BIOTECH Showcase – Clinical Advancements Update

Advanced Epigenetic Technology

January 8th, 2018

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 1b
6. Next Steps

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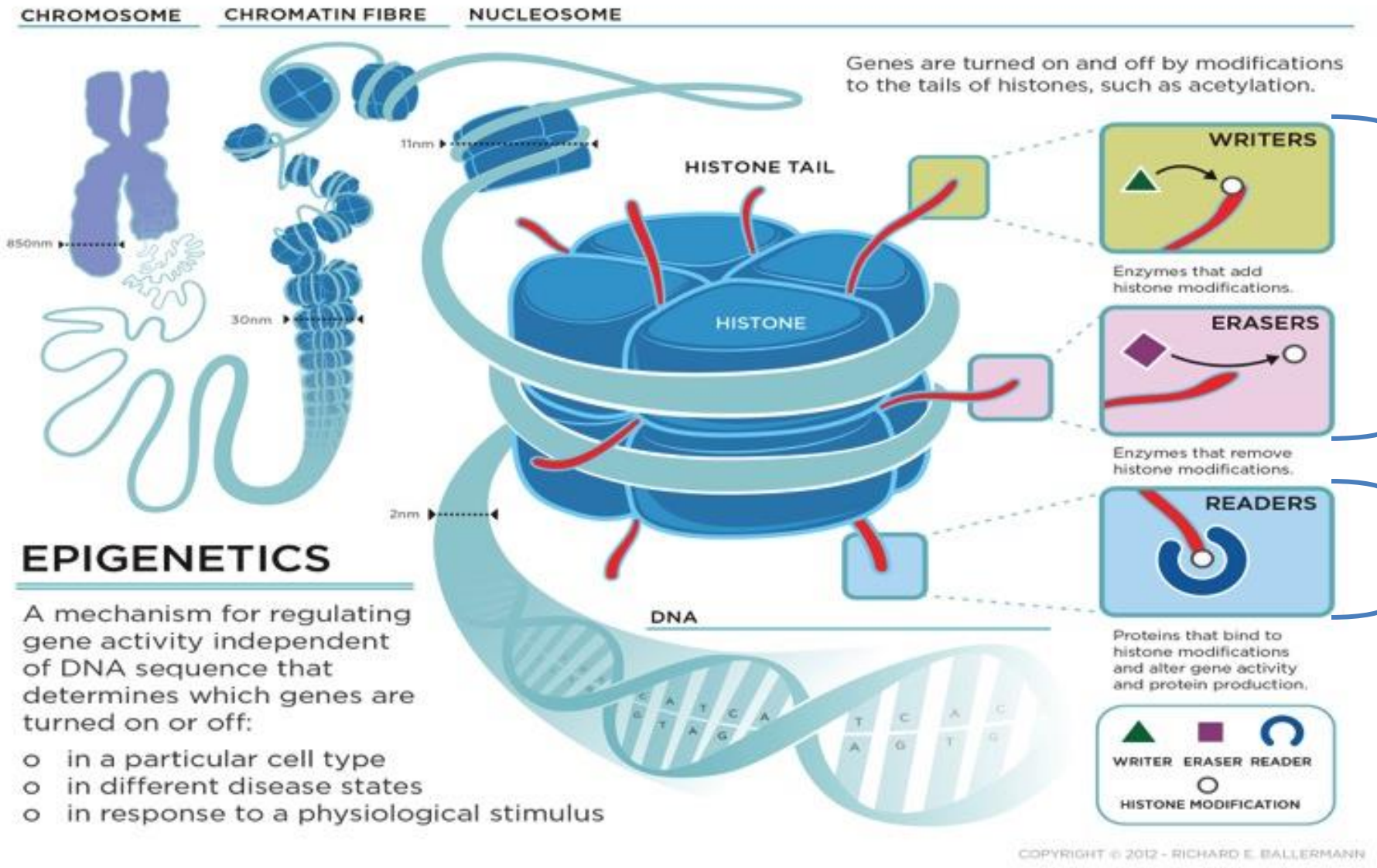
Share Structure Profile

Founded	Corporate spin out from Resverlogix in June 2013
Status	Private Company, full reporting issuer
Cash Raised 2014-2016	Approx. US$44MM @ $1.00 USD per share (all pre-clinical results based)
Enterprise Value est.	$350 to $375MM USD ($2.50 to $3.00 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

Epigenetic Mechanism

Epigenetics: the Mechanism Behind Our Approach



Early Epigenetic Approach

Advanced Epigenetic Approach

Zenith's BRD4 Targets Resistance Mechanisms

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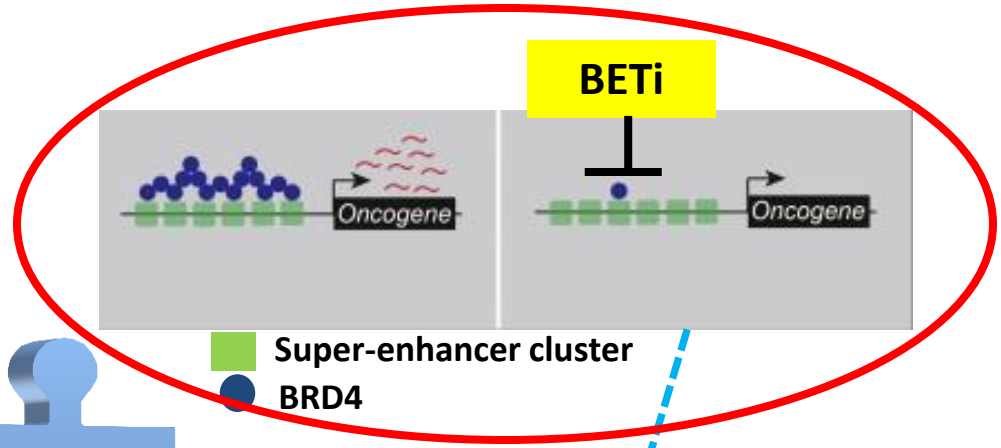
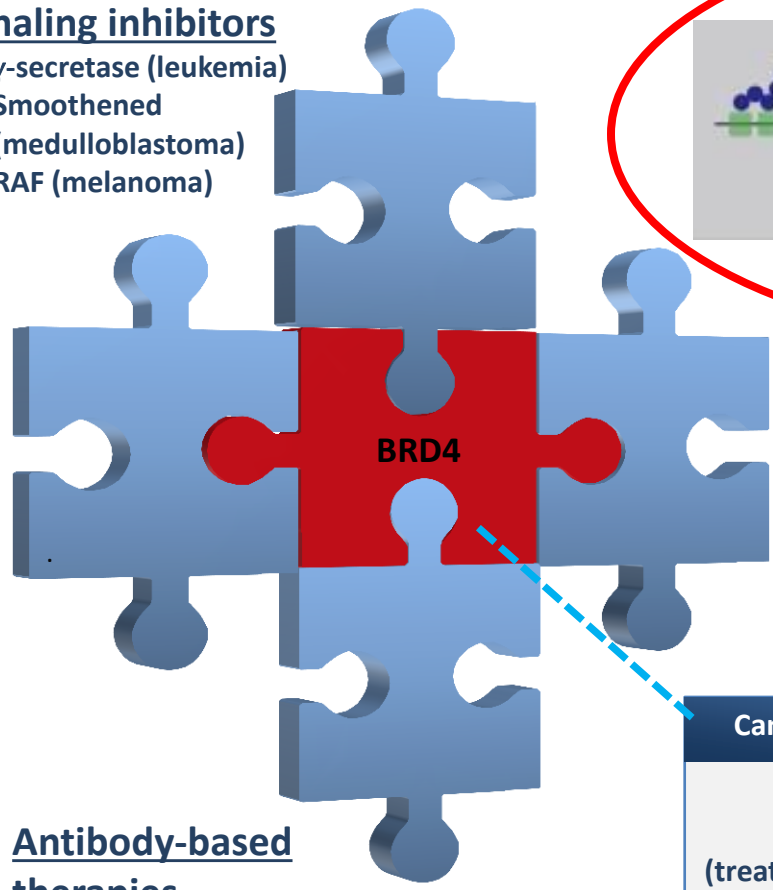


