Annual Meeting – Clinical Advancements Update

Advanced Epigenetic Technology

December 12, 2017

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
7. Intellectual Property

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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

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2. **Epigenetic Mechanism Review**
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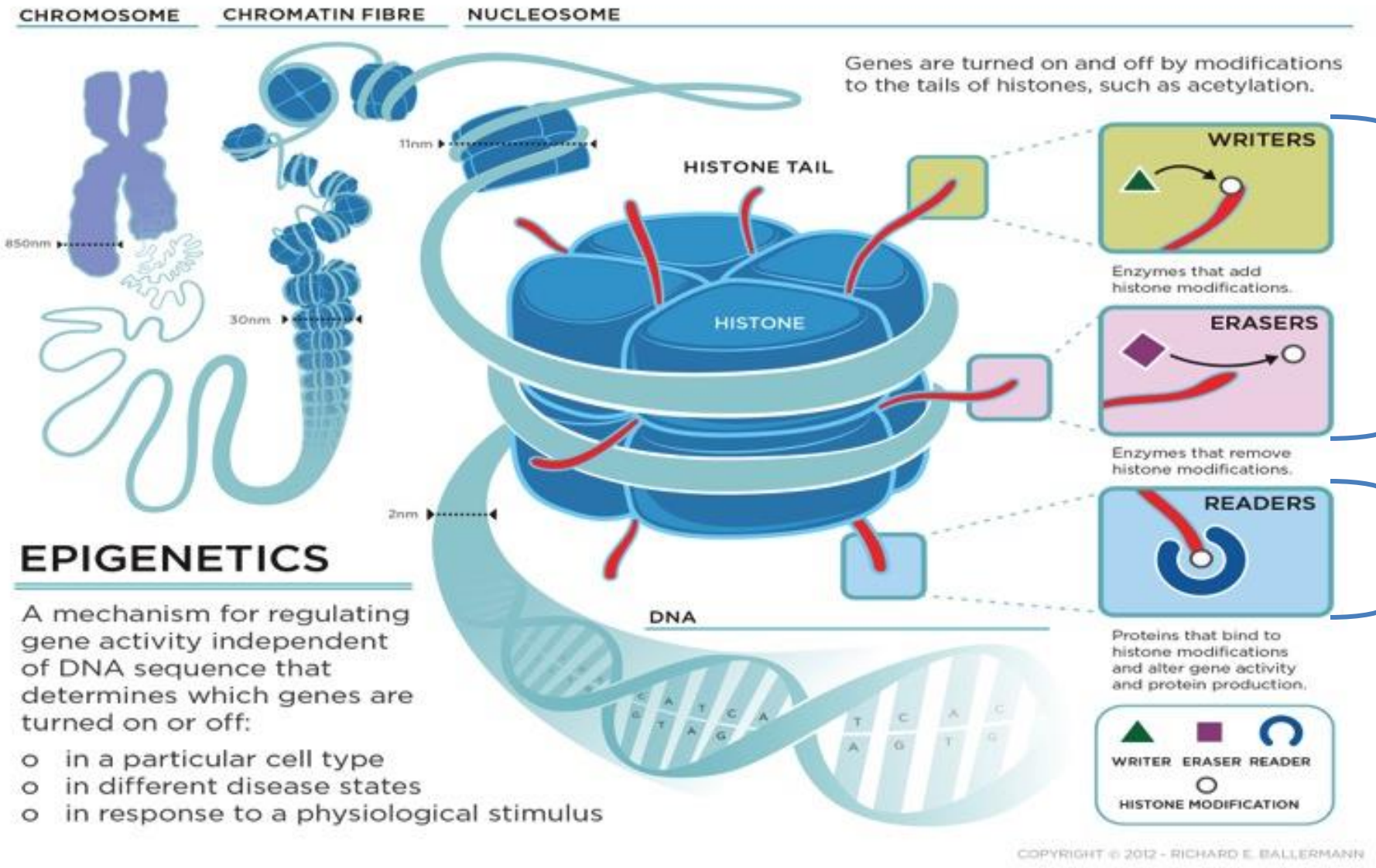
Epigenetics: the Mechanism Behind Our Approach



