BIO International Convention – June 2018

Advanced Epigenetic Technology

Todays Agenda for Zenith Capital Corp.

1. Corporate Profile
2. Epigenetic Mechanism Review
3. Prostate Cancer Rationale Review
4. Phase 1 Details & Early Results
5. Enzalutamide Combination Trial – Phase 2a
6. Next Steps

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Share Structure Profile

Founded	Corporate spin out from Resverlogix in June 2013
Status	Private company, full reporting issuer
Cash Raised 2014-2016	US$44MM @ $1.00 USD per share (all pre-clinical results based)
Enterprise Value est.	$325 USD ($2.50 USD/Share) est.
Shares Outstanding	125.2 MM 134.0 MM fully diluted 10MM additional shares will be sold shortly
Cash Burn	$2 MM per quarter - Current

Epigenetics Mechanism

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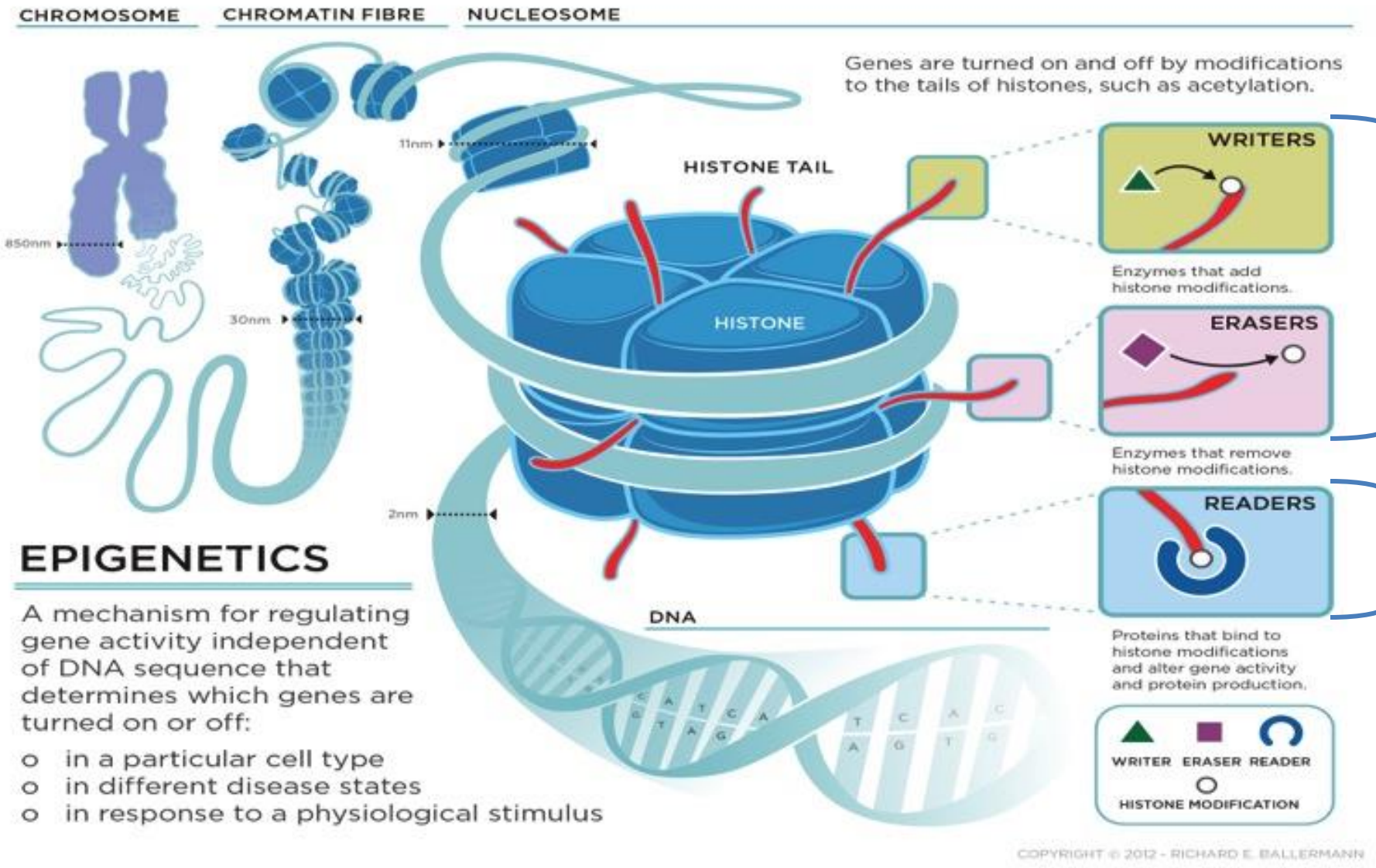
Epigenetics, the Mechanism Behind Our Approach



