

### **Todays Agenda for Zenith Capital Corp.**



- 1. Corporate Profile & Structure
- 2. Epigenetic Mechanism
- 3. Prostate Cancer Rationale
- 4. Phase 1 Details & Early Results
- 5. Enzalutamide Combination Trial Phase 1b
- 6. Next Steps
- 7. Intellectual Property



**Safe Harbor Statement.** This presentation contains forward-looking statements that involve risks and uncertainties, which may cause actual results to differ materially from the statements made. For this purpose, any statements that are contained herein that are not statements of historical fact may be deemed to be forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates," "plans," "intends," "will," "should," "expects," "projects," and similar expressions are intended to identify forward-looking statements. You are cautioned that such statements are subject to a multitude of risks and uncertainties that could cause actual results, future circumstances, or events to differ materially from those projected in the forward-looking statements. These risks include, but are not limited to, those associated with the success of research and development programs, the regulatory approval process, competition, securing and maintaining corporate alliances, market acceptance of the Company's products, the availability of government and insurance reimbursements for the Company's products, the strength of intellectual property, financing capability, the potential dilutive effects of any financing, reliance on subcontractors and key personnel. The forward-looking statements are made as of the date hereof, and the Company disclaims any intention and has no obligation or responsibility, except as required by law, to update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise. CONTACT: Donald J. McCaffrey, Chairman, President & CEO

## **Corporate Profile**



Founded	Corporate spin out from Resverlogix in June 2013
Status	Private Company, reporting issuer
Cash Raised 2014-2016	~US\$44MM @ \$1.00 USD/sh
Enterprise Value est.	\$350 MM USD
Shares Outstanding	125.3 MM 132.4 MM fully diluted
Cash Burn	\$2 MM/qtr - Current

#### Post July 31, 2016 Corporate Structure



# POST-REORGANIZATION JULY 31, 2016 STRUCTURE

ZENITH SHAREHOLDERS

125,207,692 SHARES AS OF JUNE 15<sup>TH</sup>, 2016

Private Company (Reporting Issuer)

ZENITH CAPITAL CORP. (ZCC)

Royalty PreferredShares (RVX)

Subsidiary Company (100% owned by ZCC)

