Novel Therapy for Patients with Cyclin-Dependent Kinase (CDK)4/6 Refractory, Estrogen Receptor-Positive (ER+)/HER2- Breast Cancer

TTC-352: A Phase 2 Ready, First-In-Class Selective Human ER Partial Agonist (ShERPA)

Arek Dudek, MD, PhD

Chief Executive Officer

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Raising $15,000,000

PRESENTATION HIGHLIGHTS

- Overview of TTC Oncology company and team
- Targeted cancer patient population with high therapeutic unmet need
- Introduction to TTC-352 – a unique first-in-class, best-in-class partial ER agonist
- Results of Phase 1 study of TTC-352 in heavily pre-treated patients
- Competitive landscape
- KOL support
- Planned development for TTC-352
- Fundraising
- Why TTC Oncology is a great opportunity

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COMPANY AT A GLANCE

Our Focus: Development of TTC-352 for ER+/HER2- Breast Cancer

Novel mechanism of action: selective ER partial agonist	**Completed Phase 1 clinical trial**	**Oral capsule formulation**

LLC with

$6.25M

invested to date

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- 2 US patents issued protecting novel composition
- US and international patents pending

Seeking Series A investment to complete Phase II studies to advance corporate development dialogues

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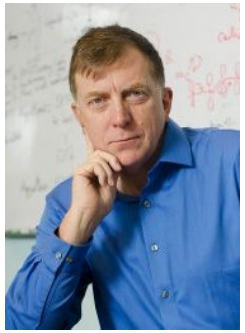
MEET OUR TEAM

Over 45 Years of Oncology Research and Over 30 Years of Drug Development Experience

Arkadiusz Dudek, MD, PhD

CEO and CMO

- Medical oncologist
- Professor, University of Minnesota
- >20 years experience in development of cancer therapeutics
  - Prior CMO of Vanquish Oncology, Luminary Therapeutics, IGF Oncology, and Squarex
  - Former CMO of Adhaere



- Professor, University of Arizona
- Designer of TTC-352 and other therapeutics

Greg Thatcher, PhD

CTO

Klara Czobor

Director of Development

- Professor, University of Illinois at Chicago
- Experienced cancer biology researcher
- Instrumental in development of biomarker for hormone resistant breast cancer

Debra Tonetti, PhD

CSO

Melody Pekarek

Manager

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THE UNMET NEED: HIGH PREVALENCE OF ER+ BREAST CANCER

2.1 Million
Total cases in the US, representing ~73% of all breast cancers[1,2]

~10% are metastatic at diagnosis[3]

Up to 60% of localized cancer relapse systemically[3]

27% Survival Rate
For metastatic ER+ breast cancer[3]

Problem:

- Majority of patients with breast cancer are treated with hormonal therapy, and all metastatic tumors develop resistance, and the only remaining treatment is toxic chemotherapy[3]

Market size:

- Ibrance (CDK4/6 inhibitor): Worldwide sales of $4.96B in 2019
- Piqray [phosphatidylinositol-3 kinase (PI3K) inhibitor]: Worldwide sales of $153 M in Q1/2 2020 following launch in 2019

1. United States Census Bureau. 2. American Cancer Society® Breast Cancer Facts & Figures 2019-2020. 3. Rozeboom B, et al. *Am J Cancer Res.* 2009; 9(12):2821-2831.

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THE UNMET MEDICAL NEED: TOXICITY ASSOCIATED WITH STANDARD OF CARE

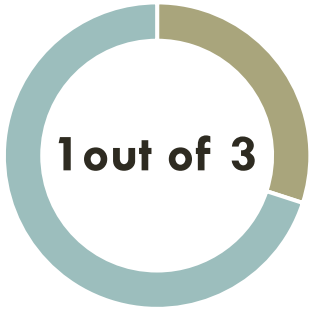
Potent ER agonists

- Estradiol
- High-dose estrogen (HDE)

"Treatment of advanced breast cancer with HDE is as effective as tamoxifen and AIs and is also effective after the development of resistance to TAM and AIs. However, HDEs have the negative reputation of having side effects."[1]