Early Epigenetic Approach

Advanced Epigenetic Approach

Zenith's BRD4 Targets Resistance Mechanisms

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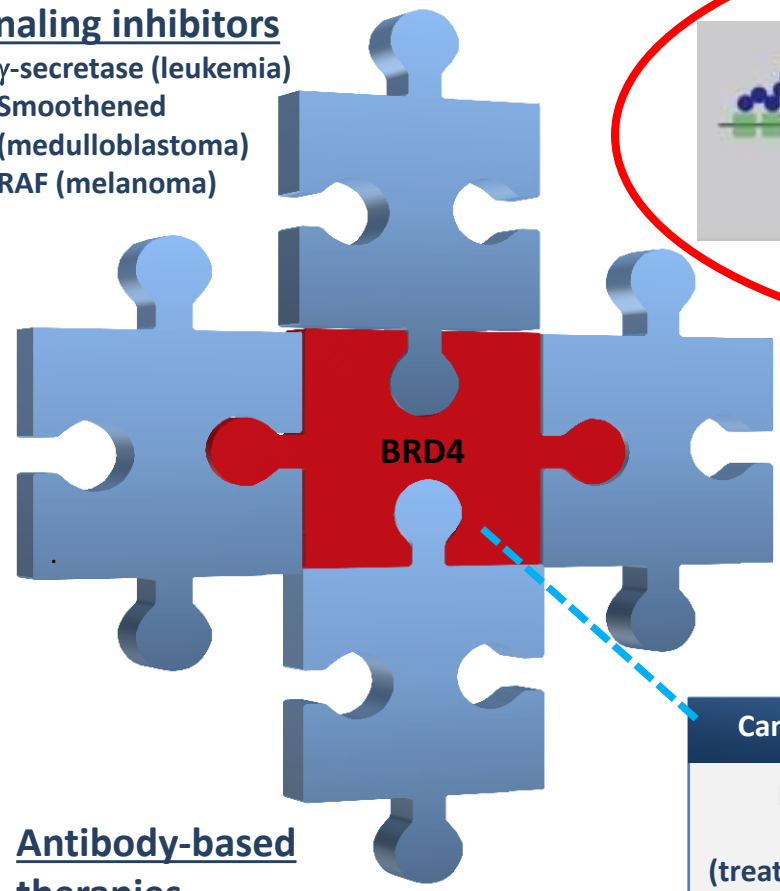
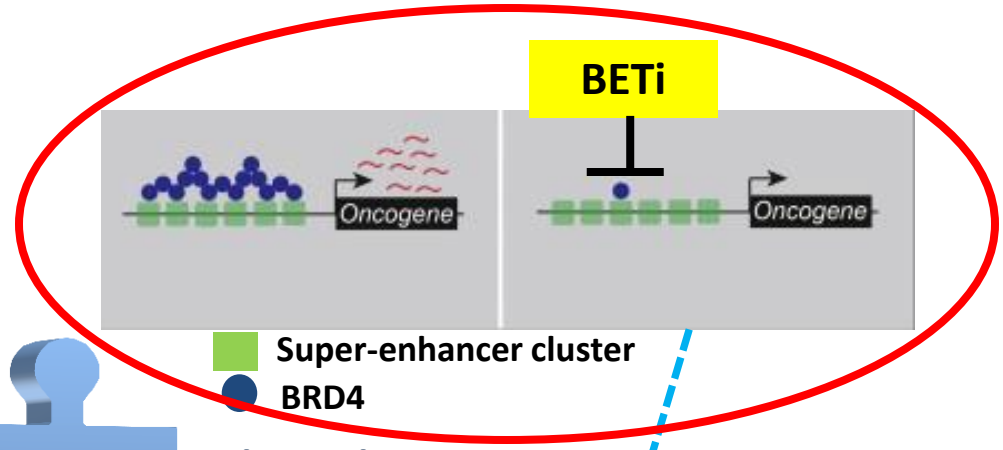
Signaling inhibitors
- γ-secretase (leukemia)
- Smoothened (medulloblastoma)
- RAF (melanoma)

Hormone-deprivation therapies
- Androgen (prostate cancer)
- Estrogen (breast cancer)



Antibody-based therapies
- Rituximab (lymphoma)



Chemotherapies
- Tamoxifen (breast cancer)
- Everolimus (breast cancer)

Cancers Escape Mechanism

Resistance mechanism involving BRD4 (treatment with BETi resensitizes cancers to these therapies)

Resistance to several standard of care treatments does not impede sensitivity to BETi

Epigenetic combination therapies - addressing resistance & increasing revenue of $B franchises

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Hormone-Modulaton
Androgen (CRPC)
Estrogen (breast cancer)

DNA Repair
PARPi (Breast, Ovarian, CRPC)

Kinase-Signaling
PI3K (breast, CRPC)
RAF (melanoma)

Immuno-Oncology
Checkpoint Inhibitors (melanoma, NSCLC, etc.)

Revenue

Current multi $B Markets
- AR antagonists (lead program)
- PD-1/PD-L1Mabs
- CDK 4/6 inh.
- PARPi

Increase duration of therapy

Increase patient pool (responders)

Differentiation

Increase IP life

Combination with ZEN-3694 (BETi)

Prostate Cancer Rationale Review

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ZEN-3694 Potential in Patients Developing mCRPC Resistance to Enzalutamide

