

A background image of a laboratory setting with various glassware, including Erlenmeyer flasks and beakers, some containing liquids. The lighting is bright, creating a clean and professional atmosphere.

ZENITH 

Annual Meeting – Clinical Advancements Update
Advanced Epigenetic Technology **December 15, 2016**

Today's 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



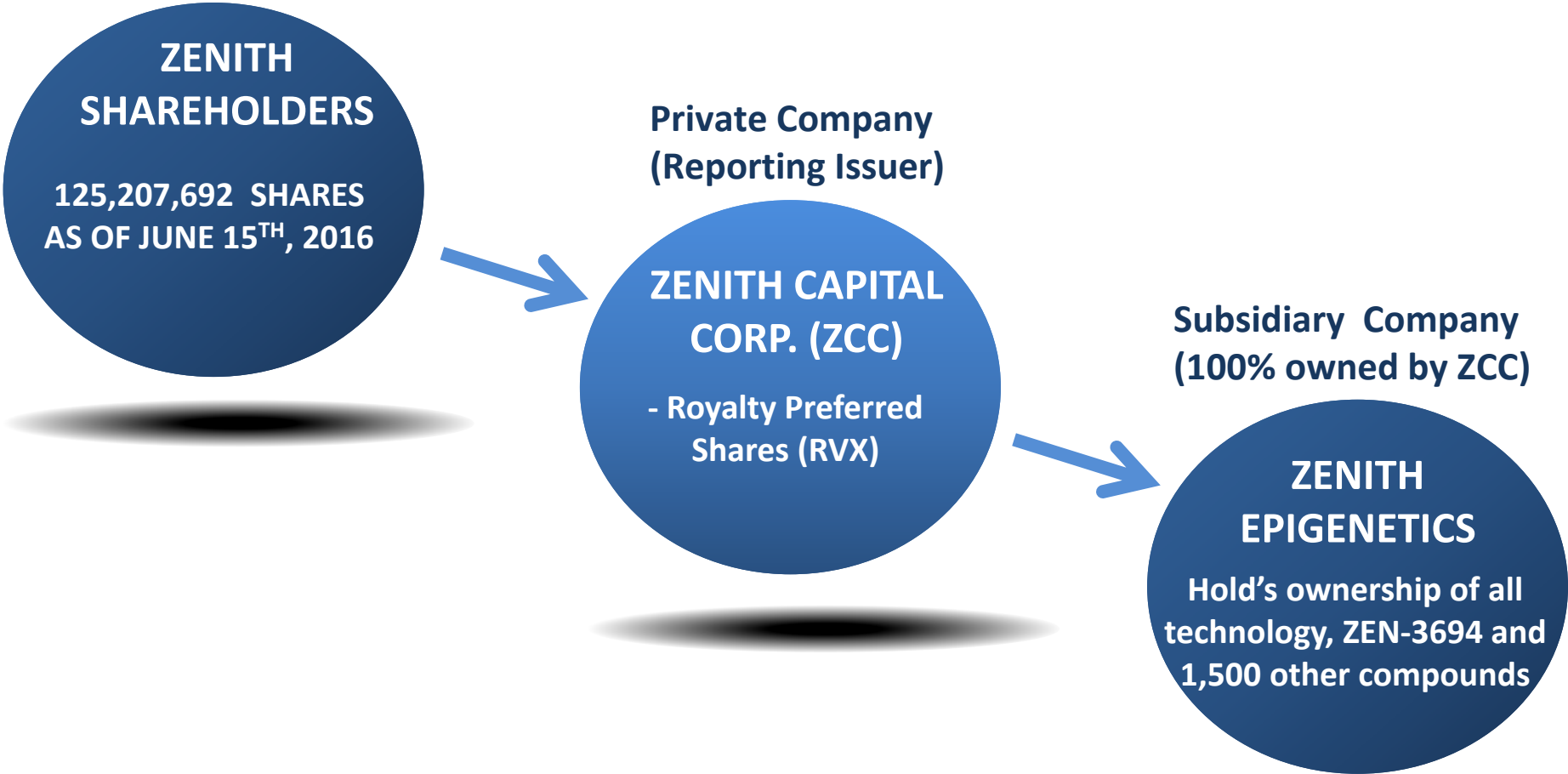
Safe Harbor Statement. This presentation contains forward-looking statements that involve risks and uncertainties, which may cause actual results to differ materially from the statements made. For this purpose, any statements that are contained herein that are not statements of historical fact may be 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
Suite 300, 4820 Richard Road S.W. Calgary, AB, Canada T3E 6L1
Tel: (403) 254-9252, Fax:(403) 256-8495, <http://www.zenithepigenetics.com>

Share Structure Profile

Founded	Corporate spin out from Resverlogix in June 2013
Status	Unlisted Possible US market IPO when conditions permit
Cash Raised 2014-2016	Approx. US\$44MM @ \$1.00 USD per share
Enterprise Value est.	\$250 MM
Shares Outstanding	125.2 MM 134.0 MM fully diluted
Cash Burn	\$2 MM per quarter - Current

Post July 31, 2016 Corporate Structure

POST-REORGANIZATION JULY 31, 2016 STRUCTURE



Historical Timeline & Strategic Progression



Company formation

Spun out of Resverlogix to focus on oncology/auto-immune

FDA approved IND for ZEN-3365

Top investigators & institutions recruited for Phase 1
Jul 2014

Challenges

Prior to the Phase 1 launch, overlapping IP published by another group, ZEN-3365 discontinued
Oct 2014

Change of plans

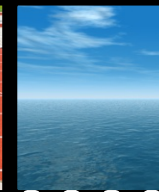
ZEN-3694 selected as DC, superior properties, multiple back ups, IP published
May 2015

