



**Creating Differentiated Therapies to Improve  
the Lives of Cancer Patients**

September 2020

# Forward-Looking Statements and Disclaimer

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Data of Fulvestrant, RAD1901, Abemaciclib, Alpelisib, AZD1775, Venetoclax and Osimertinib presented in this presentation is based on evaluation of comparable proxy chemical compounds purchased from commercial sources rather than the pharmaceutical company commercializing or developing, as applicable, the compound.

# Zentalis Overview

## ***Our Mission:***

***Discover and Develop  
Revolutionary Medicines to  
Improve the Lives of Patients  
Globally***

1

Integrated Discovery Engine has produced 4 FDA-cleared INDs in 5 years

2

Potentially differentiated lead programs: oral SERD for breast cancer (ZN-c5) and WEE1 for solid tumors (ZN-c3)

3

Additional pipeline programs targeting fundamental cancer pathways: BCL-2 (ZN-d5) and EGFR (ZN-e4)

4

Potential for internal and third-party combination strategies across portfolio

5

Experienced management, seasoned SAB, leading life sciences investors and large cap pharma partners

# Zentalis Leadership

## Experienced Management Team

**Anthony Sun, M.D., MBA**  
Chairman and Chief Executive Officer

AIKLING  
CAPITAL

UNIVERSITY OF  
PENNSYLVANIA  
HEALTH SYSTEM

**Kevin Bunker, Ph.D.**  
Chief Operating Officer

Pfizer

**Melissa Epperly, MBA**  
Chief Financial Officer

PsiOxus  
THERAPEUTICS

R-PHARM

US ANCHORAGE  
CAPITAL GROUP

Goldman  
Sachs

Morgan Stanley

**Cam Gallagher, MBA**  
Executive Director

ONCTERNAL  
therapeutics

RetroSense  
THERAPEUTICS

Zavante

dura  
PHARMACEUTICALS

**Alexis Pinto, J.D.**  
Chief Legal Officer

Celgene

MERCK

**Peter Huang, Ph.D.**  
Senior Vice President, Chemistry

Pfizer

**Ahmed Samatar, Ph.D.**  
Senior Vice President Oncology Research

MERCK

Schering-Plough

**Dimitris Voliotis, M.D.**  
Senior Vice President, Clinical Development

UREVAC  
Adv. T&D people®

Eisai

BAYER

**Orna Bornstein, Ph.D.**  
Vice President of Clinical Operations

NOVARTIS

MERCK

Schering-Plough

**Meena Rao, Ph.D.**  
Vice President of Regulatory Affairs

QUINTILES

novo nordisk

Bristol-Myers Squibb

# Zentalis Advisory Boards

## Scientific Advisory Board

Anthony Letai, M.D., Ph.D.



Ross Levine, M.D.



Donald McDonnell, Ph.D.



Kwok-Kin Wong, M.D., Ph.D.



## Mayo Clinic Advisory Board

Stephen Ansell, M.D., Ph.D.

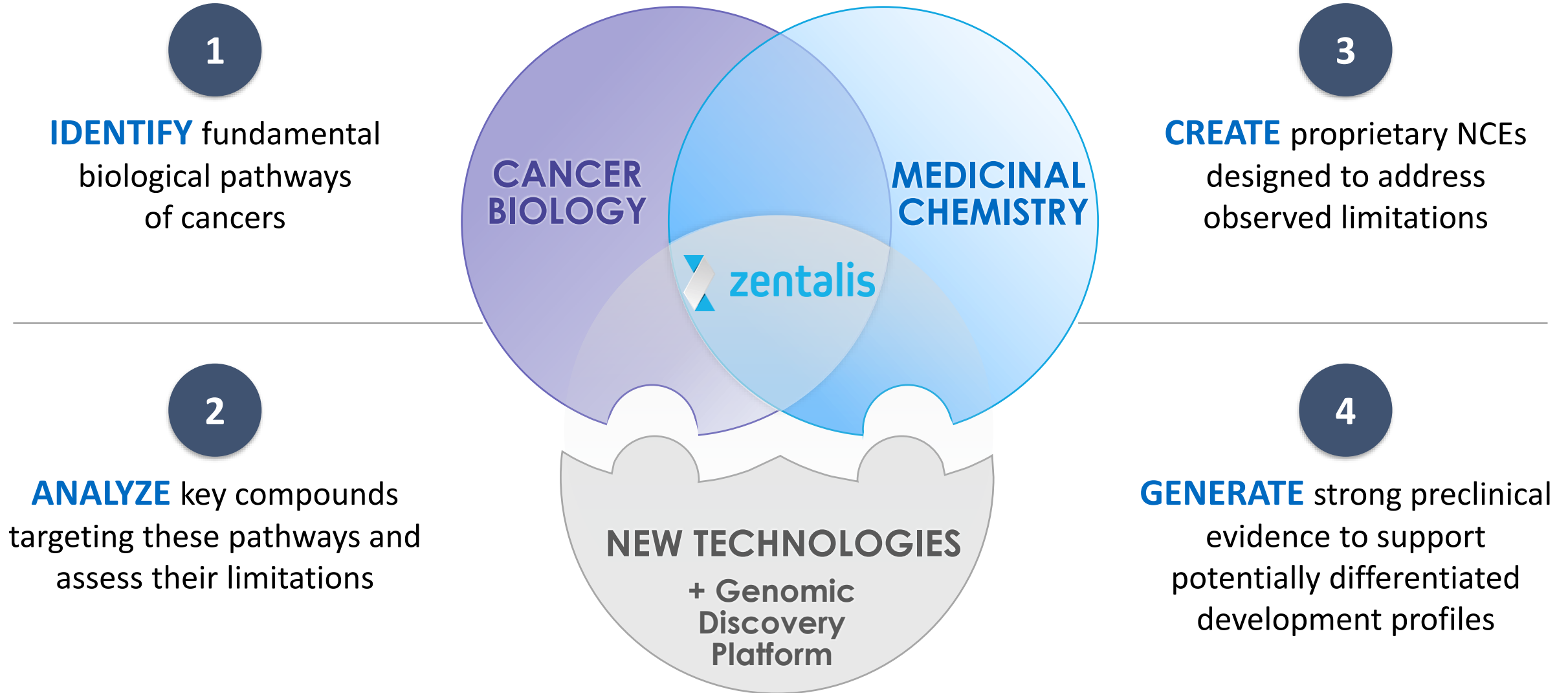
Andrew Badley, M.D.

Shaji Kumar, M.D.