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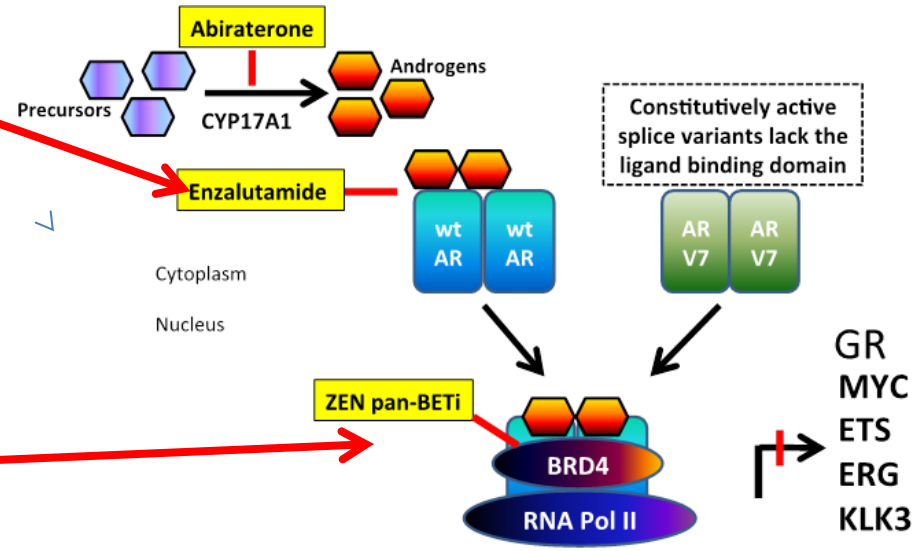
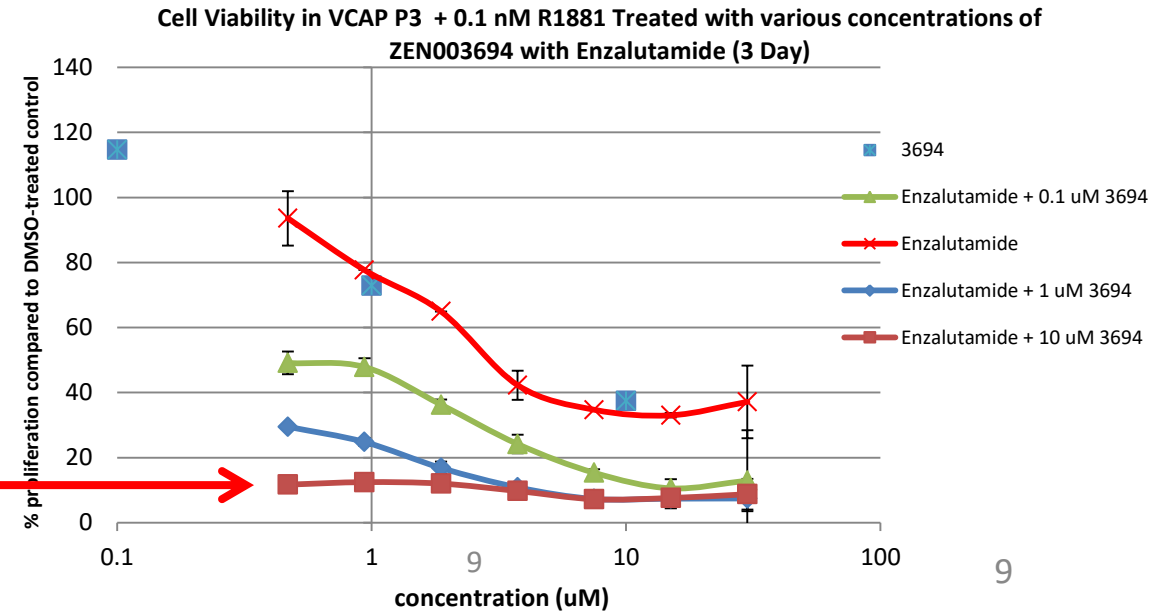
ZEN-3694 works down stream of current therapies

ZEN-3694 works where resistance to existing lead drugs, like Enzalutamide, has evolved

The combination of ZEN-3694 and enzalutamide shows strong synergy and is expected to reduce the development of resistance





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Potential Resistance Pathways in CRPC in response to Enzalutamide and/or Abiraterone

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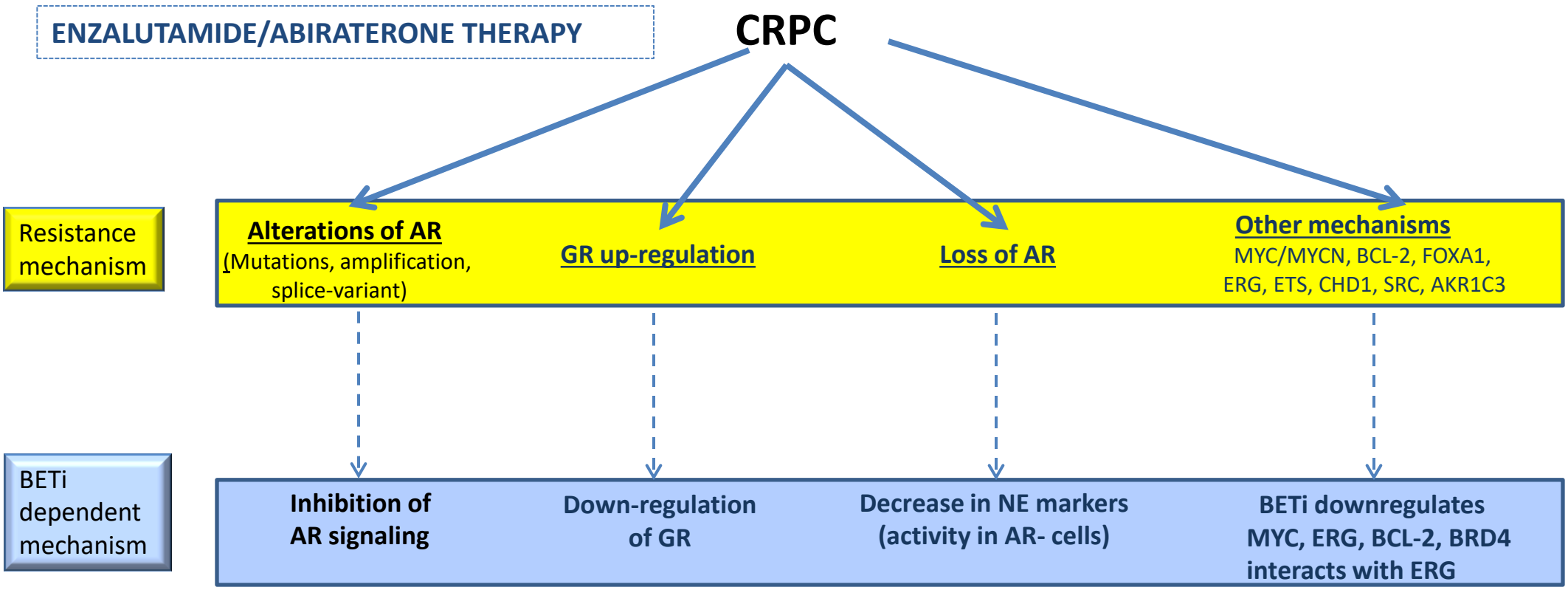

