Atossa Therapeutics to Present Pharmacokinetic and Tolerability Data from Phase 2 EVANGELINE Trial at the 2024 San Antonio Breast Cancer Symposium

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SEATTLE, Dec. 10, 2024 (GLOBE NEWSWIRE) -- Atossa Therapeutics, Inc. (Nasdaq: ATOS) ("Atossa" or the "Company"), a clinical stage biopharmaceutical company developing innovative medicines in areas of significant unmet medical need in oncology with a focus on breast cancer, today announced that three posters involving pharmacokinetic and tolerability data from the Phase 2 EVANGELINE trial will be presented at the 2024 San Antonio Breast Cancer Symposium (SABCS 2024). EVANGELINE is a randomized Phase 2 non-inferiority study investigating (Z)-endoxifen as a neoadjuvant treatment for premenopausal women with estrogen receptor-positive (ER+)/HER2-negative breast cancer.

The first poster, *"Neoadjuvant Z-Endoxifen for Premenopausal Estrogen Receptor (ER)+, Human Epidermal Receptor (HER2)- Breast Cancer (BC): Evaluation of the Pharmacokinetic (PK) Run-in for the EVANGELINE Study,"* discusses findings from the pharmacokinetic (PK) run-in phase of the trial. This phase evaluated (Z)-endoxifen monotherapy at 40 mg (data previously reported) and 80 mg (new data presented) doses, with and without goserelin (for ovarian function suppression or OFS). Findings include:

- **Primary Endpoint Achieved**: 50 percent of patients (3/6) in the group that received 80 mg of (Z)-endoxifen with goserelin met the target steady-state plasma concentrations (Css) of 500–1000 ng/mL. Approximately 38 percent of patients (3/8) in the 80 mg/day (Z)-endoxifen only group reached target Css levels. The average plasma Css level for all patients receiving 80mg/day of (Z)-endoxifen was 484 ng/mL. As previously reported, no patients in the 40 mg/day (Z)-endoxifen arm reached the target plasma Css level of 500 ng/mL.
- **Tissue Penetration**: Consistent with the recently updated trial protocol, tissue Css levels were evaluated in addition to plasma Css levels. The 80 mg/day dose, in both treatment arms, achieved tissue Css levels more than double that of plasma levels, surpassing the 500 ng/g target in 90 percent of patients—a level adequate to target PKCβ.
- **Antitumor Activity**: Substantial tumor suppression was observed across all dosing levels, with or without ovarian function suppression (OFS). The 4-week Ki-67 ≤10 percent response rate was generally above 85 percent across dose levels, with or without the presence of OFS.
- **Safety and Tolerability:** Overall, (Z)-endoxifen was well tolerated and target tissue Css levels were achieved without significant Grade 3–4 toxicities. Four gynecologic events were reported in the 80 mg groups, including one Grade 3 hemorrhagic cyst. These findings have informed protocol amendments to optimize dosing and tolerability.

The second poster, *"Evaluation of Quality of Life (QOL) Measures in the EVANGELINE Study,"* focuses on patient-reported outcomes from (Z)-endoxifen treatment in patients enrolled onto the PK run-in. Findings include:

- **Tolerability**: The QOL data presented supports (Z)-endoxifen as generally well-tolerated. Most patient-reported side effects were low grade. Symptoms like hot flashes and reduced libido were reported as mildly to moderately bothersome. Amenorrhea and menstrual suppression were common but generally reported as manageable.

The third poster, *"A Randomized Phase 2 Non-inferiority Trial of (Z)-endoxifen and Exemestane + Goserelin as Neoadjuvant Treatment for Premenopausal Women with ER+/HER2- Breast Cancer (EVANGELINE),"* outlines the design and rationale for the randomized trial:

- **Study Design**: Based on adverse events reported in 80 mg/day groups, as well as the findings reported on (Z)-endoxifen tissue and plasma Css, overall tolerability, and antitumor activity, EVANGELINE is expected to proceed based on an amended protocol as a randomized trial that compares (Z)-endoxifen 40 mg/day plus OFS to exemestane plus OFS, using the 4-week Ki-67 reduction as the primary endpoint.

  While tumor tissue (Z)-endoxifen levels were not tested at the 40 mg/day dose level, based on the ratio of plasma/tumor Css, (Z)-endoxifen tumor concentrations are expected to be >500 ng/g., meeting the required levels for PKCβ targeting.

- **Next Steps**: The process for trial initiation has begun and recruitment for this cohort is expected to begin in 2025, now that the PK run-in phase has been concluded.

"We are encouraged by the breadth of data being presented at SABCS, which collectively advances our understanding of (Z)-endoxifen's safety, efficacy, and impact on patient quality of life," said Steven Quay, M.D., Ph.D., Atossa's President and Chief Executive Officer. "Additionally, we believe we now have a clear plan for the randomized portion of the EVANGELINE trial, including a defined (Z)-endoxifen dose and study design. Our plan is to advance this arm of the study in 2025 as we seek to demonstrate the potential of (Z)-endoxifen to improve outcomes and provide a better tolerated option for premenopausal women with ER+/HER2- breast cancer."

A link to the poster presentations will be made available on Atossa Therapeutics' website at the time of the presentations on December 11. For additional information, please visit the SABCS website: https://sabcs.org.

About (Z)-Endoxifen
(Z)-endoxifen is one of the most potent Selective Estrogen Receptor Modulator (SERM) for estrogen receptor inhibition and may cause estrogen receptor degradation. It has also been shown to have efficacy in the setting of patients with tumor resistance to other hormonal treatments. In addition to its potent anti-estrogen effects, (Z)-endoxifen has been shown to target PKCβ1, a known oncogenic protein, at clinically attainable blood concentrations. Finally, (Z)-endoxifen appears to deliver similar or even greater bone agonistic effects while resulting in little or no endometrial

proliferative effects compared with standard treatments, like tamoxifen.

Atossa is developing a proprietary oral formulation of (Z)-endoxifen that is encapsulated to bypass the stomach, as acidic conditions in the stomach convert a significant 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 five Phase 2 trials: one in healthy women with measurable breast density, one in women diagnosed with ductal carcinoma in situ, and three other studies including the EVANGELINE study and two I-SPY studies in women with ER+/HER2- breast cancer. Atossa's (Z)-endoxifen is protected by four 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 using (Z)-endoxifen to prevent and treat breast cancer. For more information, please visit www.atossatherapeutics.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," "design," "predict," "future," or other comparable words. All statements made in this press release that are not statements of historical fact, including statements regarding data related to the (Z)-endoxifen program, the safety, tolerability and efficacy of (Z)-endoxifen, the potential of (Z)-endoxifen as a breast cancer prevention and treatment agent, the expected design and enrollment of trials and timing of data and related publications, and the potential milestones and growth opportunities for the Company, are forward-looking statements. 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 or preliminary and final clinical results or analysis; 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 remain compliant 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.

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