Advanced Epigenetic Technology

BIO-Europe Spring 2018

Amsterdam, The Netherlands **March 13th**

Zenith Profile

Founded	Independent company spun out from Resverlogix in June 2013, Canada
Company	Clinical stage, developing novel epigenetic and immune-oncology drugs for oncology
Status	Private company, Full reporting issuer
Products and Technology	ZEN-3694 – BETi in Phase 1b clinical testing (single agent/ combination) Pre-clinical immuno-oncology and other solid tumors programs Epigenetic platform
Location	Calgary and San Francisco
Financing 2014-2016	$ 44M from private investors @ $1.00 USD per share
Shares Outstanding	134.0 MM fully diluted

Note: The Company continues to work on securing additional financing as previously disclosed.

Historical Timeline: Rapid & Efficient Progression

ZENITH

Company formation (2013)

Spun out of Resverlogix to focus on oncology and auto-immune indications

Expanded Platform

+ 2500 compounds synthesized. Crystal structures, optimized PK/PD properties.

BETi biology & rationale

Clinical Candidate

ZEN-3694 selected as DC, superior therapeutic index, mutiple back ups, IP published

Focused clinical strategy

IND accepted

MSKCC/UCSF selected as lead clincial sites (mCRPC)

Financing

Raised $25M

FPI in single agent study, June 2016

Biology Expansion

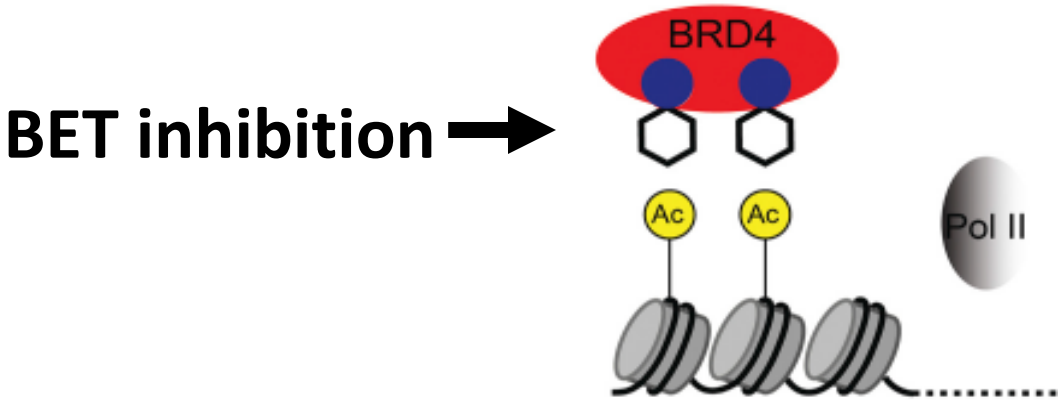
Immuno-Oncology,

HRD, ER+ BC, next indications

ZEN-3694 US patent issued in May 2017

- **Phase 1b, FPI in combination trial in Jan 2017**
- **Single agent study completed in June 2017**
- **50 patients dosed to date**