# ZENITH EPIGENETICS

-Holds ownership of all technology, ZEN-3694 and 1,500 other compounds

#### **Epigenetics Mechanism**

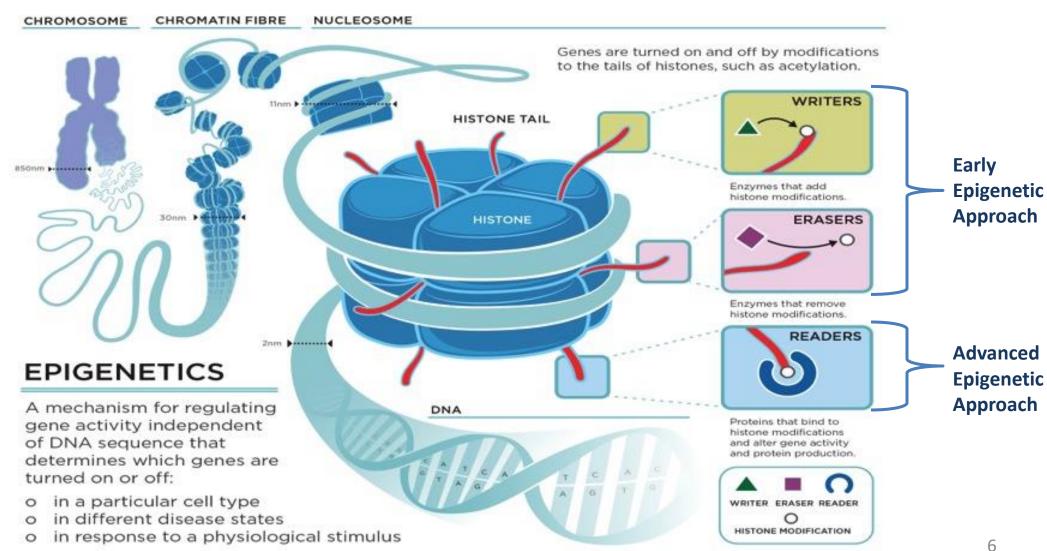


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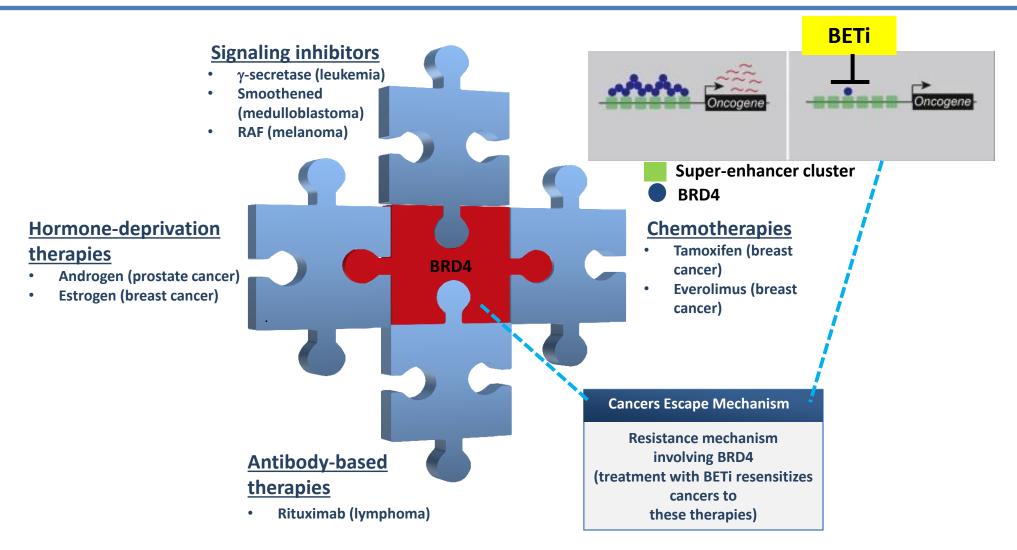
### **Epigenetics, the Mechanism Behind Our Approach**





#### **Zenith's BRD4 Targets Resistance Mechanisms**





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

#### **Prostate Cancer Rational**



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#### **Unmet Need in Metastatic Prostate Cancer (mCRPC)**



#### **Current Market and Unmet Need**

- ~135,000 annual mCRPC patients in the US/EU alone majority receive enzalutamide or abiraterone as first-line treatment
- Over \$4B in sales in 2015 for first-line enzalutamide and abiraterone
- Patients become resistant to these therapies, no effective second-line therapy yet
- Continuing high mortality rate in resistant mCRPC (50% 1 year survival, 28% in 5 years)

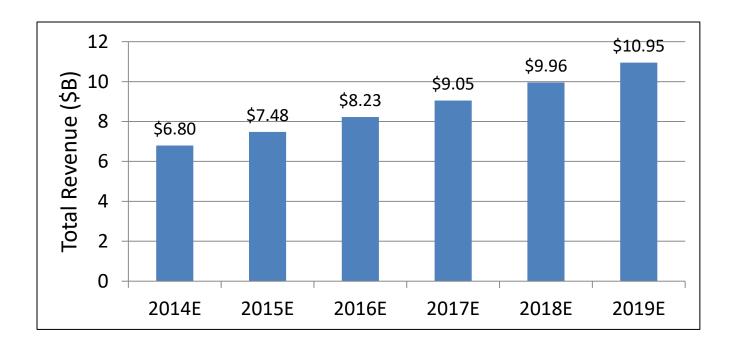
#### **Opportunity for ZEN-3694**

- Second-line single-agent treatment
  - key opinion leaders agree that there is no effective second-line treatment
  - ~60,000 second-line treatment eligible patients in US/EU alone
- Expand into first-line treatment in combination with enzalutamide or abiraterone

