Preliminary Oral Endoxifen Phase 1 Results

All Objectives Successfully Met

October 25, 2017
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Discussion Topics

- Atossa Genetics Overview
- Endoxifen
- Phase 1 Study Summaries
  - Safety
  - Tolerability
  - Pharmacokinetics
- Upcoming Milestones
Atossa Genetics Overview
About Atossa Genetics (NASDAQ: ATOS)

- Clinical-stage company
- Novel pharmaceuticals
- Novel drug delivery methods
- Breast cancer & other breast conditions
Recent capitalization improvements:

- April 2017 financing included 6M warrants and convertible Preferred
- All April warrants have now been exercised
- All April preferred stock has now been converted
- Outstanding capital now includes only 14M shares of common stock
Breast Cancer Risk Factors & Treatment Approaches

Factors that Increase Breast Cancer Risk
- Dense Breasts
- Genetic
- Lifestyle

Risk Mitigation
- Tamoxifen (Rarely used)
- Increased mammograms
- Enhanced imaging
- Lifestyle Modification
- Routine Screening

Breast Cancer Diagnosis & Treatment
- Diagnosis
- Treatment (Surgery, Chemo, Radiation)
- Long-term Therapy
- Tamoxifen or AI*

*AI = Aromatase Inhibitors
Drug Programs Using our Proprietary Endoxifen:

- **Topical Endoxifen**
  - For mammographic breast density (MBD) reduction
  - All Phase 1 objectives met
  - Phase 2 for MBD in Sweden commencing Q1 2018

- **Oral Endoxifen**
  - For “tamoxifen-refractory” patients
  - All Phase 1 objectives met
  - Phase 2 for refractory patients commencing in Q1 2018
Two Programs Using Proprietary Microcatheter Technology:

• **Microcatheters for Transpapillary CAR-T Delivery (TRAP CAR-T)** – In R&D phase with goals of reducing toxicity, improving efficacy and the potential of T-cells migrating along the lymphatic pathway

• **Intraductal Microcatheters for Drug Delivery**
  
  Enrollment underway in Phase 2 study for delivery of fulvestrant for treatment of ductal carcinoma in-situ (DCIS) and breast cancer
The Unmet Need

Topical Endoxifen for Density

- No FDA approved treatment
- 10 million women \(^{(1)}\)
- Tamoxifen use minimal

Oral Endoxifen for Refractory

- Up to 500,000 tamoxifen patients under-treated (too-little Endoxifen) \(^{(2, 3)}\)
- Raising Endoxifen levels may reduce risk of recurrent or new lesions

Intraductal Microcatheters

Provides alternative to Systemic delivery, which has:

- Systemic adverse effects
- Limited tumor drug level

ATOS microcatheter technology may:

- Increase drug to tumor ratio
- Improve efficacy
- Reduce toxicity
- CAR-T cells may follow lymphatic migration of cancer

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(1) National Cancer Inst.: Prevalence of Mammographically Dense Breasts in the United States (Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4200066/)
(2) Breast Care [Basel]: Clinical Relevance of CYP2D6 Genetics for Tamoxifen Response in Breast Cancer (Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2931018/)
Breast Cancer Timeline

Prevention Window
- High Density via Mammography

Neoadjuvant Phase
- Suspicious Lump
- Diagnosis
- Biopsy
- Surgery and Radiation/Chemotherapy
- Intraductal:
  - Fulvestrant
  - TRAP CAR-T

Adjuvant Phase
- Tamoxifen (5 years)
- Oral Endoxifen

Topical Endoxifen

Atossa GENETICS
Program Pipeline

<table>
<thead>
<tr>
<th>Drug/Device</th>
<th>Program</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA*</th>
<th>Market</th>
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<tr>
<td>Microcatheters</td>
<td>TRAP CAR-T</td>
<td>R&amp;D</td>
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<td>Ph. 2 Underway</td>
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<td>Breast Density</td>
<td>Ph. 2 starts in Q1 '18</td>
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<td>2019 2020</td>
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<td>Oral Endoxifen</td>
<td>Refractory to Tamoxifen</td>
<td>Ph. 2 starts in Q1 '18</td>
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<td>2019 2020</td>
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</tbody>
</table>

* Estimated FDA or Ex-US submission
Endoxifen
Endoxifen - Overview

- Most active metabolite of tamoxifen
- Tamoxifen has been widely studied
- Tamoxifen is a pro-drug
- Up to 50% of patients can’t make enough Endoxifen

