common Stock outstanding immediately after such dividend or distribution, and the number of Warrant Shares shall be proportionately increased; or

(ii) make any other dividend or distribution on or with respect to Common Stock, except any dividend or distribution (A) in cash, or (B) specifically provided for in any other clause of this Section 8, then, in each such case, provision shall be made by the Company such that the Warrantholder shall receive upon exercise of this Warrant a proportionate share of any such distribution as though it were the holder of the Common Stock as of the record date fixed for the determination of the stockholders of the Company entitled to receive such distribution.

(d) Notice of Certain Events. If: (i) the Company shall declare any dividend or distribution upon its outstanding Common Stock, payable in stock, cash, property or other securities; (ii) the Company shall offer for subscription pro rata to the holders of its Common Stock any additional shares of stock of any class or other rights; (iii) there shall be any Merger Event; or (iv) there shall be any voluntary dissolution, liquidation or winding up of the Company; then, in connection with each such event, the Company shall give the Warrantholder notice thereof at the same time and in the same manner as it gives notice thereof to the holders of outstanding Common Stock.

SECTION 9. REPRESENTATIONS, WARRANTIES AND COVENANTS OF THE COMPANY.

(a) Reservation of Common Stock. The Company covenants and agrees that all shares of Common Stock, if any, that may be issued upon the exercise of this Warrant will, upon issuance, be validly issued and outstanding, fully paid and non-assessable. The Company further covenants and agrees that the Company will, at all times during the term hereof, have authorized and reserved, free from preemptive rights, a sufficient number of shares of Common Stock to provide for the exercise of the rights represented by this Warrant. If at any time during the term hereof the number of authorized but unissued shares of Common Stock shall not be sufficient to permit exercise of this Warrant in full, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes.

(b) Due Authority. The execution and delivery by the Company of this Warrant and the performance of all obligations of the Company hereunder, including the grant to Warrantholder of the right to acquire the shares of Common Stock, have been duly authorized by all necessary corporate action on the part of the Company. This Warrant: (1) does not violate the Company's Charter or current bylaws and (2) does not contravene any material law or governmental rule, regulation or order applicable to it. This Warrant constitutes a legal, valid and binding agreement of the Company, enforceable in accordance with its terms, except as may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or affecting creditors' rights generally (including, without limitation, fraudulent conveyance laws) and by general principles of equity, regardless of whether considered in a proceeding in equity or at law.

(c) Consents and Approvals. No consent or approval of, giving of notice to, registration with, or taking of any other action in respect of any state, federal or other governmental authority or agency is required with respect to the execution, delivery and performance by the Company of its obligations under this Warrant, except for the filing of notices pursuant to Regulation D (as defined below) and any filing required by applicable state securities law, which filings will be effective by the time required thereby.

(d) Exempt Transaction. Subject to the accuracy of the Warrantholder's representations in Section I 0, the issuance of the Common Stock upon exercise of this Warrant will constitute a transaction exempt from (i) the registration requirements of Section 5 of the Securities Act, in reliance upon Section 4(a)(2) thereof, and (ii) the qualification requirements of the applicable state securities laws.

(e) Rule 144 Compliance. The Company shall, at all times prior to the earlier to occur of (x) the date of sale or other disposition by Warrantholder of this Warrant or all shares of Common Stock issued on exercise of this Warrant, or (y) the expiration or earlier termination of this Warrant if the Warrant has not been exercised in full or in part on such date, use all commercially reasonable efforts to timely file all reports required under the Exchange Act and otherwise timely take all actions necessary to permit the Warrantholder to sell or otherwise dispose of this Warrant and the shares of Common Stock issued on exercise hereof pursuant to Rule 144; provided that the foregoing shall not apply in the event of a Merger Event following which the successor or surviving entity is not subject to the reporting requirements of the Exchange Act. If the Warrantholder proposes to sell Common Stock issuable upon the exercise of this Warrant in compliance with Rule 144, then, upon Warrantholder's written request to the Company, the Company shall furnish to the Warrantholder, within ten (10) business days after receipt of such request, a written statement confirming the status of the Company's compliance with the filing and other requirements set forth in paragraph (c)(I) of Rule 144.

SECTION 10. REPRESENTATIONS AND COVENANTS OF THE WARRANTHOLDER.

This Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Warrantholder:

(a) Investment Purpose. This Warrant and the shares issued on exercise hereof will be acquired for investment and not with a view to the sale or distribution of any part thereof, and the Warrantholder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration or exemption. The Warrantholder has not been organized, reorganized, or recapitalized specifically for the purpose of investing in the Company.