Signaling inhibitors

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

Hormone-deprivation therapies

- Androgen (prostate cancer)
- Estrogen (breast cancer)



Chemotherapies

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

Antibody-based therapies

- Rituximab (lymphoma)

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

Developing Epigenetic Combination Therapies to Address Resistance & Significantly Increase Revenue of $B Franchises

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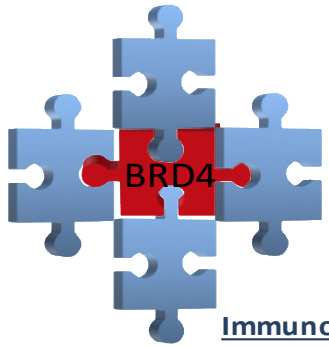
Hormone-Modulaton
Androgen (CRPC)
Estrogen (breast cancer)



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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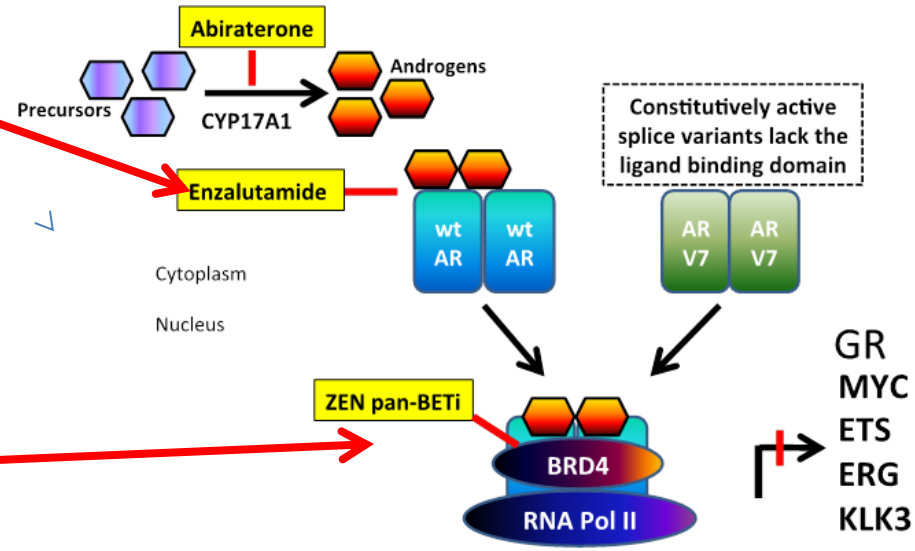
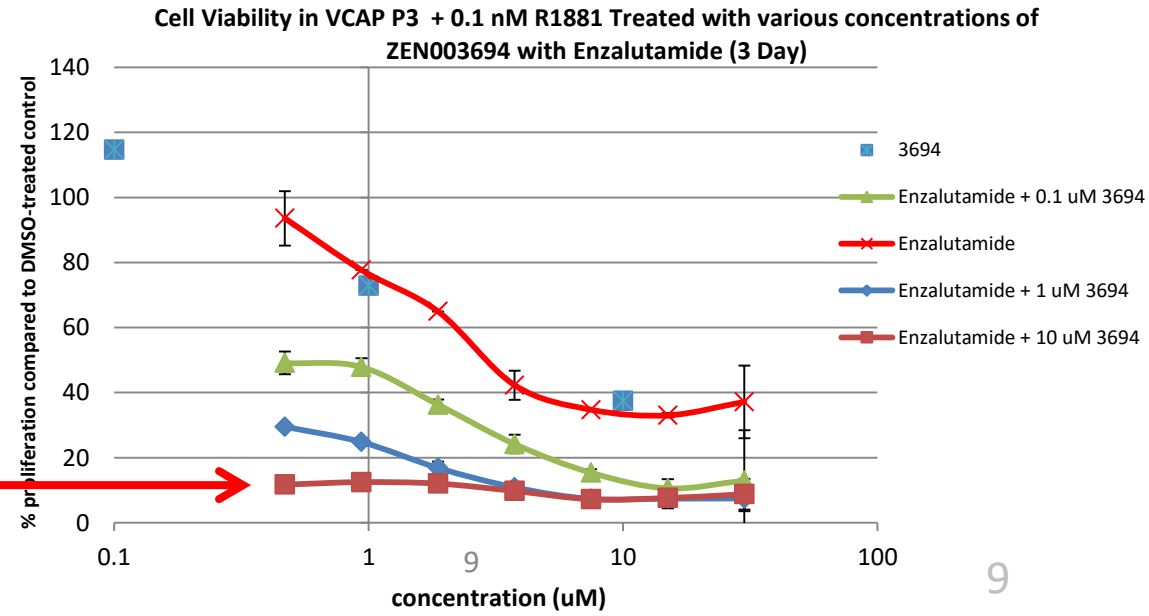
ZEN-3694 works down stream of current therapies