Early Epigenetic Approach

Advanced Epigenetic Approach

Zenith's BRD4 Targets Resistance Mechanisms

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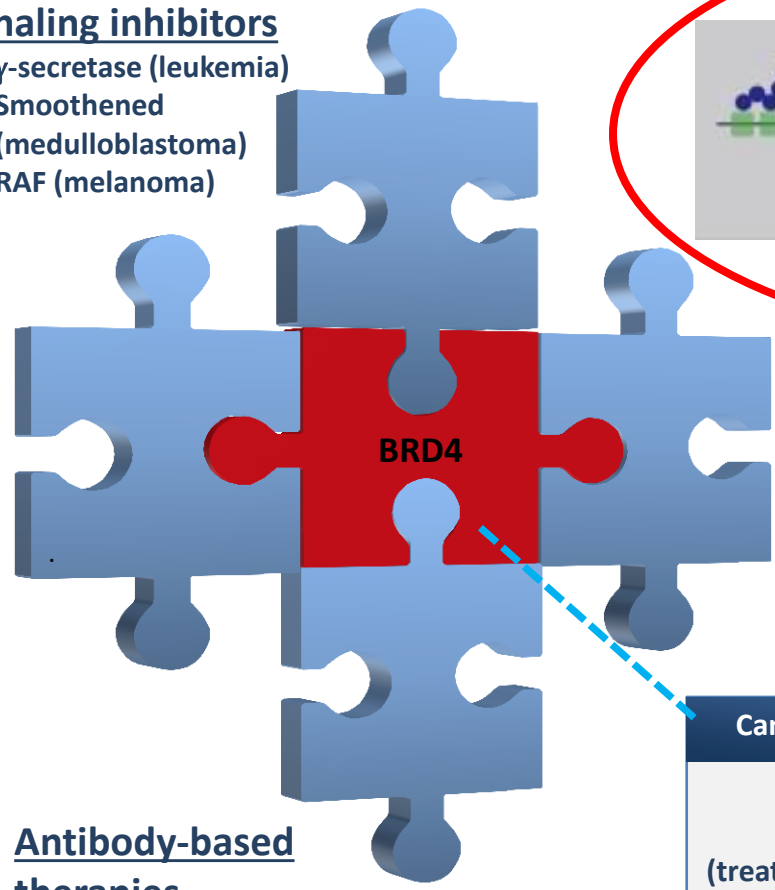
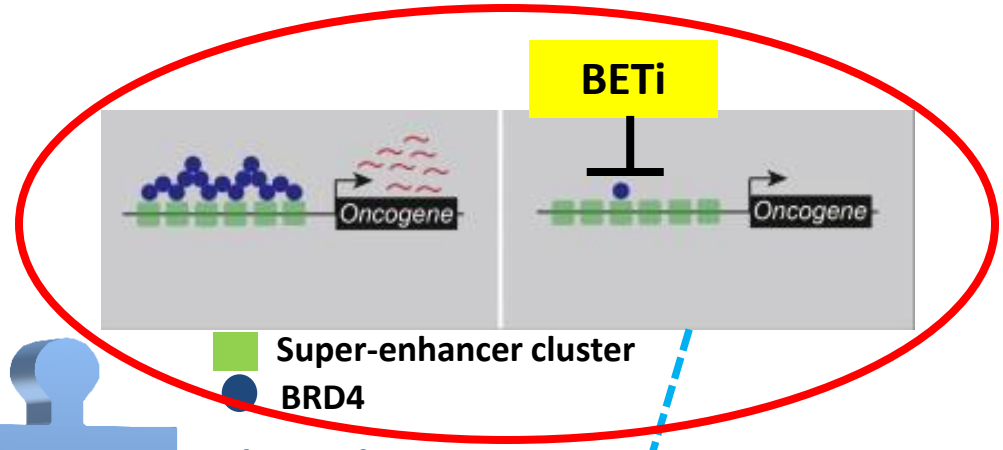
Signaling inhibitors
- γ-secretase (leukemia)
- Smoothened (medulloblastoma)
- RAF (melanoma)

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

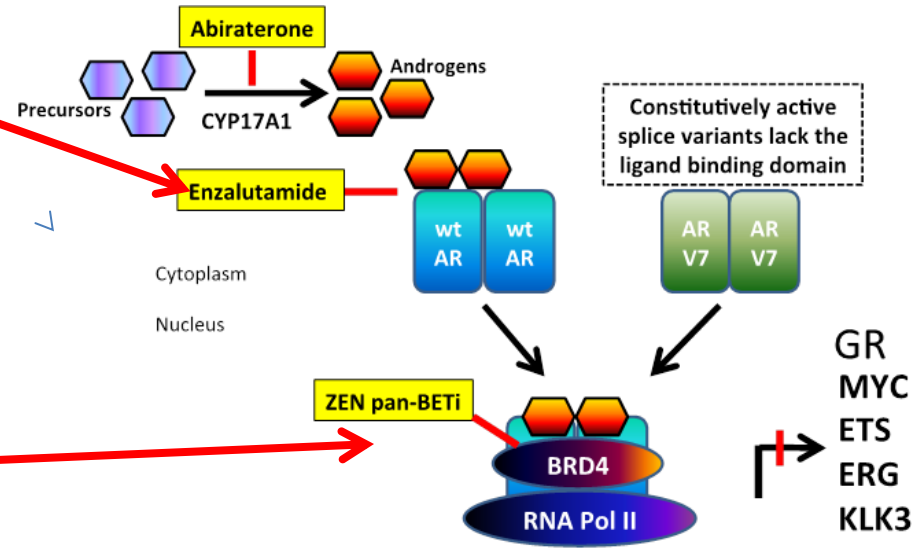
Prostate Cancer Rationale Review

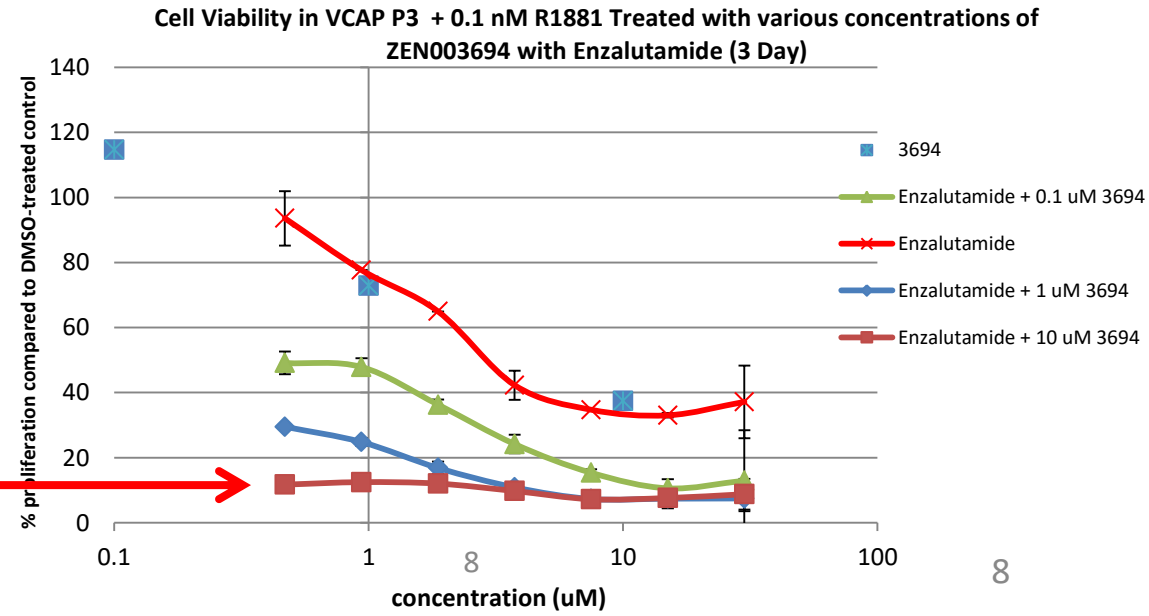
ZEN-3694 Potential in Patients Developing mCRPC Resistance to Enzalutamide