ZEN-3694 shows good efficacy in different CRPC models that are resistant to AR antagonists

Phase 1 Details & Results

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Zenith's Principal Investigators

Name	Institution	Comments
Eric Small, MD *Chief, Dept. of Medicine* **Rahul Aggarwal, MD** *Developmental Therapeutics Specialist, Genitourinary Oncologist*	University of California, San Francisco (UCSF)	Developed abiraterone - #2 CRPC drug, owned by J&J.
Howard Scher, MD *Chief, Genitourinary Oncology* **Wassim Abida, MD, PhD** *Medical Oncologist*	Memorial Sloane Kettering Cancer Center (MSKCC)	Developed enzalutamide - #1 CRPC drug, now owned by Pfizer. Developing ARN-509 for J&J
Joshi Alumkal, MD *Associate Professor*	Oregon Health Sciences University (OHSU)	Expert in epigenetics in prostate cancer research
Allan Pantuck, MD *Professor, Dept. of Urology*	University of California Los Angeles (UCLA)	Involved in enzalutamide and provenge development
Elizabeth Heath, MD *Professor, Dept. Hematology/Oncology*	Karmanos (Wayne State)	Genitourinary oncology specialist
Mark Fleming, MD *Oncologist*	Virginia Oncology Associates	Community site

ZEN-3694 development in mCRPC- Phase 1 single agent study results

2016		2017	
1H	2H	1H	2H

Single agent dose escalation; enzalutamide and/or abiraterone failures N~12

Single agent expansion at RP2D; same population as dose escalation N=12

Key Learnings

- Maximum tolerated dose (MTD) defined ✓
- Dose proportional PK ✓
- Good safety profile, prolonged dosing without dose interruption/reduction is feasible ✓
- Target modulation shown at doses below MTD ✓
- Some single agent anti-tumor activity/disease stabilization observed in multiple patients ✓

Single agent study key to understanding drug characteristics and supporting combination study

Patient X: Prolonged disease stabilization

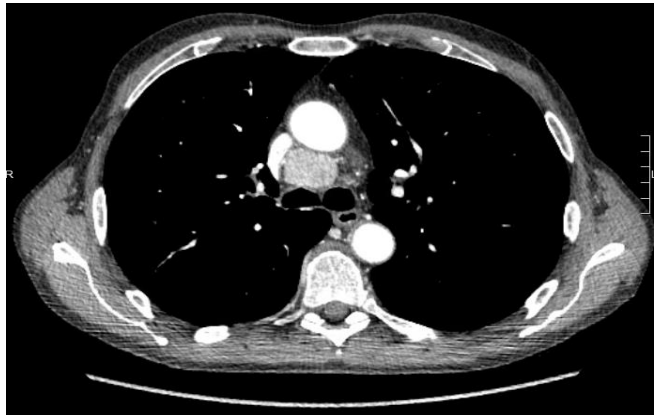
Prior Therapy for mCRPC

- Provenge
- Enzalutamide: 6/5/2014 – 5/5/2016 – acquired resistance
- Abiraterone: 5/22/2016 – 8/12/2016 – primary resistance

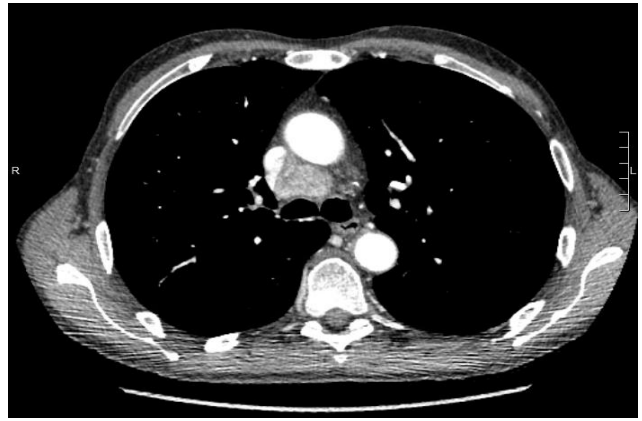
- ZEN-3694: 8/24/2016 – 7/16/2016, 45 weeks