BET Inhibitors Block Tumor Oncogene Expression



Oncogenes of addiction

MYC, BCL2
AR, ER

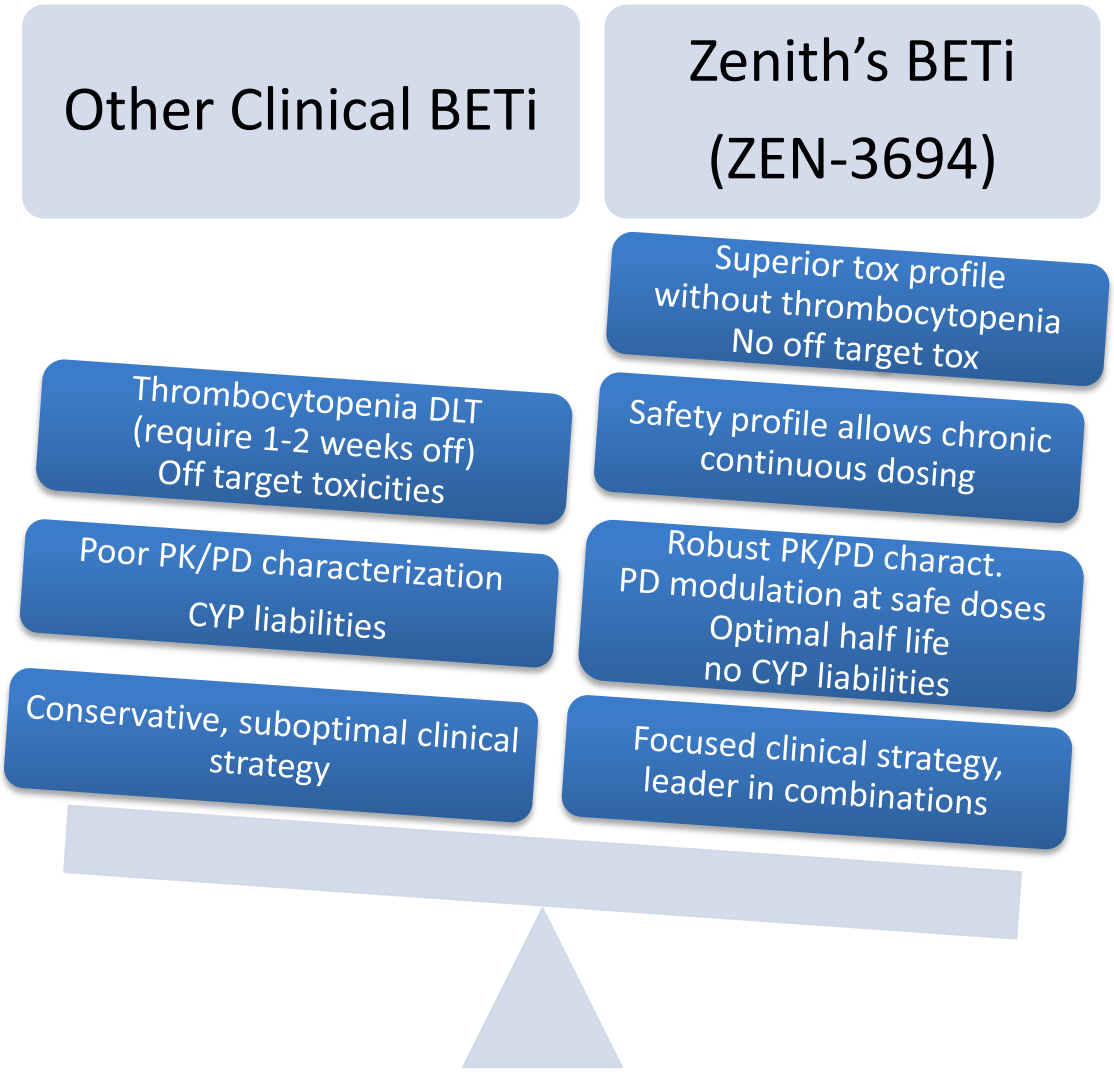
Oncogenes of immune evasion

Immune checkpoints
Regulatory cells

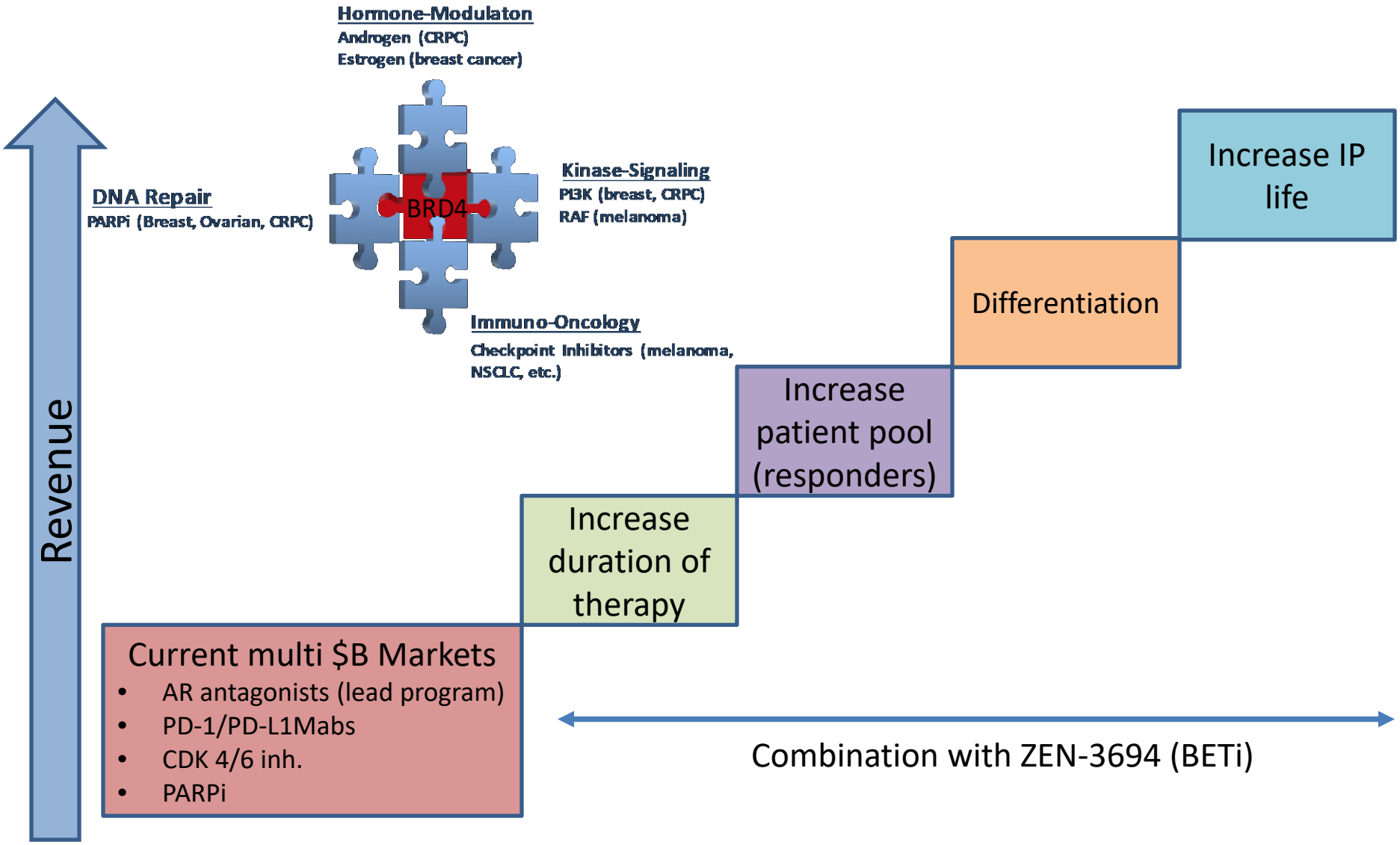
Oncogenes of metastasis

Wnt5A
VEGF
NF-kB

Zenith's BETi Program is Clinically Differentiated, Leader in Combination Approach



