ATOSSA GENETICS INC
Form 10-K
March 28, 2019

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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark one)

Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended December 31, 2018

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 Number 001-35610

ATOSSA GENETICS INC.

(Exact name of registrant as specified in its charter)

Delaware	**26-4753208**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

107 Spring Street

Seattle, WA 98104

(Address of principal executive offices)

Registrant's telephone number, including area code: **(206) 325-6068**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.18 par value	The NASDAQ Capital Market

Securities registered pursuant to 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 No

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 No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act 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 No

Indicate by check mark whether the registrant has submitted electronically, if any, 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 No

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Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, 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 Smaller reporting company

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 13a of the Exchange Act.

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

As of June 30, 2018, the last business day of the registrant’s most recently completed second fiscal quarter, the aggregate market value of the voting and non-voting common equity held by non-affiliates was $4,874,099. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Company. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's common stock, par value $0.18, as of March 25, 2019 was 9,116,490.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements made in this report on Form 10-K that are not statements of historical information are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the ***"Securities Act"***) and Section 21E of the Securities Exchange Act of 1934, as amended (the ***"Exchange Act"***). We have made these statements in reliance on the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements are subject to certain risks and uncertainties, which could cause actual results to differ materially from those projected or anticipated. Although we believe our assumptions underlying our forward-looking statements are reasonable as of the date of this report we cannot assure you that the forward-looking statements set out in this report will prove to be accurate. We typically identify these forward-looking statements by the use of forward-looking words such as "expect," "potential," "continue," "may," "will," "should," "could," "would," "seek," "intend," "plan," "estimate," "anticipate" or the ne those words or other comparable words. Forward-looking statements contained in this report include, but are not limited to, statements about:

whether we can obtain approval from the U.S. Food and Drug Administration, or FDA, and foreign regulatory bodies, to commence our clinical studies and to sell, market and distribute our therapeutics and devices under development;

our ability to successfully initiate and complete clinical trials of our pharmaceutical candidates under development, including our oral and topical Endoxifen (an active metabolite of Tamoxifen) and our intraductal microcatheters to administer therapeutics, including our study using fulvestrant;

the success, cost and timing of our product and drug development activities and clinical trials, including whether the ongoing clinical study using our intraductal microcatheters to administer fulvestrant and our study using our oral Endoxifen in the window of opportunity prior to surgery will enroll a sufficient number of subjects or be completed in a timely fashion or at all;

whether we will successfully complete our clinical study of topical Endoxifen to reduce mammographic breast density and whether the study will fail to achieve its objective, including because some participants have discontinued the study prior to completing the full six months of dosing because of skin irritation issues or for other reasons;

our ability to contract with third-party suppliers, manufacturers and service providers, including clinical research organizations, and their ability to perform adequately;

our ability to successfully develop and commercialize new therapeutics currently in development or that we might identify in the future and in the time frames currently expected;

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our ability to successfully defend litigation and other similar complaints that may be brought in the future, in a timely manner and within the coverage, scope and limits of our insurance policies;

our ability to establish and maintain intellectual property rights covering our products;

our expectations regarding, and our ability to satisfy, federal, state and foreign regulatory requirements;

the accuracy of our estimates of the size and characteristics of the markets that our products and services may address;

whether the final study results will vary from preliminary study results that we may announce;

our expectations as to future financial performance, expense levels and capital sources;

our ability to attract and retain key personnel; and

our ability to raise capital.

This Annual Report also contains estimates and other statistical data provided by third parties and by us relating to market size and growth and other industry data. These and other forward-looking statements are presented as of the date on which the statements are made. We have included important factors in the cautionary statements included in this Annual Report, particularly in the section titled “ITEM 1A. RISK FACTORS,” that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any new information, future events or circumstances that may affect our business after the date of this Annual Report. Except as required by law, we do not intend to update any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events, circumstances or otherwise.

CORPORATE INFORMATION

Our corporate website is located at *www.atossagenetics.com*. Information contained on, or that can be accessed through, our website is not a part of this report. We make available, free of charge through our website or upon written request, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other periodic SEC reports, along with amendments to all of those reports, as soon as reasonably practicable after we file the reports with the SEC.

