



## Atossa Therapeutics Proposes Potentially Groundbreaking Study Aimed at Reducing Interval Breast Cancer in High-Risk Women at AACR 2025

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SEATTLE, April 29, 2025 (GLOBE NEWSWIRE) -- Atossa Therapeutics, Inc. (Nasdaq: ATOS) ("Atossa" or the "Company"), a clinical-stage biopharmaceutical company developing innovative medicines for breast cancer, today outlined a framework for a pioneering Phase 3 clinical study titled SMART 2.0. The proposed trial would investigate the potential of oral (Z)-endoxifen, a potent Selective Estrogen Receptor Modulator (SERM) for estrogen receptor inhibition, to significantly reduce interval breast cancer in women identified as high-risk through advanced mammographic screening techniques. The proposed SMART 2.0 study was presented at the American Association for Cancer Research (AACR) Annual Meeting and represents a future research program and potential partnership opportunity to advance this critical initiative for women at high risk of breast cancer.

Interval breast cancers, diagnosed between regular mammography screenings, are typically more aggressive and challenging to treat than screen-detected cancers. Mammographic density has been recognized as a critical, modifiable risk factor for breast cancer and can complicate early detection. Previous research indicates (Z)-endoxifen, like tamoxifen, effectively reduces breast density and potentially enhances mammogram sensitivity. However, the adverse effects associated with tamoxifen limit its widespread use.

Atossa's innovative approach utilizes low-dose (1mg) Z-endoxifen, which reduced mammographic density by nearly 20 percent at six months and systemic side effects that were not statistically different than placebo in the Phase 2 KARISMA trial - an important step toward lowering the risk of interval breast cancer. The proposed SMART 2.0 trial would randomize participants identified by leveraging an AI Risk model into treatment and placebo groups to evaluate the effectiveness of (Z)-endoxifen over two years. The primary endpoint would measure the relative reduction in interval breast cancer incidence and tolerability compared to placebo over a two-year period of time.

"The SMART 2.0 study proposal represents a significant step forward for the advancement of breast cancer prevention," said Steven C. Quay, CEO of Atossa Therapeutics. "By targeting mammographic density with Z-endoxifen, we hope to establish a safer, more effective preventive therapy for women at high risk."

The company aspires to conduct a trial such as this in the future in an effort to provide the pivotal data required for regulatory approval of Z-endoxifen as a preventative treatment option.

### 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 PKC $\beta$ 1, 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 clinical studies of women with and without breast cancer. (Z)-endoxifen is currently being studied both for the treatment and prevention of breast cancer, including a program in metastatic breast cancer that was announced earlier this year.

### About Atossa Therapeutics

Atossa Therapeutics, Inc. (Nasdaq: ATOS) is a clinical-stage biopharmaceutical company dedicated to transforming breast cancer treatment through innovative science and patient-focused solutions. The company's lead product candidate, (Z)-endoxifen, is a highly potent SERM designed for use across the breast cancer spectrum, including prevention, neoadjuvant, adjuvant, and metastatic settings. Atossa is committed to advancing its robust clinical research programs to improve patient outcomes while creating sustainable value for shareholders. For more information, visit [atossatherapeutics.com](https://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 potential indications that the Company may pursue for (Z)-endoxifen, the potential for (Z)-endoxifen to receive regulatory approval, benefits of the Company's strategy of pursuing a metastatic indication for (Z)-endoxifen, the expected design and enrollment of trials and timing of data and related publications, and the potential market 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: our ability to obtain patent coverage for our product candidates; 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 regain compliance or maintain 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.

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