Anti-Estrogen Drugs

- Selective ER modulators (SERMs) (eg, tamoxifen)
- Aromatase inhibitors (AIs) (eg, anastrazole)
- Selective ER degraders (SERDs) (eg, fulvestrant)
- CDK4/6 inhibitors (eg, palbociclib)



One third of patients on hormonal therapy discontinue treatment because of toxicity.[2]

1. Benninck,et al. The use of high-dose estrogens for the treatment of breast cancer, *Maturitas* 95, (2017) 11-23. 2. Berkowitz MJ, et al. How patients experience endocrine therapy for breast cancer: an online survey of side effects, adherence, and medical team support. *J Cancer Surviv*. Published online August 17, 2020. doi:10.1007/s11764-020-00908-5

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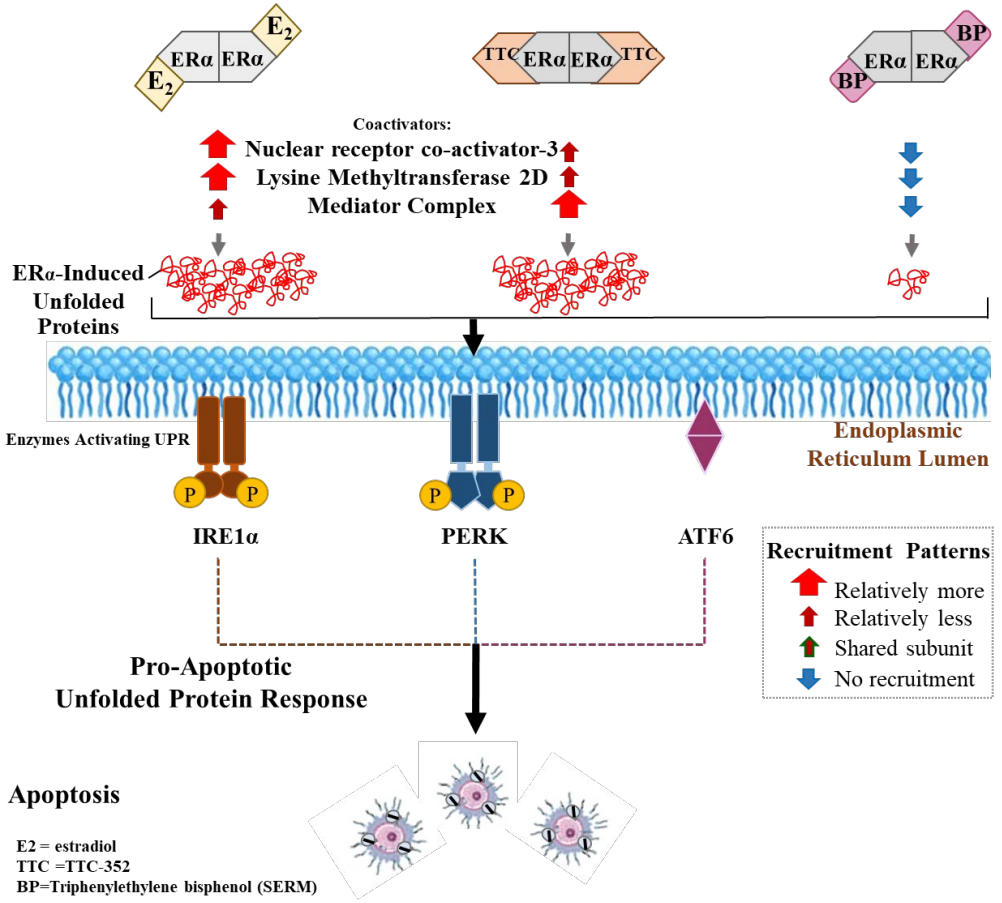
TTC-352 MECHANISM OF ACTION IN HORMONE RESISTANT BREAST CANCER

A Novel, First-in-Class, Best-in-Class Selective Human ER Partial Agonist (ShERPA) Which is Safer Than Estradiol

- Activates the estrogen signaling pathway, but differently than estradiol
- Recruits many more estradiol-enriched coactivators than SERMs
- Induces more rapid ERα-induced unfolded protein response and apoptosis compared to SERMs



Abderrahman B, et al. Rapid induction of the unfolded protein response and apoptosis by the estrogen mimic TTC-352 for the treatment of endocrine-resistant breast cancer. Author Manuscript Published OnlineFirst on November 11, 2020; DOI: 10.1158/1535-7163.MCT-20-0563.