Stable mediastinal nodes over 8 months

Study Entry



32 Weeks



Enzalutamide Combination Trial – Phase 1b/2a

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ZEN-3694 Phase 2a Study Design

Phase 2a, open label, combination, 3x3 dose escalation/confirmation

mCRPC, chemo-naïve, enzalutamide naïve, prior progression on abiraterone

X mg QD ZEN-3694
160 mg QD enzalutamide
N = 3 (planned)

Dose escalation cohorts

MTD / RP2D Confirmation

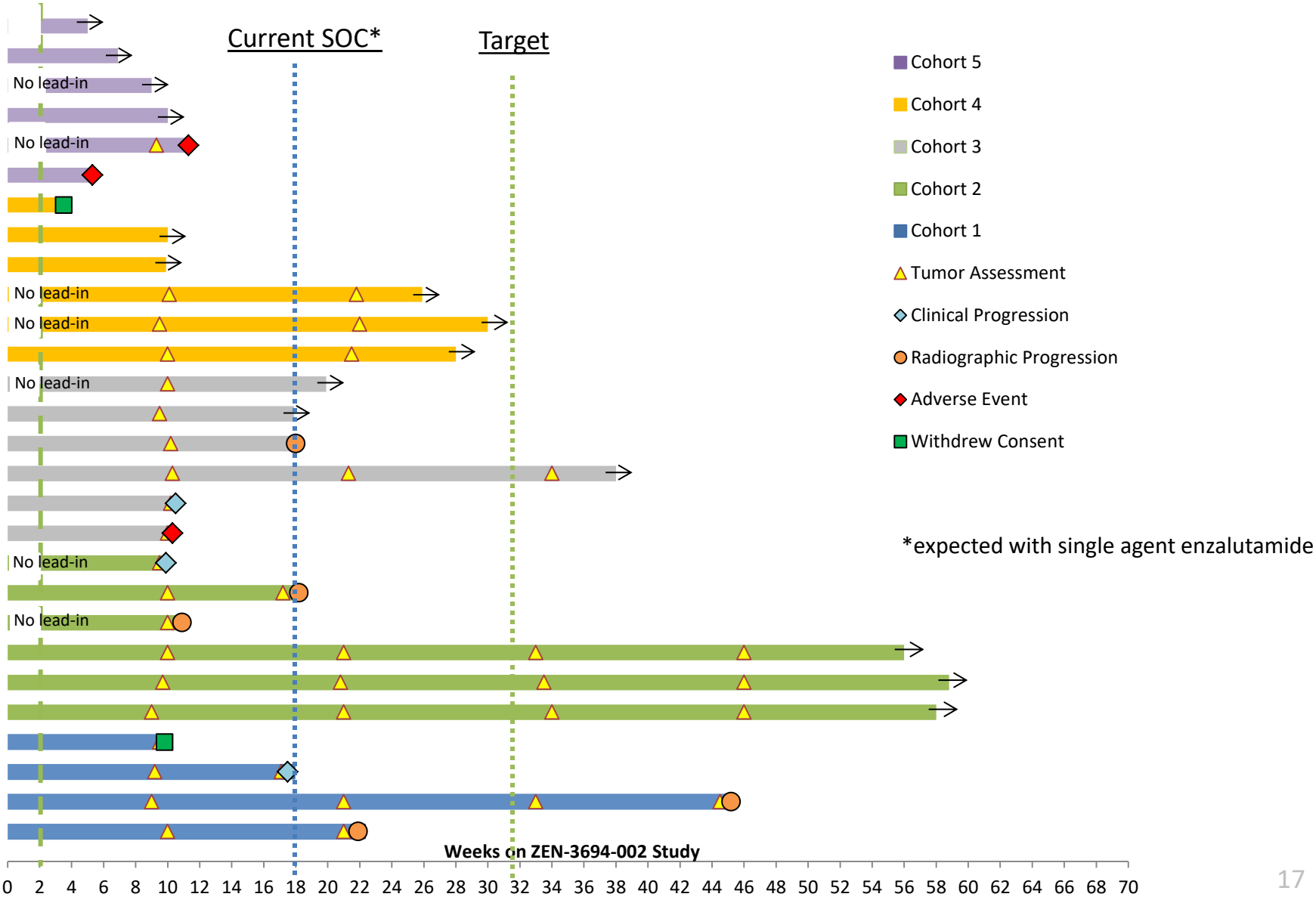
Seven sites, UCSF and MSKCC leading