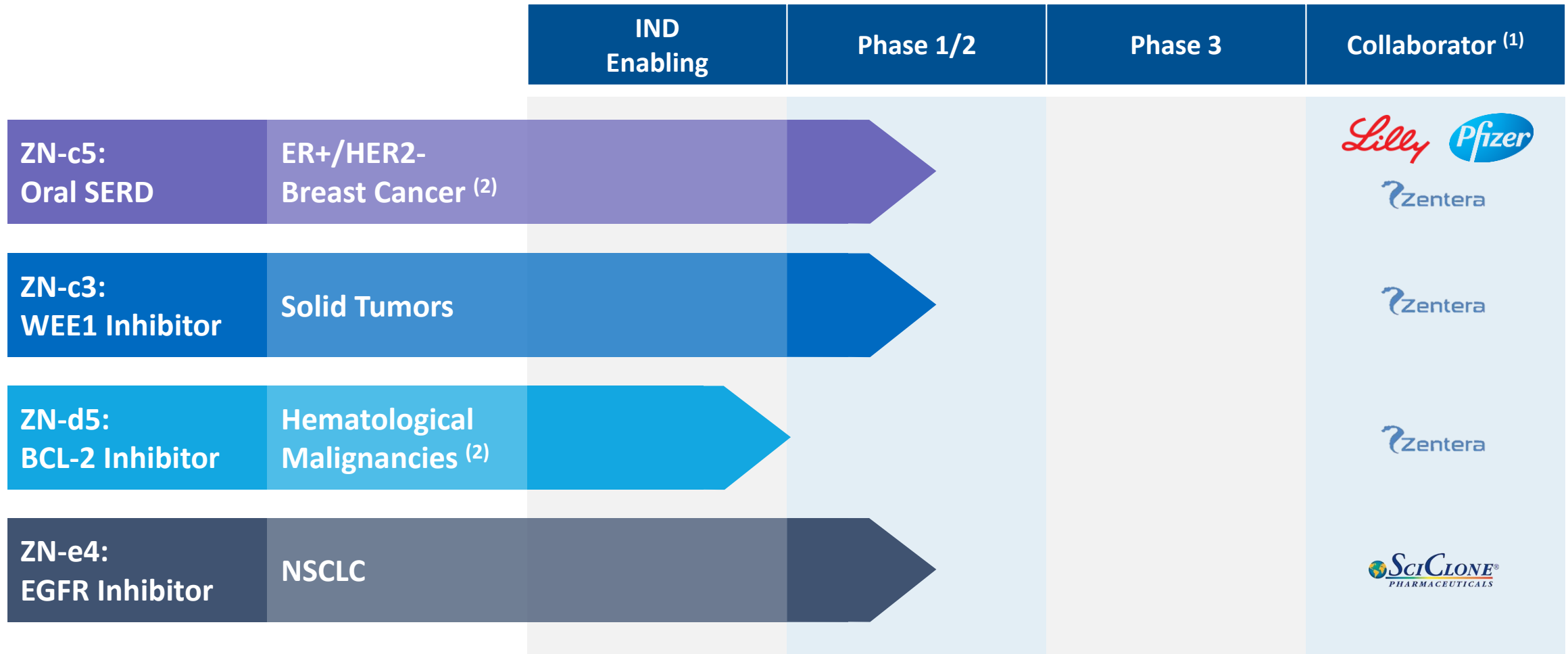


# Highly Efficient 'Integrated Discovery Engine'

Cleared four INDs in five years and expect to file fifth IND in 2021



# Pipeline of Potentially Differentiated Oncology Candidates



- (1) Zentalis is currently evaluating ZN-c5 in combination with palbociclib (Ibrance), as part of a clinical research collaboration with Pfizer, and intend to evaluate ZN-c5 in combination with abemaciclib (Verzenio), as part of a clinical research collaboration with Lilly. Zentalis maintains full ownership of ZN-c5 in each such collaboration. SciClone has development and commercial rights to ZN-e4 in Greater China (including Macau and Hong Kong), South Korea, Taiwan and Vietnam. Zentera, our majority-owned joint venture, has development and commercial rights to ZN-c5, ZN-c3 and ZN-d5 in select Asian countries (including China). Zentera intends to submit an IND in China for each of ZN-c5, ZN-c3 and ZN-d5 in 2021.
- (2) Plan to explore the combination potential of ZN-c5, our oral SERD, with ZN-d5, our BCL-2 inhibitor, for the treatment of ER+/HER2- breast cancer

# Progress Since Our IPO and Follow-on Use of Proceeds

## Recent Accomplishments

### ✓ **Multiple Clinical Milestones Achieved:**

- ZN-c5: 40% Clinical Benefit Rate (CBR) from monotherapy dose escalation study
- ZN-c3: Promising initial pharmacokinetic and safety data
- ZN-d5: IND cleared by FDA

### ✓ **Key Partnerships Announced :**

- Clinical collaboration with Eli Lilly to study ZN-c5 with abemaciclib
- Launch of majority-owned joint venture Zentera with \$20MM Series A and licensing of rights to ZN-c5, ZN-c3 and ZN-d5 in China
- Collaboration with Tavros using genomic discovery platform for next generation oncology therapies

## Proceeds Driving Expansion of Clinical Programs

### ➤ **ZN-c5: New Combination Trials and Study in Earlier-Stage Patients**

- 2H 2020: Initiate Phase 1b combination study with abemaciclib in collaboration with Eli Lilly
- 2021: Initiate Phase 1b combination study with ZN-d5
- 2021: Initiate Phase 2/3 monotherapy study in earlier-stage patients

### ➤ **ZN-c3: New Monotherapy and Combination Trials**

- 2021: Initiate Phase 2 monotherapy trial for uterine serous carcinoma (USC)
- 2021: Begin two Phase 1 combination trials including with chemotherapy and PARP inhibitors in ovarian cancer and other targeted indications

### ➤ **ZN-d5 / ZN-e4: Potential Combination Studies**



# ZN-c5: Oral SERD

# ZN-c5: Oral SERD Candidate for ER+/HER2- Breast Cancer

1

## IDENTIFY: SERD

- Clinically validated approach
- Potential use as backbone therapy
- **Fulvestrant: only FDA-approved SERD**
  - First and second-line treatment as monotherapy and in combination with CDK4/6 or PI3K $\alpha$  inhibitors

2

## ANALYZE: Fulvestrant

- Fulvestrant limitations:
  - 2 painful 5mL monthly intramuscular injections (insoluble)
  - **Capped efficacy at FDA-approved dose based on clinical and preclinical data**
  - Low convenience and high resource utilization