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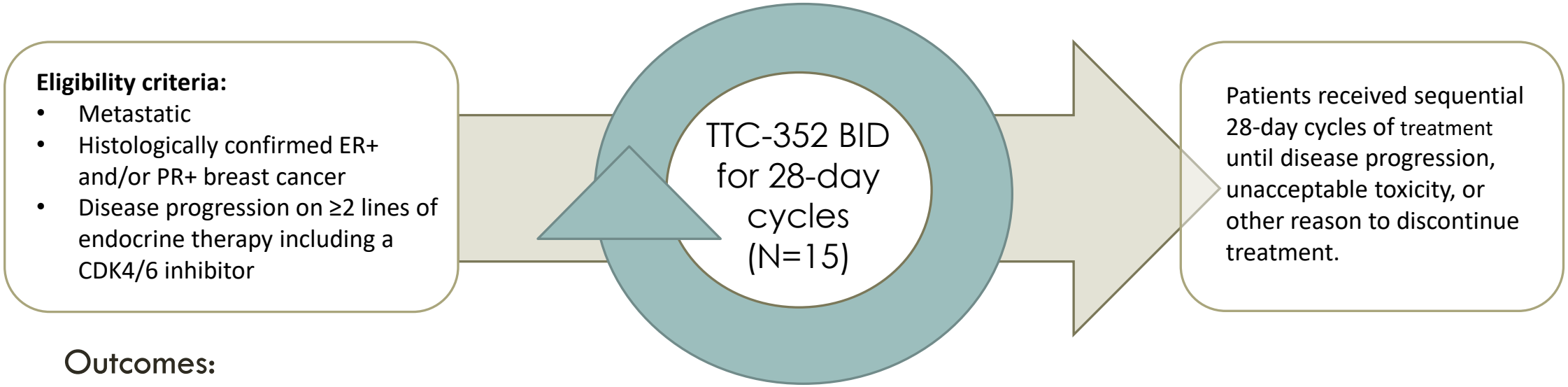
PHASE 1 STUDY OF TTC-352 IN PATIENTS WITH METASTATIC BREAST CANCER PROGRESSING ON ENDOCRINE THERAPY

Open-label, accelerated dose escalation study in patients who failed 2 or more lines of hormone therapy, including a CDK4/6 inhibitor



Outcomes:

- Established safety and dose for phase II testing
- Plasma levels of TTC-352 in patients exceed active levels in animal models
- **Observed activity in patients with heavily pretreated breast cancer, a patient population with few effective treatment options**

