



Atossa
THERAPEUTICS

Corporate Presentation

June 26, 2025

NASDAQ: ATOS

www.atossatherapeutics.com

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Multi-billion market opportunity across the rapidly growing estrogen receptor positive breast cancer market



Demonstrated broad utility across the breast cancer paradigm with first in best-in-class potential:

- ✓ Metastatic
- ✓ Prevention
- ✓ Neoadjuvant/Adjuvant



Robust and Growing IP Portfolio with broad protections in the U.S. and globally



Experienced Leadership Team and world-renowned advisors



Strong financial position with ~ two years of runway and zero debt

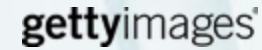
Experienced Leadership



Steven Quay, MD, PhD
Chairman, CEO and President



Heather Rees, CPA
Chief Financial Officer and Secretary



Claudia Lopez, DVM, MSC
VP, Clinical Product Development



Delly Behen, PHR, SHRM-CP
SVP, Business Operations



Michael Parks
VP, Investor and Public Relations



World-renowned Thought Leadership



Per Hall, M.D., PhD
Karisma Principal Investigator



Laura Esserman, M.D., MBA
I-Spy Principal Investigator



Matthew Goetz, M.D.
EVANGELINE Principal Investigator



David Lyden, M.D., PhD
TNBC Research Lead



Problem: High unmet need for ET in breast cancer

~40-50%

Patients Discontinue Adjuvant
Endocrine Therapy

~50%

Patients Do Not Respond to 1L
Aromatase Inhibitors + CDK4/6

~60%

Patients Do Not Benefit from 2L
fulvestrant monotherapy

Although, endocrine therapy remains the mainstay treatment for patients, there are numerous **UNMET NEEDS** that still exist for new treatment options