Unless otherwise noted, the term “Atossa Genetics” “Atossa,” the “Company,” “we,” “us,” and “our” refers to Atossa Genetics Inc., a Delaware corporation. We were incorporated in Delaware in April 2009. Our principal executive offices are located at 107 Spring Street, Seattle, Washington 98104, and our telephone number is 206-325-6086.

Our name and logo, Atossa, and Atossa Genetics (stylized) are our registered trademarks. This report also includes additional trademarks, trade names and service marks of third parties, which are the property of their respective owners. You are advised to read this Annual Report on Form 10-K in conjunction with other reports and documents that we file from time to time with the Securities and Exchange Commission (the “SEC”). In particular, please read our definitive proxy statement, which will be filed with the SEC in connection with our 2019 Annual Meeting of Stockholders, our Quarterly Reports on 10-Q and any Current Reports on Form 8-K, and any amendments thereto, that we may file from time to time. You may obtain copies of these reports after the date of this annual report from the SEC at the SEC’s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. In addition the SEC maintains information for electronic filers (including Atossa) at its website www.sec.gov. The public may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330.

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PART I

ITEM 1. BUSINESS

Overview

Company Overview

We are a clinical-stage biopharmaceutical company focused on developing novel, proprietary therapeutics and delivery methods for the treatment of breast cancer and other breast conditions. Our lead program is the development of Endoxifen, which is an active metabolite of tamoxifen, an FDA-approved drug to treat and prevent breast cancer. We are developing an oral and topical form of Endoxifen. Our Endoxifen is being developed to potentially treat a number of conditions, including: mammographic breast density (or, MBD); breast cancer in the "window of opportunity" between diagnosis of breast cancer and surgery; gynecomastia, which is male breast enlargement; and the recurrence of breast cancer in patients who do not benefit from taking tamoxifen meaning that they are "refractory" to tamoxifen. We are also developing our patented intraductal microcatheter technology to potentially target the delivery of therapies, including fulvestrant, immunotherapies and Chimeric Antigen Receptor T-cell therapies (CAR-T therapies), directly to the site of breast cancer.

In 2017, we completed a Phase 1 placebo-controlled clinical study of our proprietary oral and topical formulations of Endoxifen in 48 healthy women. All objectives were met: there were no clinically significant safety signals and no clinically significant adverse events, and both the oral and topical Endoxifen were well tolerated. In the topical arm of the study, low but measurable Endoxifen levels were detected in the blood in a dose-dependent fashion. In the oral arm of the study, participants exhibited dose-dependent Endoxifen levels that met or exceeded the published therapeutic level. The median time for patients in the study to reach the steady-state serum levels of Endoxifen while taking daily doses of oral Endoxifen was 7 days. Published literature indicates that it takes approximately 50-200 days for patients to reach steady-state Endoxifen levels from daily doses of oral tamoxifen. In September 2018, we completed a Phase 1 placebo-controlled clinical study of our proprietary topical Endoxifen in 24 healthy men. All of our objectives of safety, tolerability and pharmacokinetics were successfully met.

We are currently conducting two Phase 2 studies of our proprietary Endoxifen: one in Stockholm, Sweden using our topical Endoxifen for reduction of MBD and another in Australia using our oral Endoxifen for patients in the window of opportunity between diagnosis of breast cancer and surgery. In October 2018, the MBD study in Sweden was fully-enrolled with all 90 participants: 60 participants on two different dose levels and 30 participants on placebo. We expect dosing in this study to be completed in April 2019 and to report preliminary results in the second quarter 2019.

In December 2018, we began providing our oral Endoxifen to a pre-menopausal, estrogen-receptor positive (ER+), lacking CYP2D6 function, breast cancer patient under an FDA-approved "expanded access" program. The purpose of this therapeutic approach was to reduce activity of the cancer cells prior to surgery. The patient received daily doses of our oral Endoxifen for approximately three weeks prior to surgery. There were no safety or tolerability issues and her surgery was successfully completed. The cancer cell biological activity was reduced, based on the estrogen receptor activity of the tumor cells and a 50% reduction in Ki-67. The FDA has also issued a "safe to proceed" letter allowing the patient to continue oral Endoxifen therapy post-surgery. Under the FDA expanded access IND program, the use of our proprietary oral Endoxifen is restricted solely to this patient.