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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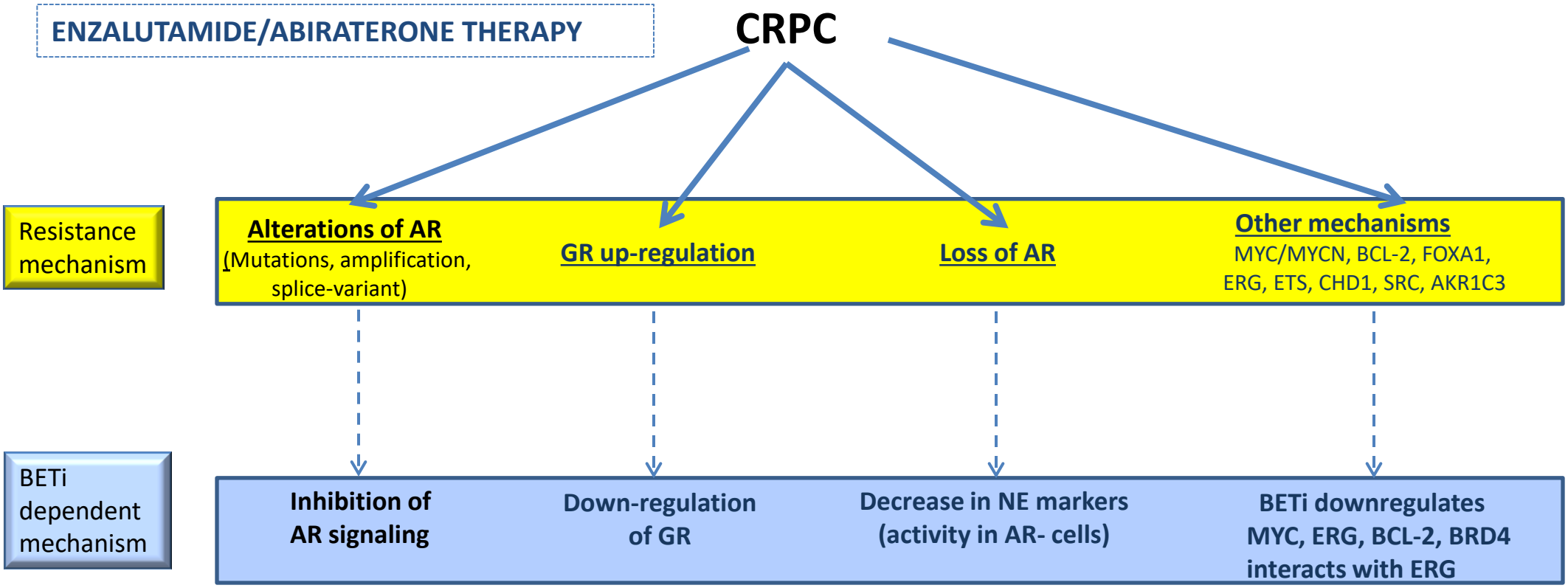

ZEN-3694 shows good efficacy in different CRPC models that are resistant to AR antagonists

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 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

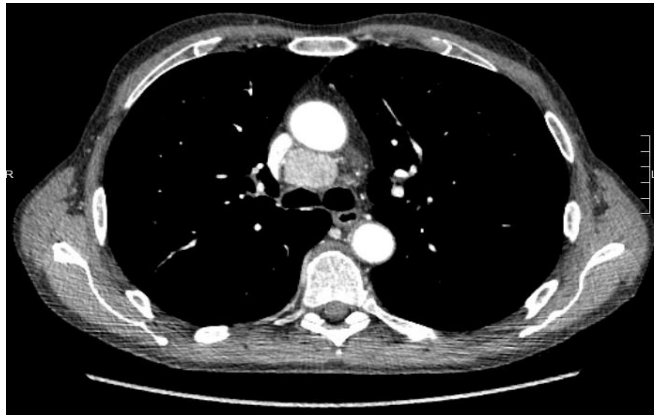
Prior Therapy for mCRPC

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

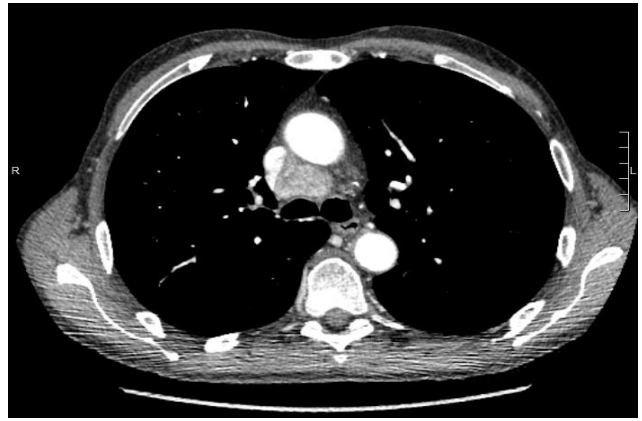
- ZEN-3694: 8/24/2016 – 7/16/2016, 45 weeks