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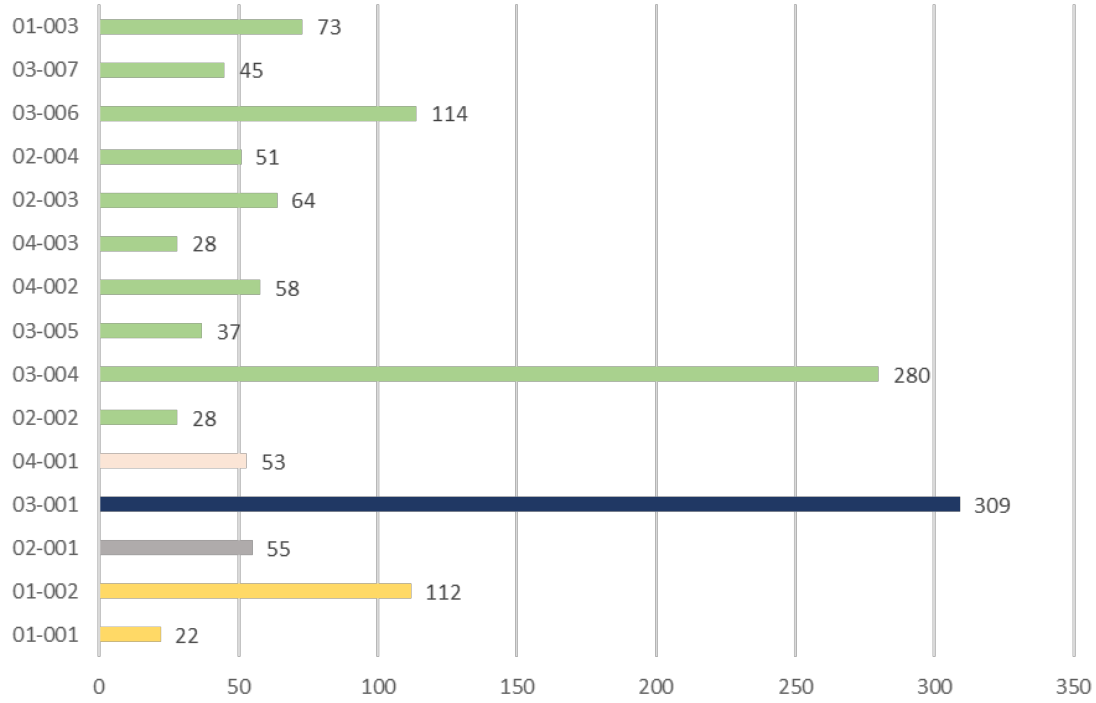
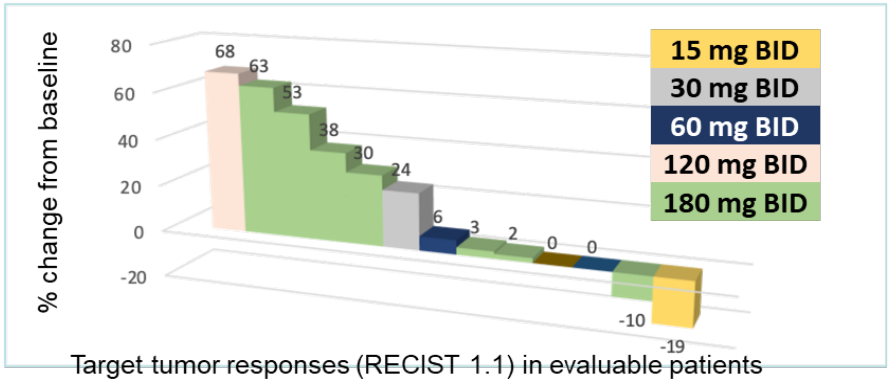
ACTIVITY IN HEAVILY PRETREATED BREAST CANCER PATIENTS

Breast cancer patients failed a median of 9 different hormonal and chemotherapy treatments before starting TTC-352

Duration of Treatment (Days)



Tumor Shrinkage



Target tumor responses (RECIST 1.1) in evaluable patients

- **7 out of 15 patients obtained stable disease**
- **Mean PFS for all patients was 89 days (range: 22-309 days)**
  - Analysis of clinical outcomes after failure of palbociclib and endocrine therapy shows time to treatment failure of only 3.8 months (95% CI 3.5-4.8)[1]