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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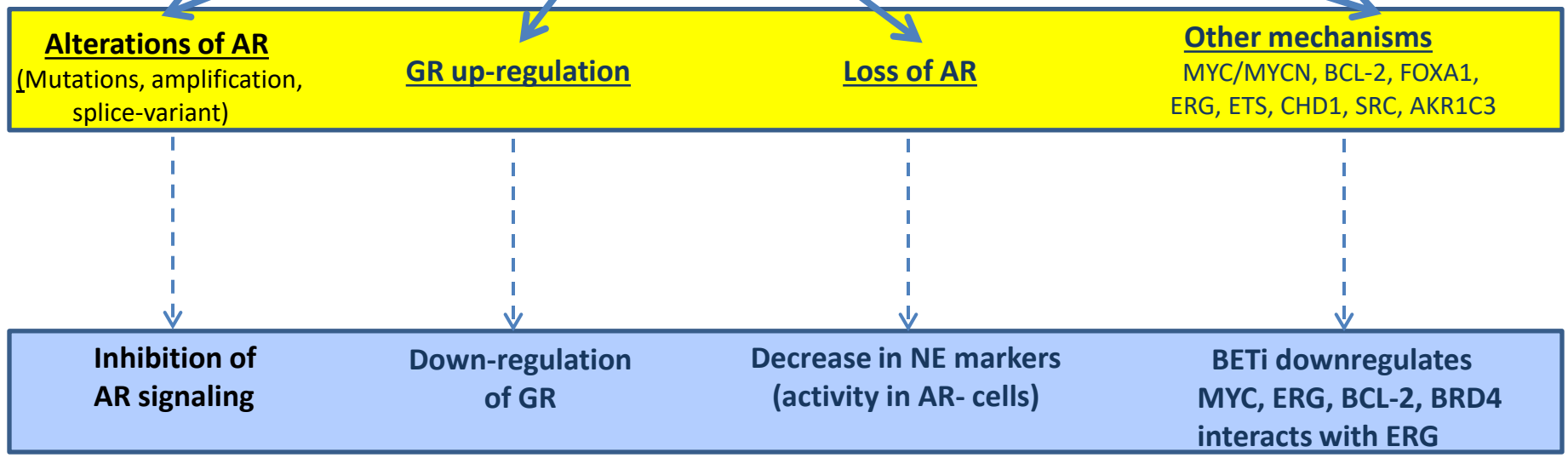
ENZALUTAMIDE/ABIRATERONE THERAPY

CRPC



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 Phase 1 Study Endpoints

Primary

- Safety, tolerability, maximum tolerated dose (MTD), and recommended Phase 2 dose (RP2D) of ZEN-3694

Secondary

- Pharmacokinetics (PK)
- Preliminary clinical activity
  - PCWG2 Criteria: PSA response rate, Radiographic response rate, PFS
  - Circulating Tumor Cell (CTC) response rate

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 ✓

Ongoing activities

- Fully enrolled and dosed,
- Study closeout ongoing, follow on data analysis continues

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

Patient X: Prolonged disease stabilization

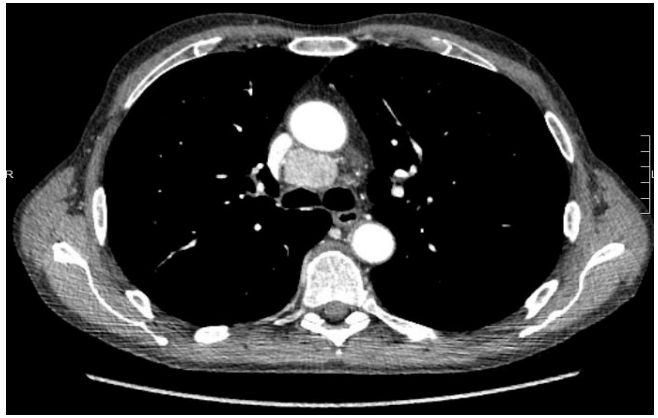
Prior Therapy for mCRPC

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

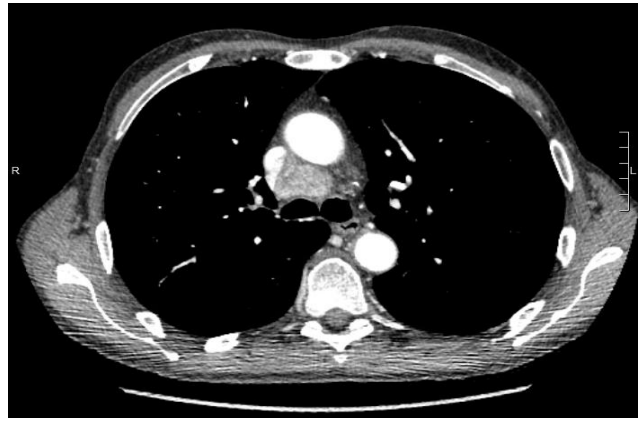
- ZEN-3694: 8/24/2016 – 7/16/2016, 45 weeks