2014



2015

2015



2016

Focused clinical strategy

IND accepted
MSKCC/UCSF selected as lead clinical sites (mCRPC)
Dec 2015

Financing

Raised \$25M
Mar 2016

First patient dosed

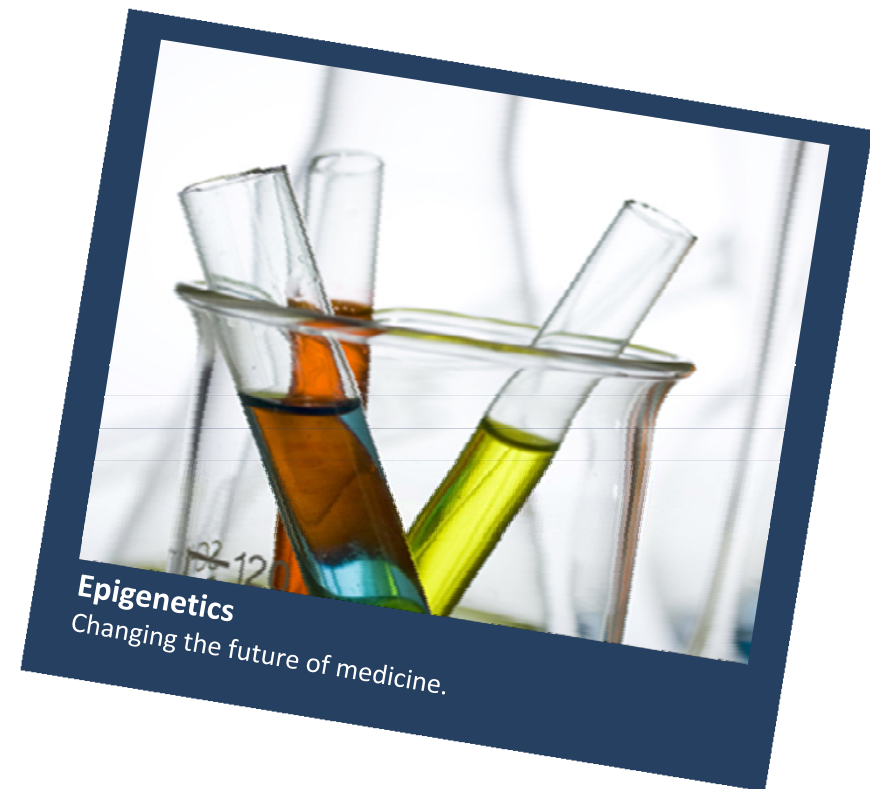
Jun 2016

Biology Expansion

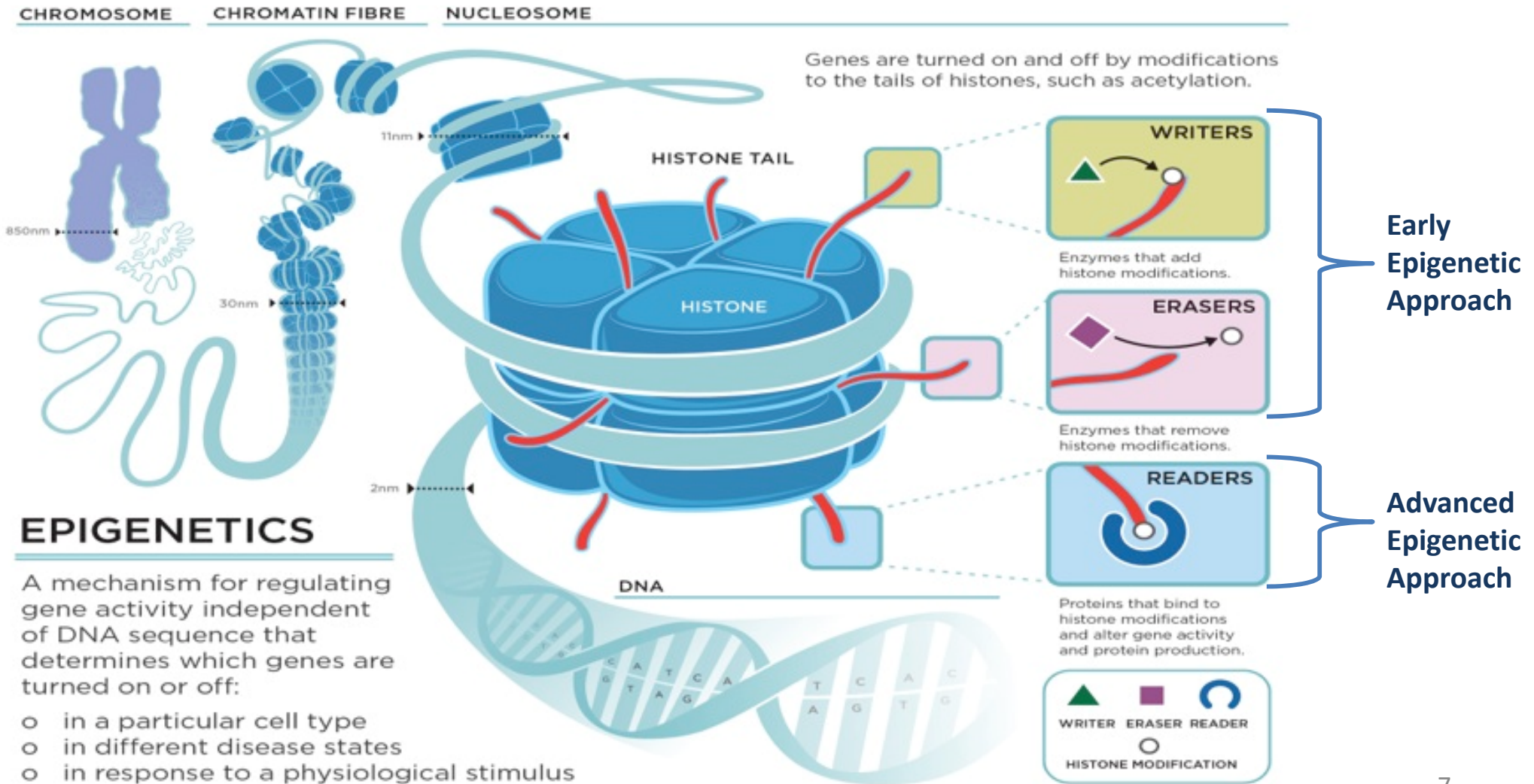
Immuno-Oncology
TNBC, NSCLC, ER+ Breast, next indications
Ongoing

Epigenetics Mechanism

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- **2. Epigenetic Mechanism**
- 3. Prostate Cancer Rationale
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Epigenetics, the Mechanism Behind Our Approach

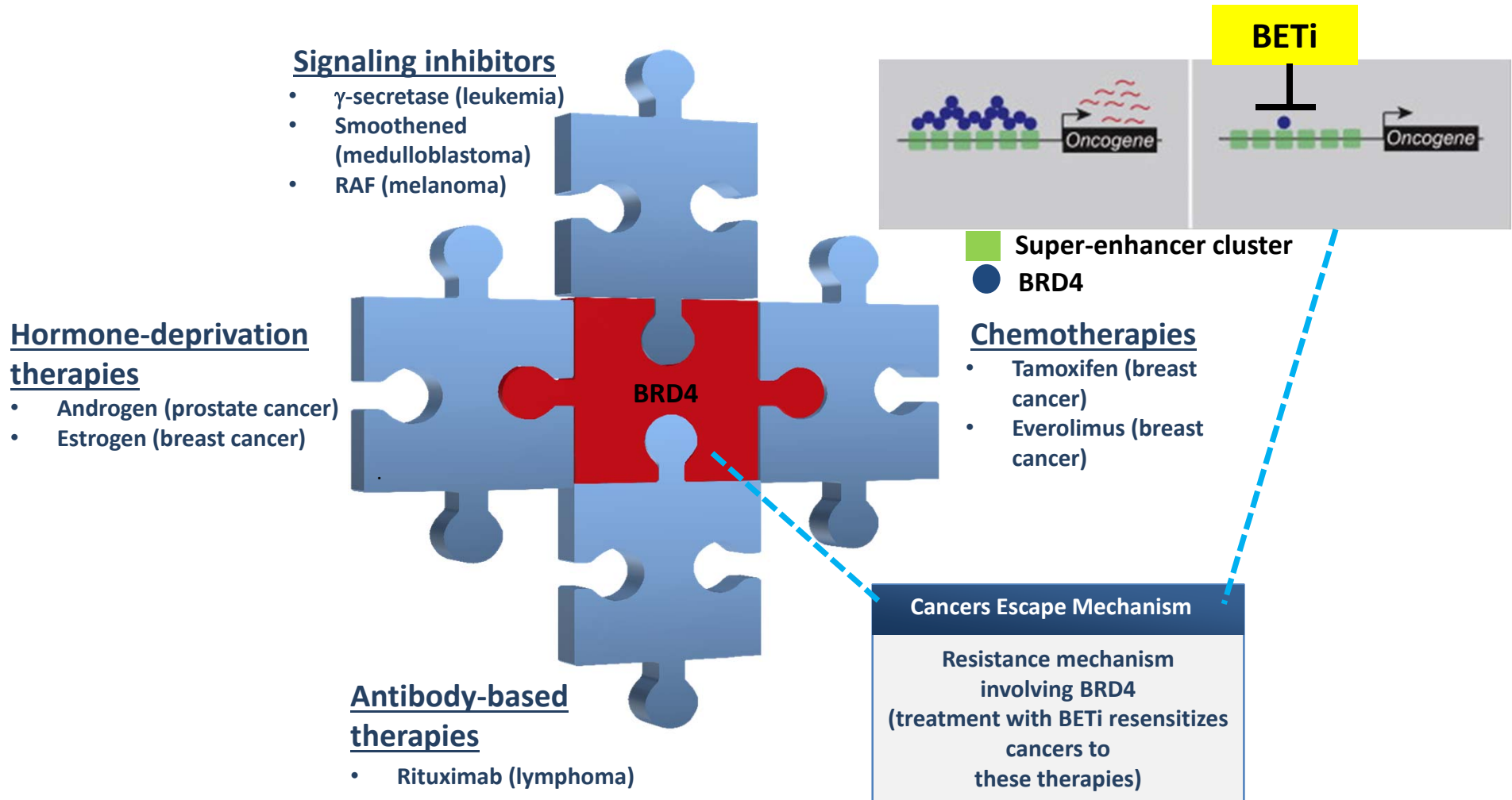


EPIGENETICS

A mechanism for regulating gene activity independent of DNA sequence that determines which genes are turned on or off:

- o in a particular cell type
- o in different disease states
- o in response to a physiological stimulus