3

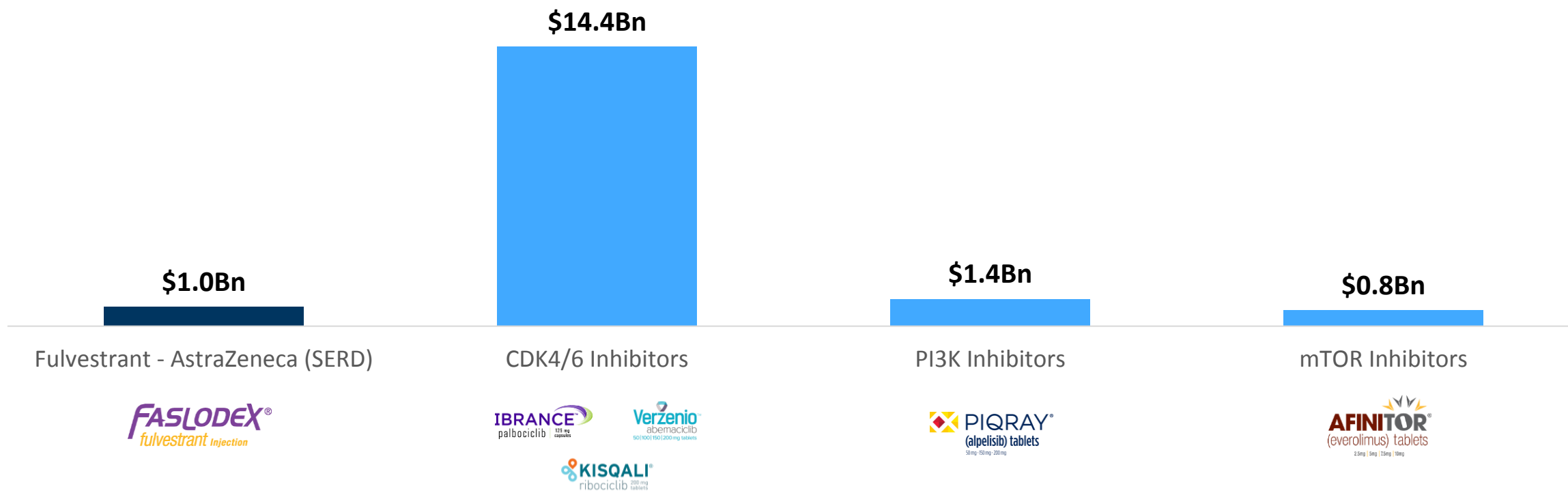
## CREATE: ZN-c5

- ZN-c5 designed as an oral SERD to have:
  - High potency and selectivity
  - Improved solubility
  - Compelling PK (long half life)
  - Favorable safety and tolerability
  - No agonist activity
- **Goal: safely establish increased drug exposure to enhance efficacy**

**Current Status: Phase 1/2 Trial (Monotherapy Dose Escalation & Expansion and Dose Escalation in Combination with Palbociclib) and Initiating Phase 1b Combination with Abemaciclib**

# Vast Market Opportunity for Oral SERDs

~\$1Bn+ Markets in Various Classes Treating ER+ Breast Cancer <sup>(1)</sup>



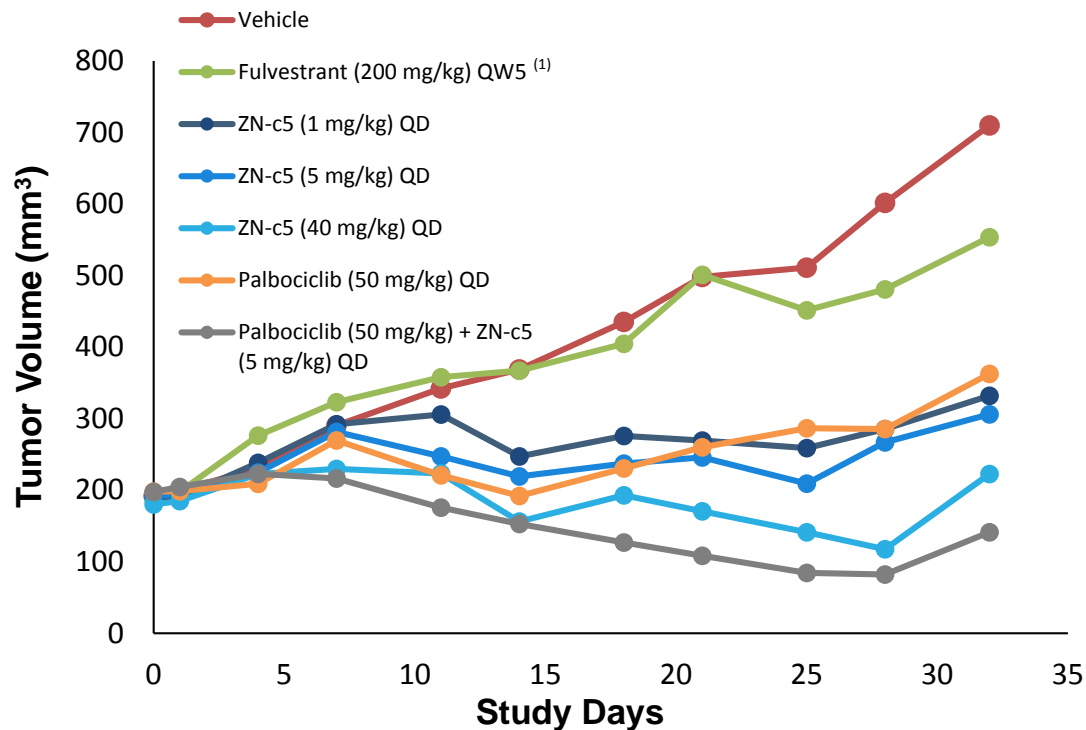
**Faslodex Sales of ~\$1.0Bn Reflect Only Part of Significant Market Potential for an Oral SERD and Only Approved for Metastatic Patients**

(1) Highest projected or historical sales for currently marketed products in breast cancer; includes historical years for drug classes with generic competition; based on data from EvaluatePharma as of July 2020

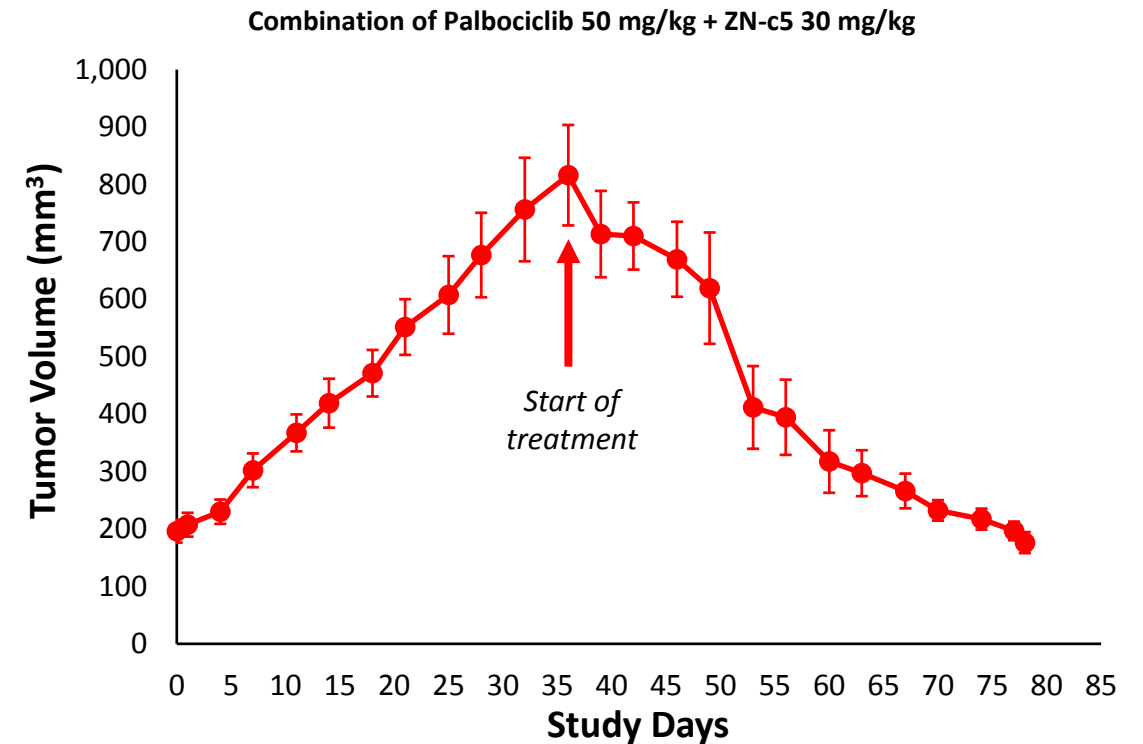
# ZN-c5: Demonstrated Strong Preclinical Anti-Tumor Activity