MTD: Highest dose with ≤1/6 patients with DLT

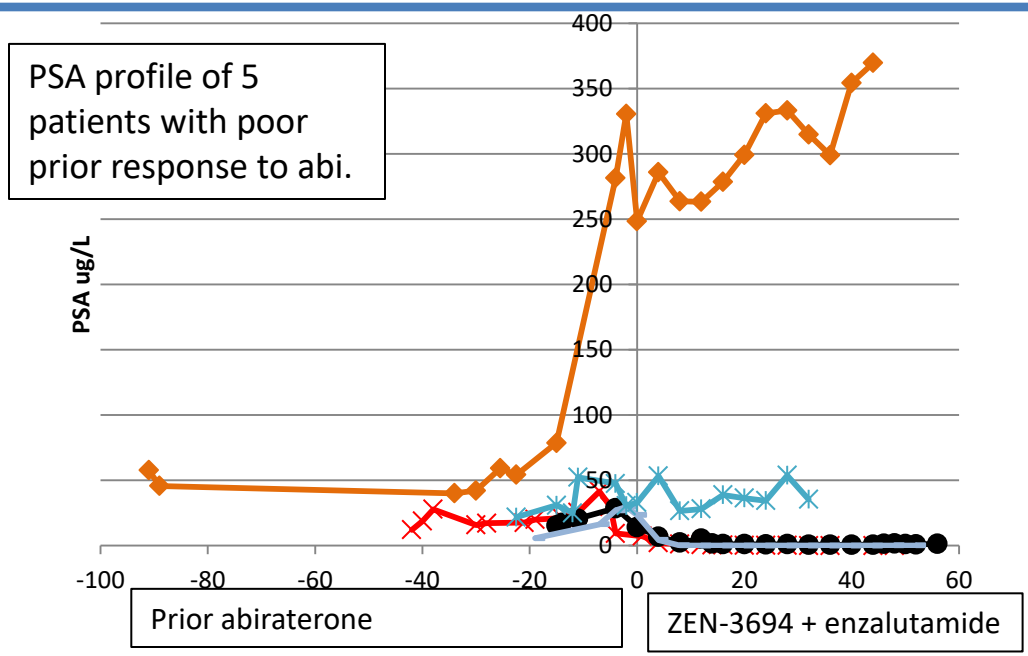
Expansion Cohort A
Enza naïve, progression on abiraterone

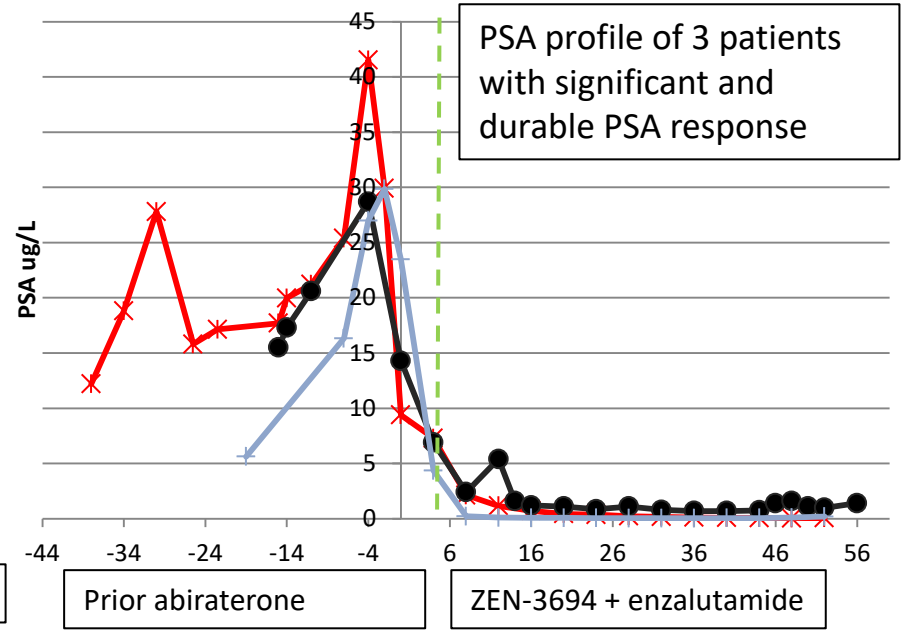
Expansion Cohort B
Biochemical progression on enzalutamide

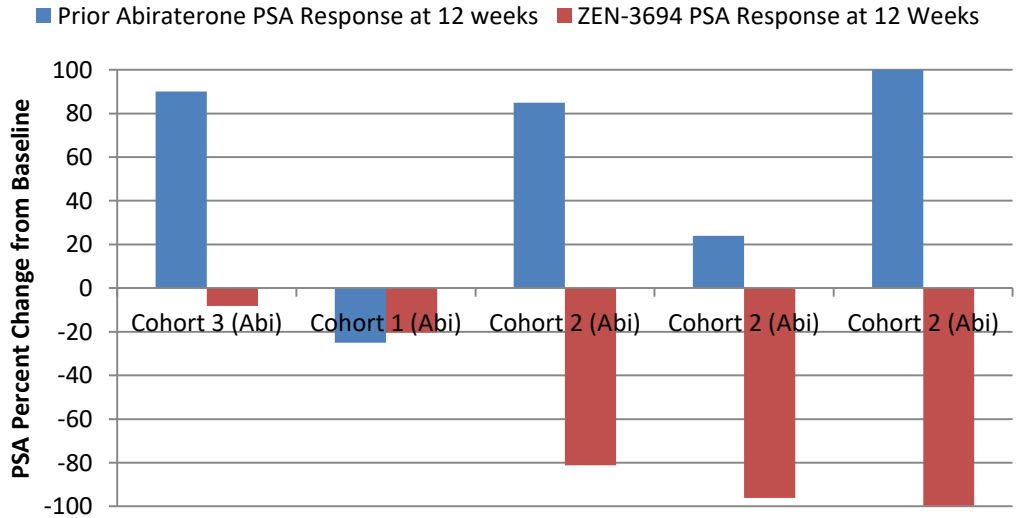
ZEN-3694 + enzalutamide is active: Increase in treatment duration relative to single agent enzalutamide



Strong PSA response with ZEN-3694 + enzalutamide in patients with poor prior response to abiraterone