Stable mediastinal nodes over 8 months

Study Entry



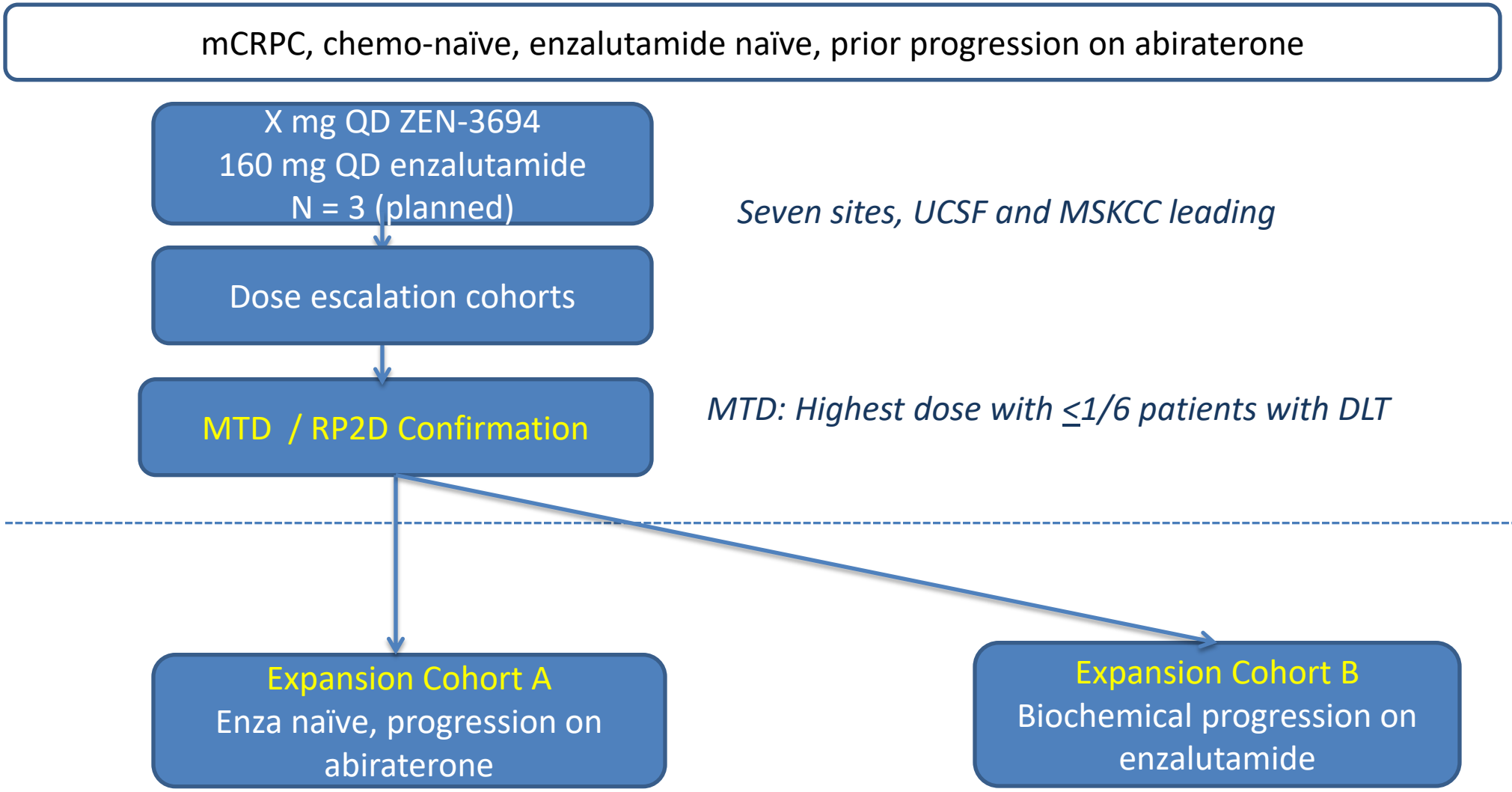
32 Weeks



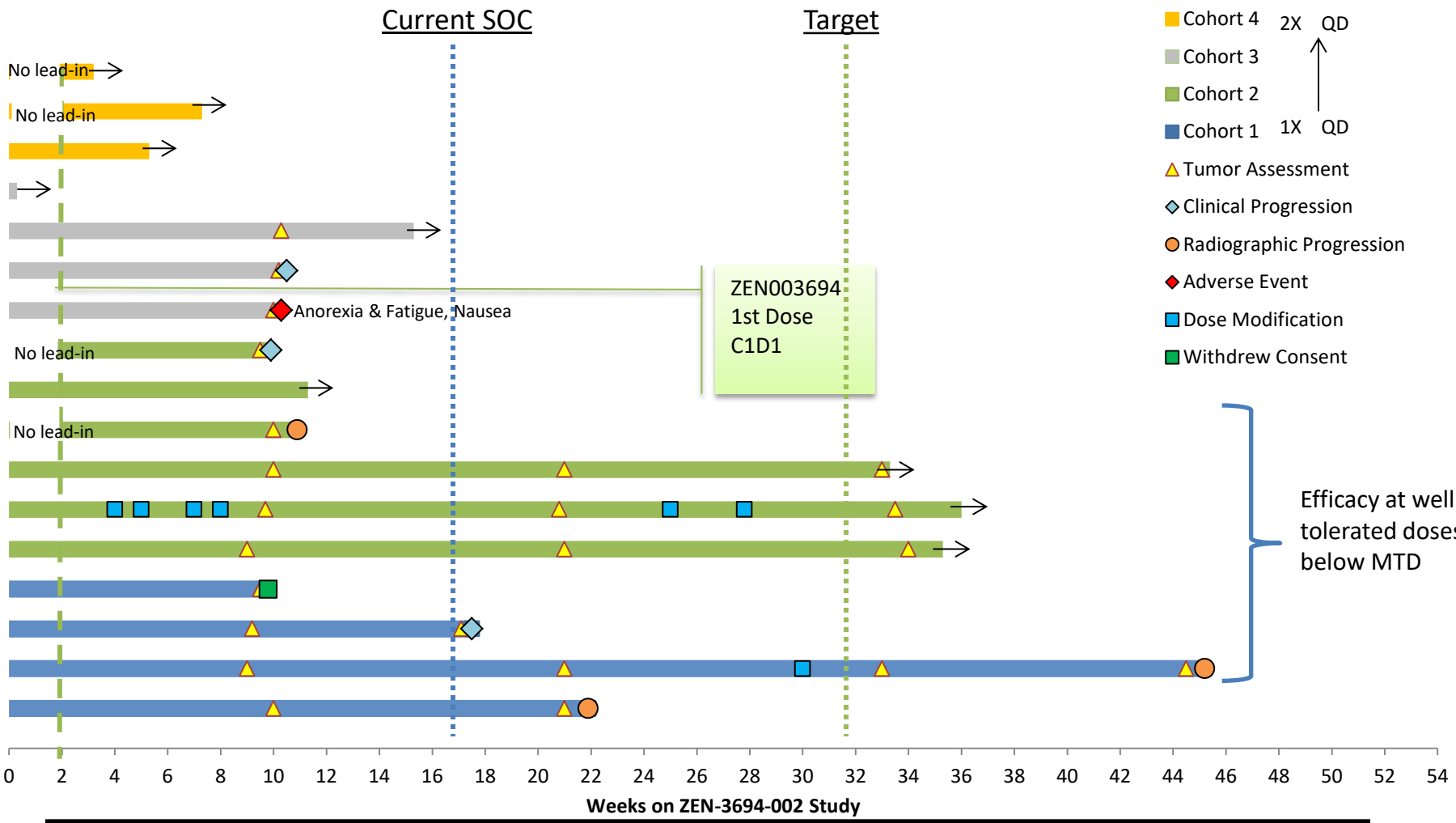
Enzalutamide Combination Trial – Phase 1b