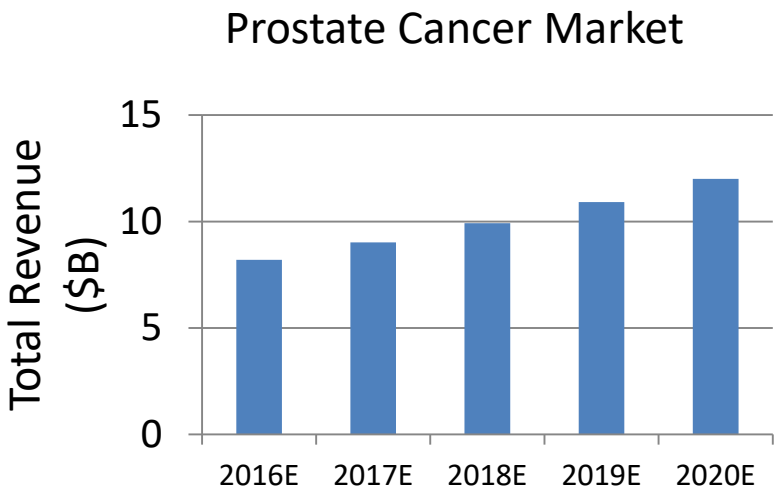
Developing Epigenetic Combination Therapies to Address Resistance & Significantly Increase Revenue of $B Franchises



Global Prostate Cancer Market and Unmet Need

Current market and unmet need

- Over $4B in sales in 2016 for enzalutamide / abiraterone,
- Almost all patients become resistant, no effective therapy in resistant patients
- Continuing high mortality rate in resistant mCRPC (50% 1 year survival, 28% in 5 years)

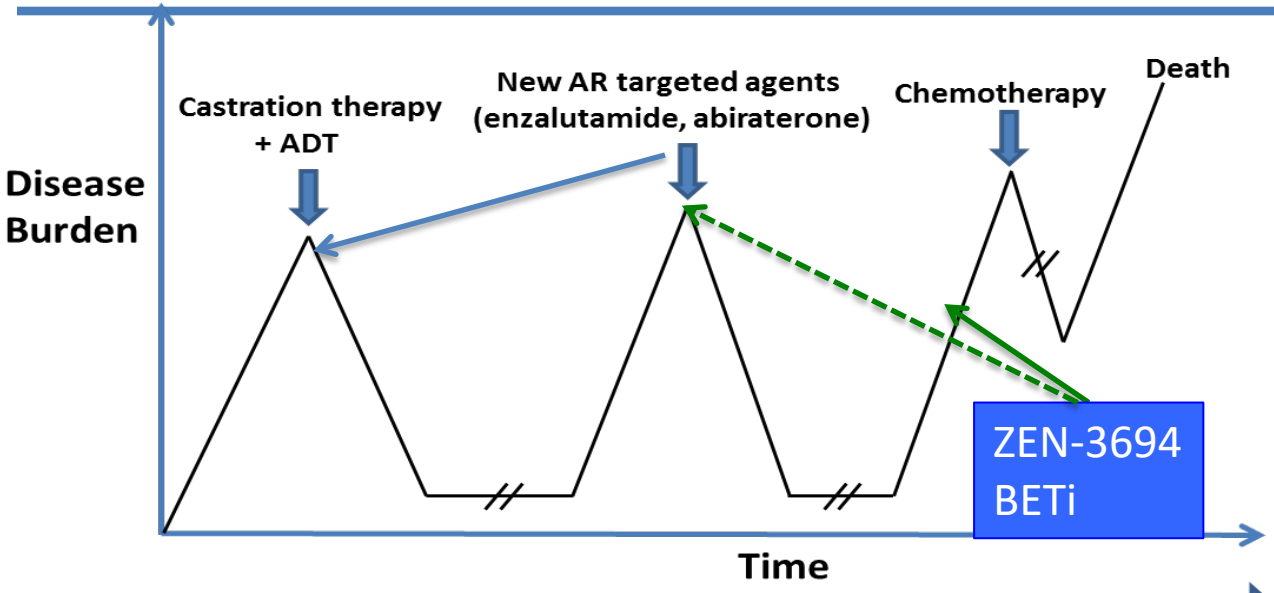


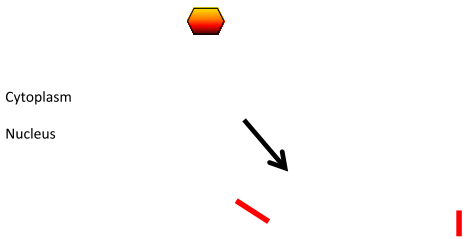
Opportunity for ZEN-3694

- Patients that progress on enza/abi
  - ~80,000 eligible patients in US/EU alone
- Enza/abi now in pre-metastatic/pre-hormone refractory setting
  - ZEN-3694 to move into 1st line mCRPC therapy, expanded population and duration on therapy
- >$1B opportunity for ZEN-3694 in mCRPC, combination

