Atossa Therapeutics Issues Letter to Shareholders

January 9, 2024 1:30 PM EST

SEATTLE, Jan. 09, 2024 (GLOBE NEWSWIRE) -- Atossa Therapeutics, Inc. (Nasdaq: ATOS), a clinical stage biopharmaceutical company developing innovative medicines in areas of significant unmet medical need in oncology with a focus on breast cancer, today announces the issuance of the following Letter to Shareholders from Steven Quay, M.D., Ph.D., the Company's President and Chief Executive Officer:

To our valued shareholders:

2023 marked another year of significant progress for Atossa. There are now four Phase 2 trials underway investigating our proprietary (Z)-endoxifen, with primary data expected from two of these trials in the second half of this year. We also initiated important research with Weill Cornell Medicine that could fundamentally transform treatment options for patients diagnosed with one of the most aggressive and deadly forms of breast cancer.

Our study that is furthest along is the Phase 2 Karisma-Endoxifen trial, which reached full enrollment in November 2023. In this study, we are looking at the effect (Z)-endoxifen has in premenopausal women with measurable breast density. Participants in the study are randomized into one of three cohorts to receive placebo, 1mg or 2mg of (Z)-endoxifen daily for six months. Mammograms are conducted to measure reduction in breast density over the treatment period and a final mammogram will be conducted at 24 months to assess the durability of density changes. If you would like to learn more about the study, please visit www.atossatherapeutics.com to view a short video interview I conducted with Dr. Per Hall, the Karsima-Endoxifen study primary investigator.

Simply put, breast density is a health crisis. Almost half of the women in the world over the age of 40 have dense breasts and this condition not only makes mammograms far less effective, but it also significantly increases the likelihood that a woman will develop breast cancer in their lifetime. Adding to the issue is the fact that there are currently no approved treatments to reduce breast density.

Breast density and the associated risk factors are not well understood by most women, although that will begin to change in the United States on September 10 of this year when a federal law requiring mammography facilities to notify patients about the density of their breasts goes into effect. The notification for patients with dense breasts will include a warning that dense tissue makes it harder to find breast cancer on a mammogram and raises their risk of developing breast cancer.

The notification will also encourage women with dense breast tissue to discuss the findings with their healthcare provider, which means the number of conversations medical professionals will be having with patients about breast density will increase exponentially starting this fall. It's our hope that one day, these conversations will include a discussion about (Z)-endoxifen and its ability to safely reduce both breast density and the increased risk that women with dense breasts have of developing breast cancer. We look forward to seeing data from the Karisma-Endoxifen study in the second half of this year and using it to further our discussions with regulatory authorities and our plans for a Phase 3 registrational study.

Late last year we announced a second breast cancer prevention study, which is investigating (Z)-endoxifen in women diagnosed with Ductal Carcinoma In Situ (DCIS). Participants receive six months of treatment with the intent of determining their suitability for long-term active surveillance without surgery. This study is led by Quantum Leap Healthcare Collaborative, which was established in 2005 by medical researchers at University of California, San Francisco and Silicon Valley entrepreneurs to speed the development of innovative breast cancer therapies like (Z)-endoxifen.

DCIS is the presence of abnormal cells inside a milk duct in the breast. It's considered the earliest form of breast cancer and is noninvasive, meaning it hasn't spread beyond the milk duct. DCIS is usually found during a mammogram done as part of breast cancer screening or to investigate a breast lump. There are approximately 63,000 DCIS diagnoses made each year in the United States alone.

Although the exact percentage is not known, it's estimated about 20-50% of DCIS cases progress to invasive breast cancer if left untreated. This presents a major clinical dilemma because with no way to predict which lesions are destined to progress, aggressive local therapy, identical to the way invasive breast cancer is treated, is the current standard of care. For most patients, this involves mastectomy or lumpectomy, radiation, and hormone therapy for five years.

The key to reducing overtreatment is to identify biomarkers that reflect the risk of progression, which is a key element of this study. DCIS patients with a lower risk of progression would be strong candidates for neoadjuvant endocrine therapy. This could potentially spare a significant percentage of patients diagnosed with DCIS from undergoing aggressive, invasive, unnecessary treatment.