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We are currently conducting a Phase 2 study at Montefiore Medical Center, Bronx, New York, using our intraductal microcatheter technology to deliver fulvestrant directly to the site of the tumor via the breast ducts. Our program to use our intraductal microcatheters to deliver CAR-T and other immunotherapies is in the pre-clinical phase.

Our key objectives are to advance our programs through Phase 2 trials and then evaluate further development independently or with partners.

Our common stock is currently quoted on The NASDAQ Capital Market under the symbol “ATOS.”

Our Programs Under Development

Endoxifen

Background

Oral tamoxifen has been widely used for over 40 years to both treat and prevent breast cancer. It is a “pro-drug”, in that it must be metabolized into active components (“metabolites”) in order to be effective. One of these active metabolites is endoxifen. Despite the success of tamoxifen in reducing the risk of estrogen-receptor-positive breast cancer, its systemic side effects have led to generally low acceptance. These systemic side effects relate to estrogen agonist activity on the endometrium and the activation of coagulation pathways, leading to an increased risk of uterine events and thromboembolism. Hot flashes and vaginal symptoms are additional barriers to acceptance.

Up to 50% of breast cancer survivors who are taking tamoxifen do not produce therapeutic endoxifen levels (meaning they are “refractory”) for a number of reasons including that they, due to their genotype, do not have the requisite liver enzymes. Additionally, it can take from 50-200 days for tamoxifen to reach “steady-state” meaning that the drug may be providing little or no benefit for up to several months after starting treatment. By providing endoxifen directly to the body, a steady-state is achieved within ~7 days.

Phase 1 Studies

In 2017 we completed a comprehensive Phase 1 study in 48 healthy women in Australia using both the topical and oral forms of our proprietary Endoxifen. The objectives of this double-blinded, placebo-controlled, Phase 1 study were to assess the pharmacokinetics of our proprietary Endoxifen dosage forms as single (oral) and repeat (oral and topical) doses, as well as to assess safety and tolerability. The study was conducted in two parts based on route of administration.

All objectives were successfully met in both arms of the study: there were no clinically significant safety signals and no clinically significant adverse events and both the oral and topical Endoxifen were well tolerated. In the topical arm of the study, there were low but detectable Endoxifen levels in the blood in a dose-dependent fashion and in the oral arm of the study participants exhibited dose-dependent Endoxifen levels consistent with published reports of the therapeutic range. The median time for patients in the study to reach the steady-state serum levels of Endoxifen while taking daily doses of oral Endoxifen was ~7 days. Published literature indicates that it takes approximately 50-200 days for patients to reach steady-state Endoxifen levels when taking daily doses of oral tamoxifen. Finally, the median time for patients in the study to reach the maximum serum level of Endoxifen after taking Atossa's oral Endoxifen ranged from 4 to 8 hours (depending on dose). The 4 mg dose of Endoxifen produced a maximum serum level of Endoxifen in 4 to 8 hours at levels above the generally accepted threshold for a therapeutic effect on estrogen-dependent breast cancer.

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Potential Treatment of MBD

Legislation that has been recently enacted in approximately 35 states requiring that women be notified if they have MBD and those notifications typically state that women with MBD have a higher risk of developing breast cancer, and that mammography may not be as effective in detecting breast cancer because the MBD can “mask” the detection of cancers. In February 2019, Federal legislation was enacted that requires that the FDA adopt rules requiring that mammography reports include information about breast density and inform women about their breast density.

We estimate that approximately ten million women in the Unites States have MBD, for which there is no FDA-approved treatment. Although oral tamoxifen is approved to prevent breast cancer in “high-risk” women (usually described as having been diagnosed with estrogen receptor positive breast cancer), it is used by less than 5% of women with an increased risk of developing breast cancer because of the actual or perceived side effects and risks of tamoxifen. We believe our Endoxifen may provide an option for women to proactively reduce the density of their breasts. Moreover, our Endoxifen may improve mammography accuracy and patient care by unmasking cancerous tumors that are otherwise hidden by breast density. In two separate reports of film-screen mammography, mammographic sensitivity decreased from a level of 85.7%–88.8% in patients with almost entirely fatty tissue to 62.2%–68.1% in patients with extremely dense breast tissue.