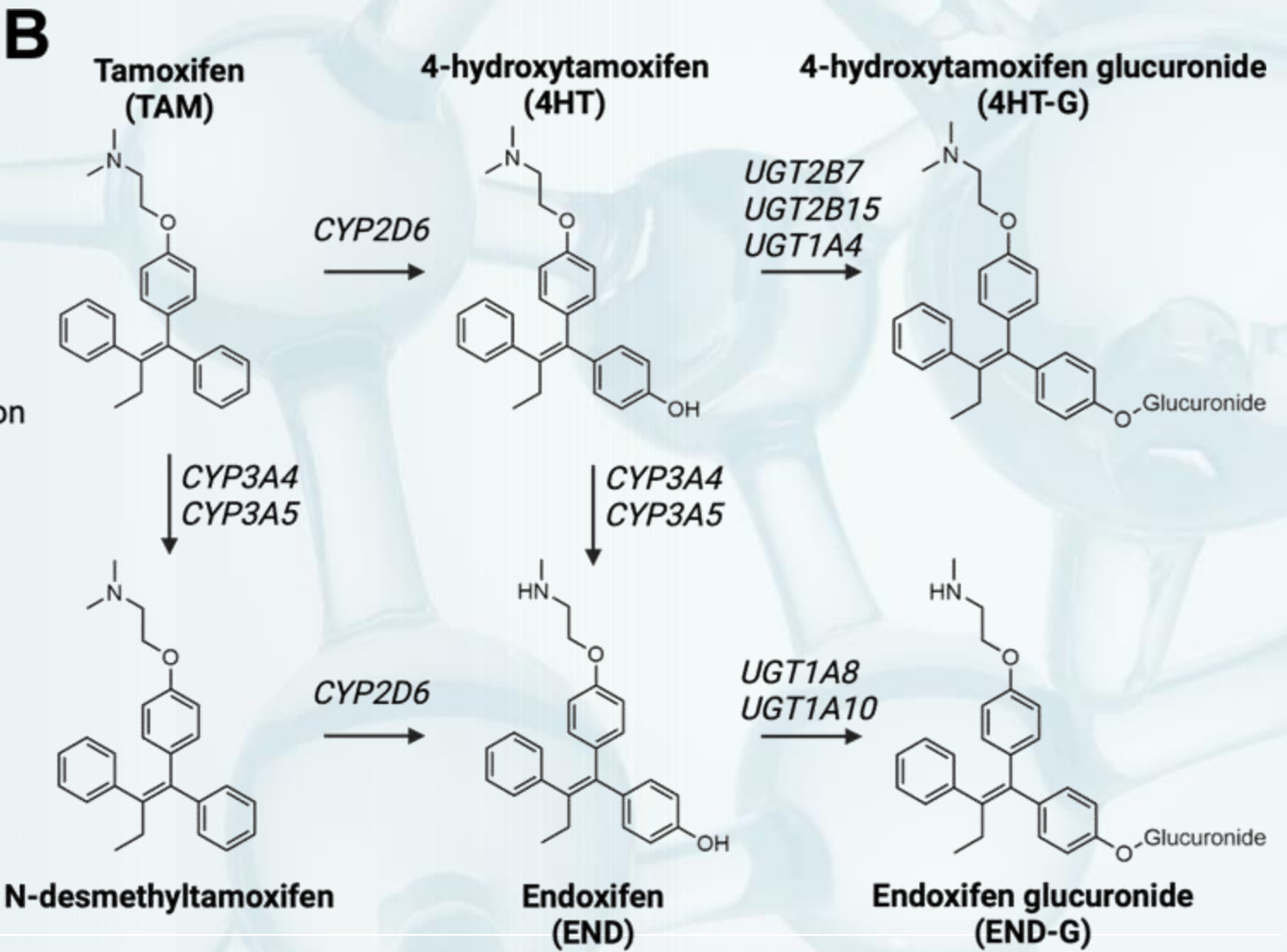
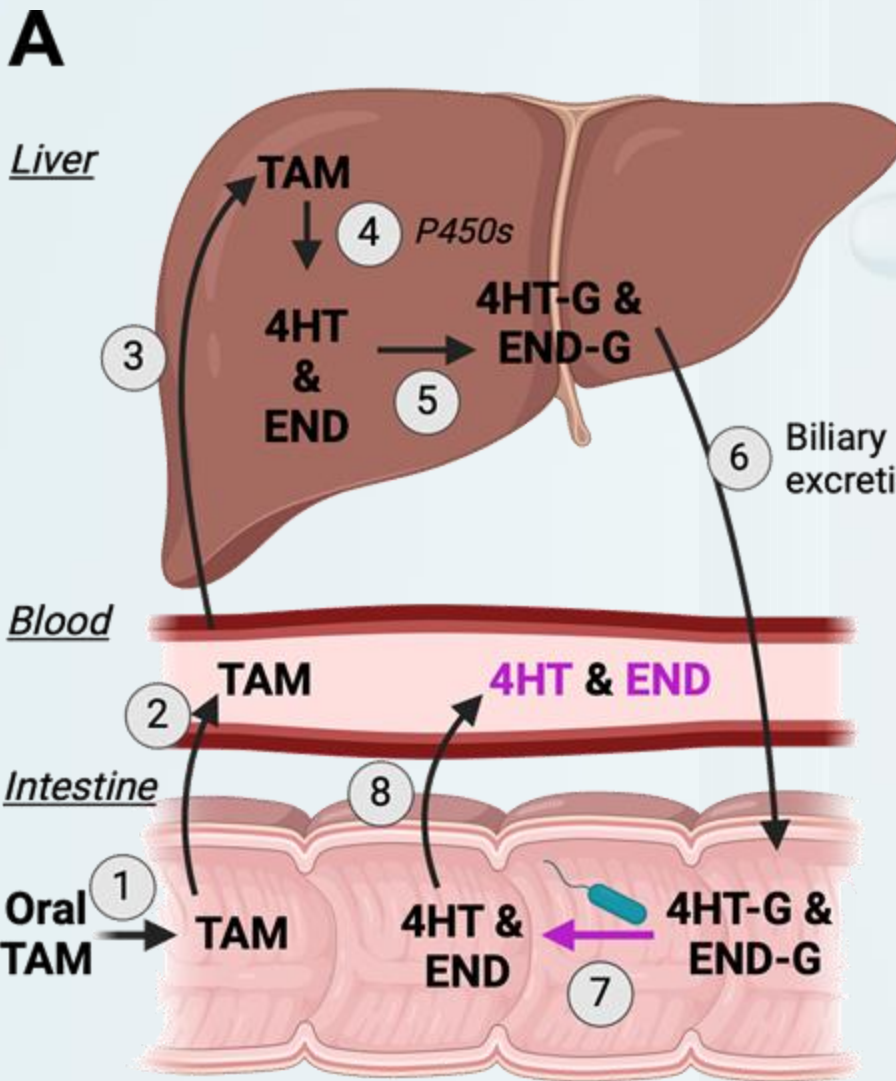
Improved efficacy