(1) Breast Care (Basel): Clinical Relevance of CYP2D6 Genetics for Tamoxifen Response in Breast Cancer (Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2931018/)
Low levels of circulating Endoxifen during tamoxifen adjuvant therapy correlate to an increased risk of recurrent or new breast cancers

- Identified as an independent risk factor
- Known and unknown causes for low endoxifen levels during tamoxifen therapy
- Most active tamoxifen metabolite
- It may save more lives
Endoxifen – Rationale for Development

• Develop **TWO** formulations for two large unmet medical needs:
  
  – Topical to reduce density – less than 5% of high risk patients will take oral tamoxifen because of actual or perceived side effects\(^{(1)}\)
  
  – Oral – up to 50% of patients taking tamoxifen are refractory\(^{(1)}\)

• Extensive existing data on tamoxifen

\(^{(1)}\) Data from DefinedHealth: SERM Report January 2017
High Breast Density Masks Tumors

Source: [http://woodtv.com/2015/05/11/are-you-dense-know-your-numbers/](http://woodtv.com/2015/05/11/are-you-dense-know-your-numbers/)
A Newly Recognized Breast Cancer Risk Factor: Mammographic Density

Several states have now mandated reporting of high breast density as seen on mammograms to both patient and primary care provider

http://slideplayer.com/slide/1557508/
10 million patients with a high risk of breast cancer are indicated for chemoprevention with oral tamoxifen.

1 million breast cancer patients take oral tamoxifen for at least five years.

Many Drugs Limit Liver Endoxifen Production from Tamoxifen

• SSRI drugs like Prozac and Paxil (paroxetine) stop liver metabolism of tamoxifen to endoxifen
  
• Before: 20 mg/day tamoxifen yields 12.4 ng/mL plasma endoxifen
  
• After: four weeks of 10 mg/day of paroxetine is administered
  
• Plasma endoxifen is reduced in 11/12 women in this study
  
• Mean endoxifen levels decreased from 12.4 ng/mL (28 nM) to 5.5 ng/mL (14 nM)
  
• Source: J Natl Cancer Inst. 2003 Dec 3;95(23):1758-64. Active tamoxifen metabolite plasma concentrations after coadministration of tamoxifen and the selective serotonin reuptake inhibitor paroxetine. Stearns V1, Johnson MD, Rae JM, Morocho A, Novielli A, Bhargava P, Hayes DF, Desta Z, Flockhart DA
• Tamoxifen Refractory Patients
  – Up to 50% of patients fail to achieve therapeutic endoxifen blood levels
    • Approximately 30 nM is therapeutic threshold
  – Only option is aromatase inhibitors
    • Significant adverse drug effects
The Need: Breast Cancer Statistics

- 250,000+ cancers and 60,000 DCIS in U.S. in 2017
- 40,000+ deaths in U.S. in 2017
- 15% of BC are triple negative; 3x deadlier in 5 years

Endoxifen: $1B U.S market
For treatment and chemoprevention of breast cancer
(Defined Health 1/17)

Intraductal Fulvestrant: $800M U.S. market
in DCIS pre-surgery and replacement to surgery
(Defined Health 1/17)

TRAP CAR-T: TBD U.S. Market
Triple neg. – 37k patients/yr.; can’t use hormone therapy
Phase 1 Study
Preliminary Phase 1 Oral Results

- Study objectives achieved
- Demonstrated:
  - Safety
  - Tolerability
  - Verification of therapeutic blood levels

Supports continued development
Product Development Timeline

- Q2 2016: Contracted to develop endoxifen API
- Q3 2016: First batch of API for clinical use
- Q4 2016: Topical formulation development in US
  Retained CRO in Australia
- Q1 2017: Retained CMO in Australia (for topical and oral presentations)
- Q2 2017: Approval to start study
  First cohort enrolled
  Shipped drug product to CRO
- Q3 2017: Last cohort completed
• **All study objectives successfully achieved**
  
  – **Safety:** There were no clinically significant safety signals and no clinically significant adverse events in participants receiving oral Endoxifen.
  
  – **Tolerability:** Oral Endoxifen was well tolerated at each dose level and for the dosing duration utilized in the study.
  
  – **Pharmacokinetics:** Oral Endoxifen demonstrated blood levels that have been associated with a therapeutic effect in the adjuvant setting in women with breast cancer.
Two-part double-blinded, placebo controlled, dose escalation trial investigating the safety and pharmacokinetics of (Z)-Endoxifen in healthy female volunteers

- Part A: Topical – liquid applied to the breasts
- Part B: Capsule – taken orally
### PART A (Topical). Cohorts, dose levels and number of participants.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose Level</th>
<th>Number of Participants</th>
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<tr>
<td></td>
<td>(mg per breast)</td>
<td>(Total mg)</td>
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<tr>
<td>1</td>
<td>1</td>
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<td>2</td>
<td>3</td>
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</tr>
<tr>
<td>3</td>
<td>5</td>
<td>10</td>
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### PART B (Oral). Cohorts, dose levels and number of participants.