ZEN-3694 Phase 1b Study Design

Phase 1b, open label, combination, 3x3 dose escalation/confirmation



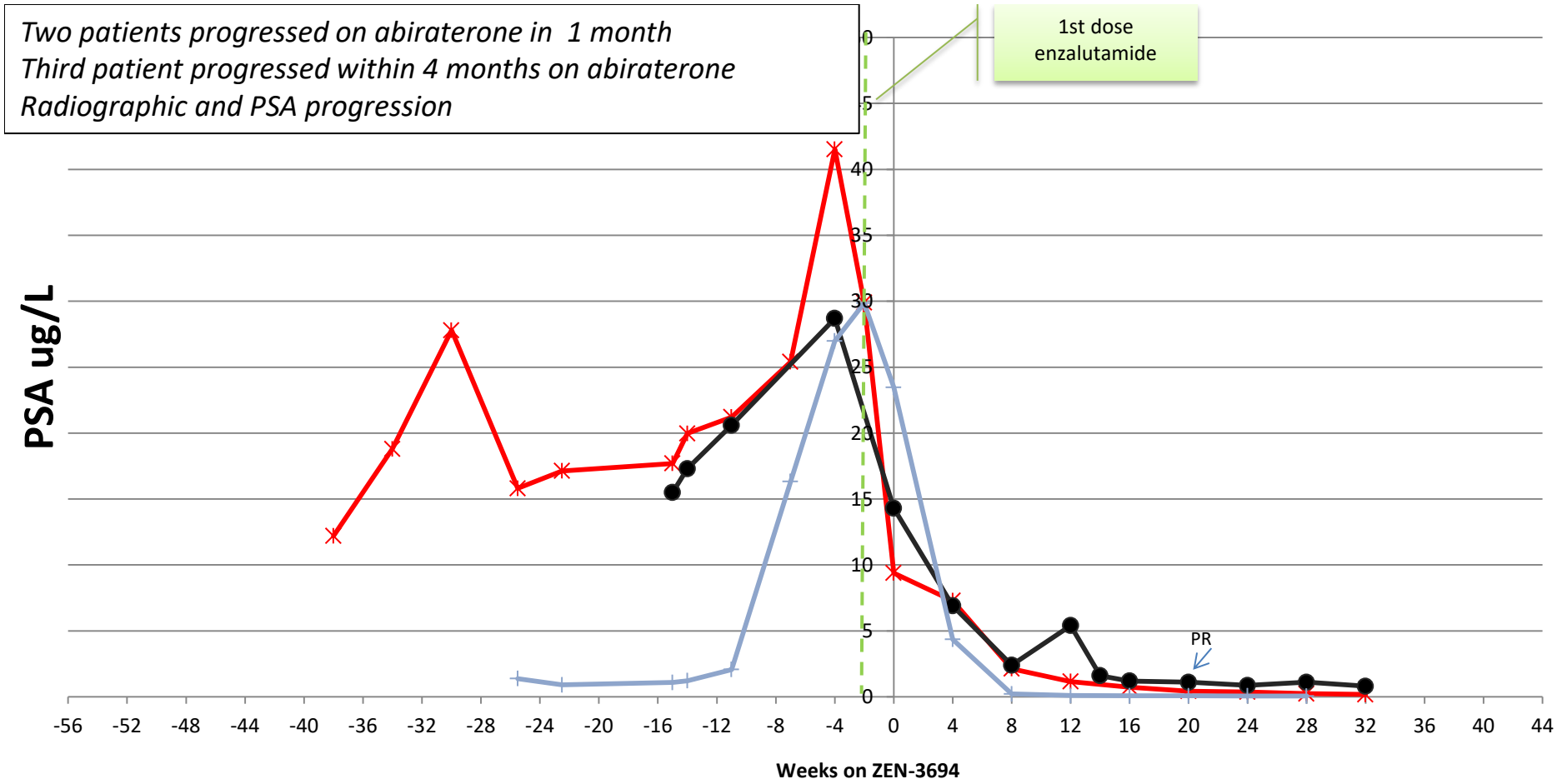
ZEN-3694-002 Treatment Duration



	Treatment days	rPFS
SOC (2nd line enza/abi)	4-5 months	4-6 months
ZEN-3694 + Enza target	> 8-9 months	> 8-9 months

ZEN-3694-002 Combination Study: PSA Response (cohort 2, 1.33X mg)

Two patients progressed on abiraterone in 1 month
Third patient progressed within 4 months on abiraterone
Radiographic and PSA progression



	PSA50 response	PSA Response duration
SOC (2nd line enza/abi)	15-25%	3-4 months
ZEN-3694 + Enza target	>40%	>8 months

Extensive Translational Medicine Plan for Deciphering MOA and Designing Future Biomarker Driven Trials

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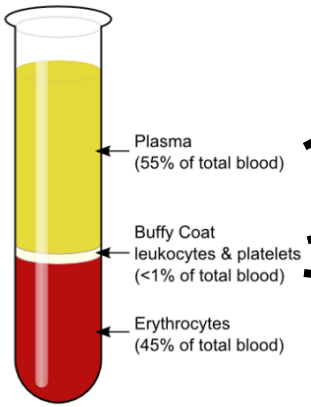
Whole blood