The global prostate cancer market forecast to reach $13B by 2024 in US/EU/Japan, driven by Zytiga (abiraterone), Xtandi (enzalutamide), Erleada (aplalutamide), others

Castration-resistant Prostate Cancer (CRPC) Disease Progression and Treatment Algorithm





Castration-sensitive → **Castration-resistant**

Non-metastatic → **Metastatic**

Restore AR signaling
(AR mutations and amplification, splice variants, androgen biosynthesis) — *BETi+ AR antagonist*

Bypass AR signaling
(GR up-regulation) — *BETi+ AR antagonist*

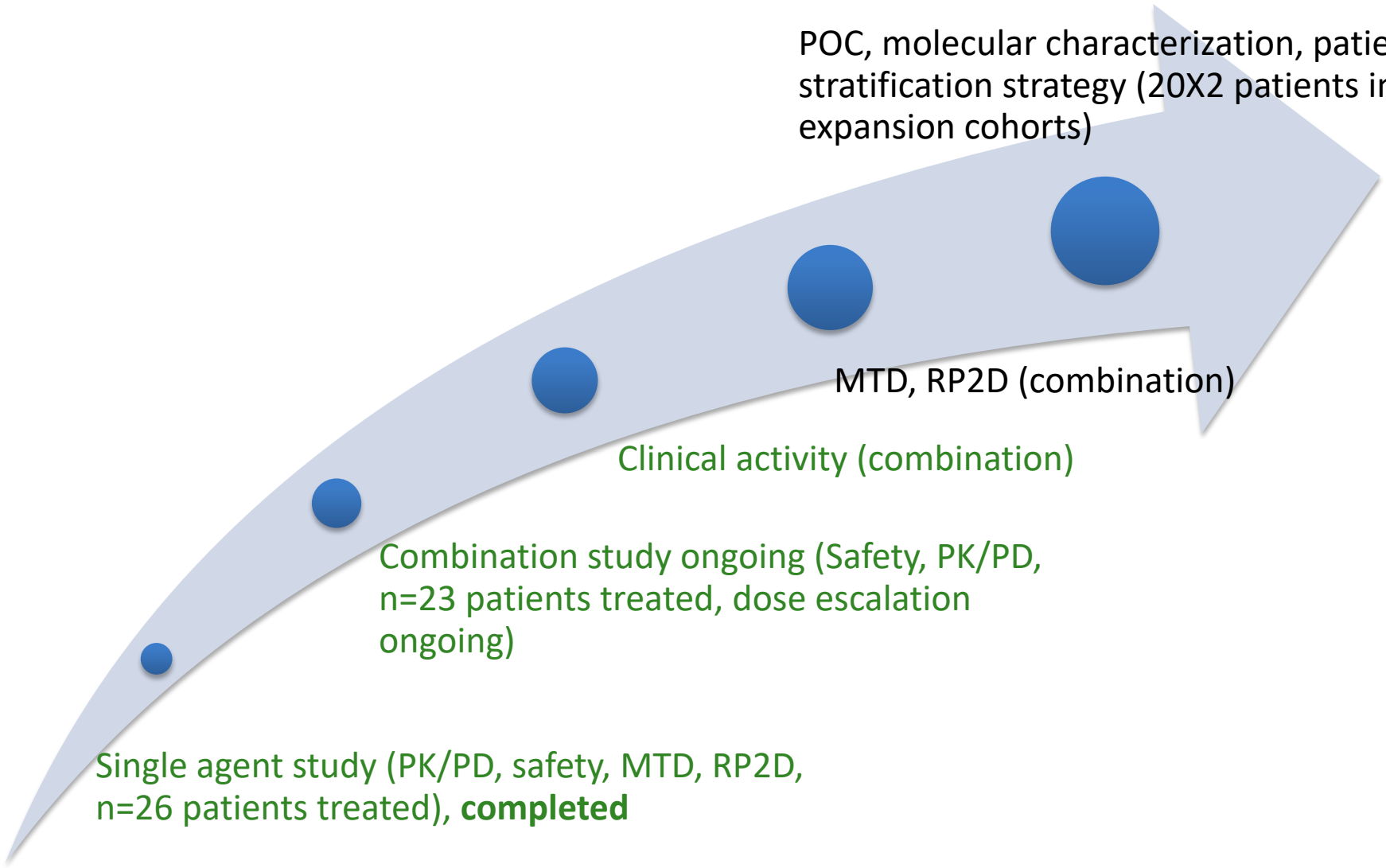
Alternate pathway (AR-)
(Transdifferentiation, IAC) — *BETi*