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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Current Market and Unmet Need

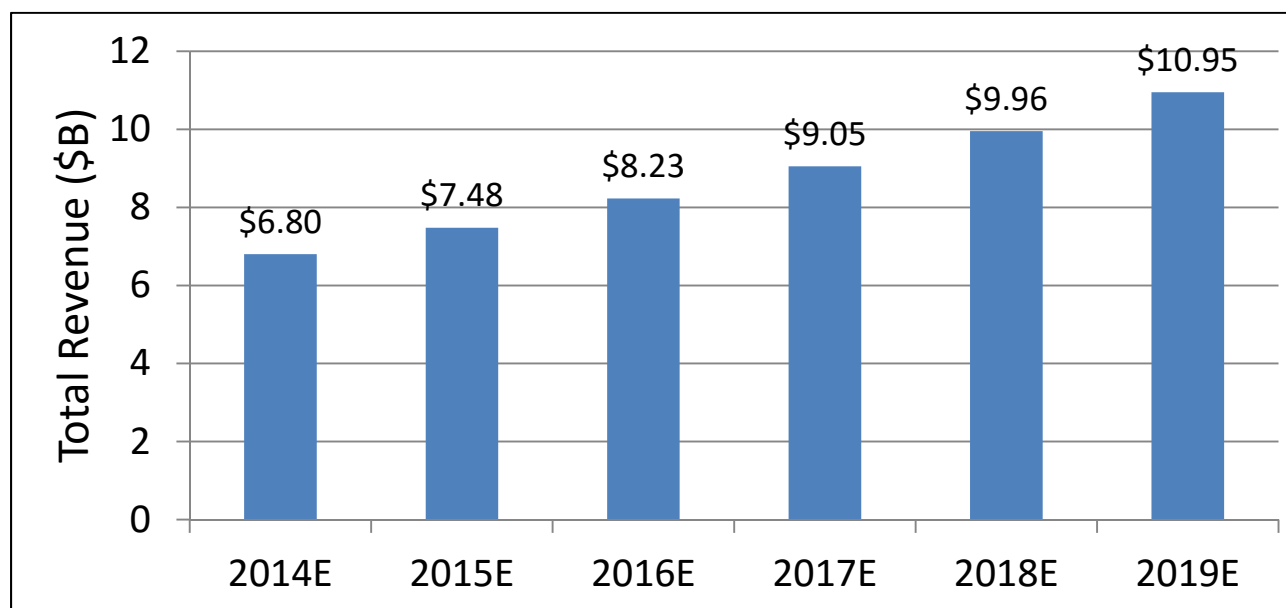
- ~135,000 annual mCRPC patients in the US/EU alone – majority receive enzalutamide or abiraterone as first-line treatment
- **Over \$4B in sales in 2015** for first-line enzalutamide and abiraterone
- Patients become resistant to these therapies, no effective second-line therapy yet
- Continuing high 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



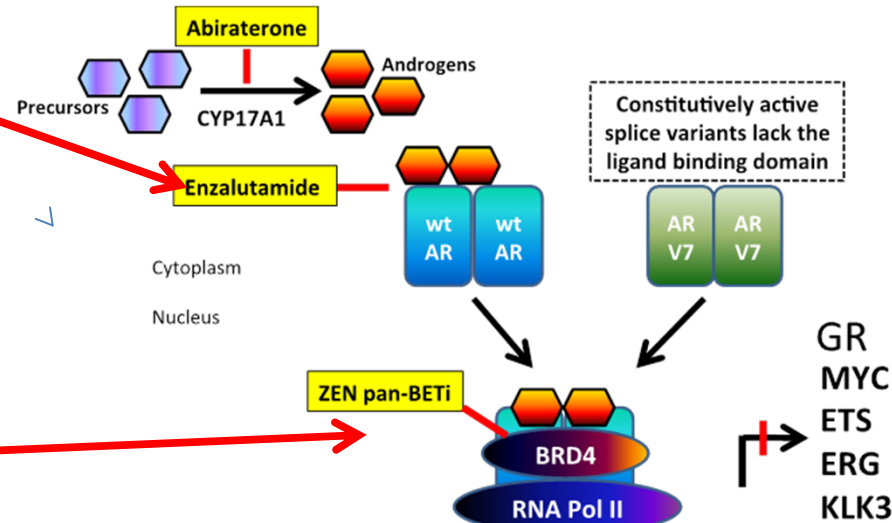
The global prostate cancer WW market is expected to reach \$11B by 2019, driven by Zytiga and Xtandi.

ZEN-3694 Potential in Patients Developing mCRPC Resistance to Enzalutamide

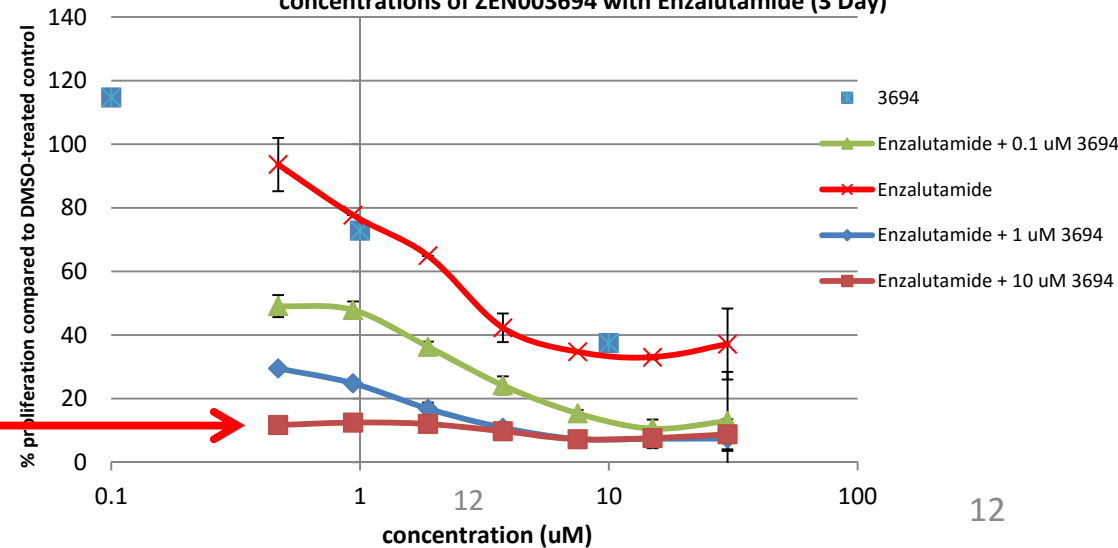
ZEN-3694 works downstream of current therapies

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

The combination of ZEN-3694 & today's top medications show strong synergism and expected reduction to resistance