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

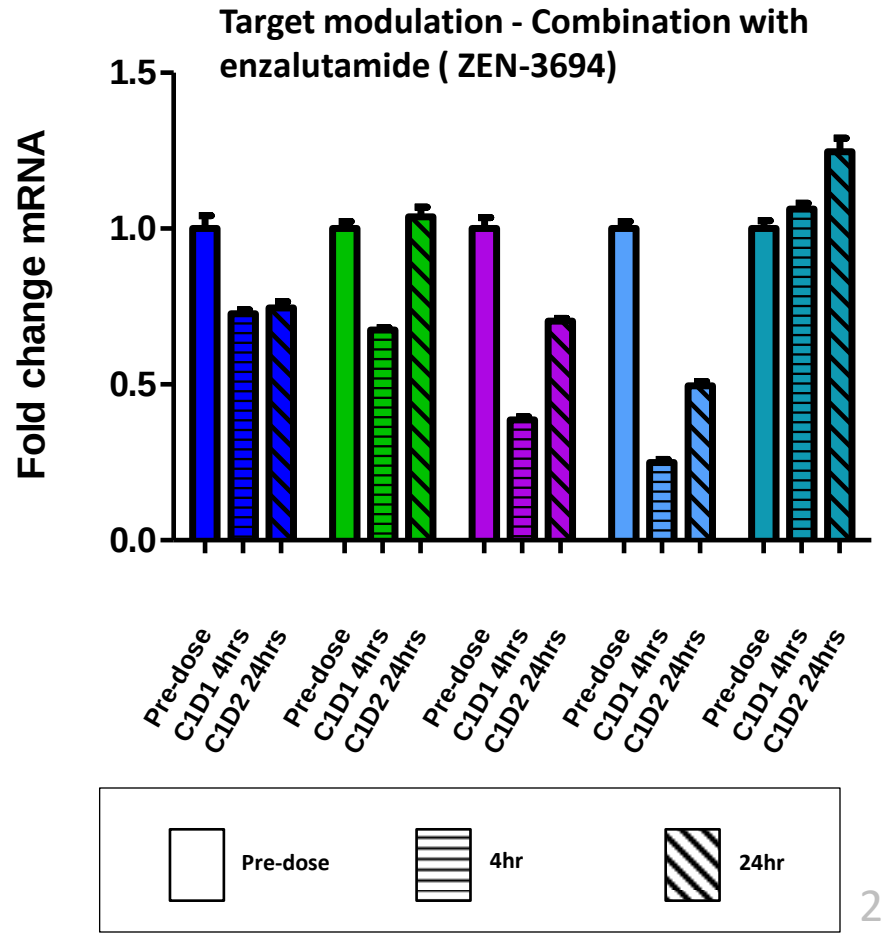
RNA-seq ==>
- Expressed mutations
- Fusions and splice variants
- Expression profiles and pathway analysis (AR/GR signaling, NFkB, etc.)
- Immuno-onc markers

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

Phase 1: Combination with Enzalutamide

ZEN-3694 combination study with enzalutamide

- Dose escalation progressing
- Dose proportional exposure
- Target modulation shown at well tolerated doses
- Combination well tolerated



Lack of Grade 3-4 Treatment-related Adverse Events (ZEN-3694-002) at Efficacious Doses

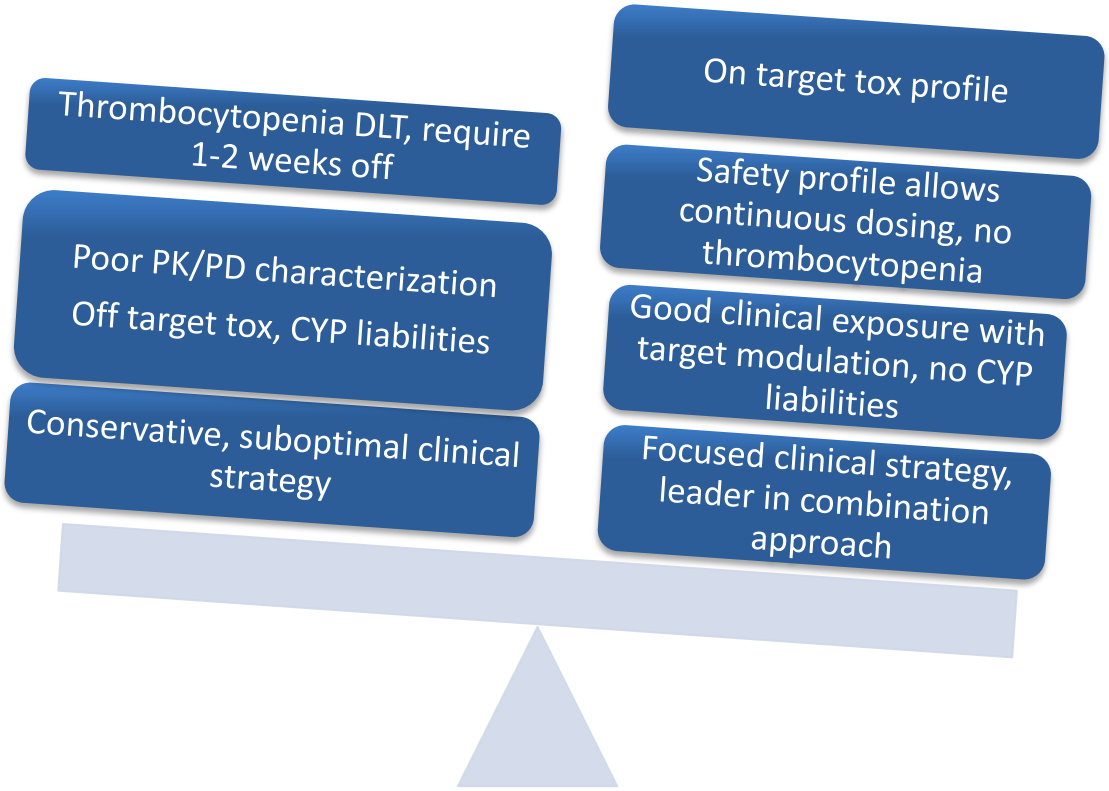
	1.0x mg N=4		1.33x mg N=6		1.66x mg N=3		2.0x mg N=4	
Grade	3	4	3	4	3	4	3	4
Fatigue			1*					
Hypokalemia							1	

Very well tolerated in combination with enzalutamide

* Patient was suffering from fatigue from enzalutamide before entering Zen-3694 trial, Event occurred after cycle 1 so not a DLT

Zenith's BETi program is Clinically Differentiated

Other Clinical BETi	Zenith's BETi (ZEN-3694)
Thrombocytopenia DLT, require 1-2 weeks off	On target tox profile
Poor PK/PD characterization Off target tox, CYP liabilities	Safety profile allows continuous dosing, no thrombocytopenia
Conservative, suboptimal clinical strategy	Good clinical exposure with target modulation, no CYP liabilities
	Focused clinical strategy, leader in combination approach



