Galera Therapeutics (GRTX) Driving Better Outcomes for Breast Cancer Patients

January 2025





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Galera Therapeutics:

Developing First-in-Class Treatments for Resistant Breast Cancer

Tilarginine (pan-NOS inhibitor) has potential to be first approved therapy in metaplastic breast cancer (MpBC)

- Fully grant funded Phase 1b/2 trial ongoing in MpBC with nab-paclitaxel and alpelisib (PI3K inhibitor)
 - 4/9 responses seen in Phase 1 portion
 - Next tranche of data expected end of 2025
- Proof of concept achieved in triple negative breast cancer (TNBC) patients in combination with docetaxel
 - 46% ORR across all patients in Phase 2
 - 82% ORR in locally advanced patients



Avasopasem (superoxide dismutase mimetic) to be repositioned into HR+ HER2- breast cancer to restore sensitivity to 1st line patients

Phase 1b/2 single arm investigator-initiated trial to begin in 1H2025



Cash balance expected to support multiple near-term data readouts

Cash runway anticipated to fund operations into 2026

Galera Therapeutics and Nova Pharma



PHARMACEUTICALS

Pan-NOS Inhibitor

tilarginine

Dismutase Mimetics avasopasem rucosopasem

Public company with small molecule dismutase mimetics in early trial for hormoneresistant breast cancer Private company with small molecule NOS inhibitor in early trials for advanced and metastatic breast cancer





Targeting treatment resistance pathways

Combined company positioned to accelerate development for tilarginine and avasopasem

Joining Forces to Bring Novel Treatments to Cancer Patients

Leadership Team



Mel Sorensen, MD President & CEO Galera, Oncopia, Ascenta GSK, Bayer, NCI, Mayo Clinic





Joel Sussman, CPA **Chief Accounting Officer** Galera, Ascenta

Judy Schnyder **Clinical Operations** Galera, Aclaris



Andie Collier **Regulatory & Quality** Galera, Gilead



Judy Fox, PhD Drug Development Genentech Sunesis, Chiron

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Galera's Breast Cancer Trials

Three Trials Targeting Highly-Resistant forms of Advanced or Metastatic Breast Cancer

	Program	Preclinical	Phase 1	Phase 2	2	Results/Status
Active / Planned	Tilarginine + nab-paclitaxel +PI3Ki	Metaplastic Breast Cancer (n=36) Phase 1-2 single-arm combo trial (HMRI)				1 CR, 3 PR, 3 SD in 1 st 9 pts Ongoing Enrollment
	Tilarginine + paclitaxel	Triple Negative Breast Cancer (TNBC) Phase 2 adaptive randomized, placebo-controlled trial (I-SPY2)				Planned to Open 2025
	Avasopasem + (fulvestrant +CDK4/6i) ¹	HR+/HER2- Metasta Phase 1b/2a single-arm co	atic Breast Cancer (r mbo trial (UT San Antonio)	=25)		Phase I portion to open 1H2025
Completed	Tilarginine + taxane	Metastatic & Locall Phase 1-2 single-arm comb	y Advanced TNBC (n bo trial (HMRI, funded by NC	=35) "		17% CR, 29% PR, 17% SD Path CRs (3), Clinical CR (1)

Tilarginine is L-NMMA (NG-monomethyl-L-arginine), a nitric oxide synthase (NOS) inhibitor, administered IV over 2 hours, with Amlodipine pretreatment TNBC = Triple-negative Breast Cancer, PI3Ki = Inhibitor of Phosphoinositide 3-kinase. Nab-paclitaxel = nanoparticle albumin-bound paclitaxel (Abraxane[®])

HMRI = Houston Methodist Research Institute; NCI=National Cancer Inst.; I-SPY 2 = Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis 2

Tilarginine in Triple Negative Breast Cancer





Promising Early Results With Tilarginine in TNBC

Long-term research with nitric oxide synthase inhibition in cancer has demonstrated potential to translate into the clinic

- A research team led by Jenny Chang, M.D., a breast medical oncologist and director of the Houston Methodist Dr. Mary and Ron Neal Cancer Center, found variants in a gene called RPL39 that work through a pathway called nitric oxide.
- Through the combination of chemotherapy and a nitric oxide synthase inhibitor, tilarginine or L-NMMA, developed at Houston Methodist, researchers were able to regress tumor growth of triple negative breast cancer and prevent the cancer from spreading.
- Historically, patients with cancers resistant to chemotherapy have about a 10-15% chance of responding when used with older drugs that target the immune system.
- The response rate using the Houston Methodist-discovered drug Tilarginine has been approximately 45% in initial trials in TNBC and Metaplastic breast cancer.