(b) Private Issue. The Warrantholder understands (i) that the Common Stock issuable upon exercise of this Warrant is not, as of the Effective Date, registered under the Securities Act or qualified under applicable state securities laws, and (ii) that the Company's reliance on exemption from such registration is predicated on the representations set forth in this Section 10.

(c) Financial Risk. The Warrantholder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment, and has the ability to bear the economic risks of its investment in the Company.

(d) Accredited Investor. The Warrantholder is an "accredited investor" within the meaning of Rule 501 of Regulation D promulgated under the Securities Act, as presently in effect ("Regulation D").

(e) No Short Sales. Warrantholder has not at any time on or prior to the Effective Date engaged in any short sales or equivalent transactions in the Common Stock. Warrantholder agrees that at all times from and after the Effective Date and on or before the expiration or earlier termination of this Warrant, it shall not engage in any short sales or equivalent transactions in the Common Stock.

SECTION 11. TRANSFERS.

Subject to compliance with applicable federal and state securities laws, this Warrant and all rights hereunder are transferable, in whole or in part, without charge to the holder hereof (except for transfer taxes) upon surrender of this Warrant properly endorsed. Each taker and holder of this Warrant, by taking or holding the same, consents and agrees that this Warrant, when endorsed in blank, shall be deemed negotiable, and that the holder hereof, when this Warrant shall have been so endorsed and its transfer recorded on the Company's books, shall be treated by the Company and all other persons dealing with this Warrant as the absolute owner hereof for any purpose and as the person entitled to exercise the rights represented by this Warrant. The transfer of this Warrant shall be recorded on the books of the Company upon receipt by the Company of a notice of transfer in the form attached hereto as Exhibit II (the "Transfer Notice"), at its principal offices and the payment to the Company of all transfer taxes and other governmental charges imposed on such transfer. Until the Company receives such Transfer Notice, the Company may treat the registered owner hereof as the owner for all purposes. Notwithstanding anything herein or in any legend to the contrary, the Company shall not require an opinion of counsel in connection with any sale, assignment or other transfer by Warrantholder of this Warrant (or any portion hereof or any interest herein) to an affiliate (as defined in Regulation D) of Warrantholder, provided that such affiliate is an "accredited investor" as defined in Regulation D.

SECTION 12. MISCELLANEOUS.

(a) Effective Date. The provisions of this Warrant shall be construed and shall be given effect in all respects as if it had been executed and delivered by the Company on the date hereof. This Warrant shall be binding upon any successors or assigns of the Company.

(b) Remedies. In the event of any default hereunder, the non-defaulting party may proceed to protect and enforce its rights either by suit in equity and/or by action at law, including but not limited to an action for damages as a result of any such default, and/or an action for specific performance for any default where the non-defaulting party will not have an adequate remedy at law and where damages will not be readily ascertainable.

(c) No Impairment of Rights. The Company will not, by amendment of its Charter or through any other means, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate in order to protect the rights of the Warrantholder against impairment.

(d) Additional Documents. The Company agrees to supply such other documents as the Warrantholder may from time to time reasonably request.

(e) Attorneys' Fees. In any litigation, arbitration or court proceeding between the Company and the Warrantholder relating hereto, the prevailing party shall be entitled to reasonable attorneys' fees and expenses and all reasonable costs of proceedings incurred in enforcing this Warrant. For the purposes of this Section 12(e), attorneys' fees shall include without limitation reasonable fees incurred in connection with the following: (i) contempt proceedings; (ii) discovery; (iii) any motion, proceeding or other activity of any kind in connection with an insolvency proceeding; (iv) garnishment, levy, and debtor and third party examinations; and (v) post-judgment motions and proceedings of any kind, including without limitation any activity reasonably taken to collect or enforce any judgment.

(t) Severability. In the event any one or more of the provisions of this Warrant shall for any reason be held invalid, illegal or unenforceable, the remaining provisions of this Warrant shall be unimpaired, and the invalid, illegal or unenforceable provision shall be replaced by a mutually acceptable valid, legal and enforceable provision, which comes closest to the intention of the parties underlying the invalid, illegal or unenforceable provision.