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

Next Steps

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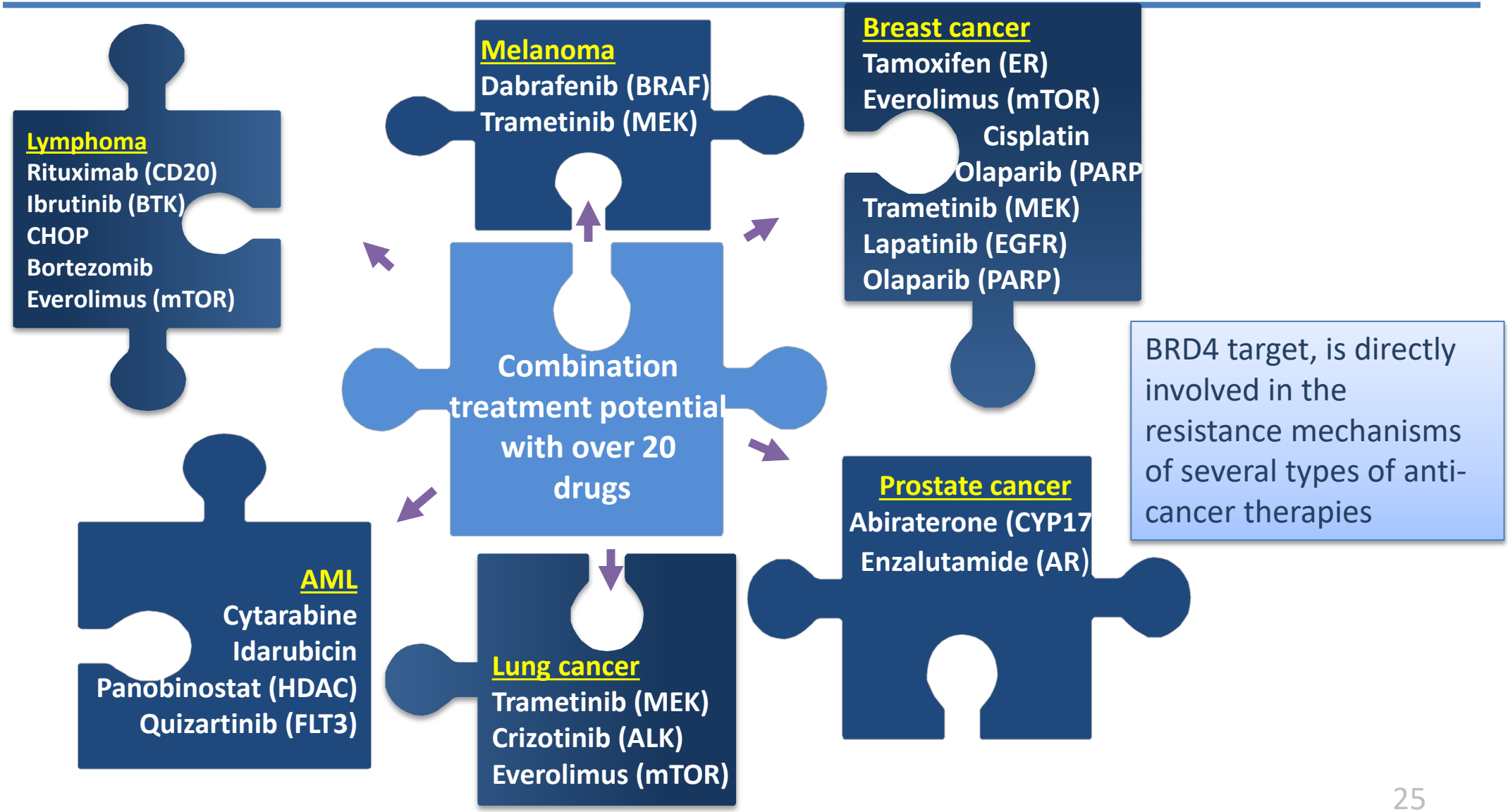
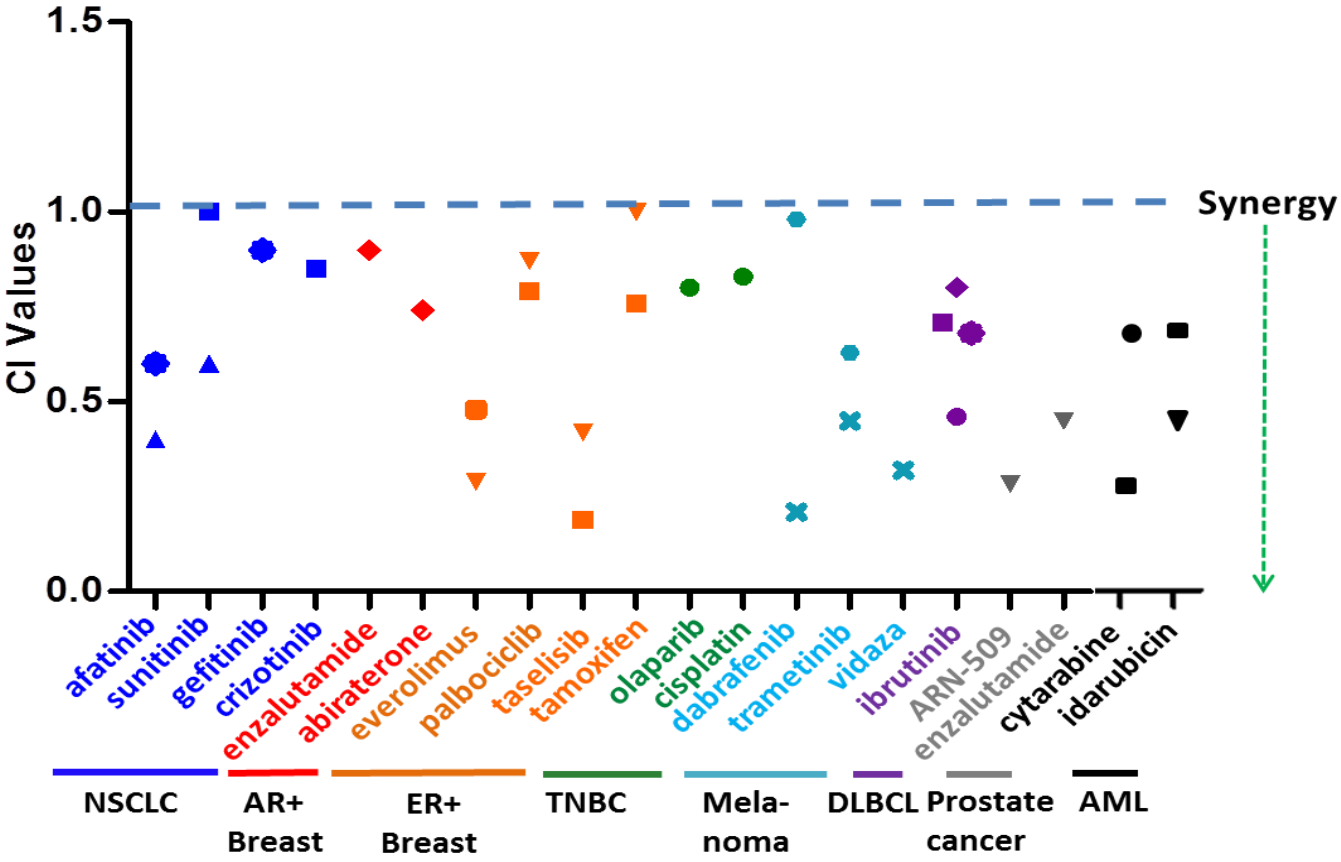
BET Inhibitors Potential as Combination Agents