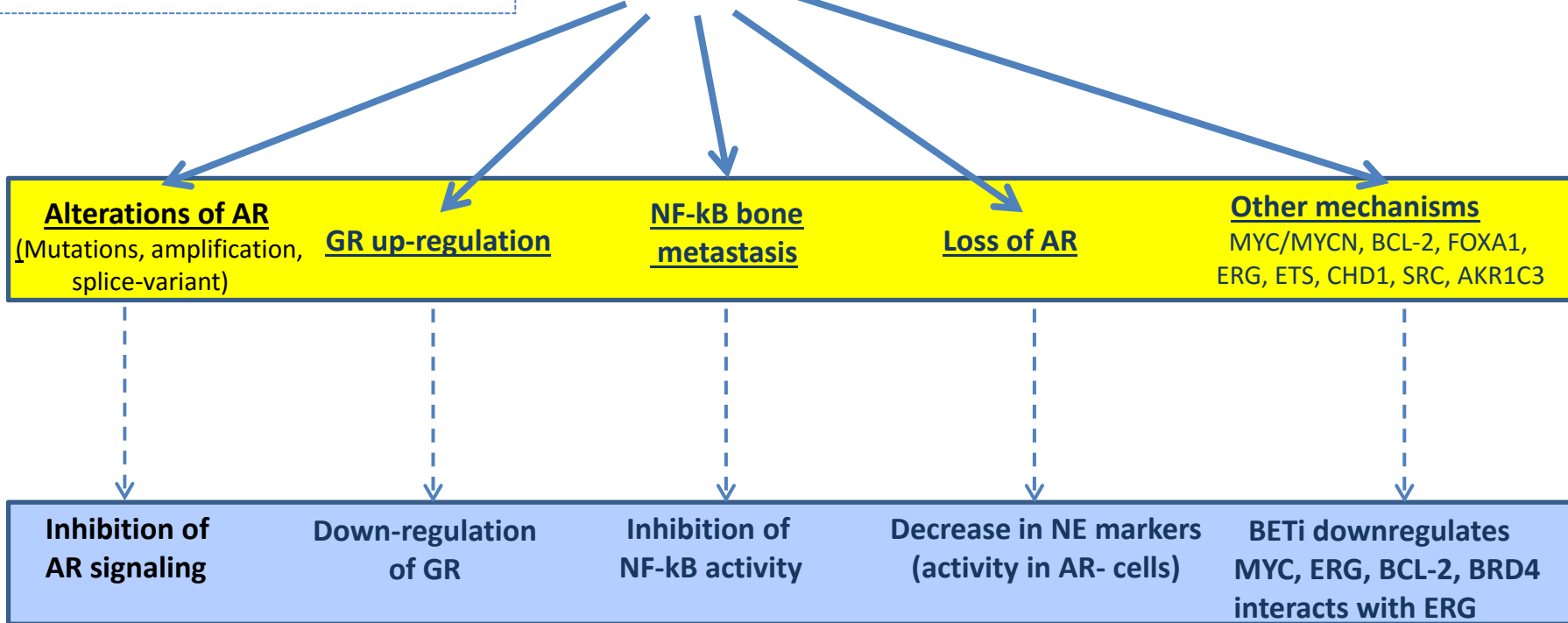
TB-03910 Cell Viability in VCAP P3 + 0.1 nM R1881 Treated with various concentrations of ZEN003694 with Enzalutamide (3 Day)



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

ENZALUTAMIDE/ABIRATERONE THERAPY

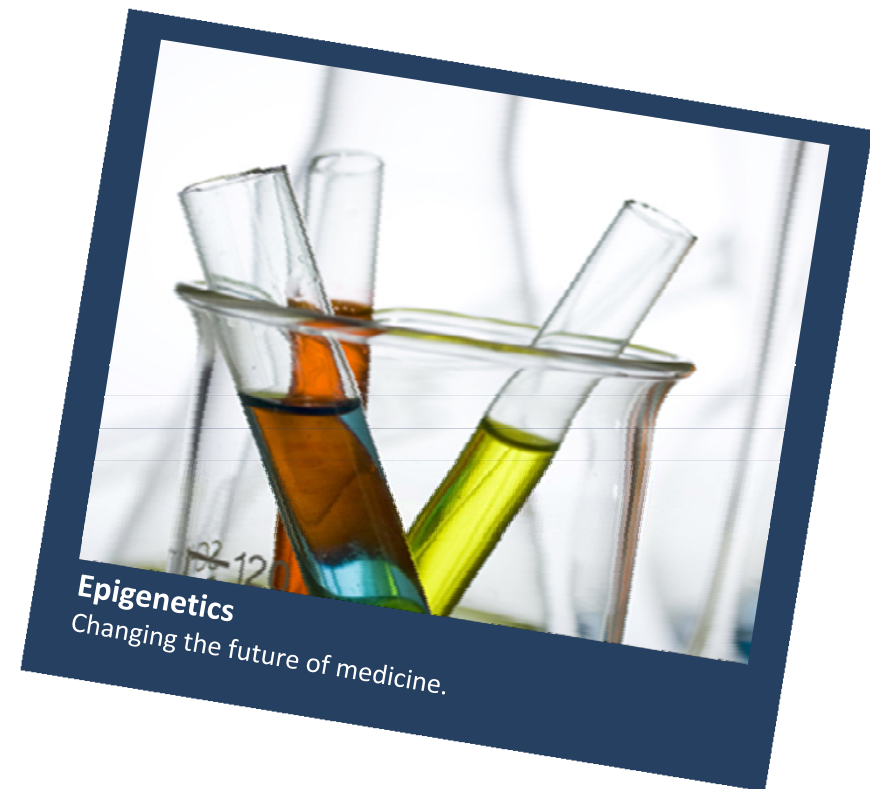
CRPC



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

Phase 1 Details & Early Results

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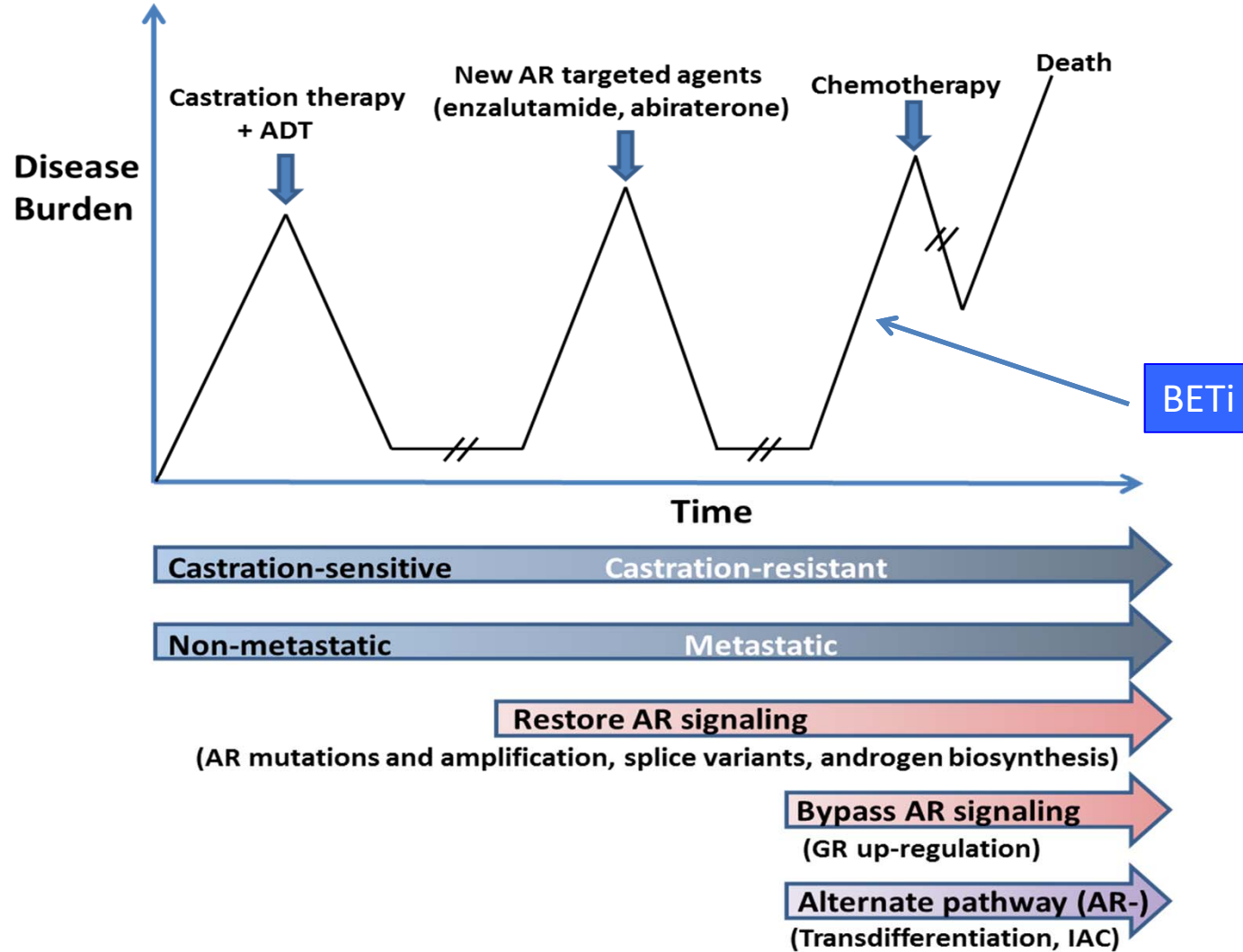