(g) Notices. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication that is required, contemplated, or permitted under this Warrant or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (a) personal delivery to the party to be notified, (b) when sent by confirmed telex, electronic transmission or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt, and shall be addressed to the party to be notified as follows:

If to Warrantholder:

AQUILO PARTNERS, L.P.
101 Main Street, 15th Floor Telephone: (617) 401-2483 Email: jdyer@aquilopartners.com

If to the Company:

CERULEAN PHARMA INC.
Attention: General Counsel 35 Gatehouse Drive
Waltham, Massachusetts 02451
Facsimile: (855) 718-2378
Telephone: (781) 996-4300 Email: acarvajal@ceruleanrx.com

With a copy to:

WilmerHale 60 State Street
Boston, Massachusetts 02109
Attention: Lia Der Marderosian, Esquire Facsimile: 617-526-5000
Telephone: 617-526-6000

or to such other address as each party may designate for itself by like notice.

(h) Entire Agreement; Amendments. This Warrant constitutes the entire agreement and understanding of the parties hereto in respect of the subject matter hereof, and supersedes and replaces in their entirety any prior proposals, term sheets, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof. None of the terms of this Warrant may be amended except by an instrument executed by each of the parties hereto.

(i) Headings. The various headings in this Warrant are inserted for convenience only and shall not affect the meaning or interpretation of this Warrant or any provisions hereof.

(j) No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Warrant. In the event an ambiguity or question of intent or interpretation arises, this Warrant shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Warrant.

(k) No Waiver. No omission or delay by either party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by the other party at any time designated, shall be a waiver of any such right or remedy to which such party is entitled, nor shall it in any way affect the right of Warrantholder to enforce such provisions thereafter during the term of this Warrant.

(l) Survival. All agreements, representations and warranties contained in this Warrant or in any document delivered pursuant hereto shall be for the benefit of Warrantholder or the Company, as the case may be, and shall survive the execution and delivery of this Warrant and the expiration or other termination of this Warrant.

(m) Governing Law. This Warrant shall be governed by, and construed and enforced in accordance with, the laws of the State of New York, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

(n) Consent to Jurisdiction and Venue. All judicial proceedings arising in or under or related to this Warrant may be brought in any state or federal court of competent jurisdiction located in the City of New York. By execution and delivery of this Warrant, each party hereto generally and unconditionally: (a) consents to personal jurisdiction in the City of New York, borough of Manhattan, State of New York; (b) waives any objection as to jurisdiction or venue in City of New York, borough of Manhattan, State of New York; (c) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (d) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Warrant. Service of process on any party hereto in any action arising out of or relating to this Warrant shall be effective if given in accordance with the requirements for notice set forth in Section 12(g), and shall be deemed effective and received as set forth in Section 12(g). Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

(o) Mutual Waiver of Jury Trial. Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes arising under or in connection with this Warrant be resolved by a judge applying such applicable laws. EACH OF THE COMPANY AND WARRANTHOLDER SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, "CLAIMS") ASSERTED BY THE COMPANY AGAINST WARRANTHOLDER OR ITS ASSIGNEE OR BY WARRANTHOLDER OR ITS ASSIGNEE AGAINST THE COMPANY RELATING TO THIS WARRANT. This waiver extends to all such Claims, including Claims that involve persons or entities other the Company and Warrantholder; Claims that arise out of or are in any way connected to the relationship between the Company and Warrantholder; and any Claims for damages, breach of contract, specific performance, or any equitable or legal relief of any kind, arising out of this Warrant.

(p) Arbitration. If the Mutual Waiver of Jury Trial set forth in Section 12(0) is ineffective or unenforceable, the parties agree that all Claims shall be submitted to binding arbitration in accordance with the commercial arbitration rules of JAMS (the "Rules"), such arbitration to occur before one arbitrator, which arbitrator shall be a retired New York state judge or a retired Federal court judge. Such proceeding shall be conducted in the City of New York, borough of Manhattan, State of New York, with New York rules of evidence and discovery applicable to such arbitration. The decision of the arbitrator shall be binding on the parties, and shall be final and nonappealable to the maximum extent permitted by law. Any judgment rendered by the arbitrator may be entered in a court of competent jurisdiction and enforced by the prevailing party as a final judgment of such court.

(q) Pre-arbitration Relief. In the event Claims are to be resolved by arbitration, either party may seek from a court of competent jurisdiction identified in Section 12(11), any prejudgment order, writ or other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by binding arbitration.

(r) Counterparts. This Warrant and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts (including by facsimile or electronic

delivery (PDF)), and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument.