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<th>(Z)-Endoxifen</th>
<th>Placebo</th>
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<tr>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
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### Oral Study Demographics

#### Table 14.1.2-B

Summary of Demographics, Part B

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<th>Cohort 4</th>
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<td></td>
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<td>1 mg (N=6)</td>
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<td>4 mg (N=6)</td>
<td>(N=18)</td>
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<td>6</td>
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<td>11.6</td>
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<td>58</td>
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<td>6 (100%)</td>
<td>6 (100%)</td>
<td>18 (100%)</td>
<td>6 (100%)</td>
<td>24 (100%)</td>
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<tr>
<td>White</td>
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<td>3 (50%)</td>
<td>4 (67%)</td>
<td>12 (67%)</td>
<td>4 (67%)</td>
<td>16 (67%)</td>
</tr>
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</table>
Safety Summary

There were no clinically significant safety signals and no clinically significant adverse events in participants receiving oral Endoxifen.
Safety Summary – Oral Study

- No safety signals observed in weekly assessments of/in:
  - Blood chemistry
  - Coagulation parameters
  - Hematology parameters
  - Urinalysis
  - Vital Signs
  - Heart
  - Physical Examinations
Serious Adverse Events

None Reported
Safety Summary – Oral Study

• AEs deemed Probable as relationship to study drug:
  – in 5 of 18 subjects receiving oral Endoxifen (28%, 7 AEs)
  – in 3 of 6 subjects receiving oral placebo (50%, 6 AEs)
  – All were assessed as “Mild”

• AEs deemed probably related to study drug for oral administration were:
  – 1 mg: Vomiting (n = 1 or one subject)
  – 2 mg: 3 x Menstruation delayed (n = 3), Metrorrhagia (n = 1)
  – 4 mg: Hot flush, Polymenorrhea* (n = 1)
  – Placebo: Acne, Breast tenderness, Nausea, Hyperesthesisa, Vulvovaginal dryness, Dysmenorrhea (n = 3)

*The medical term for cycles with intervals of <22 days
Tolerability Summary

Oral Endoxifen was well tolerated at each dose level and for the dosing duration utilized in the study.
**Tolerability Summary – Oral Study**

Based on responses from a validated questionnaire, oral endoxifen was well tolerated and similar to the placebo capsules.

**Question:** “I am bothered by side-effects of treatment”

<table>
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<th>Treatment</th>
<th>Visit Day</th>
<th>N</th>
<th>Not At All</th>
<th>A Little Bit</th>
<th>Somewhat</th>
<th>Quite a Bit</th>
<th>Very Much</th>
<th>Not Done</th>
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<td>6 (100%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 14</td>
<td>6</td>
<td>5 (83%)</td>
<td>1 (17%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 21</td>
<td>6</td>
<td>5 (83%)</td>
<td></td>
<td></td>
<td>1 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>End Of Study</td>
<td>6</td>
<td>4 (67%)</td>
<td>2 (33%)</td>
<td></td>
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<tr>
<td>C5, 2 mg</td>
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<td>6 (100%)</td>
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<td></td>
<td>Day 21</td>
<td>6</td>
<td>5 (83%)</td>
<td></td>
<td></td>
<td>1 (17%)</td>
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<tr>
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<td>6 (100%)</td>
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<td>6 (100%)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Day 14</td>
<td>6</td>
<td>4 (67%)</td>
<td>1 (17%)</td>
<td></td>
<td>1 (17%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 21</td>
<td>6</td>
<td>3 (50%)</td>
<td>2 (33%)</td>
<td></td>
<td>1 (17%)</td>
<td></td>
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<tr>
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<td>End Of Study</td>
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<td>4 (67%)</td>
<td>1 (17%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>C4-C6, Placebo</td>
<td>Day -1</td>
<td>6</td>
<td>5 (%)</td>
<td></td>
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<td></td>
<td>1 (%)</td>
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<td>2 (%)</td>
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<td>1 (%)</td>
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<td>Day 21</td>
<td>6</td>
<td>4 (%)</td>
<td>2 (%)</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>End Of Study</td>
<td>6</td>
<td>4 (%)</td>
<td>2 (%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
FACT-ES Validated Questionnaire of Endocrine Symptoms

Current therapy has a substantial effect on the FACT-ES Score
Pharmacokinetics Summary