Reduced resistance

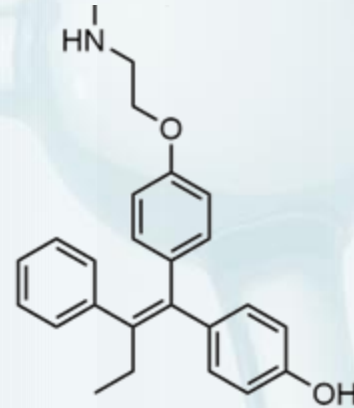
Induced apoptosis

Improved adherence

Tamoxifen: The Proven Paradigm



(Z)-endoxifen – The New Paradigm with Broad Clinical Utility



Endoxifen

**(Z)-endoxifen is NOT your grandmother's tamoxifen
or your mother's aromatase inhibitor**

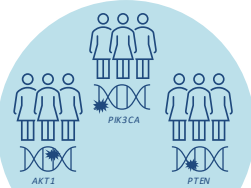
(Z)-endoxifen's points of differentiation



Superior ER Antagonist

100-fold more potent vs other SERMs

Superior antitumor efficacy in preclinical + clinical studies



PKC β 1 Inhibition

Binds to and inhibits protein kinase C beta one (PKC β 1, a known oncogenic protein)

Downregulates AKT pathway and induces apoptosis in breast cancer cells



ESR1 Mutant Inhibition

Inhibits clinically relevant *ESR1* mutants, an acquired resistance mechanism to aromatase inhibitors



Improved safety & tolerability

Potential to avoid current negative “on target off tissue” effects

May increase adherence



Superior Combination Partner

Potential to be preferred endocrine combination partner


(Z)-endoxifen is a novel, next-generation anti-estrogen with best-in-class potential across the breast cancer treatment paradigm

(Z)-endoxifen can be positioned in all stages of ER+/HER2- breast cancer treatment paradigm




Value Proposition

- Earlier detection in patients with dense breast tissue
- Prevention of cancer in at-risk patients
- Phase 2 trial completed




Value Proposition

- Potential Improvement in Breast Conservation Rate
- Premenopausal women may avoid ovarian function suppression (OFS), which results in higher use and compliance
- Phase 2 underway




Value Proposition

- Many patients are refractory to Tamoxifen / contraindicated for aromatase inhibitors
- Improved safety / tolerability profile and avoid OFS



Value Proposition

- PD effects and stable-disease responses from Ph1 study reinforce it as a potential next-generation ET.
- Tolerable safety profile makes it a promising backbone for combination regimens
- Phase 2 reporting underway



(Z)-endoxifen



Metastatic – Priority Indication and Major Focus

Metastatic provides fastest path to market, highest probability of success

- **Efficient** Clinical and Regulatory Path
- **Allows Atossa to more rapidly** bring (Z)-endoxifen to patients who need it most.
- **Strengthens foundation** for the expansion of (Z)-endoxifen into earlier-stage disease settings.
- **Right sized program** for Atossa with significant upside in a therapeutic market projected to reach **~\$42 billion by 2030.**

Value Proposition

- PD effects and stable-disease responses from Ph1 study reinforce it as a potential next-generation ET.
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(Z)-endoxifen exhibits superior anti-tumor activity to SOC agents