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

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

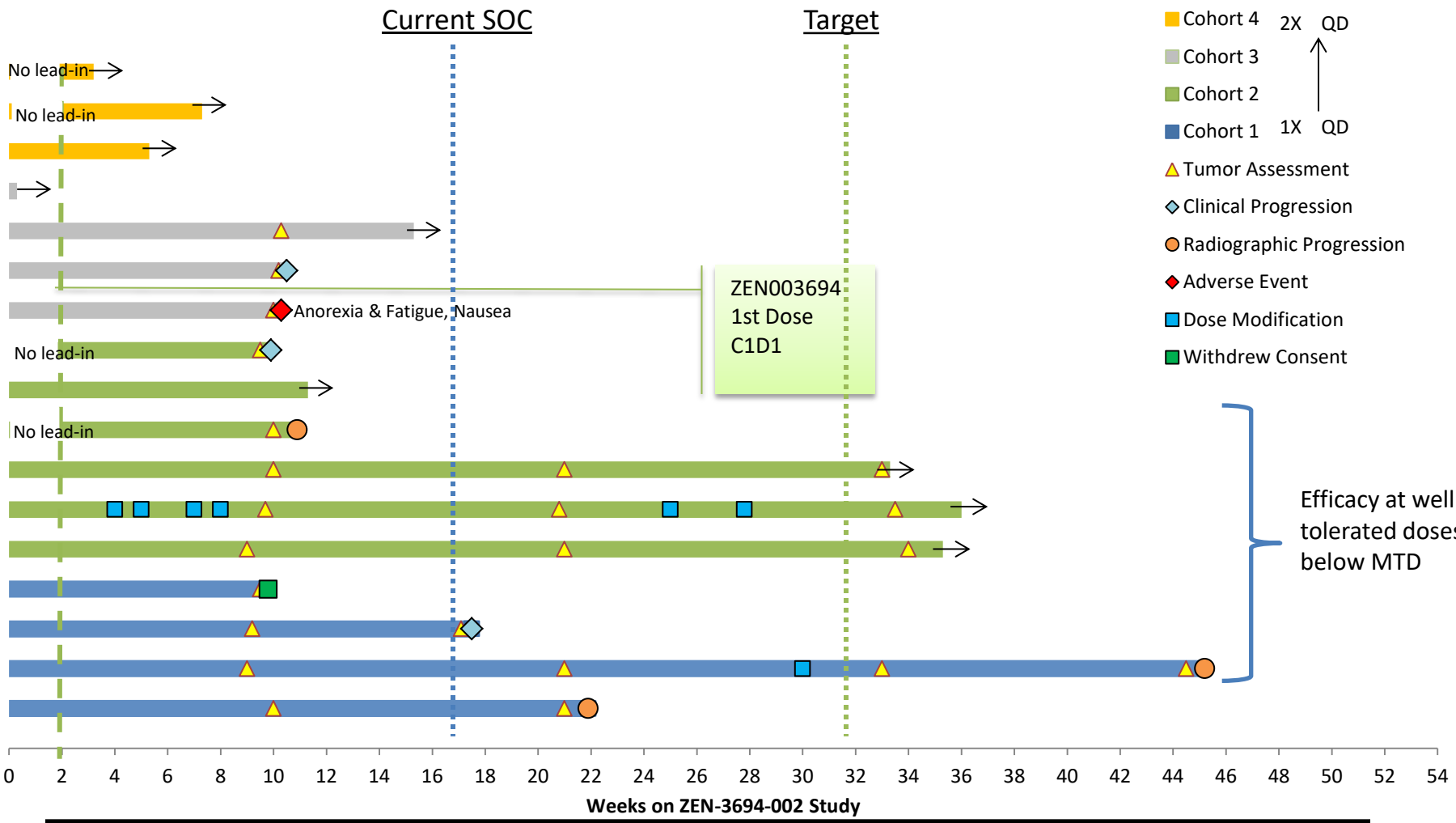
Seven sites, UCSF and MSKCC, opened for enrollment First, U Washington and Mayo Clinic joining soon.