- Medical need for targeting patients resistant to AR targeted agents
- Need for targeting downstream AR signaling and resistance pathways
- AR antagonist moving to earlier stages of disease, ZEN-3694 also shifting left, expanded market

Zenith Has Recruited Leading Clinical Investigators for Phase 1b mCRPC Clinical Study

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, apalutamide
Howard Scher, MD *Chief, Genitourinary Oncology* **Wassim Abida, MD, PhD** *Medical Oncologist*	Memorial Sloan Kettering Cancer Center (MSKCC)	Developed enzalutamide
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
Elisabeth Heath, MD *Professor, Dept. Hematology/Oncology*	Karmanos (Wayne State)	Genitourinary oncology specialist
Michael Schweizer, MD *Assistant Professor*	University of Washington	Experience with AR antagonists
David Nanus, MD *Chief, Division of Hematology and Medical Oncology*	Weill Cornell University	Genitourinary oncology specialist

ZEN-3694, Rapid mCRPC Clinical Progress



ZEN-3694 Development in mCRPC: Combination With Enzalutamide: Dose Escalation Ongoing

2017		2018	
1H	2H	1H	2H

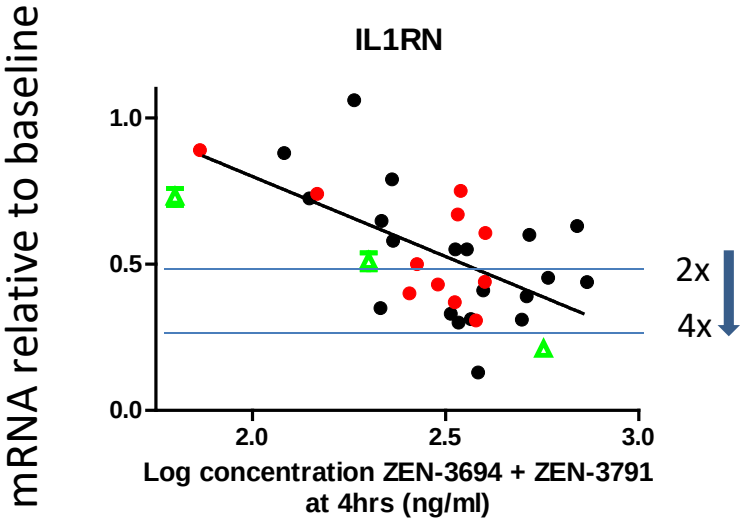
Combination dose escalation
ZEN-3694 + enzalutamide; Patients progressing on abiraterone or enzalutamide N~30

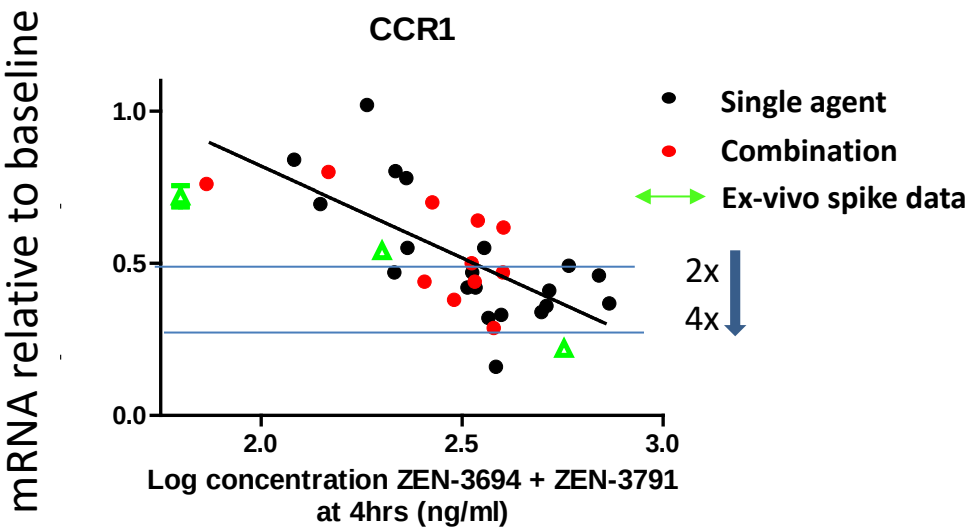
Combination expansion
ZEN-3694 + enzalutamide; Patients progressing on abiraterone N~20

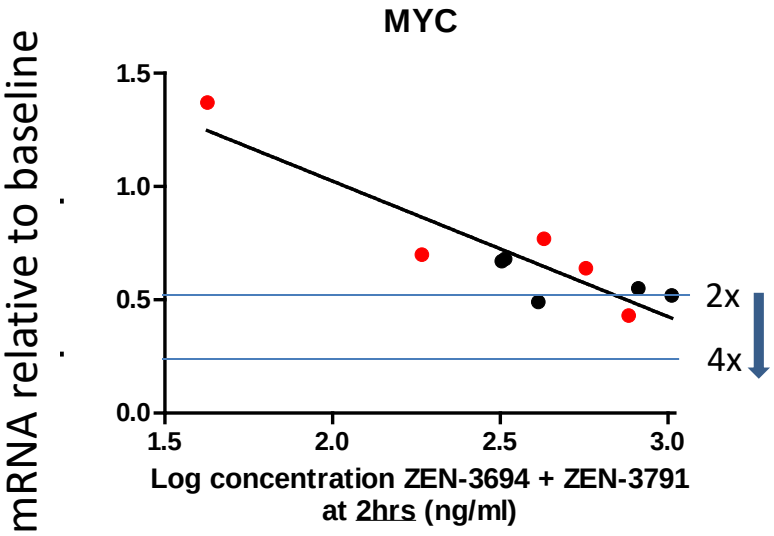
Combination expansion
ZEN-3694 + enzalutamide; Patients progressing on enzalutamide N~20