Superior anti-tumor activity

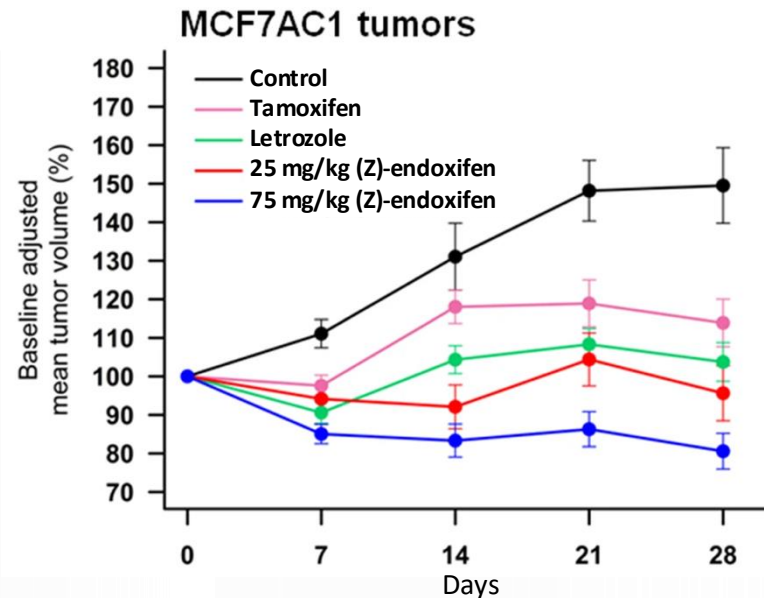
Compared to tamoxifen, (Z)-endoxifen is 100-fold more potent in anti-estrogen activity.

Preclinical studies revealed **superior antitumor activity compared to tamoxifen and aromatase inhibitors** in both endocrine-sensitive (MCF7AC1) and endocrine-resistant (MCF7LR) ER α + breast cancer models.

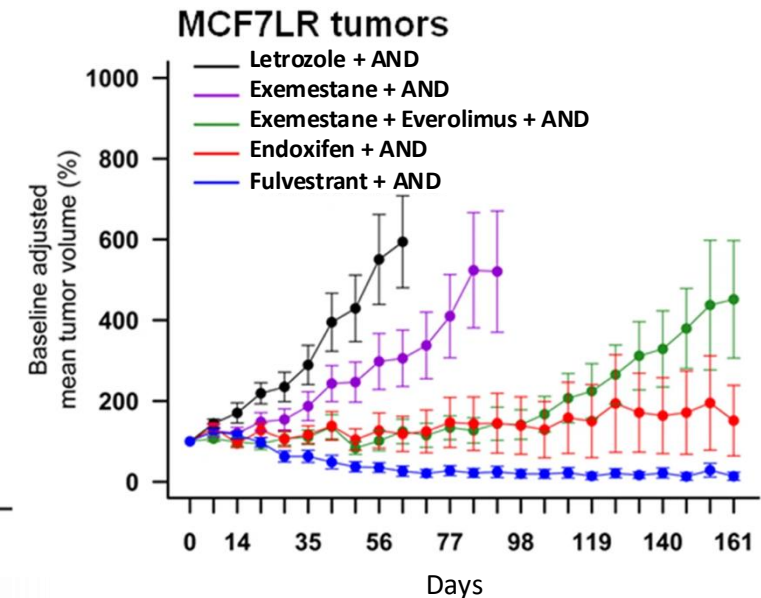
Preclinical

Superior anti-tumor and anti-estrogenic activity to current SoC

(Z)-endoxifen demonstrates promising anti-tumor activity



At both 25 and 75 mg/kg (Z)-endoxifen decreased mean tumor volume compared to tamoxifen (at 500 μ g/day) and letrozole (at 10 μ g/day) in letrozole-sensitive MCF7 aromatase expressing model (MCF7AC1).



In letrozole-resistant MCF7 models (MCF7LR), (Z)-endoxifen showed less increase in mean tumor volume than exemestane and exemestane + everolimus. Androstenedione (AND) was injected to test the efficacy of aromatase inhibitors

(Z)-endoxifen exhibits superior anti-tumor activity in the clinic

Superior anti-tumor activity

In previous **clinical studies**, (Z)-endoxifen demonstrated **promising anti-tumor activity** in endocrine-refractory metastatic breast cancer patients

In a Phase 2 trial comparing (Z)-endoxifen with tamoxifen, **CDK4/6 inhibitor naïve patients had improved PFS with (Z)-endoxifen compared to tamoxifen.**

(Z)-endoxifen has not shown unexpected safety concerns beyond what is typically seen with tamoxifen and has been better tolerated.