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

Expansion Cohort A
Enza naïve, progression on abiraterone

Expansion Cohort B
Biochemical progression on enzalutamide

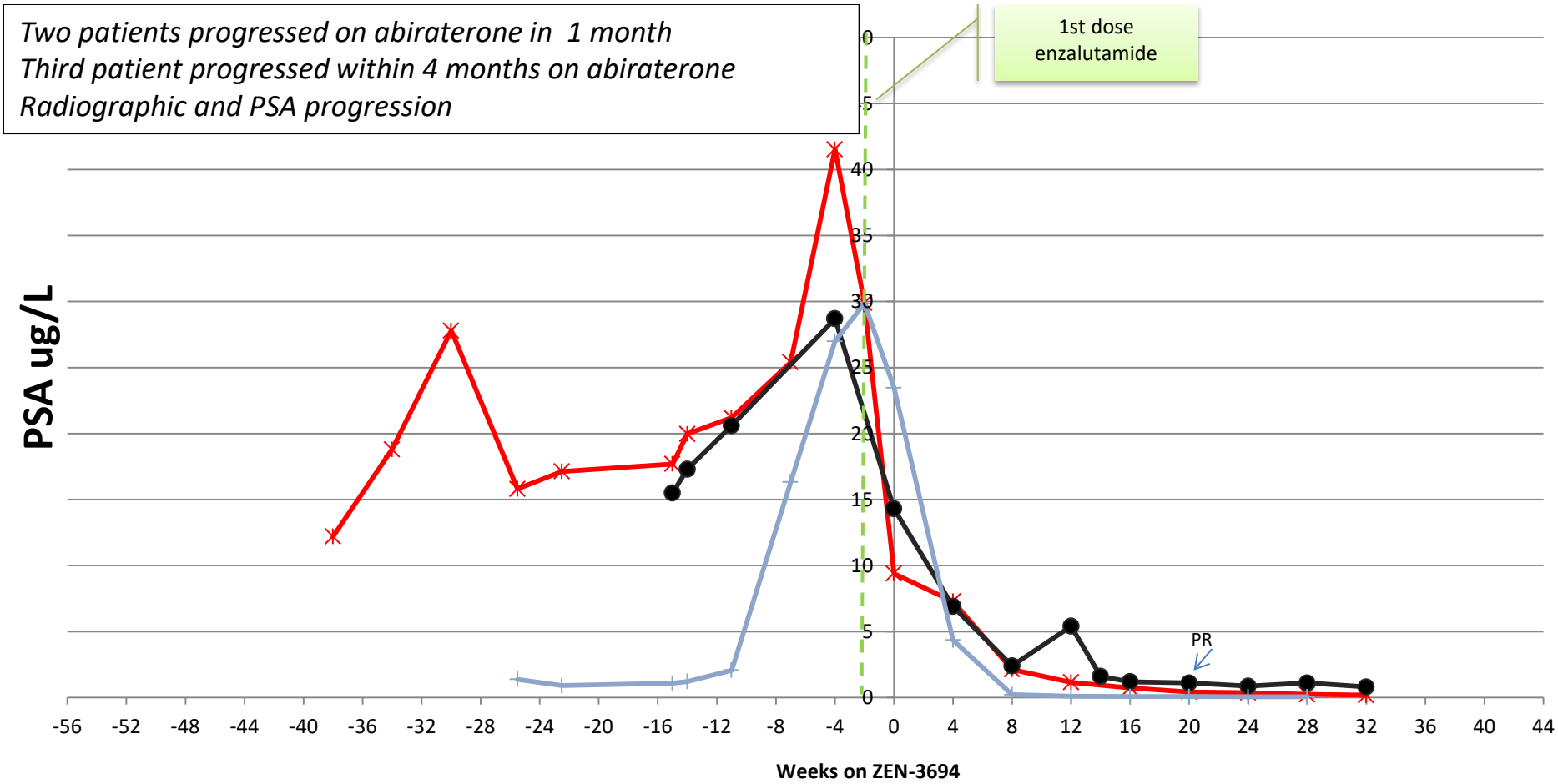
ZEN-3694-002 Treatment Duration



	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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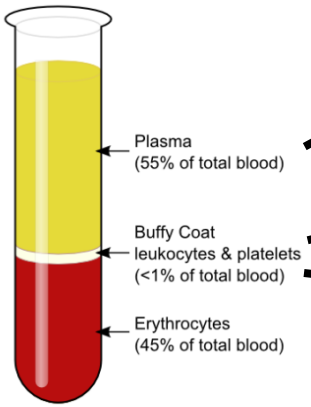
Whole blood



- **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

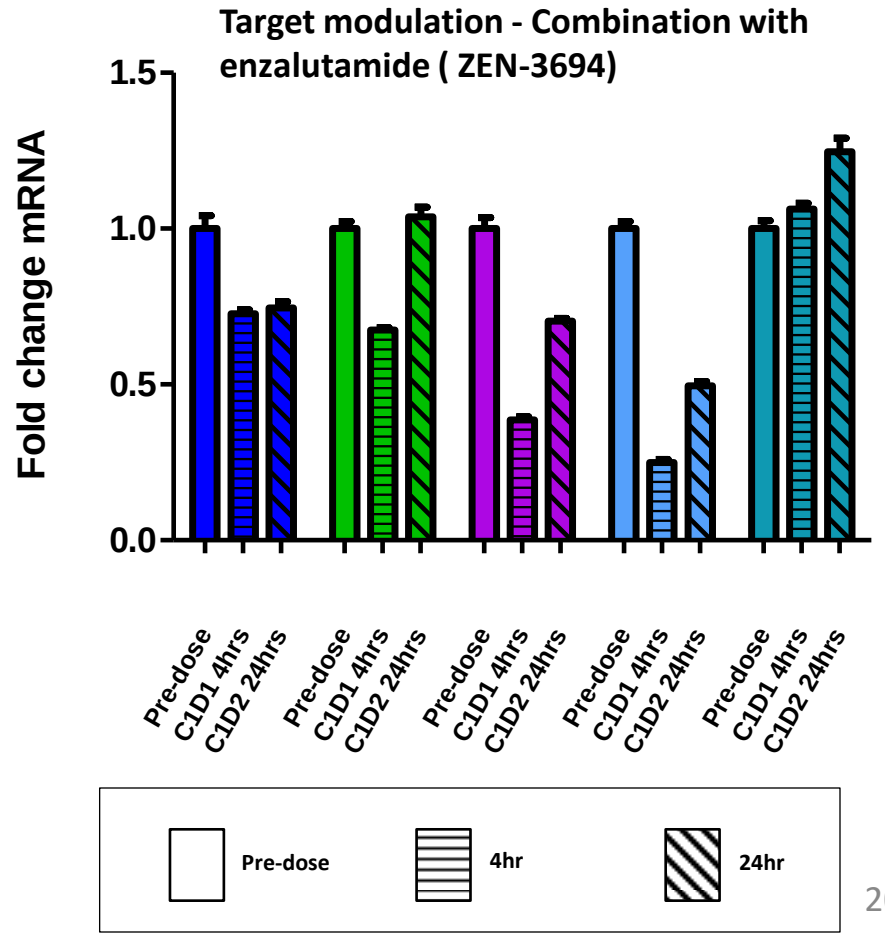
- **RNA-seq** ==>
  - Expressed mutations
  - Fusions and splice variants
  - Expression profiles and pathway analysis (AR/GR signaling, NFkB, etc.)
  - Immuno-onc markers