### **Prostate Cancer Epidemiology & Market**



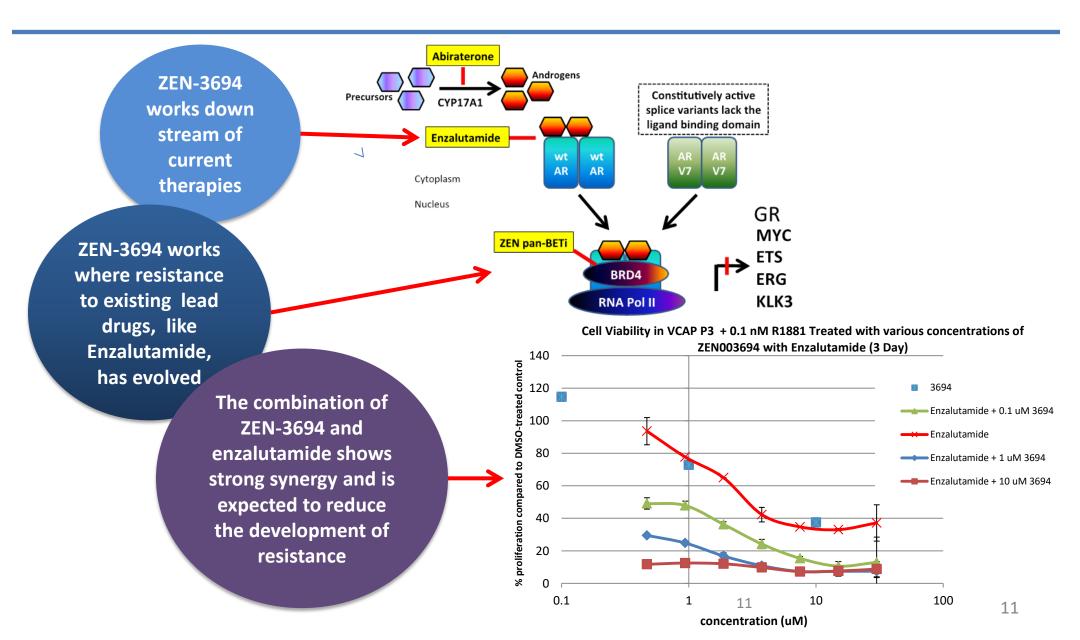
	US/EU Prevalence (2015)	5 Year Survival Rate	Japan Prevalence	Korea Prevalence	China Prevalence
mCRPC	~ 134,000	28%	~26,000	~3300	~16,000



The global prostate cancer WW market is expected to reach \$11B by 2019, driven by Zytiga and Xtandi.

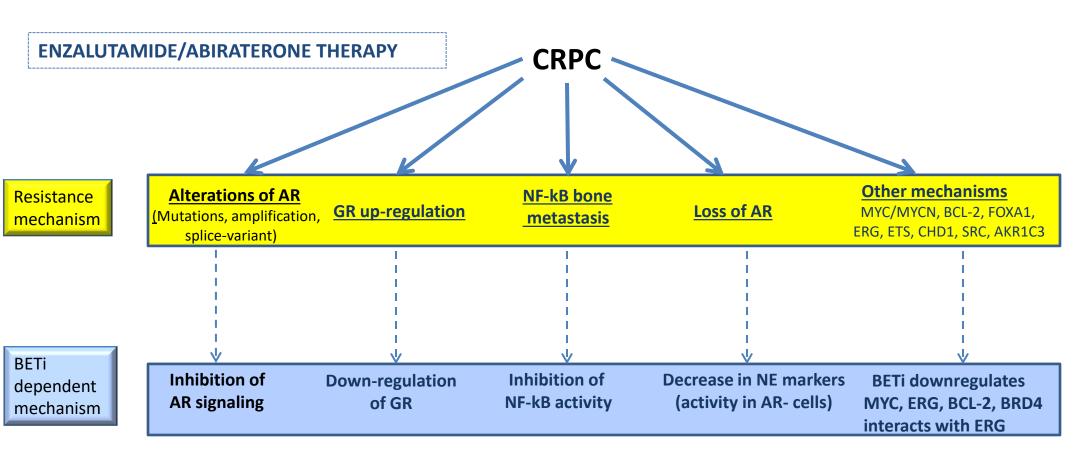
# ZEN-3694 Potential in Patients Developing mCRPC Resistance to Enzalutamide