- Dose escalation ongoing
- Dose proportional PK , no drug-drug interaction
- Very good safety profile, prolonged dosing without dose interruption/reduction is tolerated
- Robust target modulation at safe doses
- Antitumor activity, strong durable PSA responses
- 6 patients per dose to increase n for determining RP2D, 24 patients dosed to date in combination study

Robust Target Modulation at Safe Doses



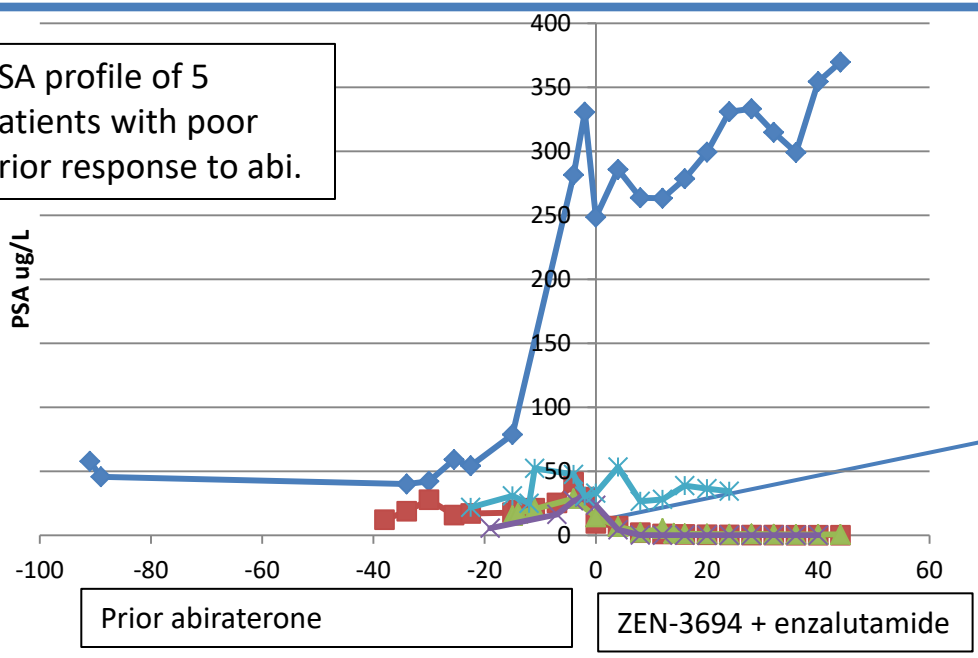




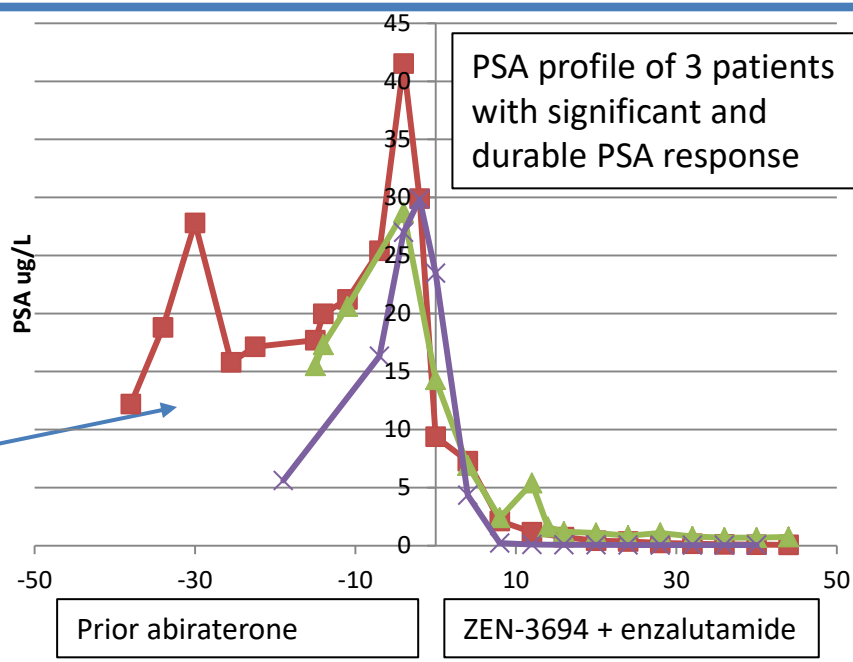
- Clear exposure-dependent pharmacodynamic effect
- Similar trend for monotherapy and combination
- Broadly, 2-fold decrease in IL1RN or CCR1 associated with plasma levels of >300 ng/ml (~1uM)
- Consistent with human ex-vivo spike data
- *MYC has a low response range in whole blood - better in hematological tumors (Yeh et al., 2017)*