Jenny Chang, MD Breast Oncologist Houston Methodist

Inhibiting NOS Reverses Resistance Mechanisms

NOS drives resistance mechanisms via reversible post-translational modifications (NT & SNO)



NOS, Nitric Oxide Synthase; NT, Tyrosine Nitration; SNO, S-nitrosylation; ASK1, Apoptosis Signal-Regulating Kinase 1; JNK, Jun N-terminal kinase; CCL2, C–C motif chemokine ligand 2; Adapted from Reddy et al., Targeting Nitric Oxide: Say NO to Metastasis. Clin Cancer Res; 29(10) May 15, 2023

Tilarginine in Metaplastic Breast Cancer and TNBC

We believe resistant TNBC and metaplastic disease are two attractive opportunities with high unmet need



²American Cancer Society Factsheet, 2019

³Wolf D et al., Redefining breast cancer subtypes to guide treatment prioritization and maximize response, Cancer Cell, 2022

Tilarginine: A Pan-NOS Inhibitor for Breast Cancer

Tilarginine: a well-characterized safety profile across hundreds of patients

- Preclinical activity seen in TNBC-PDX models as single agent and in combination with chemo and targeted therapies
- Previous clinical trial experience in CV, sepsis and oncology settings
- Pharmacodynamic activity observed in nononcology indications
- Intravenous administration
- Clinical activity & pharmacodynamic reduction in serum nitrites/nitrates observed in Phase 1b/2 study in TNBC (n=35)



Efficacy Signal in Locally Advanced TNBC

Findings from Phase 2 (n=24) portion of tilarginine + taxane trial



Pathologic Complete Response in 3 pts (27%)

Phase 2 efficacy responses

Best response	All patients (n = 24)	Metastatic (<i>n</i> = 13)	Chemorefractory LABC (<i>n</i> = 11)
Overall response	11 (45.8%)	2 (15.4%)	9 (81.8%)
CR	4 (16.7%)	0 (0%)	4 (36.4%)
PR	7 (29.2%)	2 (15.4%)	5 (45.5%)
SD	4 (16.7%)	3 (23.1%)	1 (9.1%)
PD	7 (29.2%)	6 (46.2%)	1 (9.1%)
Treatment failure	2 (8.3%)	2 (15.4%)	0 (0%)

Adapted from Chung AW et al. Sci Transl Med. 2021 Dec 15;13(624):eabj5070. doi: 10.1126/scitranslmed.abj5070. Epub 2021 Dec 15. PMID: 34910551.

Complete Response from the TNBC Trial

46-Year-Old Woman with Stage 3 Metaplastic Breast Cancer



Adapted from Chung AW et al. Sci Transl Med. 2021 Dec 15;13(624):eabj5070. doi: 10.1126/scitranslmed.abj5070. Epub 2021 Dec 15. PMID: 34910551.

Efficacy in Patient Who Failed Standard of Care

Breast Cancer Specialist affiliated with I-SPY 2 trial tested tilarginine through single patient IND