ZN-c5 exhibited dose proportional response as well as meaningful tumor shrinkage in combination with palbociclib

**Breast Cancer Model (MCF7)**

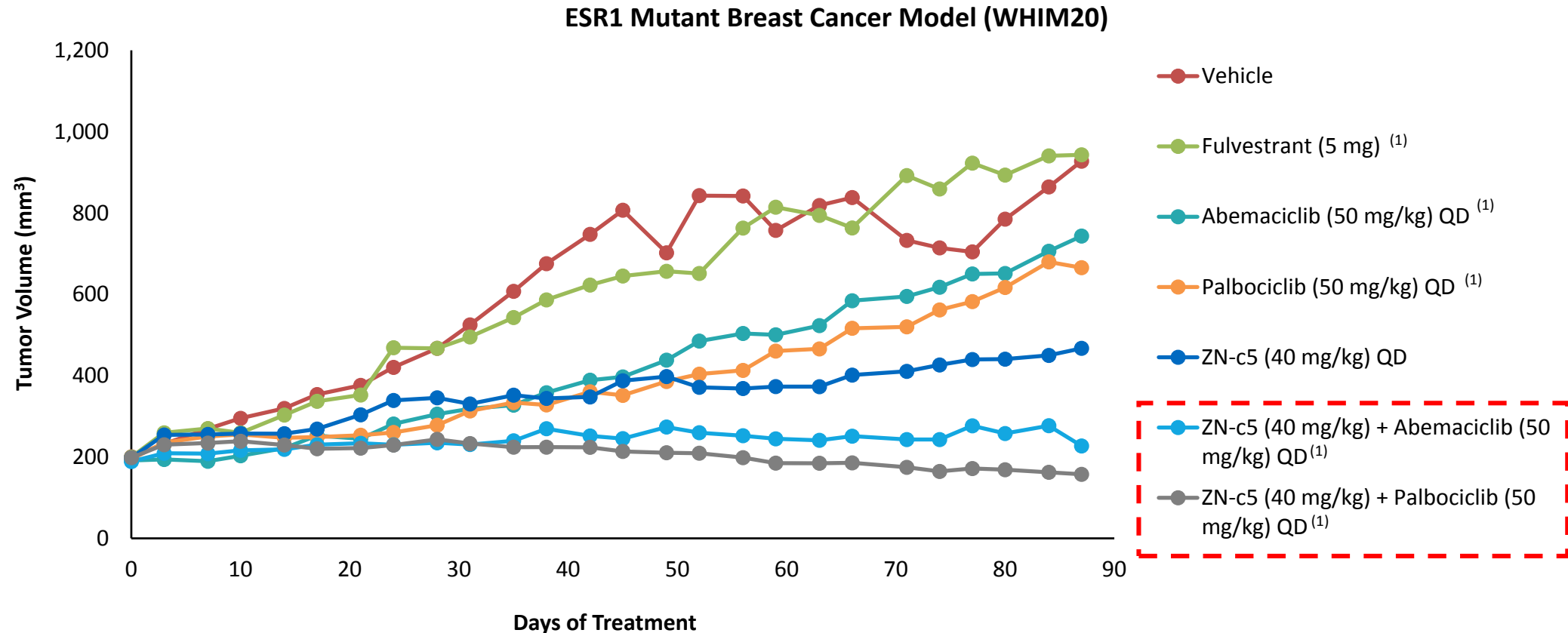


**Breast Cancer Model (MCF7), Mean ± SE**



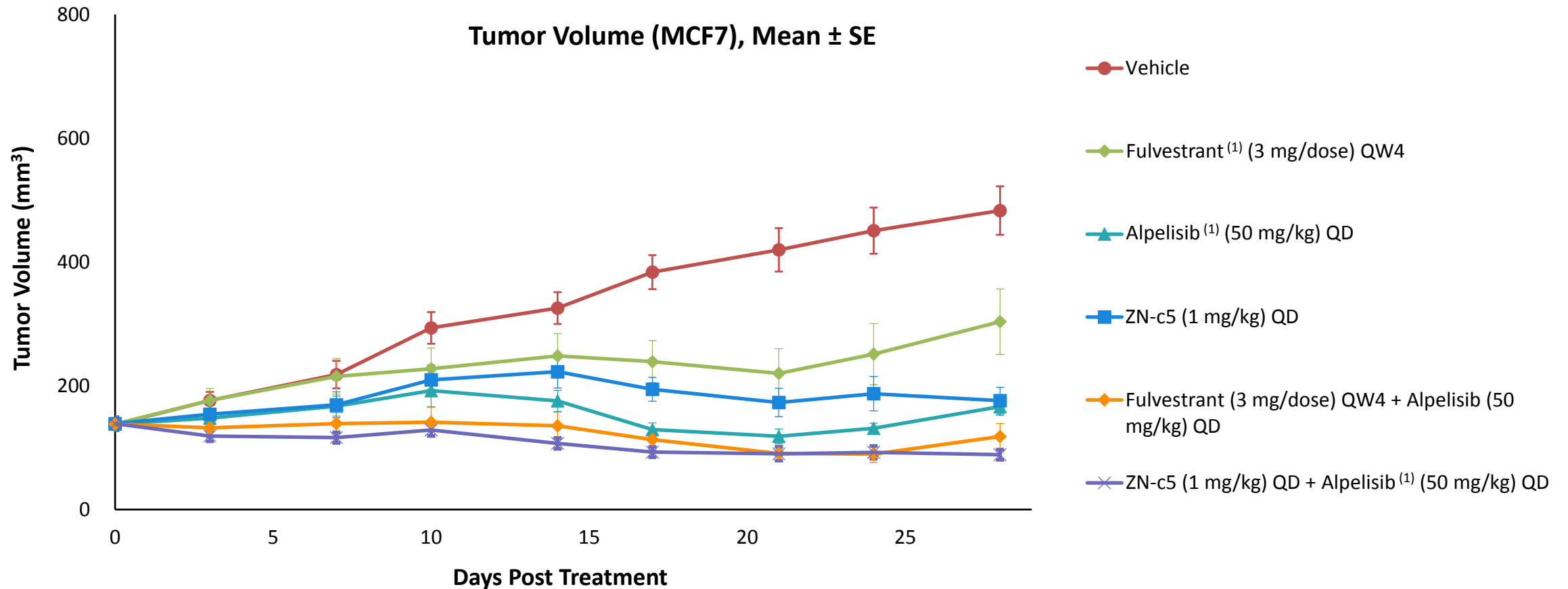
# ZN-c5: Robust Anti-Tumor Activity in Preclinical ESR1 Models as Monotherapy and in Combination with CDK4/6 Inhibitors