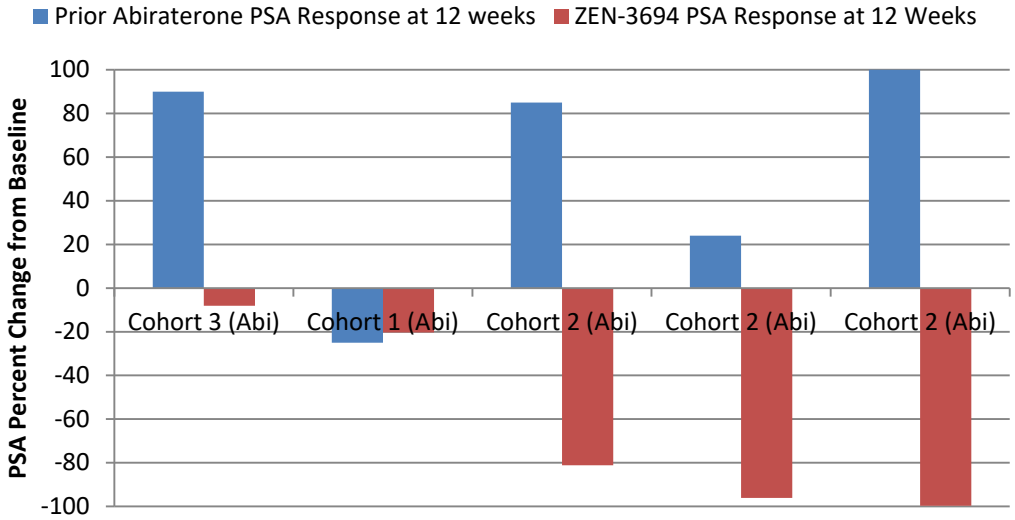
Strong PSA Response With ZEN-3694 + Enzalutamide in Patients With Poor Prior Response to Abiraterone

PSA profile of 5 patients with poor prior response to abi.