Zenith's Principal Investigators



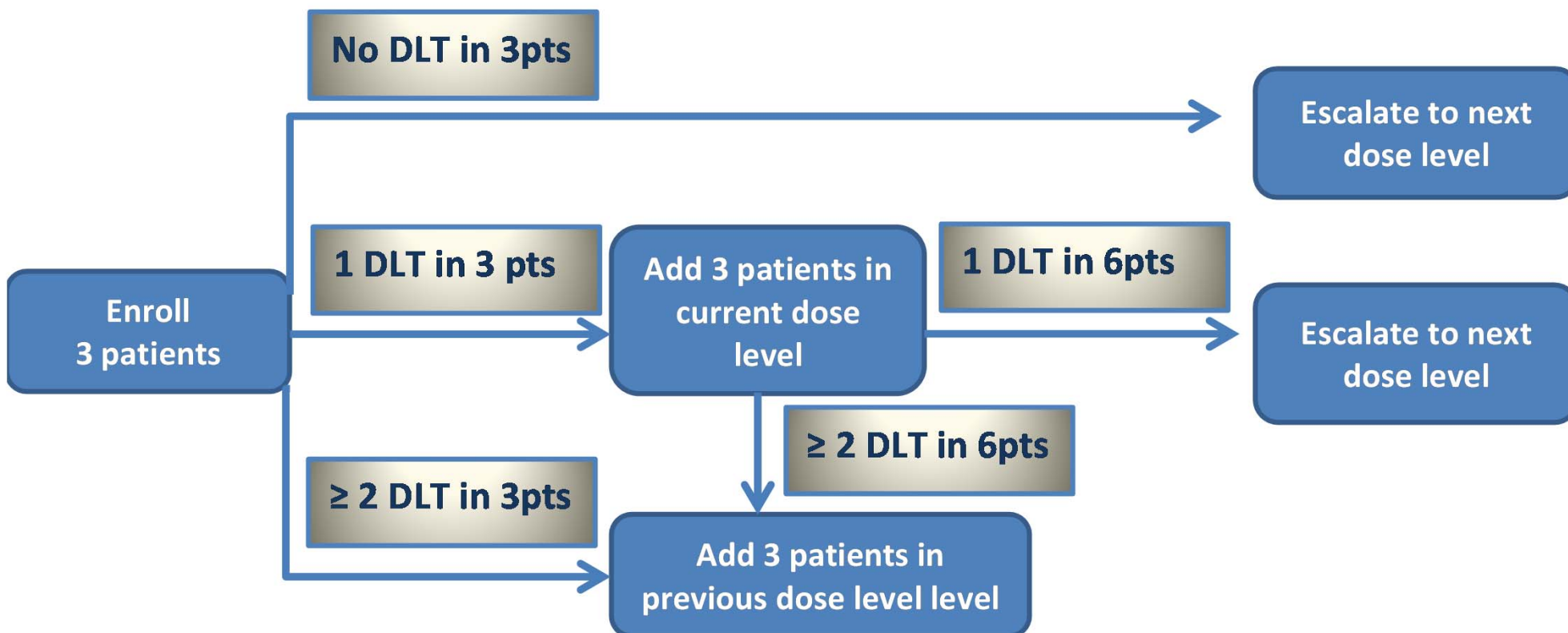
Name	Institution	Comments
Eric Small, MD <i>Chief, Dept. of Medicine</i>	University of California, San Francisco (UCSF)	Developed abiraterone - #2 CRPC drug, owned by J&J.
Rahul Aggarwal, MD <i>Developmental Therapeutics Specialist, Genitourinary Oncologist</i>	University of California, San Francisco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

3 + 3 Dose Escalation Design



Note: MTD (Maximum tolerated dose) is the highest dose with ≤ 1 DLT in 6 patients. DLT is Dose Limiting Toxicity

Primary

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

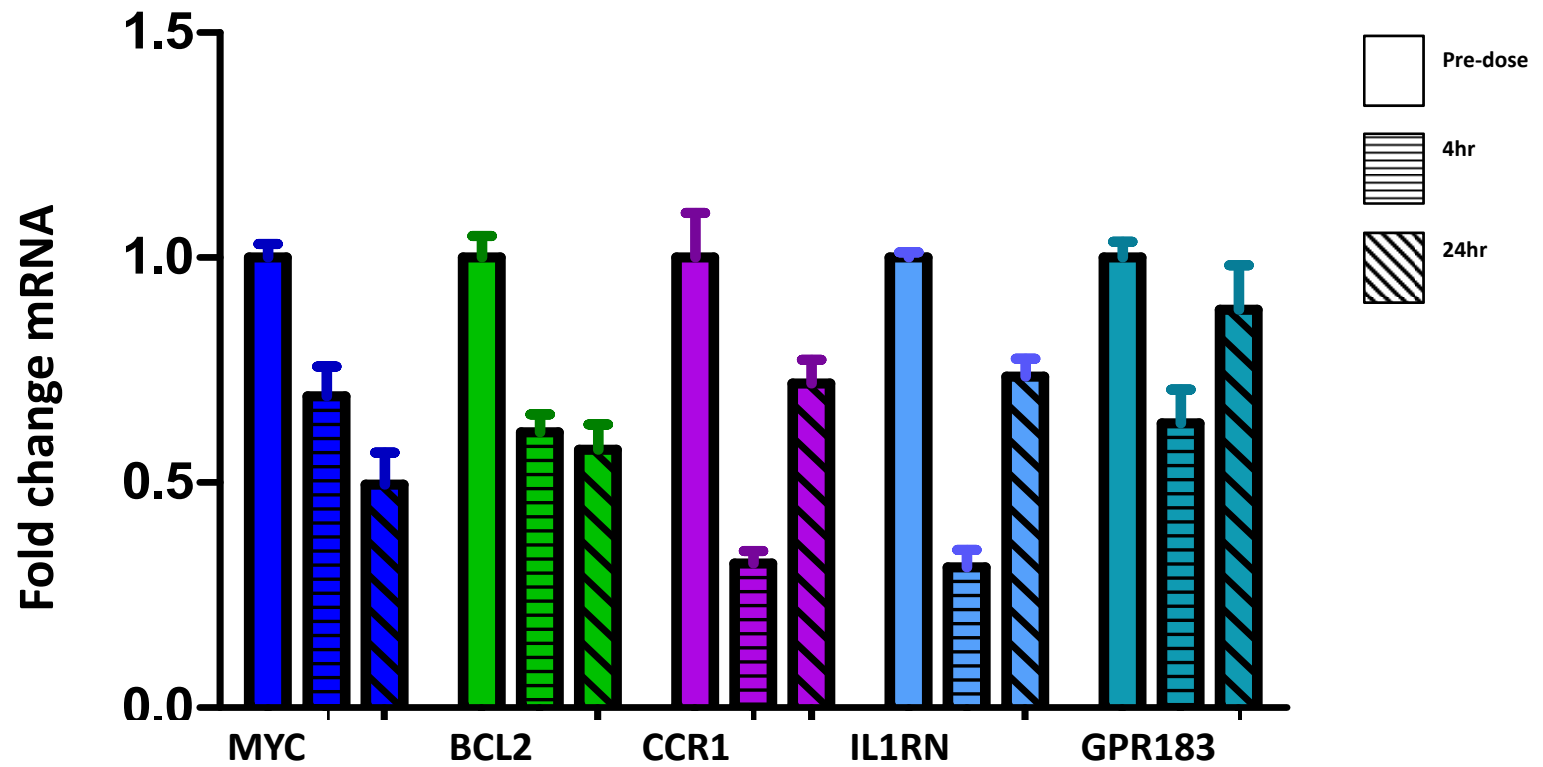
Secondary

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

ZEN-3694 single-agent study ongoing

- Maximum Tolerated Dose (MTD) confirmation
- Good PK, exposures reach IC₅₀ cell proliferation values
- **Target modulation shown**
- On-target safety profile
- Longest patient on drug now beyond 4 months
- Intermittent dosing schedule cohorts may be initiated in Q1/17 for recommended Phase 2 dose (in discussion)

