Atossa Doses First Patient in Phase 2 Neoadjuvant Clinical Study of (Z)-Endoxifen in Premenopausal Women with ER+/HER2- Breast Cancer

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SEATTLE, Feb. 23, 2023 (GLOBE NEWSWIRE) -- Atossa Therapeutics, Inc. (Nasdaq: ATOS), a clinical stage biopharmaceutical company developing innovative proprietary medicines to address significant unmet need in cancer, today announces that the first patient has been dosed in the Phase 2 EVANGELINE (Endoxifen Versus exemestANe GosEreLIn) study. EVANGELINE is a randomized non-inferiority trial of Atossa's patented Selective Estrogen Receptor Modulator (SERM), (Z)-endoxifen, and exemestane plus goserelin as a neoadjuvant treatment for pre-menopausal women with Grade 1 or 2 Estrogen Receptor positive (ER+) / Human Epidermal Growth Factor Receptor 2 negative (HER2-) breast cancer. Participants will receive neoadjuvant treatment for up to six months, followed by surgery. The study is expected to enroll approximately 175 patients at up to 25 sites across the United States.

The primary objective of the EVANGELINE study is to evaluate the endocrine sensitive disease (ESD) rate, measured by Ki-67 (a proliferation marker prognostic for disease free survival), after four weeks of treatment with (Z)-endoxifen compared to treatment with current standard of care, exemestane plus goserelin. Exemestane is an aromatase inhibitor designed to block the synthesis of estrogen and slow the growth of ER+ cancers. Goserelin is a medication given to block the ovaries from making estrogen, also called ovarian function suppression (OFS). In premenopausal women, OFS is associated with significant morbidity and inadequate compliance, which compromises efficacy and increases the risk of mortality.

(Z)-endoxifen is the most active anti-estrogen metabolite of tamoxifen that potently blocks ERa and binds to and disrupts protein kinase C beta one function (PKCb1, a known oncogenic protein). In an earlier Phase 2 study, treatment with (Z)-endoxifen resulted in a 65.1% reduction in Ki-67. This is potentially clinically meaningful because numerous studies by other groups have shown that reducing Ki-67 is prognostic for 5-year disease free survival. (Z)-endoxifen administered as monotherapy may also obviate the need for OFS in premenopausal women and potentially reduce breast cancer cell proliferation.

"We are excited to kick-off this important trial, a significant achievement in our development strategy," said Dr. Steven Quay, Atossa's President and Chief Executive Officer. "Approximately 78% of breast cancers are ER+ / HER2- and premenopausal women diagnosed with this disease need more effective and tolerable treatment options; specifically new treatments that do not require ovarian function suppression. We feel (Z)-endoxifen has the potential to change the treatment paradigm for these patients."

Atossa is also developing its proprietary (Z)-endoxifen to reduce breast density, a known risk factor for developing breast cancer. The Company has an ongoing Phase 2 trial focused on reducing mammographic breast density (MBD) in healthy, premenopausal women. Known as the "Karisma-Endoxifen" study, this randomized, double-blind, placebo-controlled trial plans to enroll 240 study participants. Participants receive daily doses of (Z)-endoxifen for six months, over the course of which mammograms are conducted to measure reduction in MBD. Participants also have a mammogram at 24 months to assess the durability of the MBD changes.

MBD affects more than 10 million women in the United States and many millions more worldwide. Increased MBD reduces the ability of mammograms to detect cancer. Studies have also shown that women with MBD have an increased risk of developing breast cancer and that the higher the MBD, the higher the incidence of breast cancer.

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 anti-estrogenic 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 has developed 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 converts 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. We are currently studying our (Z)-endoxifen in healthy women with measurable breast density and premenopausal women with ER+/HER2- breast cancer.

Atossa's (Z)-endoxifen is protected by two 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 current focus on breast cancer and lung injury caused by cancer treatments. For more information, please visit www.atossatherapeutics.com

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FORWARD LOOKING STATEMENTS
Forward-looking statements in this press release, which Atossa undertakes no obligation to update, are subject to risks and uncertainties that may cause actual results to differ materially from the anticipated or estimated future results, including the risks and uncertainties associated with any variation between interim and final clinical results, actions and inactions by the FDA, the outcome or timing of regulatory approvals needed by Atossa including those needed to commence studies of (Z)-endoxifen, lower than anticipated rate of patient enrollment, estimated market size of drugs under

development, the safety and efficacy of Atossa's products, performance of clinical research organizations and investigators, obstacles resulting from proprietary rights held by others such as patent rights, whether reduction in breast density or in Ki-67 or any other result from a neoadjuvant study is an approvable endpoint for (Z)-endoxifen, whether Atossa can complete acquisitions, and other risks detailed from time to time in Atossa's filings with the Securities and Exchange Commission, including without limitation its periodic reports on Form 10-K and 10-Q, each as amended and supplemented from time to time.