1. Rossi L, et al. *Breast Cancer Res.* 2019; 21(1):71. doi: 10.1186/s13058-019-1149-5.

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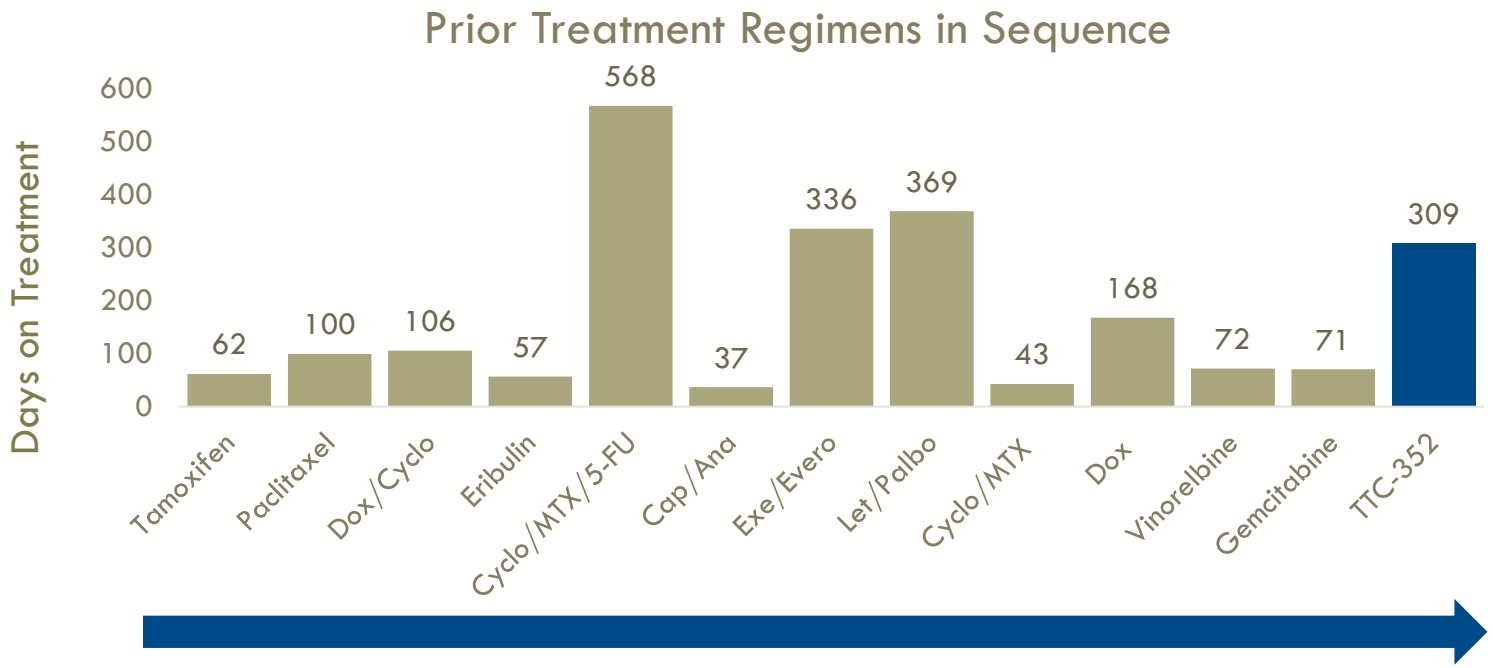
BEST RESPONDERS IN PHASE I STUDY

49-Year-Old Woman with ER+, PR+, HER2-breast cancer with visceral metastases

- After trying multiple prior lines of hormonal and chemotherapies, patient was given TTC-352 at 60 mg BID



TTC-352 induced 6% tumor shrinkage and controlled disease for 309 days with negligible toxicity.

- Patient's husband thanked the treating oncologist for giving his wife her life back

5-FU=5-fluorouracil; Ana=anastrozole; Cap=capecitabine; Cyclo=cyclophosphamide; Dox=doxorubicin; Evero=everolimus; Exe=exemestane; Let=letrozole; MTX=methotrexate; Palbo=palbociclib.