Target Modulation Measured in Clinic



Robust target modulation for 24h

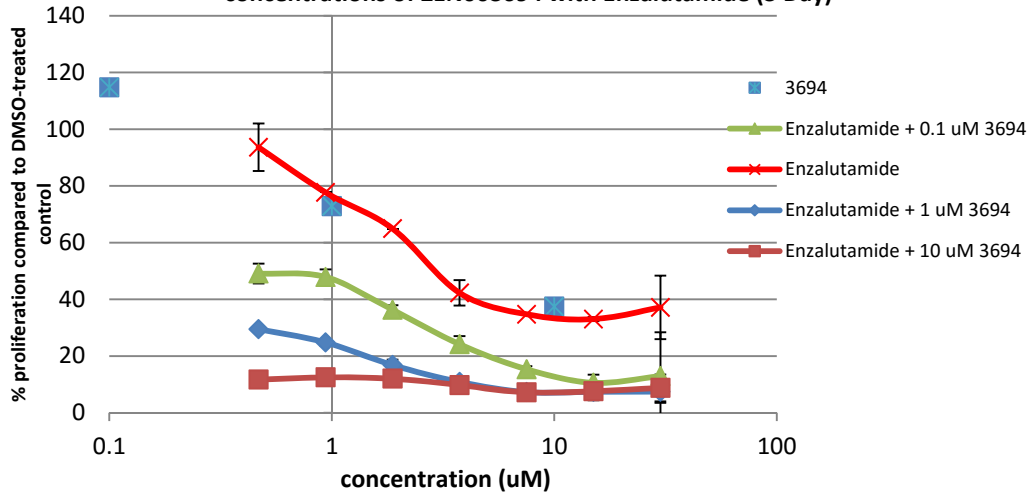
Enzalutamide Combination Trial – Phase 1b

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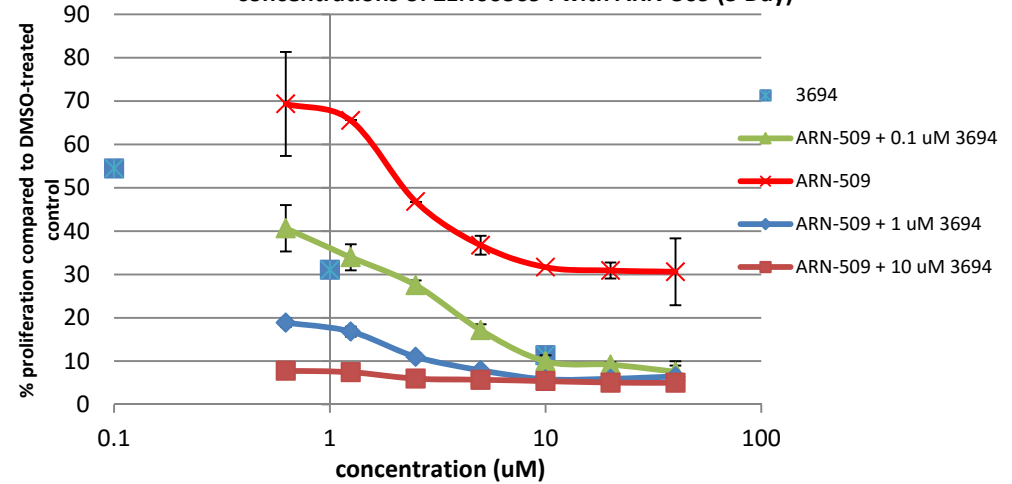
ZEN-3694 Synergizes With Enzalutamide & ARN-509

TB-03910 Cell Viability in VCAP P3 + 0.1 nM R1881 Treated with various concentrations of ZEN003694 with Enzalutamide (3 Day)



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

TB-03919 Cell Viability in VCAP P7 + 0.1 nM R1881 Treated with various concentrations of ZEN003694 with ARN-509 (3 Day)



uM ZEN3694	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

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

Two sites, UCSF and MSKCC, open for enrollment

Dose escalation cohorts

MTD / RP2D Confirmation

MTD: Highest dose with $\leq 1/6$ patients with DLT

Expansion Cohort A

Enza naïve, progression on
abiraterone

Expansion Cohort B

Biochemical progression on
enzalutamide

ZEN-3694 Phase 1b Study Endpoints

Primary

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

Secondary

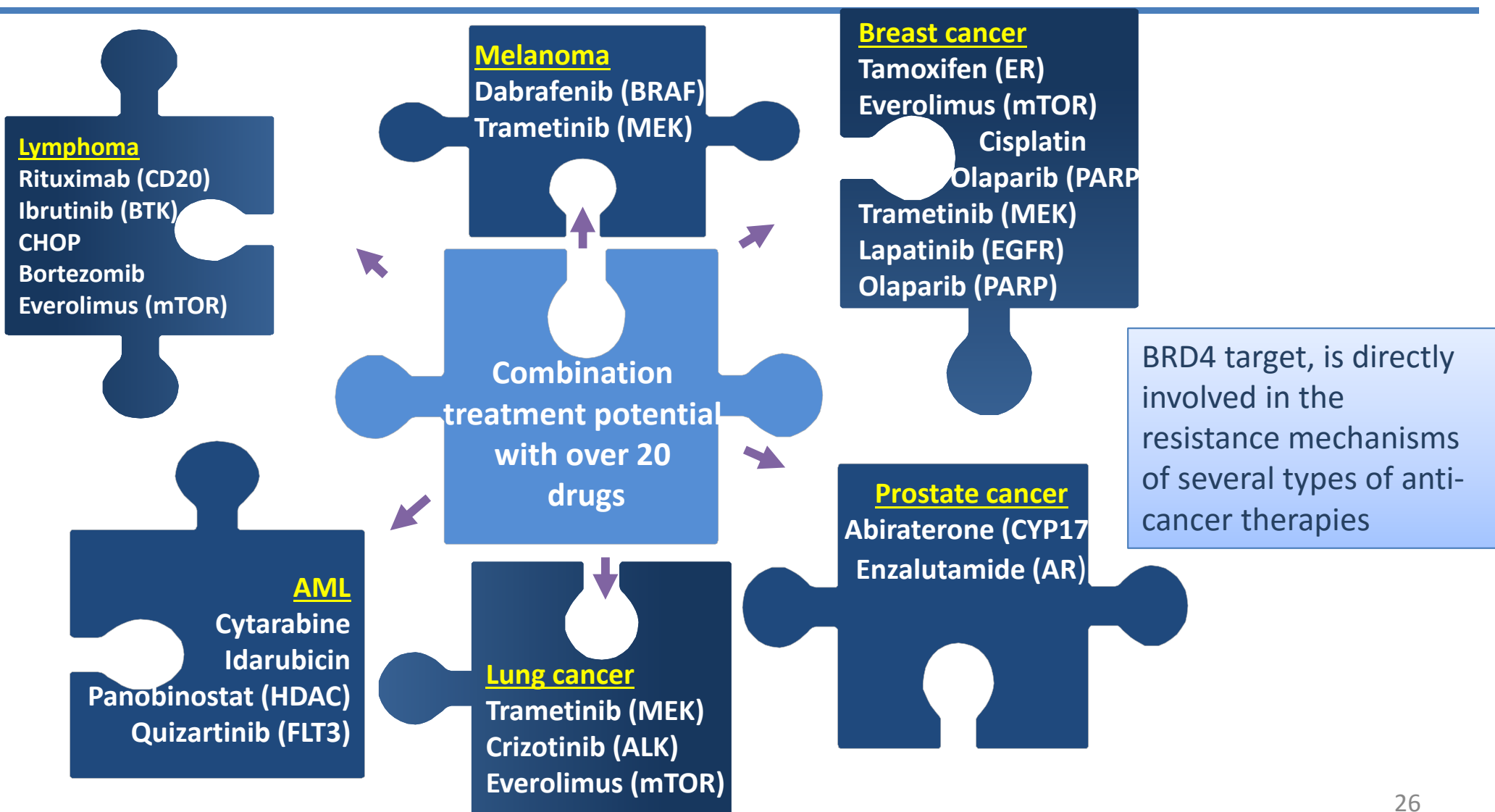
- Pharmacokinetics (PK) of ZEN-3694 and enzalutamide when given in combination
- Preliminary clinical activity
 - PCWG2 Criteria: PSA response rate, Radiographic response rate, Median PFS
 - Circulating Tumor Cell (CTC) response rate