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





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

### **Phase 1 Details & Early Results**



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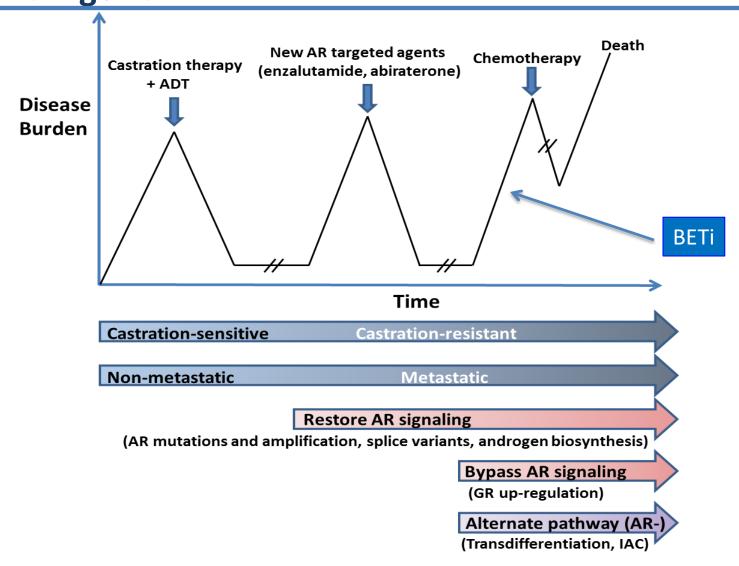
# **Zenith's Principal Investigators**



Name	Institution	Comments
Eric Small, MD Chief, Dept. of Medicine	University of California, San Francisco (UCSF)	Developed abiraterone - #2 CRPC drug, owned by J&J.
Rahul Aggarwal, MD  Developmental Therapeutics Specialist,  Genitourinary Oncologist		
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 for high enrollment

# **Castration-resistant Prostate Cancer (CRPC) Treatment Algorithm**





- Medical need for targeting patients resistant to AR targeted agents
- Need for targeting downstream AR signaling and alternate resistance pathways

### **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

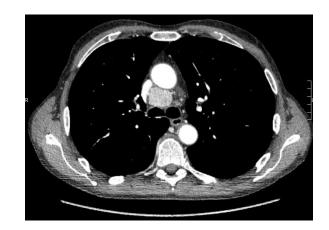
#### **Phase 1: Single Agent Study**

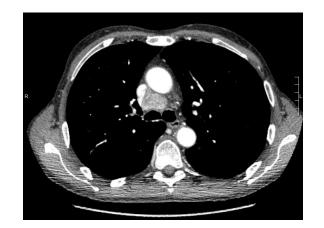


#### **ZEN-3694** single-agent study

- Maximum Tolerated Dose (MTD) confirmation
- Dose proportional PK, exposures reach IC<sub>50</sub> cell proliferation values
- Target modulation shown
- On-target safety profile
- Recommended Phase 2 dose expansion cohort has been initiated
- Longest patient on drug now beyond 11 months