In September 2017, we contracted Stockholm South General Hospital in Sweden to conduct a Phase 2 study of our topical Endoxifen in women with high MBD. The study is being led by principal investigator Dr. Per Hall, MD, Ph.D., Head of the Department of Medical Epidemiology and Biostatistics at Karolinska Institutet. The primary endpoint of this pilot study is to determine if topical Endoxifen results in an individual reduction of MBD as measured by mammography. Secondary endpoints include demonstrating safety and tolerability. The primary objective is to determine the effect size of breast density between placebo and topical Endoxifen to permit sample size calculations for statistical significance in a future Phase 3 trial. The study was fully enrolled in October 2018 with 90 participants who were equally randomized to three different groups (30 per group): placebo; lower dose topical Endoxifen; and higher dose topical Endoxifen. Participants receive the active drug or placebo for a maximum of six months. The study calls for each participant to have a baseline (pre-treatment) mammogram, and additional mammograms at month 3 and 6, or at the time of study exit. Once the study has been completed, all mammograms will be interpreted and MBD determined and any changes that occur per patient recorded. Some participants have chosen to exit the study before receiving a full six months of drug or placebo for a number of reasons: for example, some exit for non-compliance with the study protocol and some have exited because of skin rashes and irritation. As of the date of this annual report, approximately 72 participants have exited the study primarily because of skin rashes and irritation. Because the study is double blinded and results-to-date are not known, we do not know how or if the fact that some study participants exited the study before six months of dosing will result in sufficient data to achieve the primary objective which is to design a subsequent study. We expect that all dosing in the study will be completed in April 2019 with preliminary result to be reported in the second quarter of 2019.

Refractory Patients

We are developing oral Endoxifen for breast cancer patients who are refractory to tamoxifen, meaning for whatever reason, tamoxifen is not effectively metabolized into active metabolites. Approximately one million breast cancer patients take tamoxifen to prevent recurrent and new breast cancer; however, up to 50% of those patients are refractory to tamoxifen. We believe our oral Endoxifen may provide an effective treatment supplement or option for these refractory patients because Endoxifen, unlike tamoxifen, does not require liver metabolism.

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In December 2018, we began providing our oral Endoxifen to a pre-menopausal, estrogen-receptor positive (ER+) breast cancer patient under an FDA-approved "expanded access" program. The purpose of this therapeutic approach was to reduce activity of the cancer cells prior to surgery. The patient received daily doses of our oral Endoxifen for approximately three weeks prior to surgery. There were no safety or tolerability issues and her surgery was completed successfully. To determine if the oral Endoxifen reduced the biological activity of the cancer cells, the test results obtained from the initial biopsy were compared with those from the specimen obtained during surgery. There were no safety or tolerability issues and her surgery was successfully completed. The cancer cell biological activity was reduced, based on the estrogen receptor activity of the tumor cells and a 50% reduction in Ki-67. Under the FDA expanded access IND program, the use of our proprietary oral Endoxifen is restricted solely to this patient.

Window of Opportunity

We are also currently conducting a Phase 2 study of our oral Endoxifen in Australia in the window of opportunity between diagnosis of breast cancer and surgery. The Pilot Phase of the study will initially enroll up to eight newly-diagnosed patients with ER+ and HER2 negative (HER2-) stage 1 or 2 invasive breast cancer, requiring mastectomy or lumpectomy. Patients will receive our proprietary oral Endoxifen for at least 21 days from the time of diagnosis up to the day of surgery. Provided tumor activity reduction is demonstrated in at least two patients, an additional 17 patients will be enrolled for a total of 25. The primary endpoint is to determine if the administration of oral Endoxifen reduces the tumor activity as measured by Ki-67 (a measure of cellular proliferation that correlates with tumor growth). The secondary endpoints are safety and tolerability and assessment of the study drug on expression levels of both estrogen and progesterone receptors. The impact on additional markers of cellular activity will also be explored. The Phase 2 study is being conducted on behalf of Atossa by Avance Clinical (formerly CPR Pharma Services Pty Ltd.), Thebarton, SA, Australia. Avance Clinical recently completed the successful Phase 1 study of our oral and topical Endoxifen.