Clinical

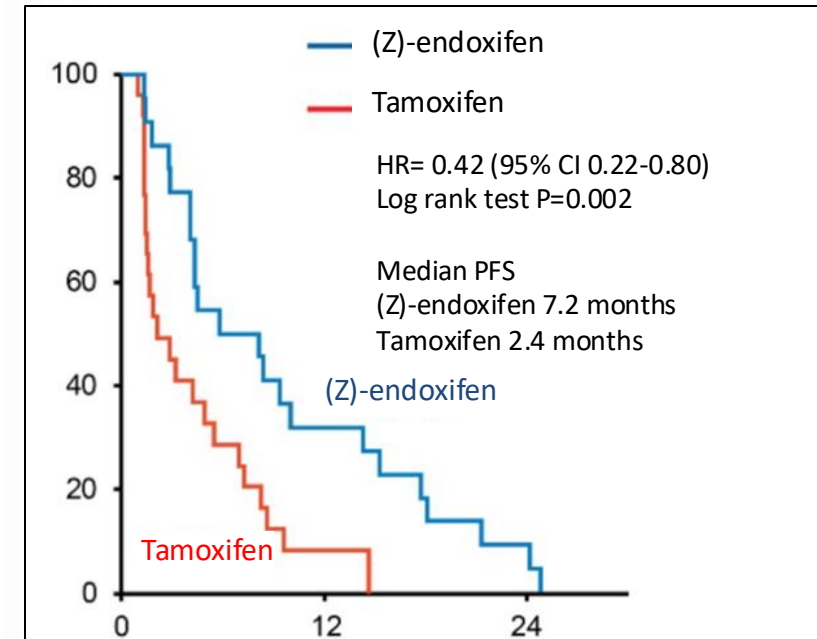
(Z)-endoxifen demonstrates promising efficacy in the relapsed/refractory setting

(Z)-endoxifen leads to disease regression



Tumor shrinkage with (Z)-endoxifen treatment in tamoxifen, aromatase inhibitor, fulvestrant and Everolimus refractory breast cancer after 9 months

Progression Free Survival (PFS) in Postmenopausal Women



Extended PFS demonstrated by (Z)-endoxifen in a Phase II randomized clinical trial, in the relapse/refractory metastatic setting. n=40 evaluable patients in each arm

(Z)-endoxifen exhibits superior anti-tumor activity in the clinic

Superior anti-tumor activity

In an ongoing neoadjuvant clinical study, (Z)-endoxifen has demonstrated promising early efficacy with **1 CR and multiple PRs**.

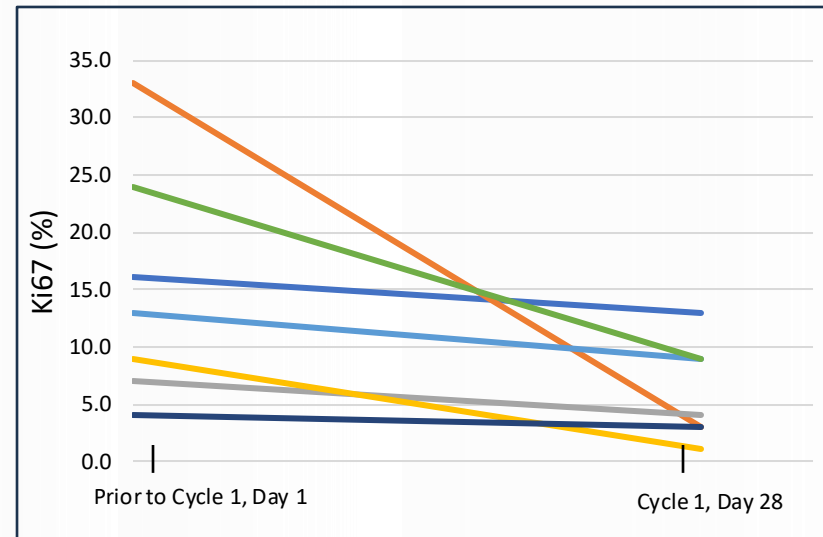
The **4-week Ki-67 $\leq 10\%$ response rate** was generally **above 85%** across dose levels, with or without the presence of OFS.