ESR1 mutations commonly drive resistance – prevalence ranges from 11% to 39%



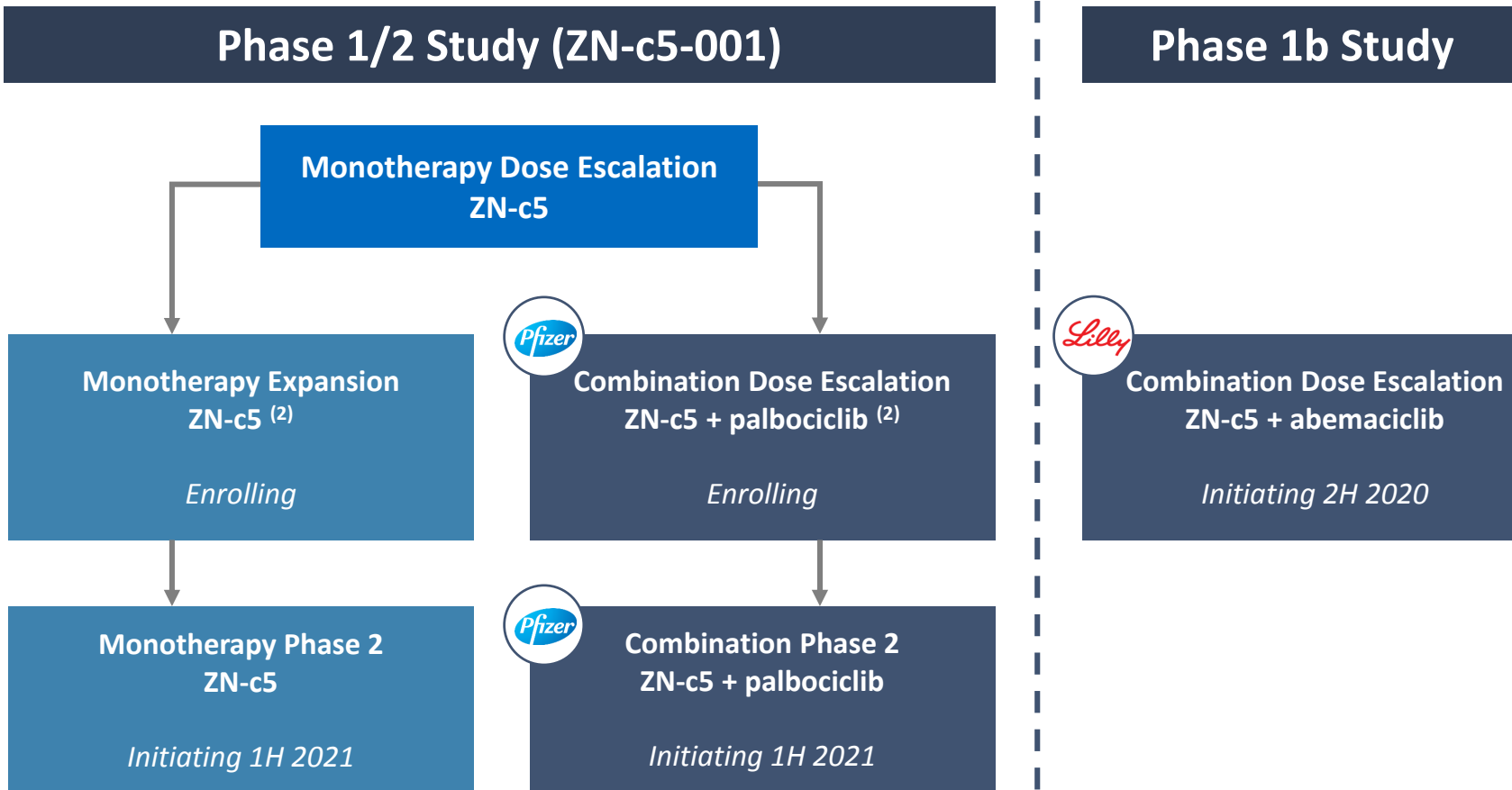
# ZN-c5: Strong Preclinical Anti-Tumor Activity in Combination with PI3K $\alpha$ Inhibitor

~1/3 of HR+ breast cancer tumors are resistant to endocrine therapy harbor activating mutations of PIK3CA



# ZN-c5: Clinical Development Plan

## Ongoing Clinical Programs



## Overview

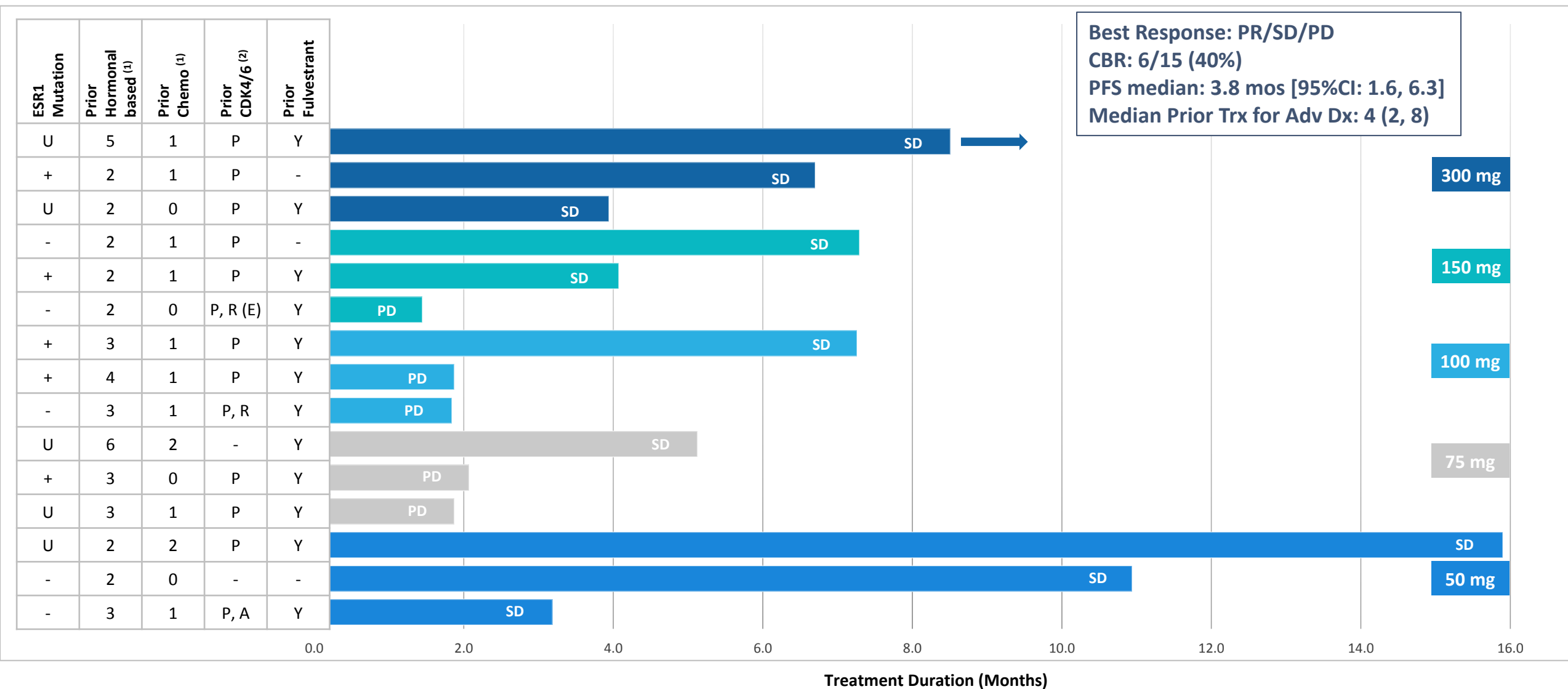
- Topline results from Phase 1 monotherapy dose escalation <sup>(1)</sup>
  - 40% CBR; Median PFS: 3.8 mo
  - Median prior therapies: 4
  - No DLTs observed and well tolerated
  - Study continues enrollment
- Window of Opportunity study initiated in 1Q 2020 to analyze levels of tumor ER degradation (8 patients enrolled)
- 2021: Intend to initiate Phase 1b combination trial with ZN-d5 & Phase 2/3 trial in earlier-stage breast cancer

(1) As of June 30, 2020, we have enrolled 15 patients in the Phase 1, monotherapy dose escalation portion of this trial, three patients each at the dose levels of 50 mg, 75 mg, 100 mg, 150 mg and 300 mg.