Extensive translational medicine plan for deciphering MOA and designing future biomarker driven trials

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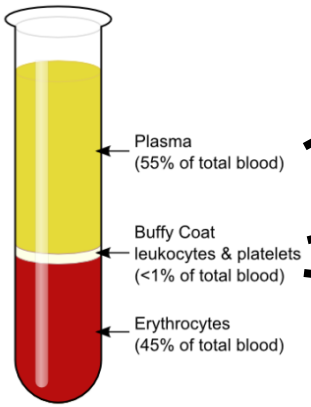
Whole blood



- **CTCs** ==>
  - Enumeration, AR-C, AR-N
  - MYC, AR-V7, GR
  - HRD signature
- **Whole blood** ==>
  - PD marker assay to measure target modulation
  - Nanostring cancer immune panel
  - AR-V7 target engagement
- **PBMCs** ==>
  - Immune Tolerance Markers, T cell subtypes, TCR sequencing
- **Plasma** ==>
  - Exploratory, Metabolomics/exosomes/protein markers, cytokine panel

Tumor biopsy

½ FFPE

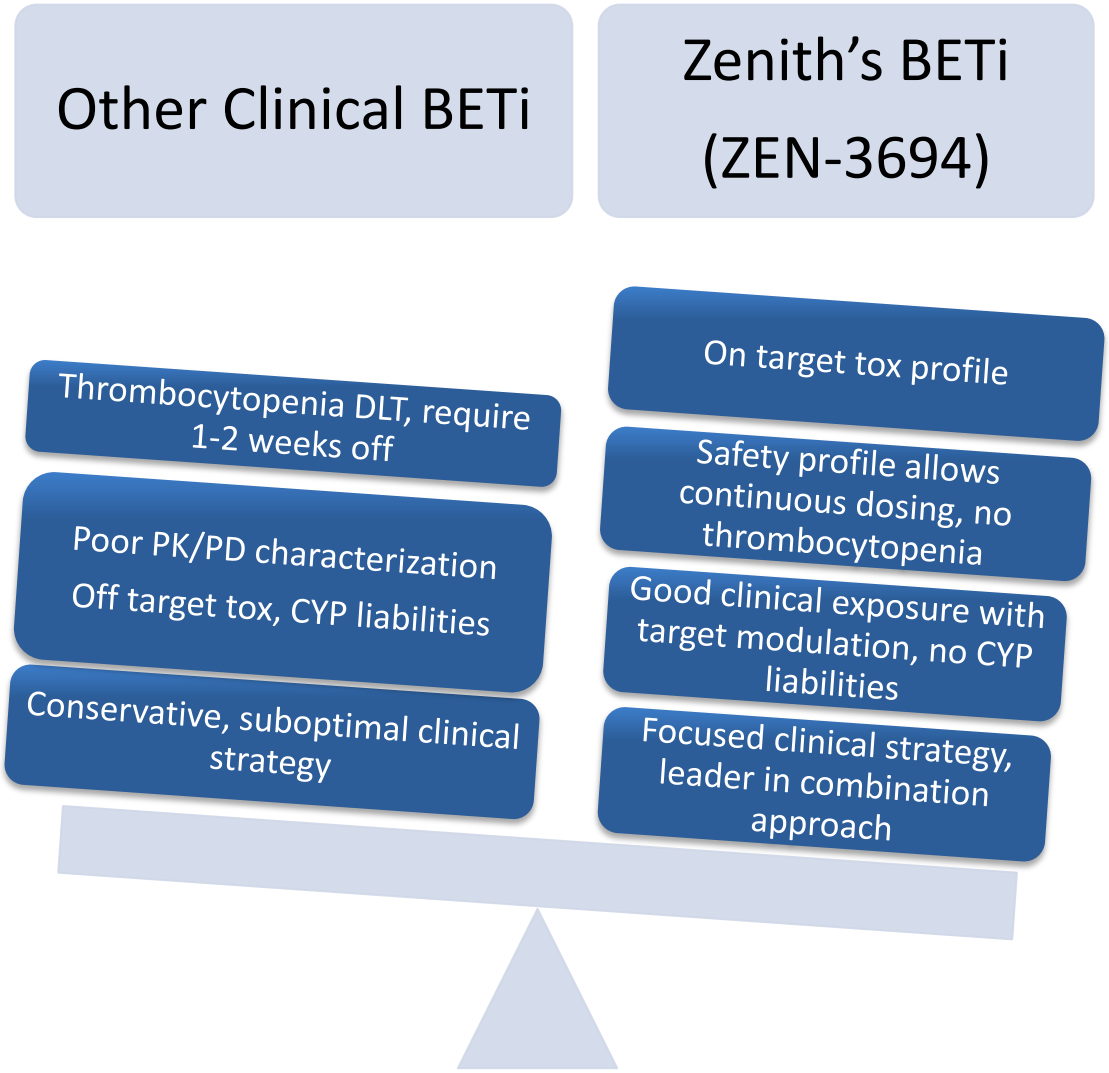
- **IHC** ==>
  - MYC
  - AR, GR
  - PD-L1, CD8+ TIL
  - Histology

½ Frozen

- **RNA-seq** ==>
  - Expressed mutations
  - Fusions and splice variants
  - Expression profiles and pathway analysis (AR/GR signaling, NFkB, etc.)
  - Immuno-onc markers