Proprietary Intraductal Delivery Technology

We believe intraductal delivery technology may be useful in delivering CAR-T, immunotherapies and a number of drugs to the ducts in the breast, the site of the majority of early breast cancers. Doing so is intended to provide a therapeutic directly to the breast tissue while at the same time reducing delivery of the drug to healthy tissue. We must obtain FDA approval of any therapy delivered via intraductal delivery technology, which will require expensive and time-consuming studies in the current regulatory framework. For example, we must complete clinical studies to demonstrate the safety and tolerability of fulvestrant using our delivery method. We may not be successful in completing these studies or obtaining approval from the FDA or other applicable foreign regulatory authority.

Breast cancers and precancerous lesions are typically treated with systemically administered agents such as tamoxifen, Faslodex®, Perjeta® and Herceptin®. However, these therapies can cause serious side effects which may lead to poor patient compliance with the treatment regimens. Providing therapies directly into the breast ducts targeting the site of

the localized cancerous lesions could reduce the need for systemic anti-cancer therapies, and potentially reduce or eliminate the systemic side effects of the therapies and morbidity in such patients, and ultimately improve patient compliance and ultimately reduce mortality.

Transpapillary CAR-T

Much of the recent success in the field of chimeric antigen receptor therapy, or CAR-T, has relied on the systemic delivery (for example a needle injection into the blood stream) of the CAR-T which is intended to treat various non-solid tumor cancers, such as blood cancers. One concern with this systemic approach is that it does not target the location of the cancer and it can have adverse effects, including deadly “cytokine storms.” Moreover, CAR-T treatments delivered systemically can be as high as $500,000 per patient.

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We are developing a novel method to deliver CAR-T cells into the ducts of the breast for the potential targeted treatment of breast cancer. This approach uses our proprietary intraductal delivery technology for the potential transpapillary, or “TRAP,” delivery of either T-cells that have been genetically modified to attack breast cancer cells or various immune-therapies. We believe this method has several potential advantages including the reduction of toxicity by limiting systemic exposure of the T-cells or immunotherapy; improved efficacy by placing the T-cells or immunotherapy in direct contact with the target ductal epithelial cells that are undergoing malignant transformation; and, lymphatic migration of the CAR-T cells or immunotherapy potentially extending their cytotoxic actions into the regional lymph system, which could limit tumor cell dissemination. Moreover, our proprietary approach may be more cost effective if lower doses of therapy can be delivered compared to systemic CAR-T. Our approach is in the R&D stage and is currently not FDA approved. We intend to commence studies that will help demonstrate safety and efficacy of this novel approach.

The TRAP delivery of pharmaceutical therapeutics in breast cancer clinical trials have demonstrated “that cytotoxic drugs can be safely administered into breast ducts with minimal toxicity” (Zhang B, et al. Chin J Cancer Res. 2014 Oct;26(5):579-87; www.ncbi.nlm.nih.gov/pubmed/25400424). In our program, we plan to remove T cells from a patient and modify them so that they express receptors specific to the patient's particular breast cancer. The T cells, which can then recognize and kill the cancer cells, are then intended to be reintroduced into the patient via natural ducts of the breast using our intraductal delivery technology. Chimeric antigen receptors (or, “CARs” and also known as chimeric immunoreceptors, chimeric T cell receptors, artificial T cell receptors or CAR-T) are engineered receptors, which graft an arbitrary specificity onto an immune effector cell (“T cell”). Typically, these receptors are used to graft the specificity of a monoclonal antibody onto a T cell, with transfer of their coding sequence facilitated by retroviral vectors. The receptors are called chimeric because they are composed of parts from different sources.

We have filed a foundational patent application with respect to the intraductal delivery of CAR-T, and we intend to continue research and development through partnership with leading investigators, institutions, and organizations around the world, bringing our technology and expertise in TRAP delivery together with experts in cancer immunology and T-cell biology.