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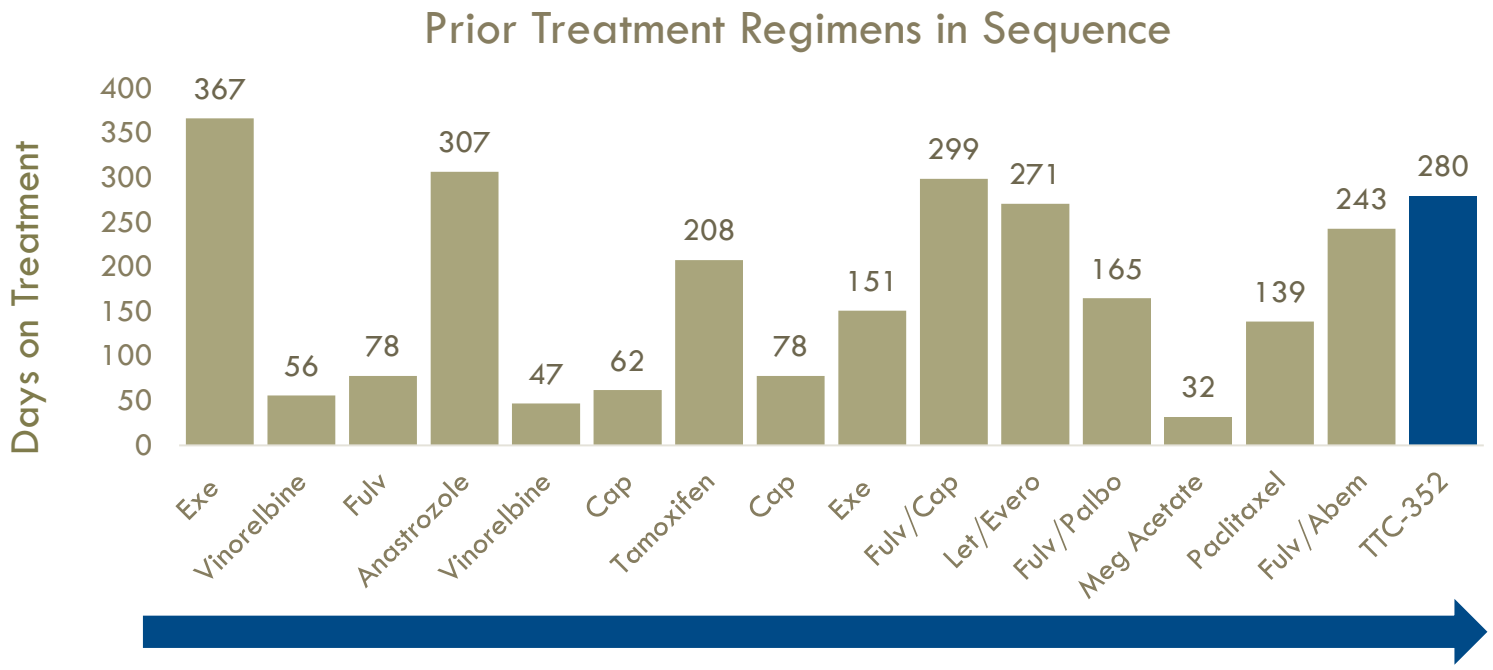
BEST RESPONDERS IN PHASE I STUDY

77-Year-Old Woman with ER+, PR+, HER2-breast cancer with bone metastases and ESR1 (D538G) mutation

- After trying multiple prior lines of hormonal and chemotherapies, patient was given TTC-352 at 180 mg BID



TTC-352 treatment resulted in stable disease, controlled for 280 days with negligible toxicity.

Abem=abemaciclib; Cap=capecitabine; Evero=everolimus; Exe=exemestane; Fulv=fulvestrant; Let=letrozole; Meg=megestrol; Palbo=palbociclib.

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COMPETITIVE LANDSCAPE

The current competition includes:

- PI3K inhibitors; examples:
  - Alpelisib
  - Taselisib
  - Pictlisib
- AKT inhibitors

However, PI3K and AKT inhibitors are effective in a small fraction of ER+ breast cancer patients **and** in combination with other agents.

TTC-352 has a key competitive advantage of being non-toxic compared with products currently in the marketplace.

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KEY OPINION LEADERS

The Platform Technology is Already Recognized by Leading KOLs

V. Craig Jordan, CMG, OBE, PhD, DSc, FmedSci
Dallas/Fort Worth Living Legend Chair of Cancer Research
Prof. of Breast Medical Oncology and Molecular and Cellular Oncology
MD Anderson Cancer Center

Ruth O'Regan, MD
Chief of Hematology, Medical Oncology and Palliative Care
Prof. of Medicine
Chair, Department of Medicine
University of Rochester

"TTC-352 provides a novel, non-toxic option for patients with hormone-refractory metastatic breast cancer."