Translational program designed for molecular profiling ARi resistant patients and effect of ZEN-3694 on resistant markers, potential correlation of response to molecular signature

Zenith's BETi program is clinically differentiated



Other companies developing BETi for CRPC
Gilead – Phase 1b/2a (Single agent and combination)
GSK – Phase 1, just initiated (combination)

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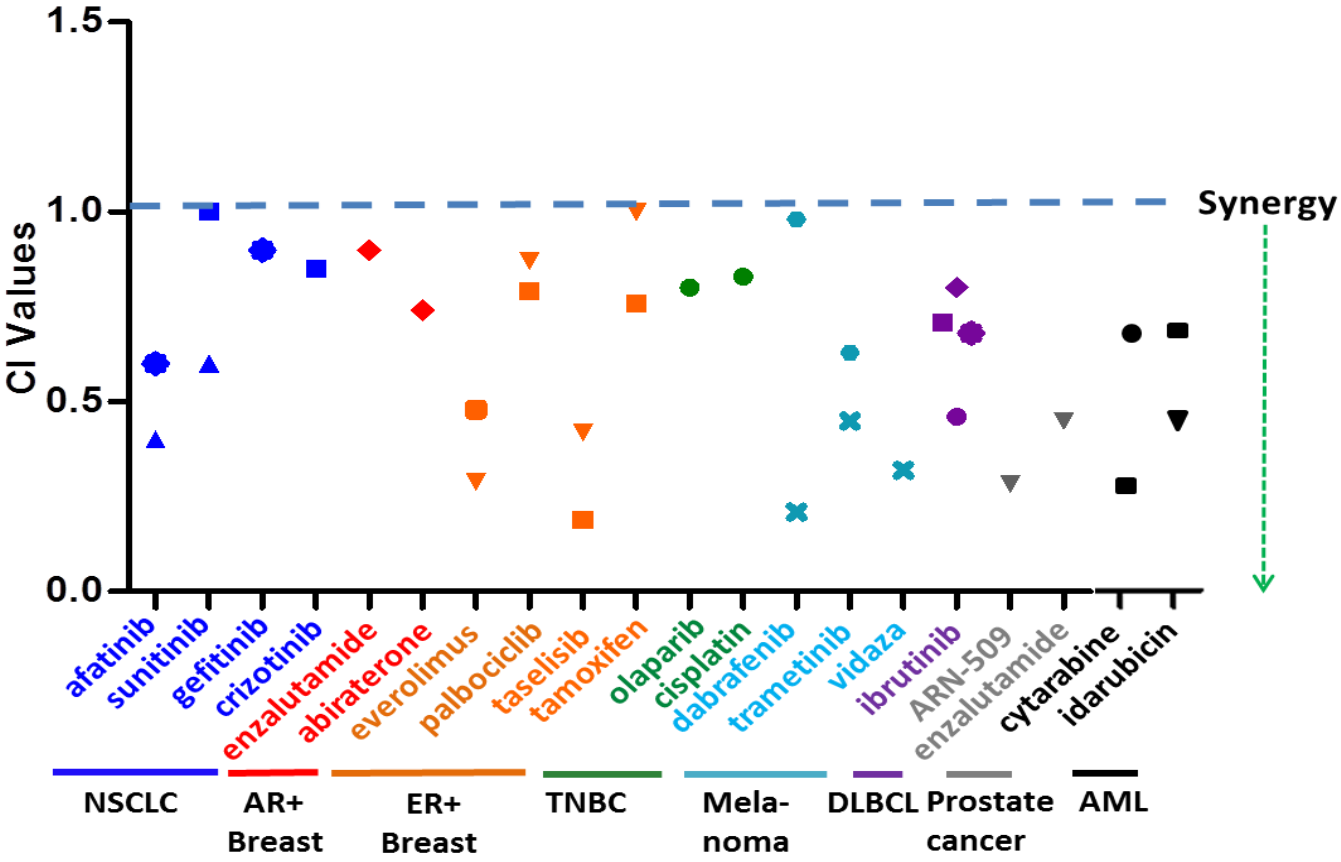
ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs



Indication		Cell line (mutation)
NSCLC	▲	H1975 (EGFR L858R T790M)
	⬢	H820 (EGFR T790M)
	■	H2228 (ALK)
AR+ Breast	◆	MDA-MB-453
ER+ Breast	■	MCF-7 (ER+)
	▼	ZR-75-1 (ER+)
TNBC	●	HCC1937 (BRCA1)
Melanoma	✖	C32 (BRAF V600E)
	⬢	A375 (BRAF)
DLBCL	⬢	CARNAVAL (MYC/BCL2)
	●	OCI-LY18 (MYC/BCL2)
	◆	NU-DUL-1
	■	OCI-LY3 (A20)
Prostate	▼	VCAP (AR AMP/AR-V7)
AML	■	MV4-11 (MLL-AF4/FLT3-ITD)
	●	OCI-AML2 (DNMT3A/MLL)
	▼	OCI-AML3 (DNMT3A/NPM1)

CANCER

Repression of BET activity sensitizes homologous recombination–proficient cancers to PARP inhibition

Article

Cancer Cell

BRD4 Inhibition Is Synthetic Lethal with PARP Inhibitors through the Induction of Homologous Recombination Deficiency

Report

Cell Reports

BET Bromodomain Inhibition Synergizes with PARP Inhibitor in Epithelial Ovarian Cancer

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