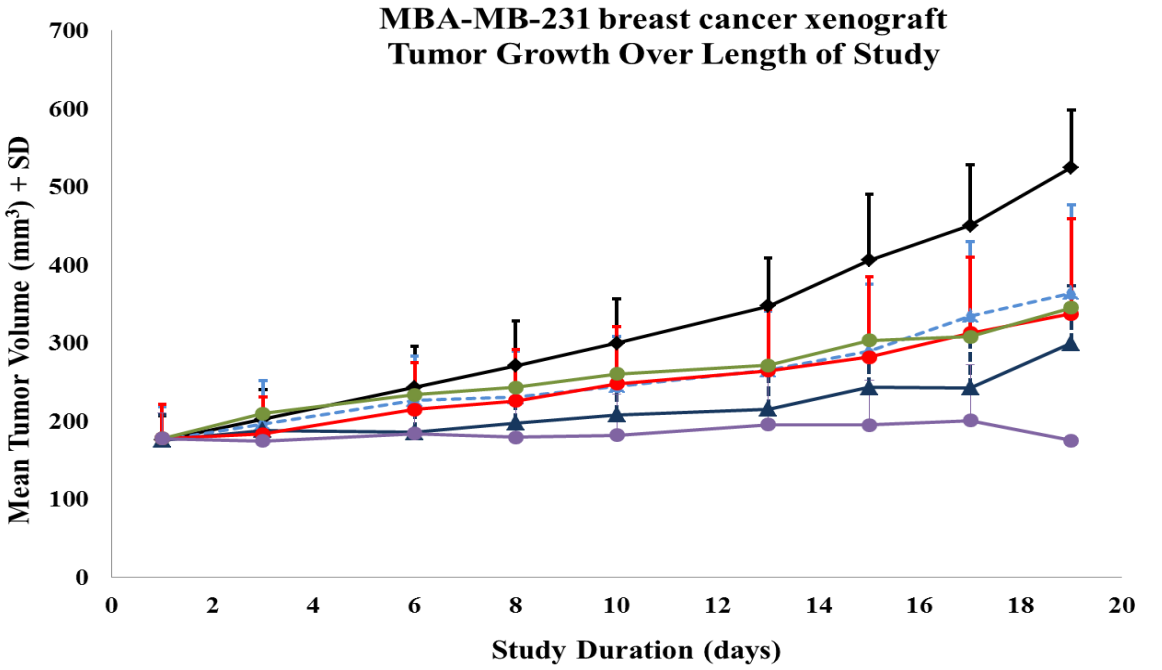
BRD4 target, is directly involved in the resistance mechanisms of several types of anti-cancer therapies

ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs

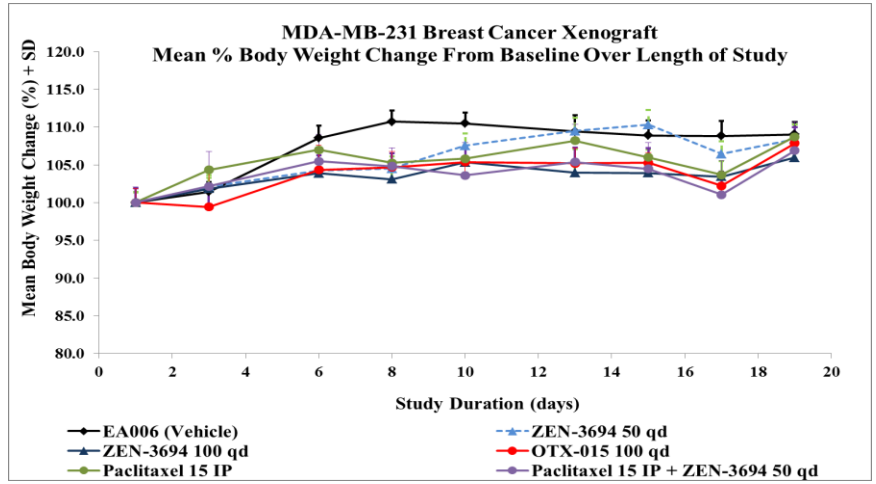


Indication		Cell line (mutation)
NSCLC	▲	H1975 (EGFR L858R T790M)
	⬢	H820 (EGFR T790M)
	■	H2228 (ALK)
AR+ Breast	◆	MDA-MB-453
ER+ Breast	▬	MCF-7 (ER+)
	▼	ZR-75-1 (ER+)
TNBC	●	HCC1937 (BRCA1)
Melanoma	✖	C32 (BRAF V600E)
	⬣	A375 (BRAF)
DLBCL	✹	CARNAVAL (MYC/BCL2)
	●	OCI-LY18 (MYC/BCL2)
	◆	NU-DUL-1
	■	OCI-LY3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

ZEN-3694 is Synergistic With Paclitaxel in Triple-negative Breast Cancer Models



Treatment Groups	TGI
EA006 (Vehicle)	0%
ZEN-3694 50 mg/kg qd	46%
ZEN-3694 100 mg/kg qd	64%
OTX-015 100 mg/kg qd	54%
Paclitaxel 15 mg/kg IP	52%
Paclitaxel 15 mg/kg IP + ZEN-3694 50 mg/kg qd	101%



- Combination regimen is well tolerated
- ZEN-3694 is more potent than OTX at equivalent dose
- ZEN-3694 is synergistic in combo with Paclitaxel (5/12 regressed tumors)

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