Delivery of Drugs via our Microcatheters

The initial drug we are studying using our microcatheters for intraductal delivery is fulvestrant. Fulvestrant is FDA-approved for metastatic breast cancer. It is administered as a monthly injection of two shots, typically into the buttocks, and costs ~$11,000 per dose.

We own several pending patent applications directed to the treatment of breast conditions, including cancer, by the intraductal administration of therapeutics including fulvestrant, and expect to file additional patent applications as and when applicable.

We are currently conducting a Phase 2 study using our intraductal delivery technology using microcatheters to deliver fulvestrant at Montefiore Medical Center in the window of opportunity. This trial is a Phase 2 study in women with ductal carcinoma in situ (“DCIS”) or Stage 1 or 2 breast cancer (invasive ductal carcinoma) scheduled for mastectomy or lumpectomy within 30 to 45 days. This study is assessing the safety, tolerability, cellular activity and distribution of fulvestrant when delivered directly into breast milk ducts of these patients compared to those who receive the same drug by injection. Of the 30 patients required for full enrollment, six will receive the standard intramuscular injection of fulvestrant and 24 will receive fulvestrant with our microcatheter device.

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The primary endpoint of the clinical trial is to compare the safety, tolerability and distribution of fulvestrant between the two routes of administration (intramuscular injection or through our microcatheters). The secondary endpoint of the study is to determine if there are changes in the expression of Ki-67 as well as estrogen and progesterone receptors between a pre-fulvestrant biopsy and post-fulvestrant surgical specimens. Digital breast imaging before and after drug administration in both groups will also be performed to determine the effect of fulvestrant on any lesions as well as breast density of the participant.

Other Studies of Intraductal Administration using our Microcatheters

An October 2011 peer-reviewed paper published in *Science Translational Medicine* reported the results of a study conducted at the Johns Hopkins Medical School demonstrating the prevention of breast cancer in rats with intraductal non-systemic chemotherapy, and a proof-of-principle Phase 1 clinical trial involving 17 women with breast cancer who subsequently received surgery. An accompanying editorial commented that “intraductal treatment could be especially useful for women with premalignant lesions or those at high risk of developing breast cancer, thus drastically improving upon their other, less attractive options of breast-removal surgery or surveillance (termed ‘watch and wait’).”

In a December 2012 peer-reviewed paper published in *Cancer Prevention Research,* Dr. Susan Love and her colleagues reported the results of a Phase I clinical trial of intraductal chemotherapy drugs administered into multiple ducts within one breast in women awaiting mastectomy for treatment of invasive cancer. Thirty subjects were enrolled in this dose escalation study conducted at a single center in Beijing, China. Under local anesthetic, one of two chemotherapy drugs, carboplatin or pegylated liposomal doxorubicin (PLD), was administered into five to eight ducts at three dose levels. Pharmacokinetic analysis has shown that carboplatin was rapidly absorbed into the bloodstream, whereas PLD, though more erratic, was absorbed after a delay. Pathologic analysis showed marked effects on breast duct epithelium in ducts treated with either drug compared with untreated ducts. The investigators concluded the study showed the safety and feasibility of intraductal administration of chemotherapy drugs into multiple ducts for the purpose of breast cancer prevention and that this was an important step towards implementing of this strategy as a "chemical mastectomy," potentially eliminating the need for surgery.

Markets

Potential Market Opportunities

We believe that, based in part on a January 2017 study by Defined Health Inc., a leading market research firm, the potential U.S. market for intraductal administration of fulvestrant or similar drugs in DCIS patients is up to $800 million annually. This estimate includes treatment of DCIS patients prior to surgery as well as patients who would use

intraductal treatment as an alternative to surgery. We believe that the potential U.S. market for our Endoxifen in the treatment and prevention settings is up to $1 billion annually.