In the continuum of invasive breast cancer, our mammographic breast density and DCIS trials are prevention studies. We also have two ongoing Phase 2 trials investigating (Z)-endoxifen in the neoadjuvant treatment setting, which is the window of time between the diagnosis and the primary treatment. The intent of neoadjuvant therapy is to slow the growth of the cancer or even shrink the cancer prior to surgery. Doing this makes surgery more effective and could alter the surgical approach; meaning some breast cancer patients could have a lumpectomy instead of a mastectomy. Neoadjuvant therapy has also been shown to reduce the likelihood that the cancer returns.

Both of our neoadjuvant trials are enrolling patients with newly diagnosed estrogen receptor-positive (ER+) invasive breast cancer. The smaller study will enroll 20 patients and is another partnership with Quantum Leap through their I-Spy network, which is the largest and most successful platform trial in the world. Patients in the (Z)-endoxifen arm are treated with 10mg daily for up to 24 weeks prior to surgery. The (Z)-endoxifen treatment cohort is expected to fully enroll the first quarter of 2024, which means we should see data the second half of this year.

Our EVANGELINE (Endoxifen Versus exemestANe GosEreLIn) study is much larger with an enrollment target of 175 patients. Another important distinction is that patients in the EVANGELINE study are being treated with a higher daily dose of (Z)-endoxifen. As we communicated last year, the

study commenced with a 40mg pharmacokinetic (PK) run-in cohort. While the 40mg/day dose was well tolerated and showed encouraging efficacy, it did not achieve plasma concentrations to optimally target protein kinase C beta (PKC-β) inhibition. We have since opened an 80mg PK cohort, which we strongly believe will deliver the desired steady-state plasma concentrations and further enhance (Z)-endoxifen's antitumor mechanism of action.

We know that (Z)-endoxifen binds to estrogen receptors in breast cells and stops the body's own natural estrogen from attaching to them. We also know that (Z)-endoxifen has estrogen receptor degrader characteristics, meaning it can both block and destroy the receptor. This cuts off the cancer's fuel source and prevents it from growing and spreading, which alone is incredibly powerful, but the significance of additionally targeting PKC-β cannot be overstated.

The opportunity here is to induce apoptosis, which is programmed cell death where the malignant cells are in a way, committing suicide. It's the cellular equivalent of a self-destruct button and where we expect to see a reduction in the size of the tumor and potentially pathologic complete response (pCR), which is defined as the absence of residual invasive cancer upon evaluation of the resected breast tissue and regional lymph nodes. Multiple neoadjuvant studies in breast cancer have shown that pCR is associated with a reduction in disease recurrence and improved overall survival, two endpoints that the FDA highly values when reviewing regulatory submissions for oncology indications.

Endoxifen's ability to induce apoptosis was explored in detail in a recent paper published in *npj Breast Cancer,* which is a Nature Portfolio journal published by Springer Nature in partnership with Breast Cancer Research Foundation (BCRF). The paper, titled "Endoxifen downregulates AKT phosphorylation through protein kinase C beta 1 inhibition in ERα+ breast cancer," can be found here - https://www.nature.com/articles/s41523-023-00606-2.

One of the authors is Dr. Matthew Goetz who is deputy director of translational research for the Mayo Clinic Comprehensive Cancer Center and co-leader of the Mayo Clinic Women's Cancer Program. Dr. Goetz is also the primary investigator of our EVANGELINE study and has more experience with endoxifen, in the lab and treating patients, than anyone in the world.

Beyond the progress made in our four ongoing Phase 2 studies this year, we also initiated important research with Weill Cornell Medicine to study the potential of inducing estrogen receptor expression in triple-negative breast cancer (TNBC). TNBC accounts for about 10-15% of all breast cancers and it differs from other types of invasive breast cancer in that it tends to grow and spread faster, has fewer treatment options, has a higher risk of recurrence, and tends to have a worse prognosis.

The goal of the research we are doing with Weill Cornell is to determine if treating TNBC with extracellular vesicles carrying the estrogen receptor will change the cancer phenotype and turn on the estrogen receptor. Converting the tumor to ER+ would make it sensitive to hormone therapy, including treatment with (Z)-endoxifen. This would fundamentally transform the treatment approach and outlook for these patients.

As important as 2023 was for our Company, 2024 promises to be an opportunity for unparalleled progress. Fortunately, we are well positioned to take advantage of the opportunities that lie ahead. We have an extremely talented team in place and a growing network of investigators and partners who share our belief that (Z)-endoxifen has the potential to play an important role in both the prevention and treatment of breast cancer. We also have a strong balance sheet with no debt and cash, cash equivalents and restricted cash of $94 million as of September 30, 2023.