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



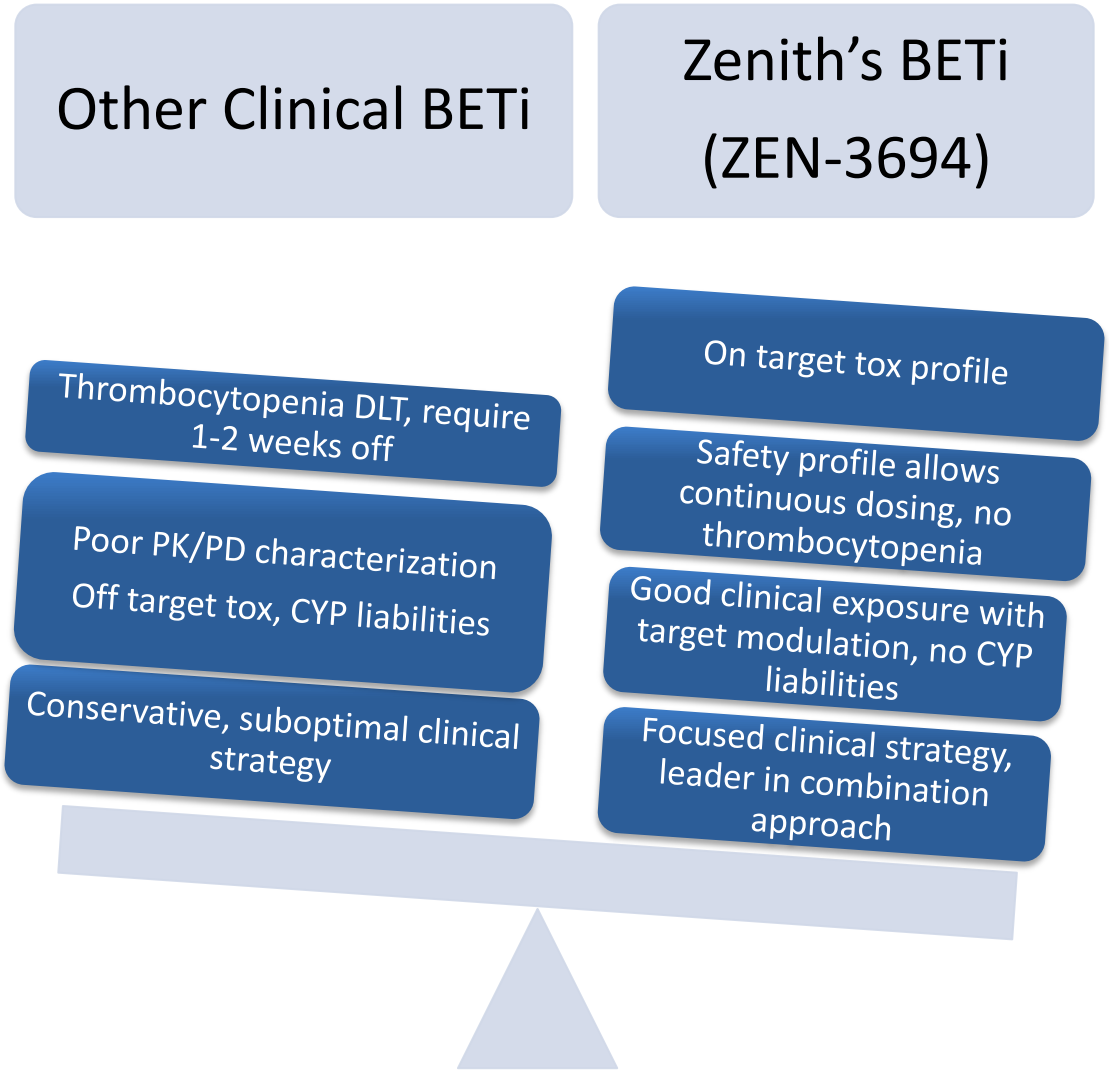
Lack of Grade 3-4 Treatment-related Adverse Events (ZEN-3694-002) at Efficacious Doses

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

ZEN-3694 is Well Differentiated From Competing BETi

Differentiator	Clinical Impact
Lack of thrombocytopenia	Can be dosed without dose interruption, other BETi have intermittent schedule (2 weeks on / 1-2 weeks off) that can effect efficacy
Very low GI event frequency	Good drug compliance
On target tox profile	MTD will not be limited by off target tox, on target tox (low grade GI events) are very manageable through PRN use of anti-emetics and hydration
No interaction with enzalutamide	Dose adjustment will not be needed for individual patients, reduces variability
Well characterized PK/PD	Dose dependent exposure, low variability Good half life, target modulated for sufficient duration with QD dosing Exposures are at levels that have shown efficacy in pre-clinical models Very well characterized PK/PD correlation to guide selection of RP2D
Clinical Strategy	Zenith leader in combination approach, BETi are combination agents Phase 1b trials designed to show POC in carefully selected populations