(s) Specific Performance. The parties hereto hereby declare that it is impossible to measure in money the damages which will accrue to the non-defaulting party by reason of the other party's failure to perform any of the obligations under this Warrant. If such non-defaulting party institutes any action or proceeding to specifically enforce the provisions hereof, any person against whom such action or proceeding is brought hereby waives the claim or defense therein that such non-defaulting party has an adequate remedy at law, and such person shall not offer in any such action or proceeding the claim or defense that such remedy at law exists.

(t) Lost, Stolen, Mutilated or Destroyed Warrant. If this Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as this Warrant so lost, stolen, mutilated or destroyed.

(u) Legends. To the extent required by applicable laws, this Warrant and the shares of Common Stock issuable hereunder (and the securities issuable, directly or indirectly, upon conversion of such shares of Common Stock, if any) shall bear a legend substantially in the following form:

THIS SECURITY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS, AND MAY NOT BE SOLD, PLEDGED OR OTHERWISE TRANSFERRED WITHOUT AN EFFECTIVE REGISTRATION THEREOF UNDER THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS, OR PURSUANT TO RULE 144 OR AN EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have caused this Warrant to be executed by its officer thereunto duly authorized as of the Effective Date.

COMPANY: CERULEAN PHARMA INC.

By: /s/ Christopher D.T. Guiffre
Name: Christopher D.T. Guiffre
Title: President and Chief Executive Officer

WARRANTHOLDER: AQUILO PARTNERS, L.P.

By: /s/ John Dyer
Name: John Dyer
Title: Managing Director

EXHIBIT I

NOTICE OF EXERCISE

To: __

(1) The undersigned Warrantholder hereby elects to purchase [_____] shares of the Common Stock of [__ _] pursuant to the terms of the Warrant dated the [___] day of October 2016 (the "Warrant") between Cerulean Pharma Inc. and the Warrantholder, and tenders herewith payment of the Purchase Price (as defined in the Warrant) in full, together with all applicable transfer taxes, if any.

(2) Please issue a certificate or certificates representing said shares of Common Stock in the name of the undersigned or in such other name as is specified below.

_____
(Name)

_____
(Address)

WARRANTHOLDER: _____

By: _____
Name: _____
Title: _____

EXHIBIT II TRANSFER NOTICE

(To transfer or assign the foregoing Warrant execute this form and supply required information. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby transferred and assigned to

_____
(Please Print)

whose address is _____

_____

Dated: _____

Holder's Signature: _____

Holder's Address: _____

_____

Signature Guaranteed: _____

NOTE: The signature to this Transfer Notice must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Exhibit 21.1

SUBSIDIARIES OF THE REGISTRANT

Name	**Jurisdiction of Organization**
Daré Bioscience Operations, Inc.	Delaware
Daré Bioscience Australia Pty Ltd	Australia
Pear Tree Pharmaceuticals, Inc.	Delaware
Daré MBI Inc.	Delaware

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements on Form S-3 (File Nos. 333-254862, 333-238299, and 333-206396) and Form S-8 (File Nos. 333-254864, 333-237473, 333-230802, 333-226904, 333-211697, 333-204007, and 333-198126) of our report dated March 31, 2022, with respect to our audits of the consolidated financial statements of **Daré Bioscience, Inc. and Subsidiaries (Company)** and Subsidiaries Company) as of and for each of the two years in the period ended December 31, 2021 (which includes an explanatory paragraph relating to the uncertainty of the Company's ability to continue as a going concern), which report is included in this Annual Report on Form 10-K.

/s/ Mayer Hoffman McCann P.C.

San Diego, California
March 31, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Sabrina Martucci Johnson, certify that:

1. I have reviewed this annual report on Form 10-K of Daré Bioscience, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2022

/s/ Sabrina Martucci Johnson
Sabrina Martucci Johnson
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Lisa Walters-Hoffert, certify that:

1. I have reviewed this annual report on Form 10-K of Daré Bioscience, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2022

/s/ Lisa Walters-Hoffert
Lisa Walters-Hoffert
Chief Financial Officer
(principal financial officer and principal accounting officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of Daré Bioscience, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2021 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 31, 2022

/s/ Sabrina Martucci Johnson
Sabrina Martucci Johnson
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of Daré Bioscience, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2021 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 31, 2022

/s/ Lisa Walters-Hoffert
Lisa Walters-Hoffert
Chief Financial Officer
(principal financial officer and principal accounting officer)