Next Steps

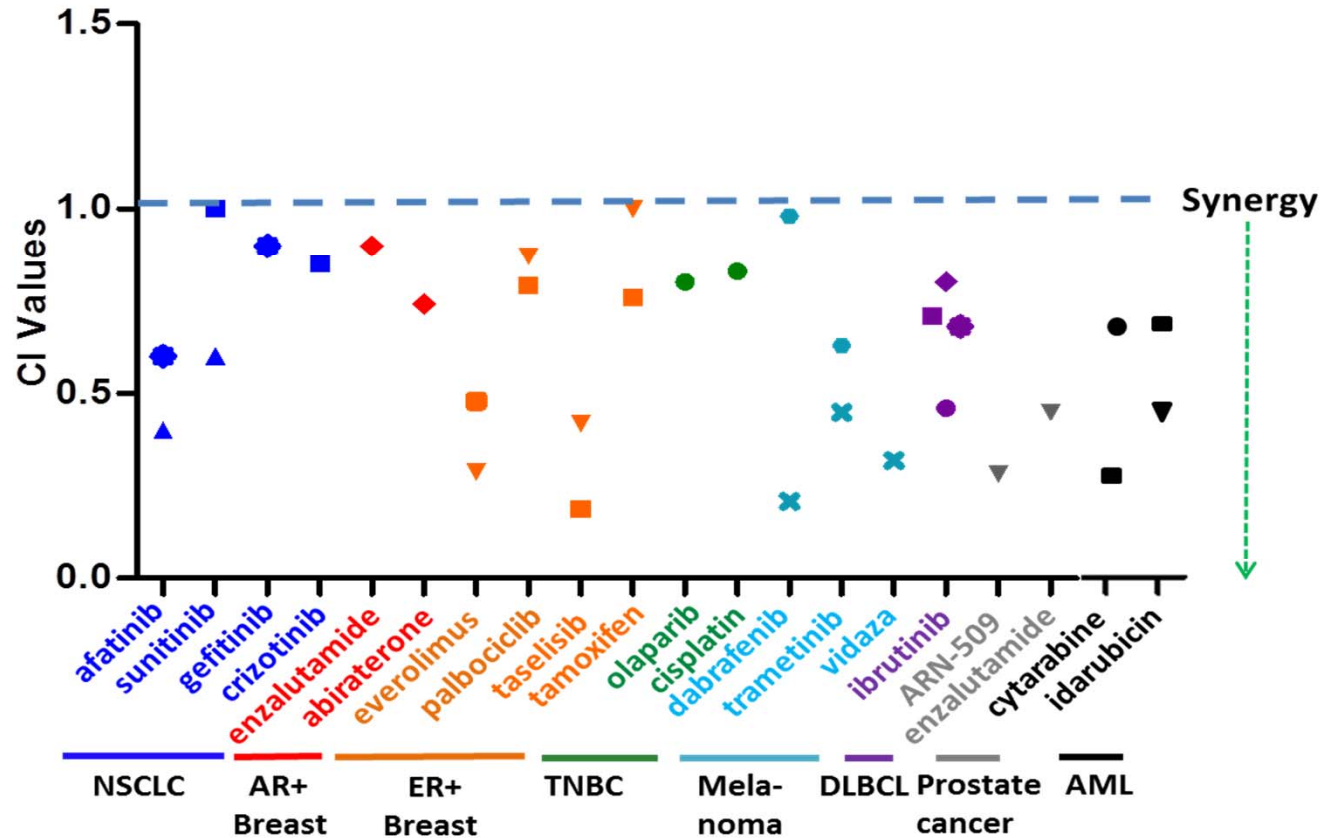
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BET Inhibitors Potential as Combination Agents



ZEN-3694 Synergizes With Several Standard of Care Cancer Drugs



Indication		Cell line (mutation)
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)

Potential Resistance Pathways in TNBC in Response to Chemotherapy

AC-T

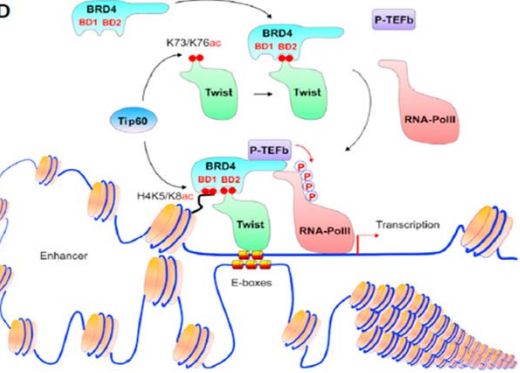
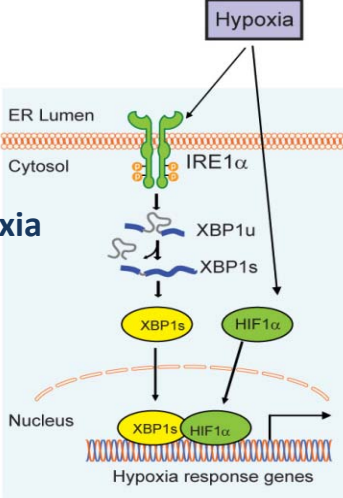
TNBC

Resistance mechanism

EMT

WNT signaling

XBP1s driven hypoxia



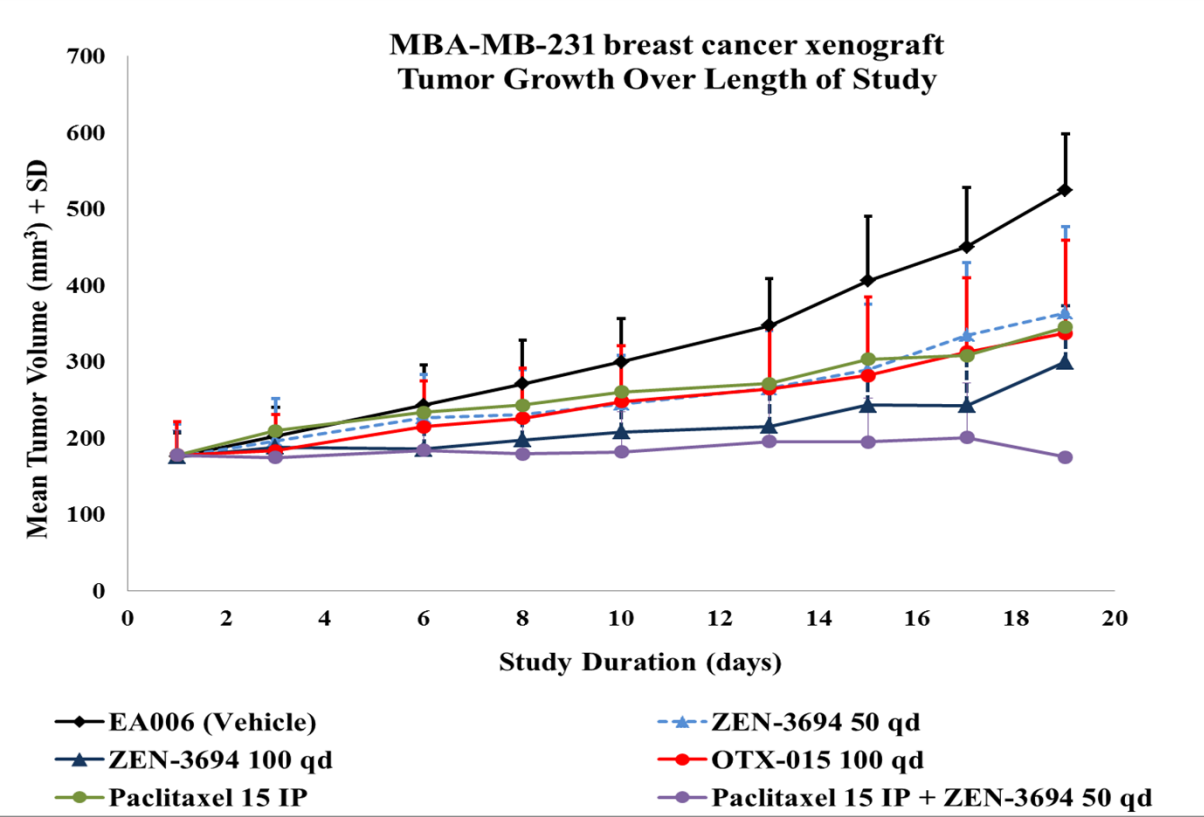
**BETi down
Regulates
Several key players
Twist targets (Wnt5a)**