As we consider our cash position, we remain intently focused on deploying capital to drive long-term value for stockholders, which is why in June of last year we announced a share repurchase program with authorization to purchase up to $10 million of our common stock through December 31, 2023. Through that program, we purchased 1.32 million shares of our stock at a cost of $1.475 million in 2023.

As we continue to believe that our current share price and the long-term prospects of our business present an attractive and strategic buying opportunity, the Atossa Board of Directors recently extended the share repurchase program authorization through December 31, 2024. The authorization continues to be for the purchase up to $10 million of our common stock, inclusive of purchases made in 2023.

On behalf of the board of directors, management, and employees of Atossa Therapeutics, we thank you for your investment and continued support of our Company.

Sincerely,

Steven C. Quay, MD, Ph.D.
President and Chief Executive Officer

About (Z)-Endoxifen
(Z)-endoxifen is the most active metabolite of the FDA approved Selective Estrogen Receptor Modulator (SERM), tamoxifen. Studies by others have demonstrated that the therapeutic effects of tamoxifen are driven in a concentration-dependent manner by (Z)-endoxifen. In addition to its potent anti-estrogen effects, (Z)-endoxifen at higher concentrations has been shown to target PKCβ1, a known oncogenic protein.

Atossa is developing a proprietary oral formulation of (Z)-endoxifen that does not require liver metabolism to achieve therapeutic concentrations and is encapsulated to bypass the stomach as acidic conditions in the stomach convert a greater proportion of (Z)-endoxifen to the inactive (E)-endoxifen. Atossa's (Z)-endoxifen has been shown to be well tolerated in Phase 1 studies and in a small Phase 2 study of women with breast cancer. (Z)-endoxifen is currently being studied in four Phase 2 trials: one in healthy women with measurable breast density, one in women diagnosed with ductal carcinoma in situ, and two other studies including the EVANGELINE study in women with ER+/HER2- breast cancer. Atossa's (Z)-endoxifen is protected by three issued U.S. patents and numerous pending patent applications.

About Atossa Therapeutics
Atossa Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing innovative medicines in areas of significant unmet medical need in oncology with a focus on breast cancer. For more information, please visit www.atossatherapeutics.com

Contact
Eric Van Zanten
VP, Investor and Public Relations
610-529-6219
eric.vanzanten@atossainc.com

FORWARD LOOKING STATEMENTS

This press release contains certain information that may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We may identify these forward-looking statements by the use of words such as “expect,” “potential,” “continue,” “may,” “will,” “should,” “could,” “would,” “seek,” “intend,” “plan,” “estimate,” “anticipate,” “believe,” “future,” or other comparable words. Forward-looking statements in this press release are subject to risks and uncertainties that may cause actual results, outcomes, or the timing of actual results or outcomes, to differ materially from those projected or anticipated, including risks and uncertainties associated with: macroeconomic conditions and increasing geopolitical instability; the expected timing of releasing data; any variation between interim and final clinical results; actions and inactions by the FDA and foreign regulatory bodies; the outcome or timing of regulatory approvals needed by Atossa, including those needed to continue our planned (Z)-endoxifen trials; our ability to satisfy regulatory requirements; our ability to regain compliance with the continued listing requirements of the Nasdaq Stock Market; our ability to successfully develop and commercialize new therapeutics; the success, costs and timing of our development activities, including our ability to successfully initiate or complete our clinical trials, including our (Z)-endoxifen trials; our anticipated rate of patient enrollment; our ability to contract with third-parties and their ability to perform adequately; our estimates on the size and characteristics of our potential markets; our ability to successfully defend litigation and other similar complaints and to establish and maintain intellectual property rights covering our products; whether we can successfully complete our clinical trial of oral (Z)-endoxifen in women with mammographic breast density and our trials of (Z)-endoxifen in women with breast cancer, and whether the studies will meet their objectives; our expectations as to future financial performance, expense levels and capital sources, including our ability to raise capital; our ability to attract and retain key personnel; our anticipated working capital needs and expectations around the sufficiency of our cash reserves; and other risks and uncertainties detailed from time to time in Atossa’s filings with the Securities and Exchange Commission, including without limitation its Annual Reports on Form 10-K and Quarterly Reports on 10-Q. Forward-looking statements are presented as of the date of this press release. Except as required by law, we do not intend to update any forward-looking statements, whether as a result of new information, future events or circumstances or otherwise.