Tilarginine Phase 2 Toxicity Profile

Tavidates	Grade 1 or 2	Grade ≥3	Any grade	Likely attributed to	Likely attributed to taxane
loxicity	79.2% (19 of 24)	20.8% (5 of 24)	83.3% (20 of 24)	L-NMMA	
Constitutional	10 (41.7%)	1 (4.2%)	11 (45.8%)	No	Yes
Gastrointestinal	10 (41.7%)	0 (0%)	10 (41.7%)	No	Yes
Peripheral neuropathy	7 (29.2%)	1 (4.2%)	8 (33.3%)	No	Yes
Dermatological	7 (29.2%)	1 (4.2%)	8 (33.3%)	No	Yes
Musculoskeletal	5 (20.8%)	0	5 (20.8%)	No	Yes
Hematological	5 (20.8%)	0	5 (20.8%)	No	Yes
Mucositis	4 (16.7%)	0	4 (16.7%)	No	Yes
Pulmonary	4 (16.7%)	0	4 (16.7%)	Yes	No
nfectious	0	2 (8.3%)	2 (8.3%)	No	Yes
Cardiovascular	2 (8.3%)	0	2 (8.33%)	Yes	No
Renal	0	1 (4.16%)	1 (4.16%)	No	Yes
Elevation of AST/ALT	0	1 (4.16%)	1 (4.16%)	No	Yes
Dehydration	0	1 (4.16%)	1 (4.16%)	No	Yes
Electrolyte imbalance	1 (4.16%)	0	1 (4.16%)	No	Yes
Hypotension	1 (4.16%)	0	1 (4.16%)	Yes	No
Neurological	1 (4.16%)	0	1 (4.16%)	No	Yes
Sinus tachycardia	1 (4.16%)	0	1 (4.16%)	Yes	No

Table 2. Phase 2 toxicities. AST, aspartate aminotransferase; ALT, alanine aminotransferase

Tilarginine is L-NMMA (NG-monomethyl-L-arginine) is a nitric oxide synthase (NOS) inhibitor, administered IV over 2 hours, with amlodipine pretreatment Amlodipine and aspirin were used as supportive care.

Adapted from Chung AW et al. Sci Transl Med. 2021 Dec 15;13(624):eabj5070. doi: 10.1126/scitranslmed.abj5070. Epub 2021 Dec 15. PMID: 34910551.

Metaplastic Breast Cancer is First Approval Opportunity

A highly treatment-resistant subset of TNBC with no FDA approved therapies

12 Month Median OS in iNOS high patients¹ Low iNOS High iNOS 0.8 Cumulative proportion surviving 0.2 0.1 P = .003No. at risk

Rare Subset with High Unmet Need

Incidence 1% of all breast cancer²

- First classified in 2000 by WHO
- No currently agreed treatment guidelines

Carcinomatous & sarcomatous features

- Similar to basal-like triple-negative breast cancer (TNBCs)
- Closely related to the claudin-low BC (loss of cell-cell adhesion genes)
- Enriched for stem cell-like and EMT characteristics
 - EMT = epithelial-to-mesenchymal transition

Highly chemo-refractory (10-15% ORR), poor survival²

3-year overall survival for LN+ Patients is 40% (v. 70% for basal-TNBC)

¹Role of RPL39 in Metaplastic Breast Cancer. Dave B et al. (j. Chang) JNCI J Natl Cancer Inst (2017) 109(6): djw292
 ²A comprehensive overview of metaplastic breast cancer: Features and treatments. Yan Q et al., Cancer Sci, 2024
 ³Classification of Metaplastic Carcinomas of the Breast. Tavassoli FA. Pathology Annual, Volume 27, Part 2, pages 89–119. 1992

Ongoing Fully Funded NIH Trial in Metaplastic Breast Cancer

4/9 patients in Phase 1 portion responded (PR + CR). 7/9 had clinical benefit (PR + CR + SD).



Clinical Trial in Metaplastic Breast Cancer



Patient Population (n=~35 pts)

1st and 2nd line locally advanced or metastatic metaplastic breast cancer patients



Design & Drug Regimen Open label single arm Phase 1/2 study Tilarginine + nab-paclitaxel + alpelisib



Trial Logistics 3 Sites: (Houston Methodist, MD Anderson, NCI Clinical)



Desired Outcomes ORR (primary), PFS (primary), OS (secondary),

¹Data derived from cBioPortal database of 7548 patients across 12 breast cancer studies Figure 3 in Reddy TP, Rosato RR, Li X, Moulder S, Piwnica-Worms H, Chang JC. A comprehensive overview of metaplastic breast cancer: clinical features and molecular aberrations. Breast Cancer Res. 2020 Nov 4;22(1):121. doi: 10.1186/s13058-020-01353-z.