(2) As of June 30, 2020, 14 patients were enrolled in the Phase 1, monotherapy expansion portion of this trial, 12 patients at the 150 mg dose and two patients at the 300 mg dose. Of these 14 patients, five are still on treatment and nine discontinued due to disease progression. As of June 30, 2020, we have enrolled 15 patients in the Phase 1, combination dose escalation portion of this trial. Of these 15 patients, nine are still on treatment and six discontinued due to disease progression (n = 5) and physician decision (n = 1).

# ZN-c5: Initial Topline Results from Monotherapy Dose Escalation

Treatment Duration (months) and Response by Dose as of June 30, 2020



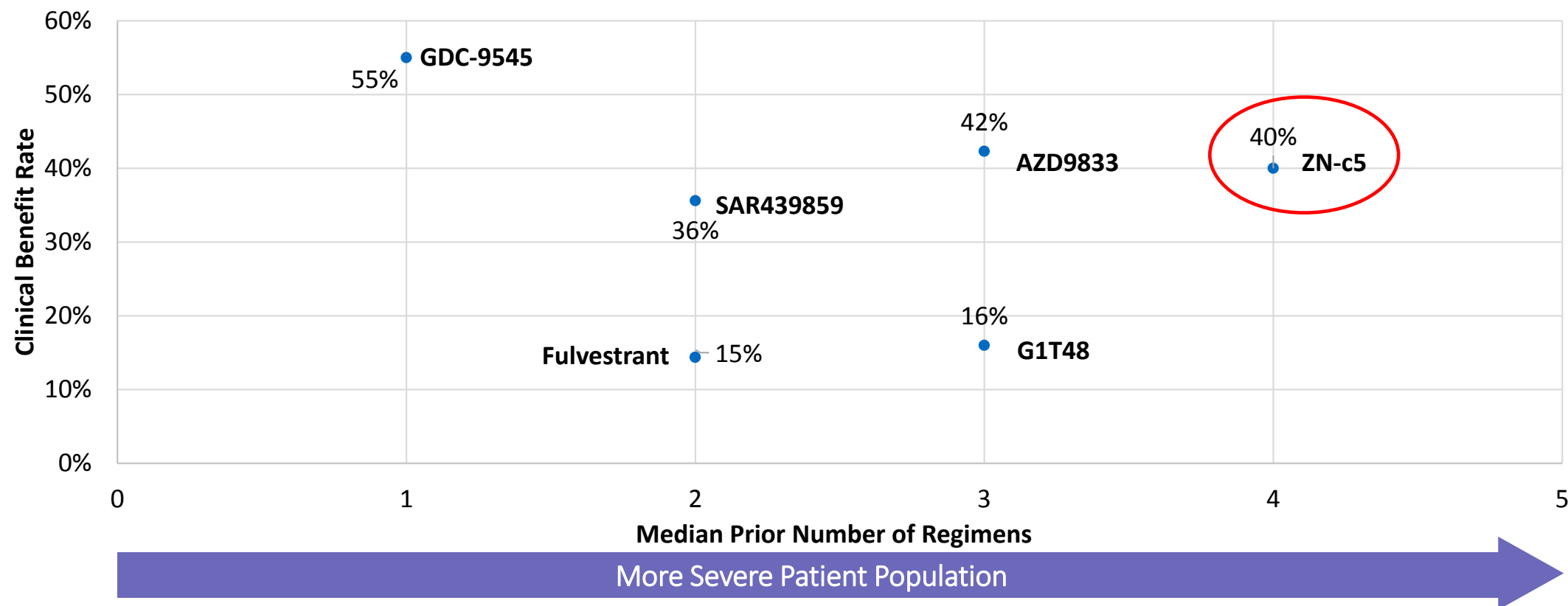
(1) Number of treatments reflect advanced or metastatic setting, not neo/adjuvant; also reflects combinations with targeted therapies CDK4/6, mTOR, PI3Ki

(2) P-palbociclib, A- abemaciclib, R-ribociclib, E-experimental treatment, could be placebo



# Summary of Oral SERD Competitor Clinical Benefit Rates

40% Clinical Benefit Rate in severe and heavily pre-treated patient population



**Sources:** Fulvestrant BELLE-3 Publication; AZD9833 ASCO 2020 Presentation; GDC-9545 SABCS 2019 Poster; SAR439859 ASCO 2019 Poster; G1T48 ESMO 2019 Poster

(1) Clinical Benefit Rate, various studies and lines of therapies

(2) The data presents a non-head to head summary comparison. While we believe the comparison is useful in evaluating the observed interim results of ZN-c5 in the Phase 1/2 clinical trial, our Phase 1/2 clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials were separate trials conducted at different sites with other differences, including, for example, that the subjects in the GDC-9545 clinical trials had 1 median line of prior treatment while the subjects in our Phase 1/2 clinical trial had 4 median lines of prior treatment. In this regard, we have not conducted a head-to-head comparison of ZN-c5 and any of the presented oral SERDs in a clinical trial. Results of a head-to-head comparison may differ significantly from those set forth in the table. In addition, because our Phase 1/2 clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials were separate trials and because we have interim data for 15 patients in our Phase 1/2 clinical trial from the Phase 1, monotherapy dose escalation portion as of June 30, 2020, differences between the results of our clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials may not be statistically or clinically meaningful. For these reasons, you should not place undue weight on the table.