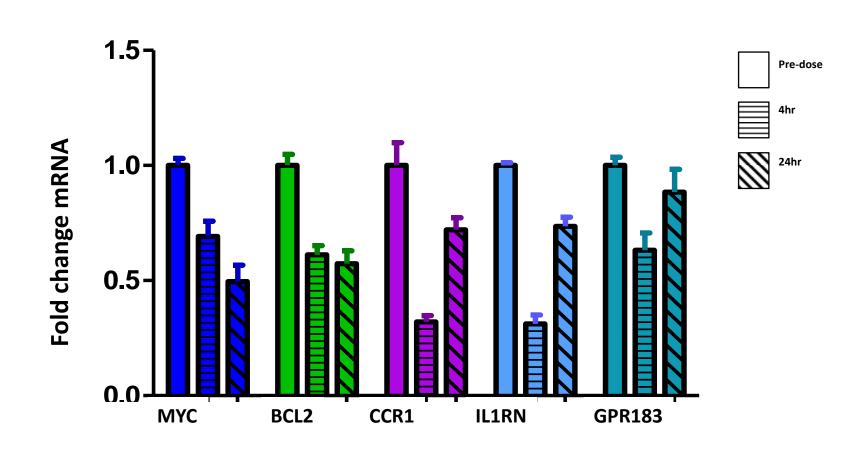
Stable mediastinal nodes over past 10 months





### **Target Modulation at Well Tolerated Doses**





Robust target modulation for 24h at a safe dose

#### **Enzalutamide Combination Trial – Phase 1b**

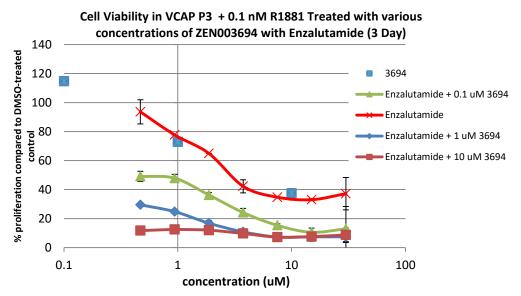


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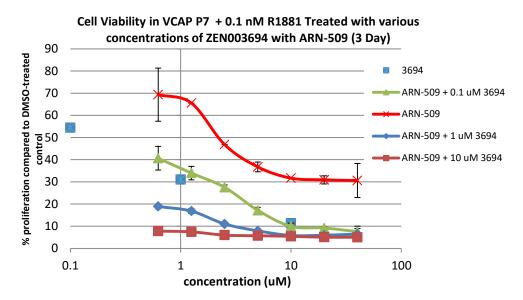


## ZENITH

#### **ZEN-3694 Synergizes With Enzalutamide & ARN-509**



uM ZEN3694	IC50 uM of Enzalutamide in VCAP + 0.1 nM R1881		
0	4.98		
0.1	0.58		
1	0.09		
10	< 0.09		



u <b>M ZEN</b> 3694	IC50 uM of ARN-509 in VCAP + 0.1 nM R1881			
0	2.24			
0.1	0.36			
1	0.02			
10	< 0.02			

VCAP curve shift: Enzalutamide and ARN-509 sensitive, ZEN003694 highly synergistic

#### **ZEN-3694 Phase 1b Study Design**



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

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

enrollment

QD ZEN-3694 160 mg QD enzalutamide (2 cohorts completed)

Dose escalation cohorts

MTD / RP2D Confirmation

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

All sites, including UCSF and MSKCC, open for

Expansion Cohort A
Enza naïve, progression on
abiraterone

Expansion Cohort B Progression on enzalutamide

### **ZEN-3694 Phase 1b Study Endpoints**



#### **Primary**

• Safety, tolerability, MTD, and RP2D of ZEN-3694 in combination with enzalutamide