Oral Endoxifen demonstrated blood levels that have been associated with a therapeutic effect in the adjuvant setting in women with breast cancer.
Pharmacokinetics Objective

- The typical plasma endoxifen levels after 20 mg daily tamoxifen in women who are poor metabolizers of tamoxifen (PM), intermediate metabolizers (IM), and excellent metabolizers (EM)

Therapeutic level is reported by others to be approximately 30 nM
Single Dose Pharmacokinetics

Pharmacokinetics Summary – Oral Study

- Placebo
- 1 mg/day
- 2 mg/day
- 4 mg/day

Plasma Enoxifen, nM

Time, Hr

0 5 10 15 20 25

0 10 20 30 40 50 60 70 80 90 100
Pseudo-Steady State Levels:

21 Day Sample

Plasma endoxifen levels after 20 mg/day tamoxifen, based on CYP2D6 status, published data

- EM
- IM
- PM

<table>
<thead>
<tr>
<th>Dose</th>
<th>Plasma Endoxifen, nM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>2</td>
</tr>
<tr>
<td>1 mg/day</td>
<td>39.8</td>
</tr>
<tr>
<td>2 mg/day</td>
<td>89.1</td>
</tr>
<tr>
<td>4 mg/day</td>
<td>187.8</td>
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</table>
Preliminary Study Conclusions

• All primary and secondary endpoints successfully met
  – **Safety:** There were no clinically significant safety signals and no clinically significant adverse events in participants receiving oral endoxifen.
  – **Tolerability:** Oral endoxifen was well tolerated at each dose level and for the dosing duration utilized in the study.
  – **Pharmacokinetics:** At doses between 1 and 4 mg/day, oral endoxifen produced significant plasma levels of endoxifen; doses of 2 and 4 mg/day exceeded endoxifen levels in “excellent metabolizers” taking 20 mg/day tamoxifen

**Therefore, oral Endoxifen is suitable for continued development**
Entry Criteria: ER$^+$ breast cancer patients on tamoxifen

Measure Endoxifen Levels

- >TBD nM Endoxifen: Continue on tamoxifen (20 mg/day)
- ≤TBD nM Endoxifen: Add Oral Endoxifen (1-2 mg/day)
Program could qualify for designation under the 505(b)(2) status. Advantages:

✧ A single clinical study of safety and efficacy
✧ Limited additional clinical or pre-clinical studies
✧ Leverage published clinical study data
✧ Multi-year market exclusivity possible
Intraductal Microcatheters
Intraductal Microcatheters

- Potential advantages: higher local drug/CAR-T exposure; lower systemic concentrations (lower toxicity) vs systemically delivered agents; potential for lymphatic migration of T-cells
- 1 issued and 3 pending patent app’s (US and PCT) for intraductal delivery of drugs and CAR-T
- Kite Pharma acquisition by Gilead; FDA approved Novartis's Kymriah™ for B-cell Acute Lymphoblastic Leukemia
• Phase 2 study for delivery of fulvestrant in patients with DCIS or breast cancer (initiated at Columbia; transferred to Montefiore)

• Advantages: potentially higher local drug exposure and lower systemic concentrations vs systemically delivered agents

• Fulvestrant is FDA approved for intramuscular admin (AstraZeneca); opportunities with other drugs and biotherapeutics
Microcatheter Fulvestrant - Clinical Trial Study

Thirty women with ER+ DCIS or Invasive Breast Cancer

Drug Administered 30-45 days Before Surgery

Assessments

- Efficacy
  - Pathological Response, Ki-67 Expression
- Safety
  - FACT-ES Tolerability
- Pharmacokinetics
  - Tissue and Blood Levels of Fulvestrant

Intramuscular Administration

Intraductal Administration
Microcatheters – TRAP CAR-T

**Step 1:** Remove blood and genetically modify T-cells to kill cancer

**Step 2:** Atossa’s Transpapillary (TRAP) microcatheters delivery CAR modified T-cells to breast ducts containing cancer cells
Upcoming Milestones

Oral Endoxifen: Phase 2 study for patients refractory to Tamoxifen is planned to start Q1 ‘18

Topical Endoxifen: Phase 2 study of MBD to start in Q1 ‘18 with Karolinska Institute Investigator in Stockholm

TRAP CAR-T - Seeking partners
Seasoned Management

Steven Quay, MD, PhD
Chairman, CEO and President

Kyle Guse, CPA, ESQ, MBA
CFO and General Counsel

Janet Rose Rea, MSPH, RAC
VP Regulatory, Quality and Clinical Affairs
NASDAQ: ATOS