Potential Registrational Pathway in Metaplastic Breast Cancer

Based on previous rare cancer approvals, one additional randomized trial may be sufficient

nab-paclitaxel + alpelisib + tilarginine

- Participants in this study will receive nab-paclitaxel, alpelisib and tilarginine, administered q3w cycles until disease progression, toxicity or until the participant withdraws from the study.
- Alterations in the Pl3K/Akt pathway have been linked with chemoresistance, especially in MpBC.
- As a result, this study includes alpelisib, a PI3K inhibitor, in the treatment regime.
- This study is targeting 36 participants at Houston Methodist, MD Anderson and the NIH
- This study is ongoing with 14 patients to date

nab-paclitaxel +/- tilarginine

- Targeting 40 60 subjects, first-line or second-line
- Purpose of study is to explore activity of tilarginine with chemo versus chemo alone
- Global study with multiple centers excluding those in ongoing PI3K study
- Treatment to be continued until disease progression, unacceptable toxic effects, withdrawal from the trial, or death, whichever occurs first.
- Primary endpoint will be ORR and PFS.
- Secondary endpoints include OS

alpelisib (Piqray[®], Novartis): FDA Approved May 2019 for use in combination with fulvestrant for HR+/HER-/PIK3CA-mutated, breast cancer following progression on endocrine-based regimen nab-paclitaxel (Abraxane[®], BMS) albumin nanoparticles: FDA approved in Jan 2005

Indication Expansion Opportunity in Neoadjuvant TNBC

26% of TNBC patients do not have adequate treatment options in the neoadjuvant setting



I-SPY KOLs believe NOS inhibition benefits some Immune-/DRD- patients via reversing immune exclusion

Ctr: paclitaxel; VC: veliparib-carboplatin-paclitaxel; Pembro: pembrolizumab Adapted from Wolf D et al., Redefining breast cancer subtypes to guide treatment prioritization and maximize response, Cancer Cell, 2022

Avasopasem in HR+ HER2- Breast Cancer





Avasopasem Restored Sensitivity to SoC in HR+ Cancers

Avasopasem is active preclinically in both HR+ breast cancer and prostate cancer cell lines with AcK68 alteration



HR+, Hormone Receptor positive; AcK68 = acetylation of lysine 68 on MnSOD enzyme; Q68 = model for AcK68 mutation; SoC = standard of care; ENZ = enzalutamide Adapted from Zhu Y et al., Lysine 68 acetylation directs MnSOD as a tetrameric detoxification complex versus a monomeric tumor promoter, Nature Communications, (2019)10:2399

Planned Grant Funded Ph1b/2 Trial in HR+ HER2- Breast Cancer

Opportunity to evaluate ability of dismutase mimetic to reverse resistance to fulvestrant and CDK4/6 inhibitors

Avasopasem **replaces** deactivated AcK68-modified endogenous superoxide dismutase, **resolving superoxide accumulation** and **resistance to SoC**



Patient Population

- 25 Patients with metastatic ER+/HER2- breast cancer patients
- Progressed on CDK4/6 & fulvestrant

Design & Drug Regimen

- Open label single arm Phase 1b/2
- Avasopasem + CDK4/6 inhibitor + fulvestrant

Adapted from Zhu Y et al., Lysine 68 acetylation directs MnSOD as a tetrameric detoxification complex versus a monomeric tumor promoter, Nature Communications, (2019)10:2399

Executive Summary and Key Milestones

Tilarginine potential to be first approved therapy in metaplastic breast cancer (MpBC)

- Fully grant funded Phase 1b/2 trial ongoing in MpBC with nab-paclitaxel and alpelisib (PI3K inhibitor)
 - 4/9 responses seen in Phase 1 portion
 - Next tranche of data expected end of 2025
- Proof of concept achieved in TNBC patients in combination with docetaxel
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 - 82% ORR in locally advanced patients



Avasopasem to be repositioned into HR+ HER2- breast cancer to restore sensitivity to 1st line patients

• Phase 1b/2 single arm investigator-initiated trial to begin in 1H2025



Cash balance supports multiple near-term data readouts

• Cash runway anticipated to fund operations into 2026

Galera Therapeutics Capitalization and Cash Position



Financial & Investor Information

OTC: GRTX

In December 2024, Galera entered into a private placement financing

- Net proceeds of \$3M combined with Galera's net cash of \$5.7M is expected to provide cash runway into 2026
- On an as-converted basis after accounting for the acquisition of Nova Pharmaceuticals, Inc. and the financing, the total shares
 of Galera common stock outstanding would be 217.8M