The Breast Cancer and Related Markets

The American Cancer Society ("ACS") estimates that in 2019, 269,000 women will be diagnosed with breast cancer in the United States. Every two minutes an American woman is diagnosed with breast cancer and 42,000 die each year. Although about 100 times less common than in women, breast cancer also affects men. The ACS estimates that the lifetime risk of men getting breast cancer is about 1 in 1,000; 2,670 new cases of invasive breast cancer will be diagnosed in 2019; and 500 men will die from breast cancer in 2019.

We were incorporated in April of 2009 and our common stock is currently quoted on The NASDAQ Capital Market under the symbol "ATOS."

Our Medical Devices

The use of our intraductal delivery technology is being developed for the targeted delivery of potential drugs, CAR-T and immunotherapies, as described above.

Our medical devices also include the ForeCYTE Breast Aspirator and the FullCYTE Breast Aspirator, which collect specimens of nipple aspirate fluid (NAF) for cytological testing at a laboratory, and a universal transport kit to assist with the packaging and transport of NAF samples to a laboratory. We also own the exclusive rights to manufacture and sell various medical devices consisting primarily of tools to assist breast surgeons, which we acquired from Acueity Healthcare in 2012. We are not currently commercializing our breast aspirator devices, transportation kits, tools for breast surgeons and NAF cytology tests nor do we maintain an inventory of our medical devices.

Additionally, we, as a pharmaceutical company, are not maintaining the device patents directed to any of our medical devices due to the short patent term remaining on them.

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Our Capital Resources

We have not yet established an ongoing source of revenue sufficient to cover our operating costs and allow us to continue as a going concern. Our ability to continue as a going concern is dependent on obtaining adequate capital to fund operating losses until we become profitable. We plan to obtain additional capital resources by selling our equity securities and borrowing from stockholders or others when needed. However, we cannot assure you that we will be successful in accomplishing any of these plans and, if we are unable to obtain adequate capital, we could be forced to cease operations. We do not anticipate any revenue until our pharmaceutical programs are developed, including receiving all necessary regulatory approvals, and until we successfully commercialize these programs.

As of December 31, 2018, we had cash and cash equivalents of $10,380,493 and in March 2019 we received approximately $11.3 million from the exercise of warrants that were issued on May 30, 2018. Our capital raising activity in 2017 and 2018 consisted of the following (all share and per-share amounts in this report have been adjusted to reflect the 1:12 reverse stock split we effectuated on April 20, 2018):

2017 Financing Activities

On March 28, 2017, the Company entered into an underwriting agreement with Aegis Capital Corp. relating to a public offering which closed on April 3, 2017. The offering generated gross proceeds to the Company of approximately $4.4 million and net proceeds of approximately $3.9 million after deducting underwriting discounts and commissions and other offering expenses paid by the Company.

On October 26, 2017, the Company entered into an underwriting agreement with Maxim Group LLC relating to a public offering of common stock which closed on October 30, 2017. The offering generated gross proceeds to the Company of approximately $5.5 million and net proceeds of $4.9 million after deducting underwriting discounts, commissions and other offering expenses paid by the Company.

On December 20, 2017, the Company entered into a placement agent agreement with Maxim Group LLC relating to the sale of the Company’s securities. Pursuant to the placement agent agreement, on December 20, 2017, the Company entered into a securities purchase agreement with certain purchasers named therein relating to the offering and sale of 441,667 shares of Company common stock at a public offering price of $3.24 per share. The offering generated gross proceeds to the Company of approximately $1.4 million and net proceeds of $1.2 million after deduction of underwriting discounts, commissions, and other offering expenses paid by the Company.

2018 Financing Activities

On May 30, 2018, we completed a rights offering pursuant to which we sold an aggregate of 13,624 units consisting of an aggregate of 13,624 shares of Series B convertible preferred stock, convertible into 3,869,216 shares of common stock, and 3,869,216 warrants, with each warrant exercisable for one share of common stock at an exercise price of $4.048 per share, resulting in net proceeds to us of approximately $12.3 million, after deducting expenses relating to the rights offering, including dealer-manager fees and expenses, and excluding any proceeds received upon exercise of any warrants.

Research and Development Phase

All of our programs are in the pre-clinical or clinical research and development phase. Research and development costs are generally expensed as incurred. Our research and development expenses include, for example, manufacturing expenses for our drugs under development, expenses associated with clinical studies and associated salaries and benefits. Research and development expenses for the years ended December 31, 2018 and 2017 were $4,209,981 and $2,328,087, respectively.