# Summary of Potential Oral SERD Competitors

	AZD9496 (AstraZeneca)	AZD9833 (AstraZeneca)	GDC-9545 (Roche)	SAR439859 (Sanofi)	LSZ102 (Novartis)	G1T48 (G1 Therapeutics)	ZN-c5 <sup>(1)</sup> (Zentalis)
<b>Dose</b>	600 mg BID (Maximal Feasible Dose)	75 mg QD* (Initial Reported Data)	90 mg QD (10, 30 and 100 mg Taken Forward)	400 mg QD	600 mg QD	1,000 mg QD (600 and 1,000 mg Taken Forward)	100 mg
<b>AUC (ng*hr/mL)</b>	8,676	683	12,200	~36,600 <sup>(2)</sup>	25,600	2,690	106,000
<b><u>Treatment-Related AEs: % Patients Treated with Drug (All Doses Tested)</u></b>							
<b>Diarrhea</b>	36%	0-10% <sup>(3)</sup>	17%	8%	62%	27%	3%
<b>Nausea</b>	22%	18%	21%	8%	56%	15%	10%
<b>Bradycardia</b>	N/A	45%	10%	N/A	N/A	N/A	0%
<b>Visual Disturbances</b>	N/A	53%	0-10% <sup>(3)</sup>	N/A	N/A	N/A	0%
<b><u>Other Notable Adverse Events: All Doses Tested</u></b>							
<b>Other Notable Adverse Events</b>	AST/ALT Increase; Hot Flush, Fatigue	QTcF DLT; Dizziness	Hot Flush; Dizziness Reported; Fatigue; Arthralgia; QTc Reported	Hot Flush	N/A	Hot Flush; Fatigue	Full AE Tables on Following Page

**Sources:** AZD9496 Phase 1 Publication; AZD9833 ASCO 2020 Poster; GDC-9545 SABCS 2019 Poster; LSZ102 Poster SABCS 2017; SAR439859 ASCO 2020 Poster; G1T48 ESMO 2019 Poster

(1) The data presents a non-head to head summary comparison. While we believe the comparison is useful in evaluating the observed results of ZN-c5 in the Phase 1/2 clinical trial, our Phase 1/2 clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials were separate trials conducted at different sites with other differences, including, for example, that the subjects in the GDC-9545 clinical trials had 1 median line of prior treatment while the subjects in our Phase 1/2 clinical trial had 4 median lines of prior treatment. In this regard, we have not conducted a head-to-head comparison of ZN-c5 and any of the presented oral SERDs in a clinical trial. Results of a head-to-head comparison may differ significantly from those set forth in the table. In addition, because our Phase 1/2 clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials were separate trials and because we have interim data for 29 patients in our Phase 1/2 clinical trial from the Phase 1, monotherapy dose escalation portion as of June 30, 2020, differences between the results of our clinical trial and the AZD9496, AZD9833, GDC-9545, SAR439859, LSZ102 and G1T48 clinical trials may not be statistically or clinically meaningful. For these reasons, you should not place undue weight on the table.

18 (2) Visual estimation based on graph

(3) Ranges represent adverse events where posters do not disclose events <10%

# ZN-c5: Well Tolerated as Monotherapy and in Combination with Palbociclib

## Monotherapy Treatment-Related AEs\*

	Monotherapy ZN-c5 50 mg (N=3)					Monotherapy ZN-c5 75 mg (N=3)					Monotherapy ZN-c5 100 mg (N=3)					Monotherapy ZN-c5 150 mg (N=15)					Monotherapy ZN-c5 300 mg (N=5)					Total (N=29)				
Grade (CTCAE v4.03)	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Any Adverse Event	2	1				1										5	3				3	1				11	5			
Fatigue																2					1					3				
Hot flush																2					1					3				
Nausea																1					1	1				2	1			
Alanine aminotransferase increased			1													1										1	1			
Affect lability																1										1				
Anaemia																1										1				
Aspartate aminotransferase increased																1										1				
Bone pain																1										1				
Diarrhoea		1																								1				
Dyspepsia																1										1				
Flatulence						1																				1				
Gamma-glutamyltransferase increased																					1					1				
Lymphocyte count decreased																1										1				
Musculoskeletal pain		1																								1				
Myalgia																1										1				
Oral pain																1										1				
Pain																1										1				
Platelet count decreased																1										1				
Vaginal discharge																1										1				
Vomiting																						1				1				
Vulvovaginal dryness																1										1				
Vulvovaginal pain																1										1				
White blood cell count decreased																1										1				

## Combination Treatment-Related AEs\*\*

	Combination Therapy ZN-c5 50 mg + Palbociclib 125 mg (N=3)					Combination Therapy ZN-c5 100 mg + Palbociclib 125 mg (N=9)					Combination Therapy ZN-c5 150 mg + Palbociclib 125 mg (N=3)					Total (N=15)				
Grade (CTCAE v4.03)	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Any Adverse Event	2	1				3	2	3			1		1			4	4	5		
White blood cell count decreased		2	1				4	2	1				1			4	4	3		
Neutrophil count decreased		2	1				2	3					1			4	5			
Anaemia	2					2					1					5				
Fatigue	1					1					1					3				
Platelet count decreased	1					1					1					3				
Lymphocyte count decreased						2										2				
Affect lability						1										1				
Alanine aminotransferase increased						1										1				
Arthralgia	1															1				
Aspartate aminotransferase increased						1										1				
Decreased appetite							1										1			
Dermatitis acneiform						1										1				
Hot flush	1															1				
Hypophosphataemia		1															1			
Rash maculo-papular											1					1				
Stomatitis												1					1			
Vomiting						1										1				

\*Based on first 29 patients from Phase 1 monotherapy dose escalation/expansion as of Jun 30, 2020

\*\*Based on first 15 patients from Phase 1 Combination Dose Escalation as of June 30, 2020

# ZN-c3: WEE1 Inhibitor

# ZN-c3: Oral WEE1 Inhibitor for Solid Tumors

1

## IDENTIFY: WEE1

- Highly attractive DNA damage response target
- Active across multiple tumor types with potential for combination
- **No approved WEE1 inhibitor** and currently only a few in development (i.e. AstraZeneca's AZD1775)

2

## ANALYZE: AZD1775

- Promising efficacy across tumor types (ovarian and pancreatic cancer)
- Potentially limited by **narrow therapeutic window**

3

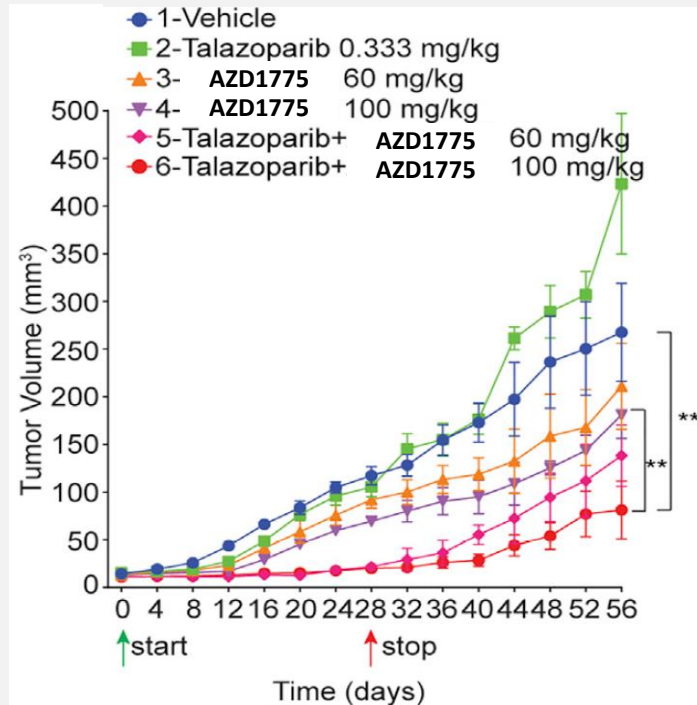
## CREATE: ZN-c3

- Designed as an improved oral WEE1 inhibitor with respect to:
  - Solubility
  - Selectivity
  - PK properties
- **Goal: broader therapeutic window**
- Potential to have broad applicability as monotherapy and in combination