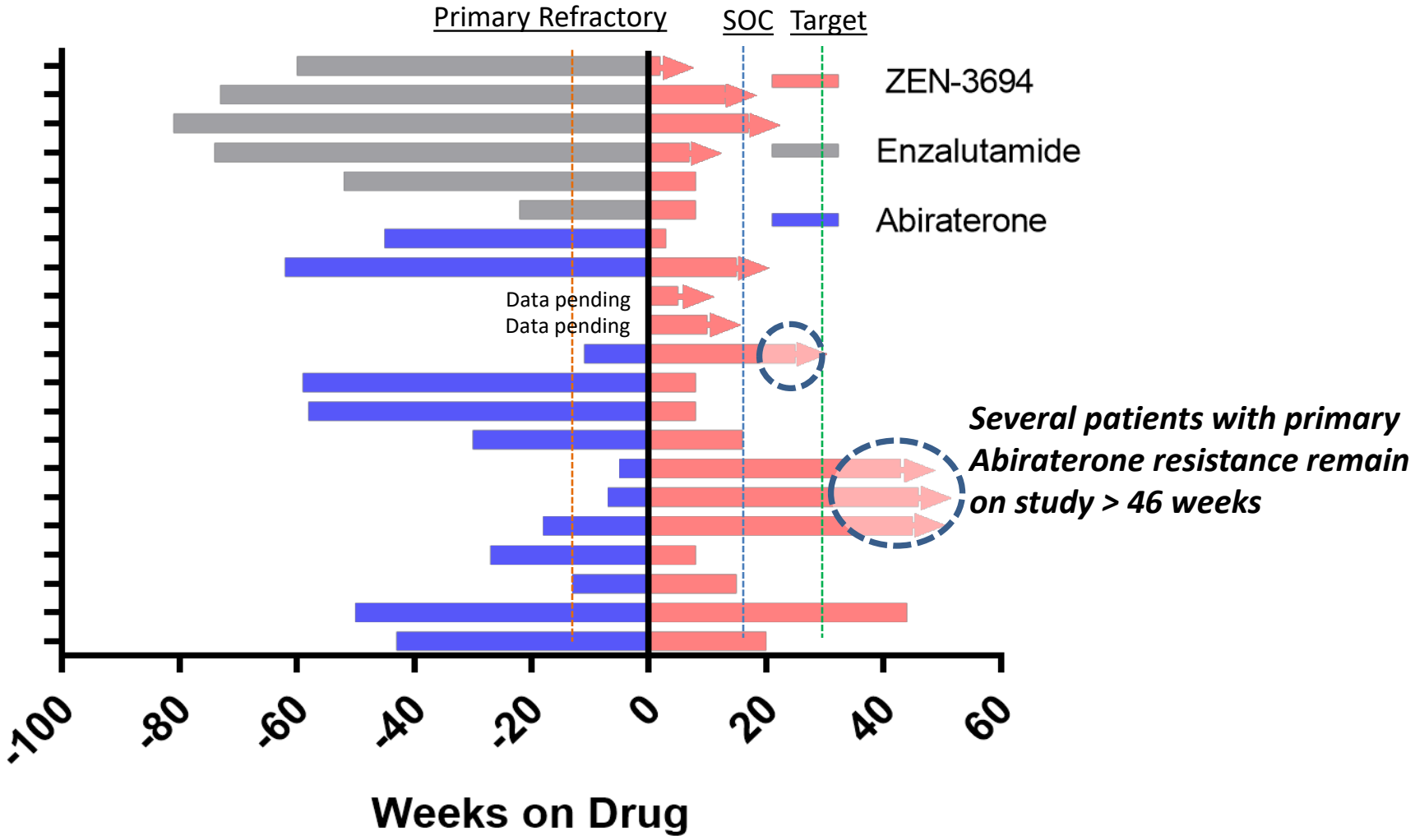


PSA profile of 3 patients with significant and durable PSA response



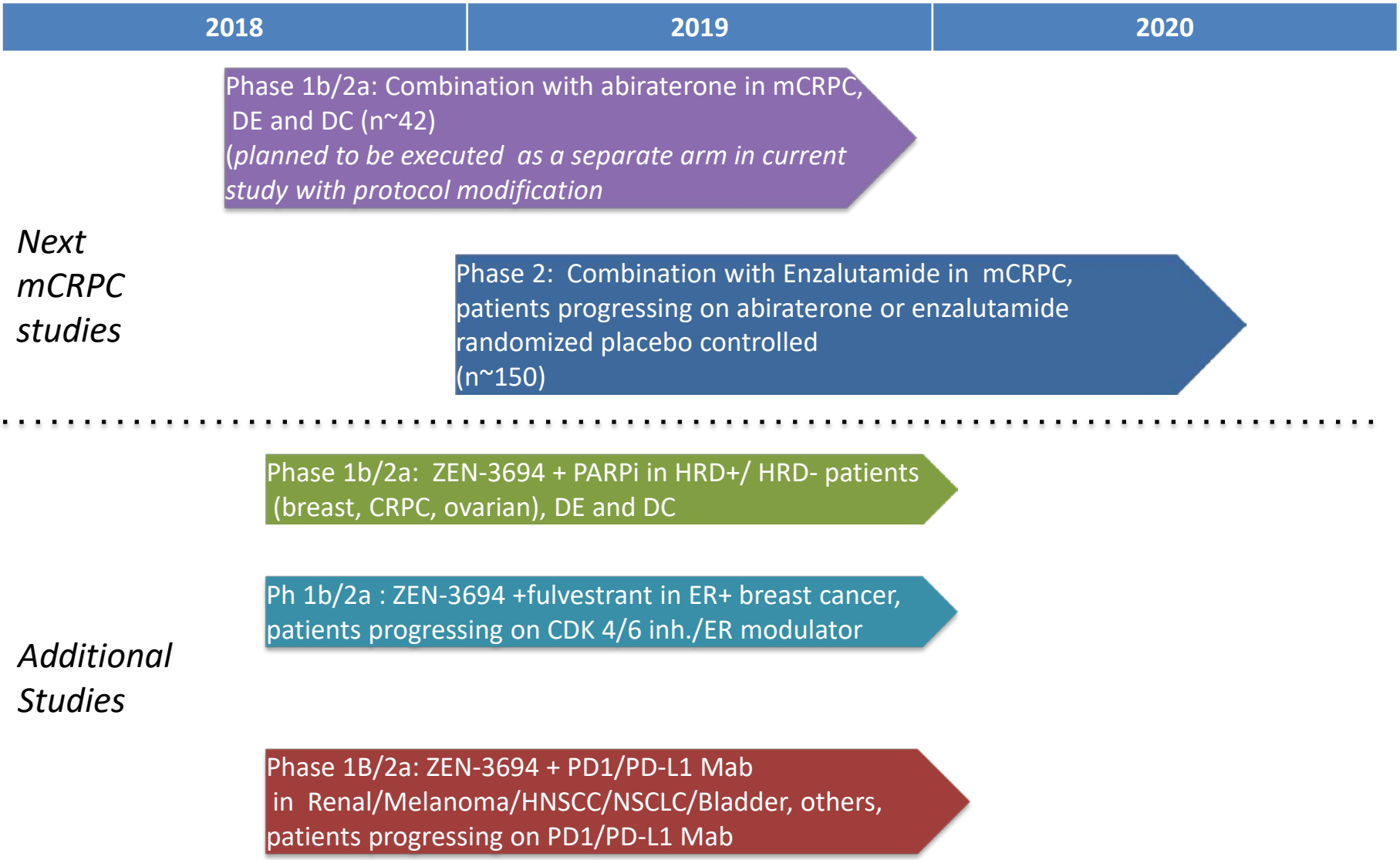


Long Duration of ZEN-3694 + Enzalutamide Therapy Without Radiographic Progression in Primary Abi Refractory Patients



Potential signal in abiraterone primary resistance patients, historically these are poor responders to enzalutamide

ZEN-3694 Clinical Planning: Focus on Efficient Biomarker Driven and Combination Trials



ZEN-3694: Clinical Safety, PK/PD, and Activity Summary

- Robust target modulation at safe doses
- Dose dependent exposure
- Activity signal in primary ARi refractory patients
- Comprehensive translational program in place, data analysis ongoing
- ZEN-3694 is clinically differentiated from other BETi