Intellectual Property

Our owned and licensed patents and patent applications are directed to Endoxifen and Fulvestrant, and immunotherapies such as CAR-T therapy. We commonly seek patent claims directed to compositions of matter, including Endoxifen, Fulvestrant, and other Selective Estrogen Receptor Modulators (SERMs), Selective Estrogen Receptor Downregulators (SERDs), and Aromatase Inhibitors (AI), as well as methods of using such compositions. When appropriate, we also seek claims to related technologies, such as treatment methods via transpappillary and intraductal delivery of therapeutics to breast ducts of an individual. For each of our products, we filed and expect to file multiple patent applications . As of February 28, 2019, and based on a recent periodic review of our patent estate, we own 13 issued patents (11 US and 2 international) and 29 pending patent applications (5 in the United States, and 24 international applications) directed to our programs on Endoxifen, Fulvestrant, CAR-T therapeutics and intraductal delivery of therapeutics using devices such as microcatheters. This list above does not identify all patents and patent applications currently in Atossa's patent portfolio. For example, the foregoing patent counts exclude certain applications and device patents with short patent terms remaining on them and those covering our ForeCyte, FullCyte and Acueity devices and various tests that are no longer core to our business. We continue to evaluate our patent portfolio and, as a clinical-stage pharmaceutical company, will no longer maintain our device and test patents and applications.

Of the 29 pending patent applications in Atossa's patent portfolio, 3 of the 5 United States pending applications and 16 of the 24 pending international applications include at least one claim directed to Endoxifen; 4 of the 5 United States pending applications and 16 of the 24 pending international applicatons include at least one claim directed to Fulvestrant; and 1 of the 5 United States pending application and 2 of the 24 international pending applications are directed to our intraductal program delivering CAR-T therapeutics and other immunotherapy.

The following table provides the patent counts[4] related to our programs.

	Pending Applications[1, 2]		Approximate Expiry Date[3]
	U.S.	International	
Endoxifen Program	3	16	2034 - 2037
Fulvestrant Program	4	16	2034 - 2037
Immunotherapy/ CAR-T Program	1	2	2037 - 2038

[1] Each patent application includes at least one claim directed to a listed therapeutic/program.

[2] The patent counts in the table above are greater than the total numbers of the patent applications in the Atossa portfolio as the patent counts in the table above reflect that a patent application may have claims directed to more than one type of therapeutic/program.

[3] The patent counts and the approximate expiry dates disclosed herein and in our patent estate are subject to change, for example, in the event of changes in the law or legal rulings affecting our patents and applications or if we become aware of new information. The standards that the U.S. Patent and Trademark Office, or USPTO, and foreign patent offices use to grant patents are not always applied predictably or uniformly and can change. Consequently, our pending patent applications may not be allowed and, if allowed, may not contain the type and extent of patent claims that will be adequate to conduct our business as planned. Additionally, any issued patents we currently own or obtain in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our products.

[4]The standards that the U.S. Patent and Trademark Office, or USPTO, and foreign patent offices use to grant patents are not always applied predictably or uniformly and can change. Consequently, our pending patent applications may not be allowed and, if allowed, may not contain the type and extent of patent claims that will be adequate to conduct our business as planned. Additionally, any issued patents we currently own or obtain in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our product .

Atossa and Atossa Genetics (stylized) are our registered trademarks.

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Manufacturing, Clinical Studies and Associated Operations

Our drug development strategy utilizes third party contractors for the procurement and manufacture, as applicable, of raw materials, active pharmaceutical ingredients and finished drug products, as well as for storage, and distribution of our products and associated supply chain operations. We also plan to rely on third parties to conduct pre-clinical and clinical studies of our drugs and microcatheter technology under development. As our development programs advance, we expect that our manufacturing, pre-clinical and clinical studies, and related operational requirements will correspondingly increase. Each third-party contractor undergoes a qualification process by Atossa subject matter experts prior to signing any service agreement and initiating any third-party work.