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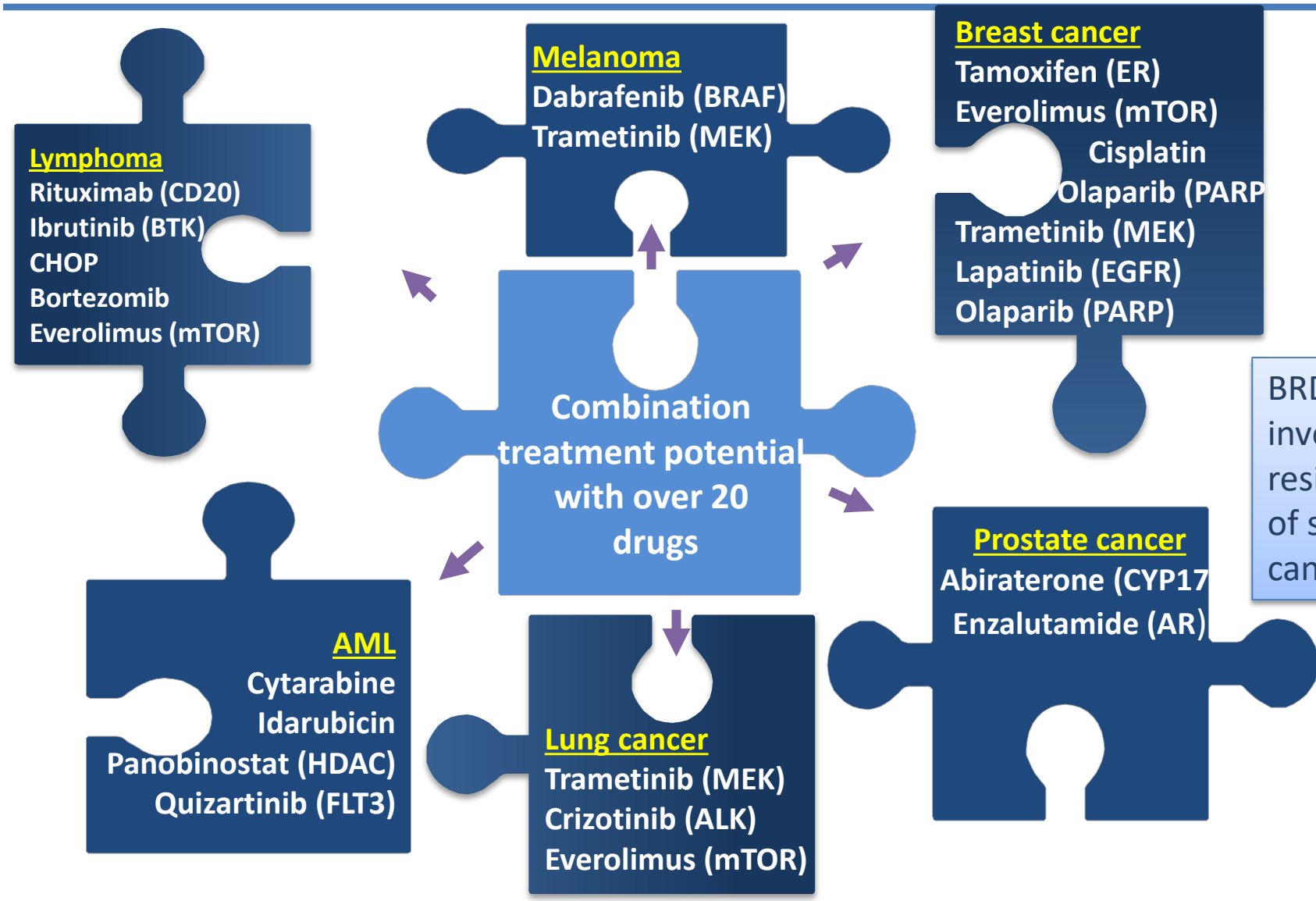
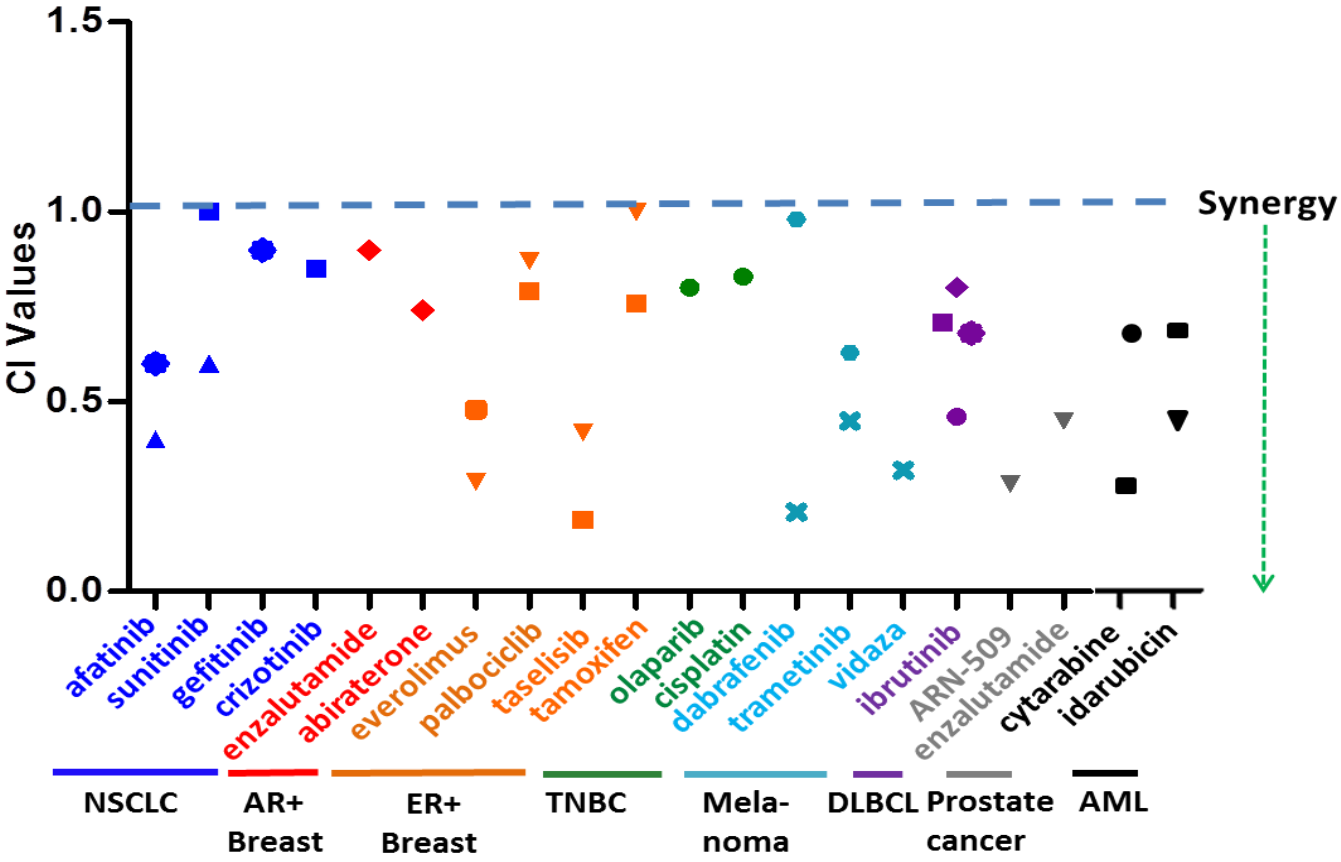
BET Inhibitors Potential as Combination Agents