#### **Secondary**

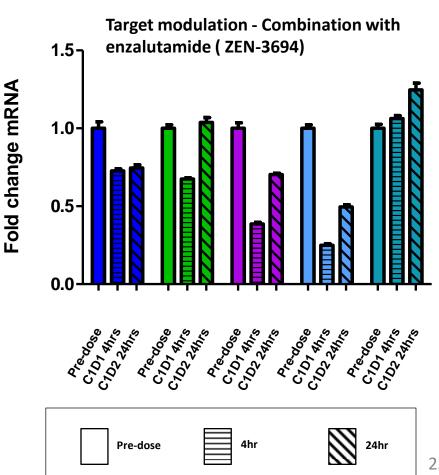
- Pharmacokinetics (PK) of ZEN-3694 and enzalutamide when given in combination
- Preliminary clinical activity
  - PCWG2 Criteria: PSA response rate, Radiographic response rate, Median PFS
  - Circulating Tumor Cell (CTC) response rate

#### 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



### **Next Steps**

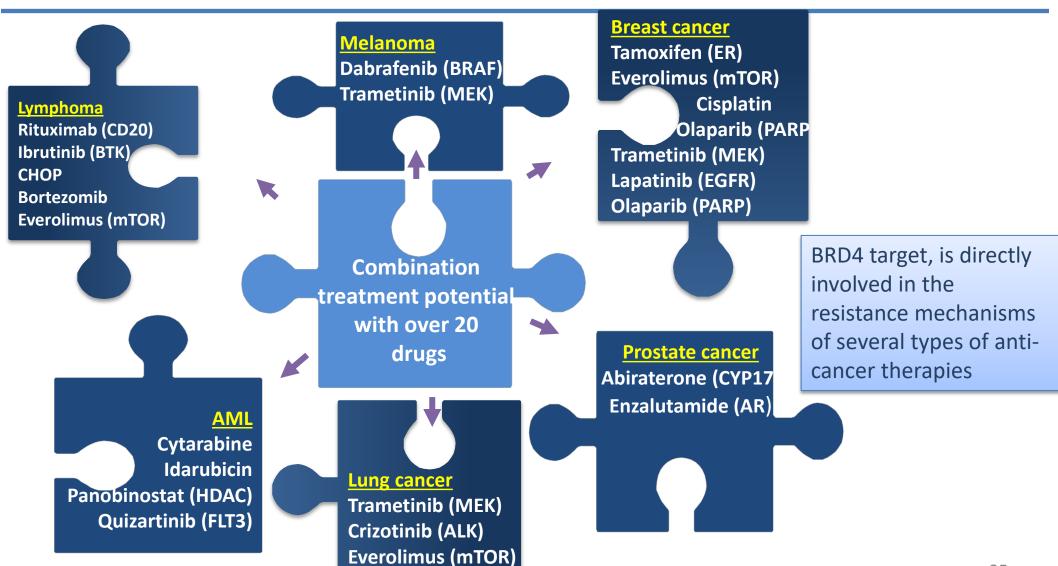


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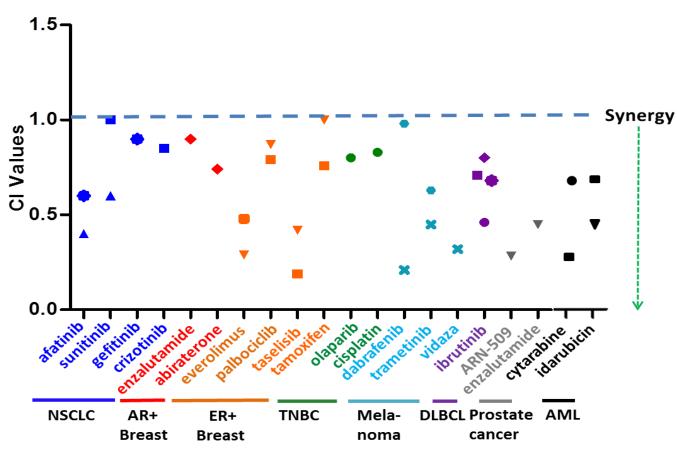
### **BET Inhibitors Potential as Combination Agents**