The following data is as of September 30, 2024

- Cash and cash equivalents \$8.455M
- Outstanding shares of common stock 54.4M

Appendix





Other Completed Trials

Two Completed Trials

Program	Preclinical	Phase 1	Phase 2	Results/Status
Avasopasem + SBRT x 5 days	Locally-Advanced Panc Pilot randomized Phase 1-2 o	reatic Cancer (n=42) combo trial		Improved response rate, tumor control, PFS and OS
Tilorginino				
+ pembrolizumab	Ph 1b single-arm combo tria	l (HMRI)		Combination Well tolerated
Tilargining is L. NMMA (NG, monomoth)	(L orginino), o pitrio ovido punthogo (NG	29) inhibitor, administered IV over	2 hours with Amladining pro	trootmont

Tilarginine is L-NMMA (NG-monomethyl-L-arginine), a nitric oxide synthase (NOS) inhibitor, administered IV over 2 hours, with Amlodipine pretreatment SBRT is Stereotactic Body Radiotherapy, where high doses are administered over a 1-2 week period HMRI = Houston Methodist Research Institute

NOS Inhibition Reverses Immune Exclusion of T Cells

Excess nitric oxide creates an immunosuppressive tumor microenvironment



1) Ridnour et al., Cancer Research Communications, 2024; 2) Jayaraman et al., J. Immunology, 2012; 3) Glynn et al., J. Clin., Invest., 2010

Combining Tilarginine with Immune Checkpoint Blocker

Opportunity to evaluate NOS inhibition in combination with pembrolizumab



Patient Population²

- 12 Patients with refractory solid tumors who are naïve to anti-PD1 therapy
- Metastatic ER+/HER2- breast cancer patients who have progressed on CDK4/6 & fulvestrant

Design & Drug Regimen²

- Single center (Houston Methodist)
- Open label single arm Phase 1b/2a of Tilarginine and pembrolizumab

¹Tcyganov et al., Cancer Cell, 2022; 2) NCT03236935

Avasopasem

in Locally Advanced Pancreatic

Cancer





Synergy with High-Dose RT (SBRT)

High-fraction focal irradiation of human tumor xenografts (H1299 NSCLC) in mice



Preclinical results; Sishc, et al., Science Translational Medicine 12 May 2021:Vol. 13, Issue 593

H_2O_2 build-up in Cancer Cell \rightarrow Synergy with SBRT

Synergy eliminated with doxycycline-induced catalase in genetically modified H1299^{CAT} cells



Preclinical results; Sishc, et al., Science Translational Medicine 12 May 2021:Vol. 13, Issue 593

Proof of Concept Trial in Pancreatic Cancer

Completed 42-Patient Double-blind, Placebo-controlled, Randomized Trial



Final Safety Analysis - Regimen Generally Well Tolerated

12-Month Safety Follow-up (% of Patients)

Baseline Patient Characteristics					
Baseline Characteristics	Placebo (n=18)	GC4419 (n=24)			
Median age in years	68	72			
Male / Female	39% / 61%	67% / 33%			
Borderline resectable / Unresectable	11% / 89%	29% / 71%			
ECOG Performance status 0/1	50% / 50%	50% / 46%			
Prior chemo, duration median (range)	22 weeks (12.0–36.3)	18 weeks (9.1–67.1)			
CA19-9 at randomization, median (range)	71 (0.5–5505)	31 (0.3–719)			
Smokers/Nonsmokers	17% / 83%	8% / 92%			

Similar SBRT Toxicity Across Arms

AEs Conside by Investigat	ered related tor to SBRT	SBRT + PBO	SBRT + AVA
≤90 davs	Any AE	67%	46%
after	GI AE	44%	42%
SBRT	Severe AE	0%	0%
>90 davs	Any AE	22%	25%
after	GI AE	17%	21%
SBRT	Severe AE	11%	8%

• No bleeding ulcers by 12-week endoscopy

AE = Adverse Event, GI AE = Gastrointestinal AE

Efficacy Signal in Locally Advanced Pancreatic Cancer (N=42)

Regimen consisted of radiotherapy (SBRT) + avasopasem vs radiotherapy + placebo



¹Adapted from Figure 2 in Taniguchi CM et al, Lancet Oncol 2023; 24: 1387–98



Best in-field tumor response from baseline²

²Adapted from Figure 3 in Taniguchi CM et al, Lancet Oncol 2023; 24: 1387–98