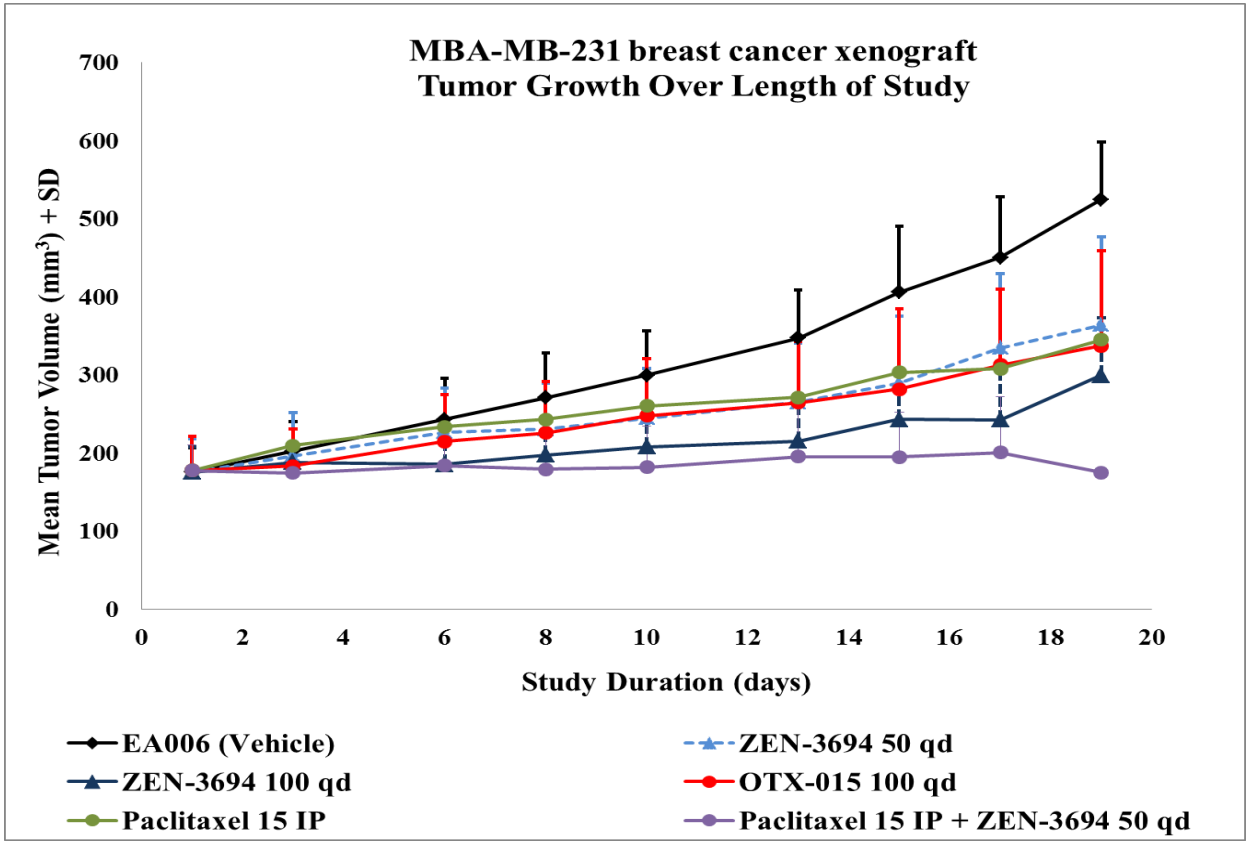
BRD4 target, is directly involved in the resistance mechanisms of several types of anti-cancer therapies

ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs

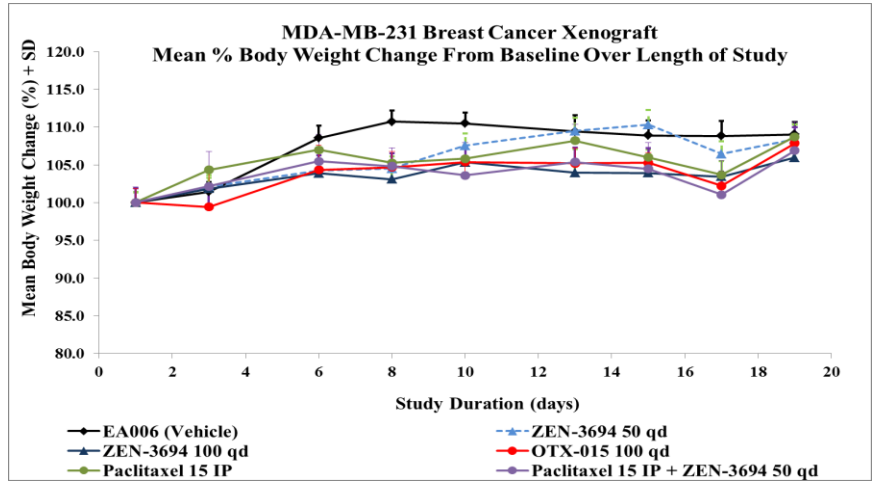


Indication		Cell line (mutation)
NSCLC	▲	H1975 (EGFR L858R T790M)
	⬢	H820 (EGFR T790M)
	■	H2228 (ALK)
AR+ Breast	◆	MDA-MB-453
ER+ Breast	■	MCF-7 (ER+)
	▼	ZR-75-1 (ER+)
TNBC	●	HCC1937 (BRCA1)
Melanoma	✖	C32 (BRAF V600E)
	⬢	A375 (BRAF)
DLBCL	⬢	CARNAVAL (MYC/BCL2)
	●	OCI-LY18 (MYC/BCL2)
	◆	NU-DUL-1
	■	OCI-LY3 (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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Zenith's IP Portfolio: Overview

Composition Patents						
Zenith Reference Number	Provisional Patent Application	Patent Application	Publication	National Stage	Examination	Issuance
22981-36						
22981-37						
22981-38						
22981-40*						
22981-41						
22981-46						
22981-47						
22981-49						
22981-50						
22981-51						
22981-57						

*Patent family 22981-40 contains claims to the clinical development compound ZEN-3694

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