# **ZEN-3694** Synergizes With Several Standard of Care Cancer Drugs

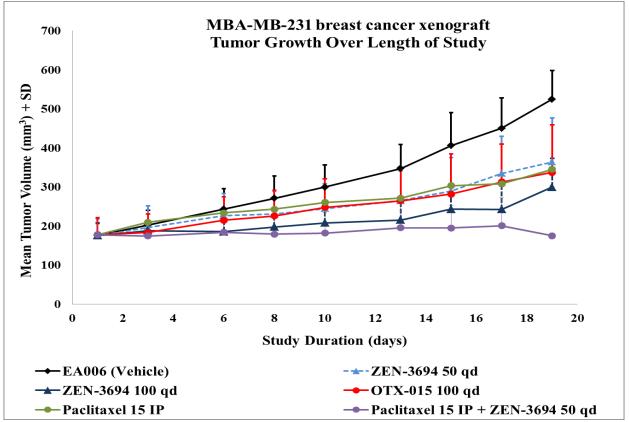




Indication		Cell line (mutation)	
	_	H1975 (EGFR L858R T790M)	
NSCLC		H820 (EGFR T790M)	
		H2228 (ALK)	
AR+ Breast	•	MDA-MB-453	
ED. Durant	-	MCF-7 (ER+)	
ER+ Breast	Þ	ZR-75-1 (ER+)	
TNBC	<ul> <li>HCC1937 (BRCA1)</li> </ul>		
Melanoma	*	C32 (BRAF V600E)	
Meianoma	•	A375 (BRAF)	
		CARNAVAL (MYC/BCL2)	
DLBCL	•	OCI-LY18 (MYC/BCL2)	
	•	NU-DUL-1	
	•	OCI-LY3 (A20)	
Prostate	₩	VCAP (AR AMP/AR-V7)	
		MV4-11 (MLL-AF4/FLT3-ITD)	
AML	•	OCI-AML2 (DNMT3A/MLL)	
	▼	OCI-AML3 (DNMT3A/NPM1)	

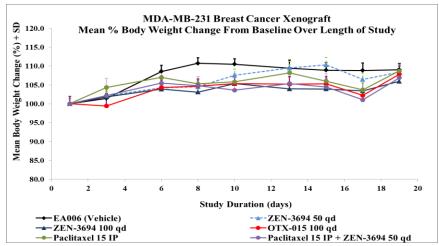
# ZEN-3694 is Synergistic With Paclitaxel in Triple-negative Breast Cancer Models





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	<b>52</b> %
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)



### **Intellectual Property**



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# **Broad Intellectual Property Portfolio: ZEN-3694 Patent Issued**



Zenith Epigenetics Ltd. owns numerous patent families, including seven issued US patents and +60 pending applications. The portfolio includes a number of US applications and world-wide equivalents.

	Composition Patents					
Zenith Reference Number	Provisional Patent Application	Patent Application	Publication	National Stage	Examination	Issuance
22981-36						
22981-37						2x
22981-38						2x
22981-39						
22981-40						
22981-41						
22981-45						
22981-46						
22981-47						
22981-49						
22981-50						
22981-51						
22981-57						

# How can you determine the true potential of a new clinical drug candidate in oncology?



There are hundreds of biotech companies with potential drug candidates

Drug candidates require 3<sup>rd</sup> party Principle Investigators (PIs) to act as independent clinical investigators

The best oncology units and principle investigators in the United States are highly sought after

Zenith's cutting edge technology has attracted the top two U.S. PIs in prostate cancer research as well as the Prostate Cancer Clinical Trials Consortium (PCCTC)

Zenith has confirmed
-Dr. Eric Small - Univ. of
California, San Francisco
-Dr. Howard Scher,
Memorial-Sloan
Kettering, NY

Both Dr. Small & Dr. Scher were involved in the developed of the top two current prostate drugs in use, abiraterone & enzalutamide, respectively

Four of the last five FDA approved prostate drugs have come from the PCCTC, which is highly selective and only champions the most promising drugs