Douglas Yee , MD, PhD
Director of the Masonic Cancer Center
Prof. of Medicine and Pharmacology
University of Minnesota

Gini F. Fleming, MD
Prof. of Medicine
Director, Gynecologic Oncology
University of Chicago

"Degree of disease stabilization on TTC-352 in patients with prior CDK4/6 inhibitor therapy makes this treatment worth pursuing. It is certainly less toxic option than chemotherapy."

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DEVELOPMENT STRATEGY

Lead drug, TTC-352, is a first-in-class ShERPA effective in tamoxifen-resistant, ER+ breast cancer

Completed Phase 1 Study

- Patient population was heavily pre-treated with at least 2 lines of hormonal/chemotherapy including a CDK4/6 inhibitor
- Results:
  - TTC-352 was very well tolerated across all tested dose levels
  - TTC-352 induced remarkable disease stability in 4 patients (range, 112 -309 days)
  - Clinical evidence of biomarker predicting benefit from TTC-352

Planned Phase 2 Studies Leading to Partnerships

- TTC-352 vs physician's choice second line therapy of ER+ breast cancer after failure of hormonal therapy and CDK4/6 inhibitors
- Single agent therapy of ESR1-mutated breast cancer
- Combination of TTC-352 with CDK4/6 inhibitor (study in partnership with pharma)
- Combination of TTC-352 with PI3K inhibitor (study in partnership with pharma)

Planned Phase 3 Study Leading to Series B Approval

- Biomarker driven randomized study of TTC-352 versus physician's choice standard of care

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DEVELOPMENT STRATEGY

A Deeper Dive Into One of the Planned Phase 2 Studies

"TTC352-201: Randomized Phase 2 Study of TTC 352 versus Physician's Choice in Patients with Metastatic Breast Cancer Progressing on Endocrine Therapy and CDK4/CDK6 inhibitor"

- 171 patients
- Study performed internationally to accelerate accrual
- PI: TBA
- Primary Endpoint: Progression Free Survival
- Validation of PKCa expression as biomarker for benefit of therapy

Timeline to completion: September of 2024

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SERIES A FINANCING

Seeking $15 M Funding to Support Multiple Planned Studies

- Randomized Phase 2 Study with Biomarker Validation
- Two-Stage Simon Design Phase 2 Study of TTC 352 in ESR1-Mutated Breast Cancer
- Phase 1B/2 of TTC-352 with PI3K Inhibitor or CDK4/6 Inhibitor in Partnership

		2020			2021											2022								
		Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
		Q1			Q2			Q3			Q4			Q1			Q2			Q3			Q4		
Bridge Tasks	**Bridge Investment (4 Million)**																								
	Seeking $4 M Funding																								
	GMP Production of 30 kg of Drug Substance and Product																								
	Discussion with FDA Regarding Path to Approval																								
Series A Tasks	**Series A Investment (15 Million)**																								
	Randomized Phase 2 Study with Biomarker Validation																					Study will end in September 2024			
	Two Stage Simon Phase 2 of TTC 352 in ESR1 Mutated Breast Cancer																					Study will end in December 2023			
	Phase 1B/2 of TTC 352 with PIK3A Inhibitor in Partnership																					Study will end in September 2023			
	Phase 1B/2 of TTC 352 with PIK3A Inhibitor in Partnership																					Study will end in September 2023			

WHY TTC ONCOLOGY IS A UNIQUE OPPORTUNITY

- Novel MoA for hormonal therapy of breast cancer; effective in CDK4/6-resistant ER+ breast cancer after failure of AIs and SERDs
- Biomarker predicting activity in development (PKCa overexpression)
- Oral capsule delivery
- Human safety established
- IP protected until October 2033 (novel composition and use)
- Pipeline focused on breast cancer: brain bioavailable oral SERD, BET/P300 dual inhibitor, BD1-selective inhibitor
- Significant KOL support in breast cancer for novel, non-toxic breast cancer therapy

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Thank you!

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