Endocrine therapies are generally observed to be cytostatic and do not cause tumor shrinkage.

Clinical

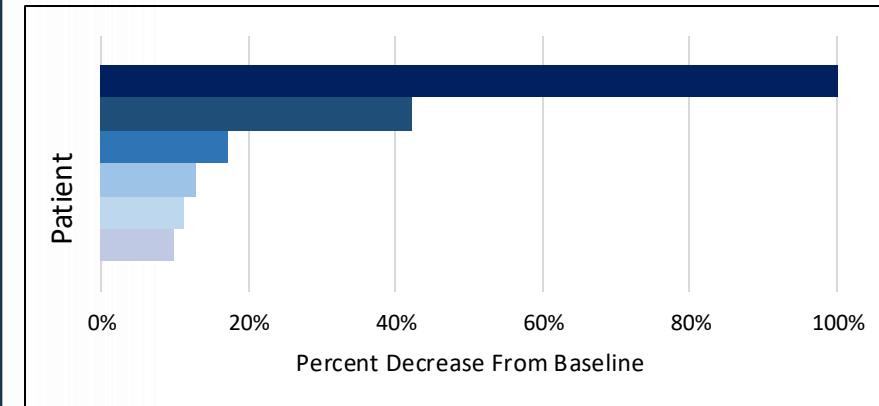
(Z)-endoxifen demonstrates promising efficacy in the neoadjuvant setting

Ki67 From Baseline to Cycle 1, Day 28



One pt discontinued due to wk4 Ki-67 (marker for cell proliferation) remaining > 10%. The remaining 6 had endocrine sensitive disease and underwent surgery after 24 weeks.

% Decrease in Tumor Size at Cycle 3, Day 28 by MRI Imaging



5 PR and 1 CR were observed in the neoadjuvant setting with (z)-endoxifen treatment in post-menopausal ER+/HER2- breast cancer patients.

EVANGELINE estimated enrollment will be ~180 patients

(Z)-endoxifen has the potential to be the preferred endocrine therapy for combination partners

(Z)-endoxifen as the preferred combination partner for CDK4/6 inhibitors

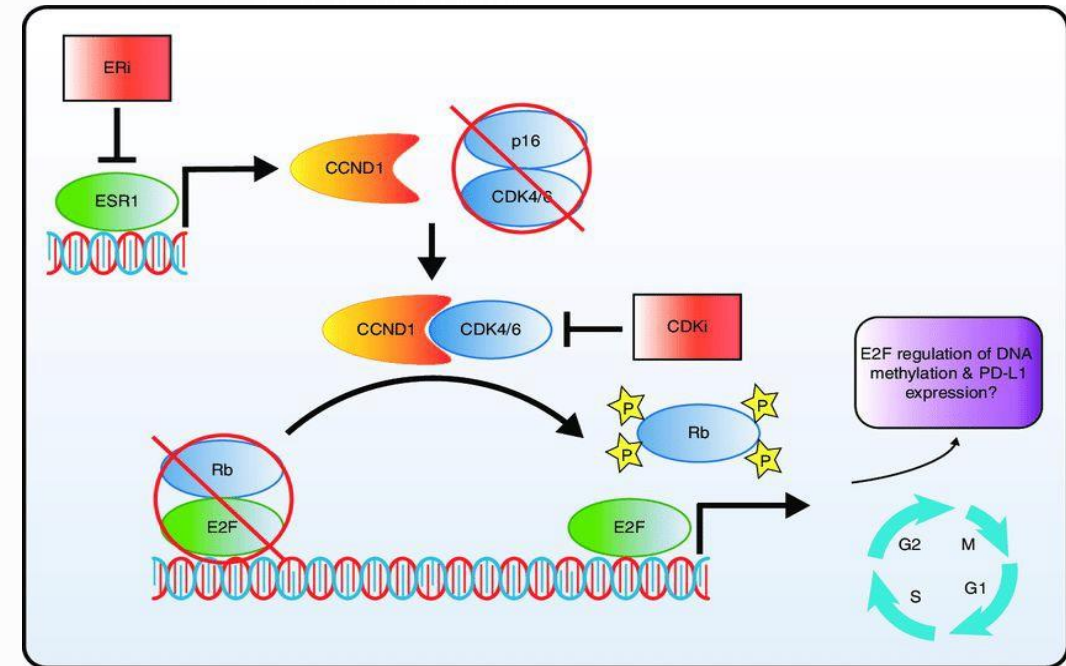
CDK4/6 inhibitors are FDA-approved combination partners for tamoxifen, aromatase inhibitors and fulvestrant