**BETi modulates WNT
pathways**

BETi downregulates XBP1s

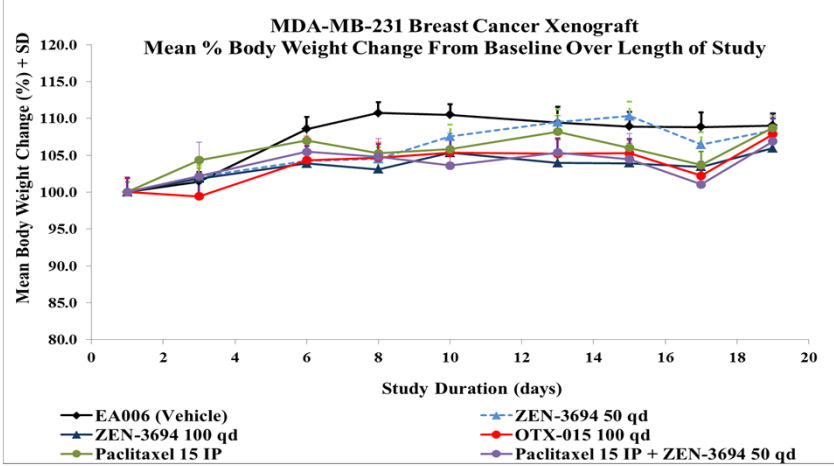
Rationale for ZEN-3694 to show activity in different TNBC models that are resistant to chemotherapy

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



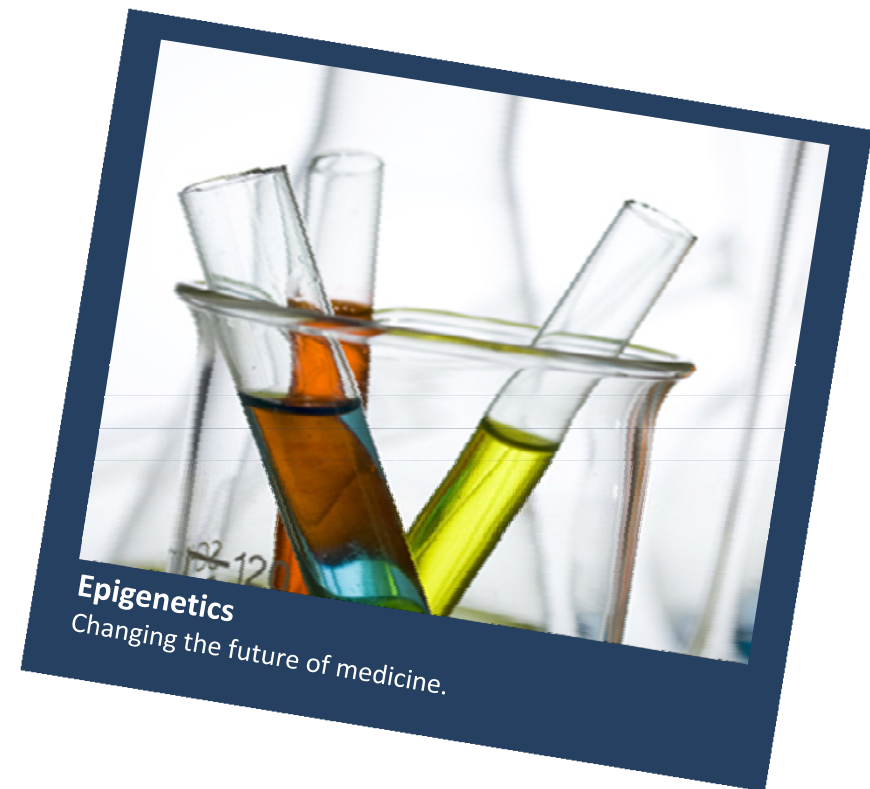
Treatment Groups	TGI
EA006 (Vehicle)	0%
ZEN-3694 50 mg/kg qd	46%
ZEN-3694 100 mg/kg qd	64%
OTX-015 100 mg/kg qd	54%
Paclitaxel 15 mg/kg IP	52%
Paclitaxel 15 mg/kg IP + ZEN-3694 50 mg/kg qd	101%

- 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)



Intellectual Property

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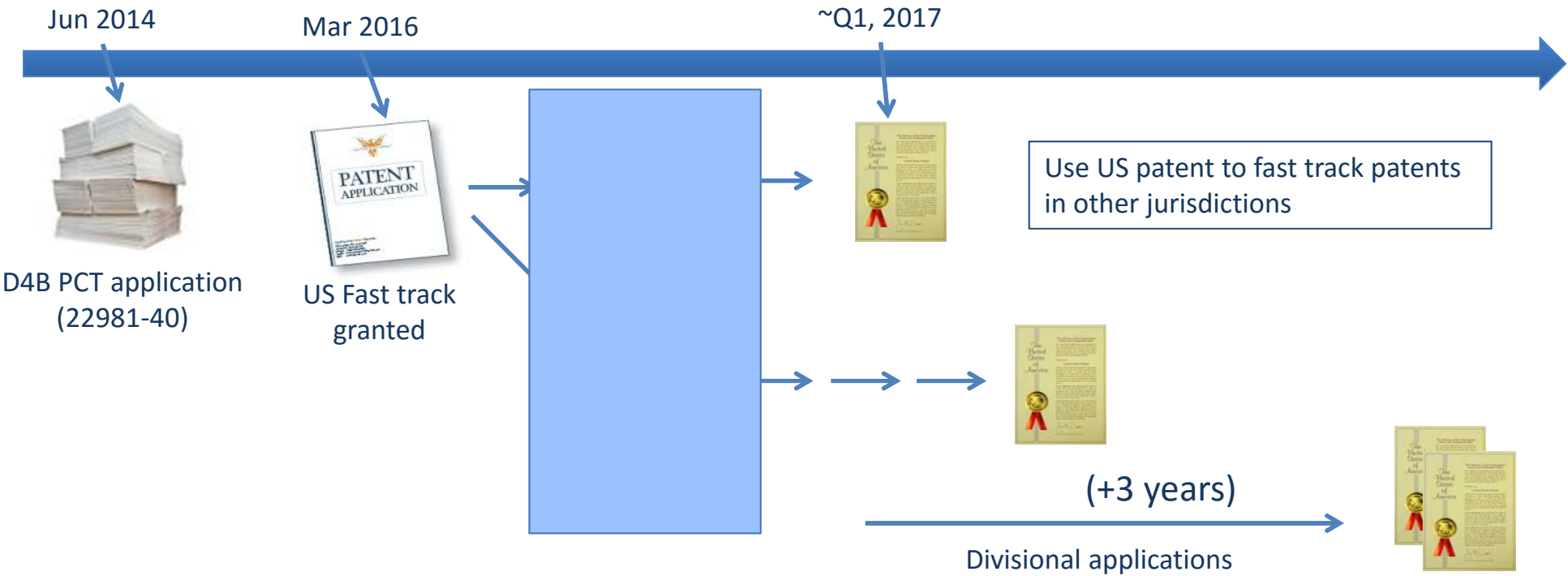
Intellectual Property: Status Update



Zenith Epigenetics Ltd. owns numerous patent families, including three 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						
22981-39						
22981-40						
22981-41						
22981-45						
22981-46				National phase mid 2017		
22981-47				National phase mid 2017		
22981-49				National phase mid 2017		
22981-50				National phase mid 2017		
22981-51				National phase mid 2017		
22981-57		Convert mid Dec.2016				

ZEN-3694 Patent Application



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

There are hundreds of biotech company's with potential drug candidates

Drug candidates require 3rd party Principle Investigators (PI's) 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. PI's in prostate cancer research as well as the Prostate Cancer Clinical Trials Consortium (PCCTC)

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

Both Dr's Small & Scher where involved in the developed of the top 2 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

A background image of a laboratory setting with various glassware, including Erlenmeyer flasks and beakers, some containing liquids. The lighting is bright, creating a clean and professional atmosphere.

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