(Z)-endoxifen's superior safety and efficacy could make it the preferred endocrine therapy combination partner.

The recently initiated I-SPY2 trial will help confirm the hypothesis that (Z)-endoxifen is the preferred endocrine therapy for CDK4/6 combination.

Other potential combinations have been preclinically tested and suggested, including **PI3Ki, MDM2i and others.**

CDK4/6 and ER pathways converge on regulation of cell cycle and Rb phosphorylation



(Z)-endoxifen is safe and well tolerated in preclinical and early clinical trials

Preclinical

- Preclinical data supports that (Z)-endoxifen **does not induce bone loss and does not affect uterine wet weight** in ovariectomized animals.

Clinical

- **Overall:** In studies conducted by other groups, (Z)-endoxifen was **well tolerated at doses up to 360 mg/day, for up to 5 years with relatively few adverse events reported** demonstrating a relatively **wide therapeutic window**.
- **Metastatic:** In Phase I studies (including heavily pretreated metastatic ER+ breast cancer patients), (Z)-endoxifen was escalated from 20 mg to as high as 160 mg/day **without identifying a clear maximum tolerated dose (MTD)**. Most adverse events were **mild-to-moderate**.
- **EVANGELINE** is currently ongoing in premenopausal women with Grade 1 or 2 ER+/HER2- breast cancer in the neoadjuvant setting (40 and 80 mg/day; 22 participants to date).
 - (Z)-endoxifen has been **generally well-tolerated**, the **majority of AEs** have been **mild or moderate in severity**, one **SAE** was reported related to study drug (hemorrhagic ovarian cyst).

Current Clinical Strategy – Early Disease

(Z)-endoxifen



Prevention

Neoadjuvant/Adjuvant

KARISMA:

- Unmet need to prevent breast cancers.
- (Z)-endoxifen has demonstrated 1 mg dose of (Z)-endoxifen reduced MBD by 17.3 percentage points ($p < 0.01$), compared to a minimal change in the placebo group of 0.27 percentage points.
- Plasma concentrations for (Z)-endoxifen was measured at 4.8 ng/mL for the 1 mg, highlighting the effectiveness of the lower dose in achieving significant reductions.
- Importantly, no significant differences in adverse events were observed between the 1 mg dose and placebo

Greater than \$20B TAM based on eligible high-risk women with average 5-years of treatment.

EVANGELINE:

- The 4-week Ki-67 $\leq 10\%$ response rate was generally above 85% across dose levels, with or without the presence of OFS

I-SPY2:

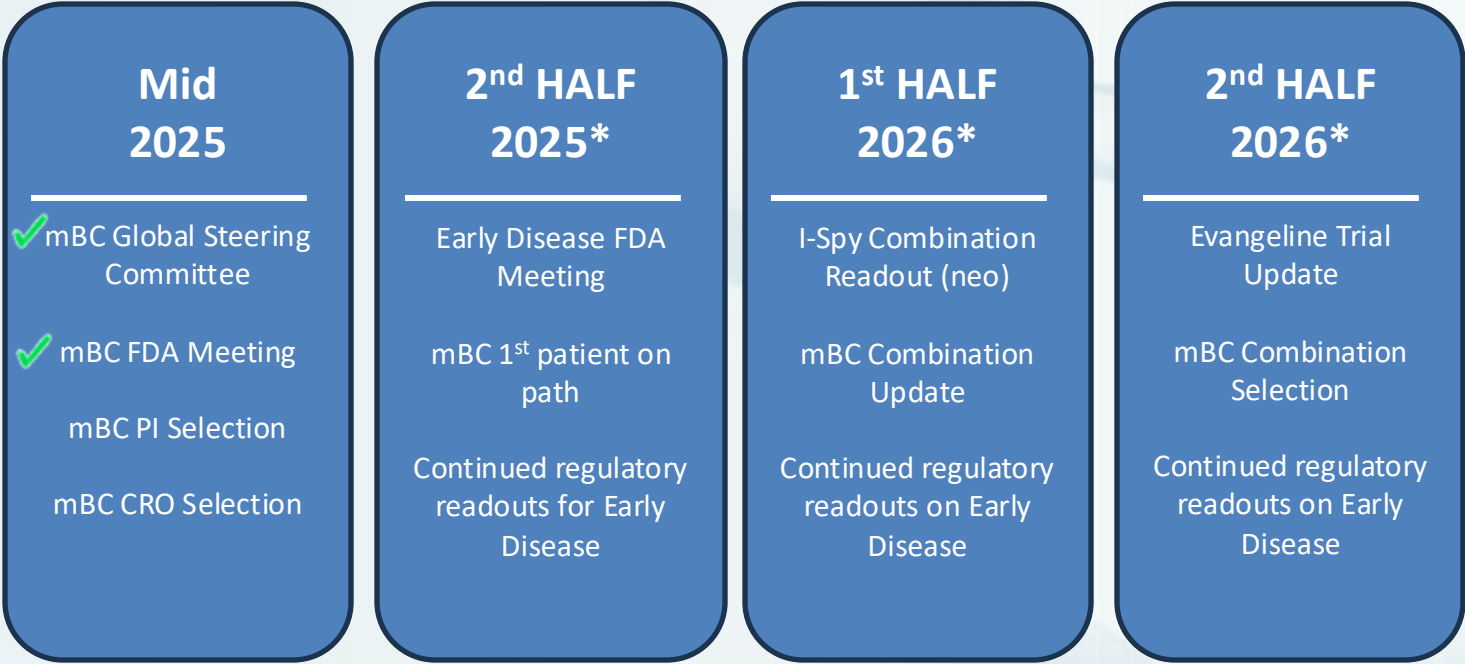
- Primary feasibility goal surpassed – 95% of participants completed at least 75% of planned dosing
- Early anti proliferative activity – Median Ki-67 fell from 10.5 percent at baseline to 5 percent by Week 3 in 65% of patients, and suppression was maintained at surgery.
- Robust imaging response – Median FTV measurement decreased 77.7 percent from baseline to surgery.

~240k ER+ BC cancers diagnosed annually with average 6mo neoadjuvant and 5-years of adjuvant treatment.

(Z)-endoxifen is highly differentiated from current SoC

(Z)-endoxifen is a novel, next generation anti-estrogen with best-in-class potential				
	(Z)-endoxifen	Tamoxifen	Aromatase Inhibitors	Fulvestrant
Novel Agent	✓	FDA Approved	FDA Approved	FDA Approved
Level of Antiestrogenic Activity	✓✓✓	✓	✓	✓
Safety	✓✓	✓	✓	✓
ER-dependent & -independent MoA	✓	✗	✗	✗
Addressable Patients	✓✓✓	✓	✓	✓
Combination Potential	✓✓✓	✓	✓✓	✓✓

Anticipated Upcoming Milestones



Approximately two years of cash on hand at current burn rate and zero debt

*timing subject to FDA feedback

KEY STATISTICS

\$ 65.1 M Cash (as of 03/31/25)

Approximately 2 years of working capital and NO debt

- **Nasdaq: ATOS Market Cap - \$107M (as of 06/25/25)**
 - Share Price - \$0.86
 - 52 Week Range - \$0.55 - \$1.66
 - Outstanding Shares - 129,170,004

8.7% Beneficial Ownership – Management & the Board of Directors

12.3 MM Shares

Outstanding Warrants

17.8 MM warrants

\$1.00 to \$2.88/share; June to September 2025



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Questions