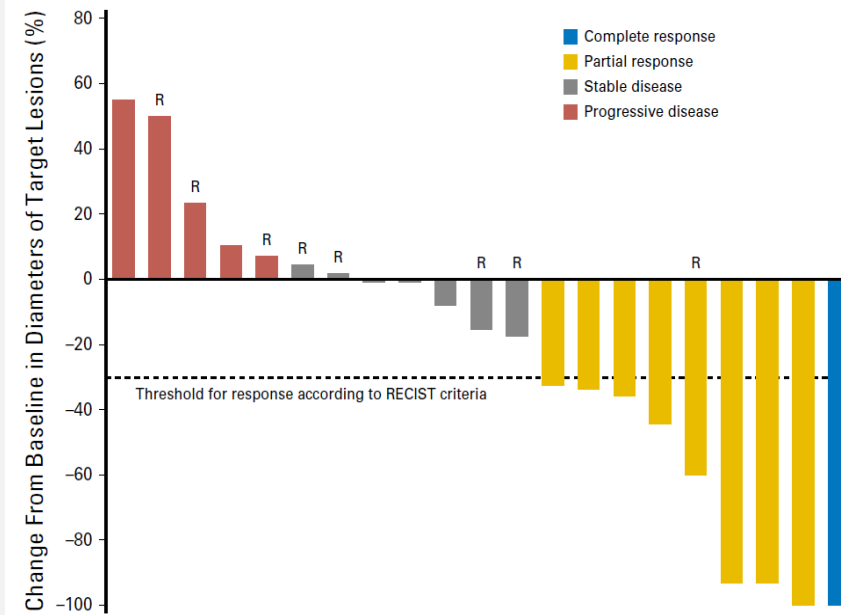
**Current Status: Phase 1/2 Trial in Monotherapy Dose Escalation (22 Patients Dosed)**

# Third-Party WEE1 Inhibitor Shows Strong Preclinical Activity and Clinical Responses

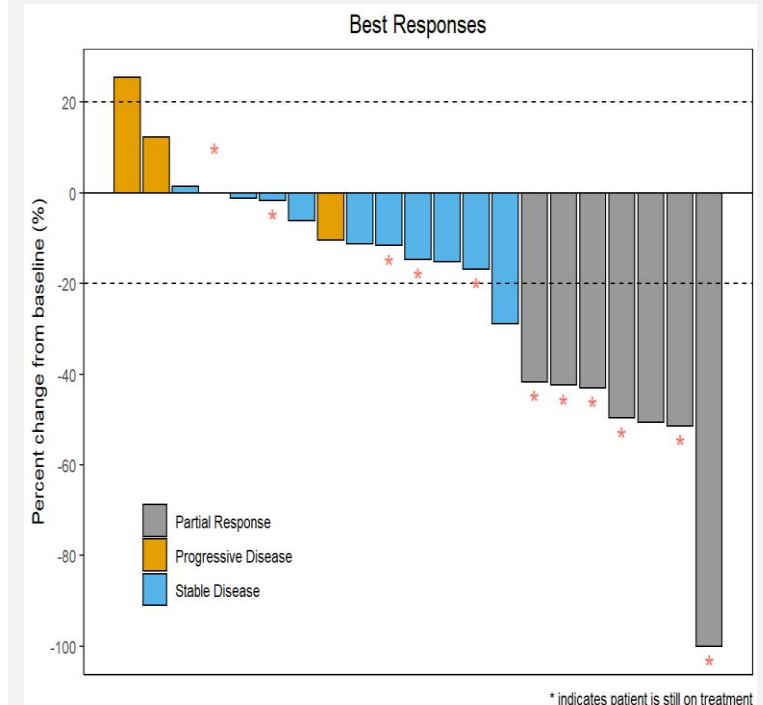
Combination of WEE1 and PARP Inhibitors Showed Improved Anti-Tumor Activity as Compared to the Use of Each as Monotherapy <sup>(1)</sup>



Phase II Study of WEE1 Inhibitor AZD1775 Plus Carboplatin in Patients With *TP53*-Mutated Ovarian Cancer Refractory or Resistant to First-Line Therapy Within 3 Months <sup>(2)</sup>



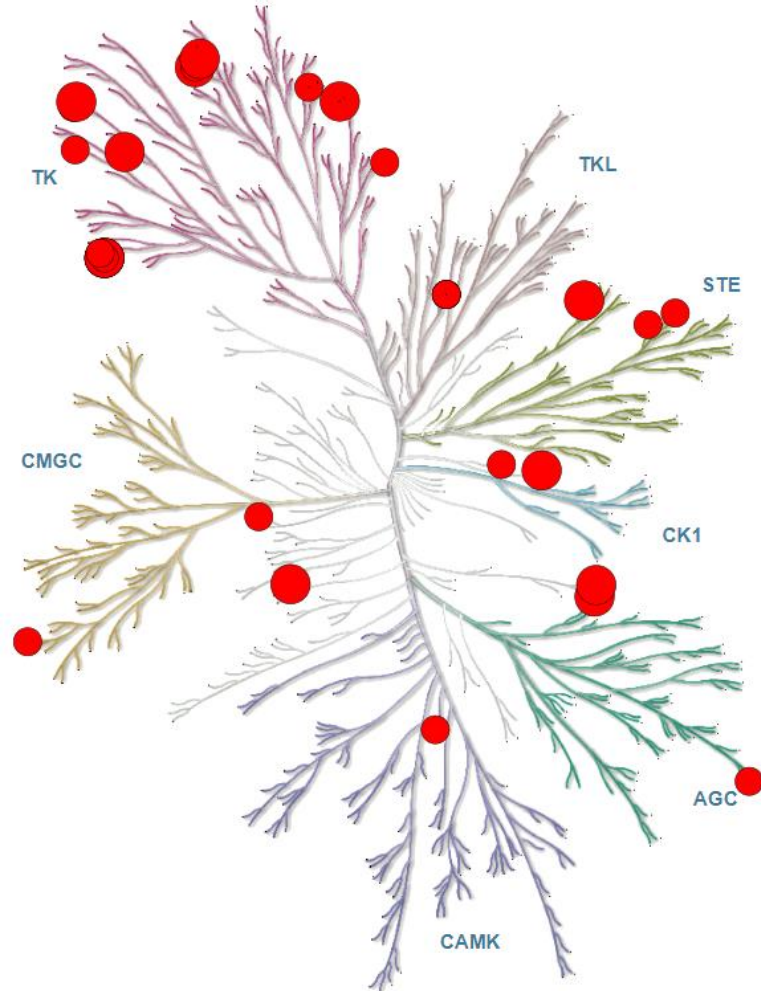
Phase II Trial of WEE1 Inhibitor in recurrent Uterine Serous Carcinoma (USC) <sup>(3,4)</sup>



- (1) Fang, Y. Cancer Cell (2019). A total of 2 x 10<sup>6</sup> OVCAR8 were injected subcutaneously (s.c.) and grown for 2 weeks in nude mice. Mice were randomized with six in each group and treated as indicated. Average tumor volume ± SEM are displayed. p value: one-way ANOVA. \*\*p < 0.01
- (2) Leijen, R. Journal of Clinical Oncology (2016)
- (3) Liu, J.F. AZD1775 SGO Presentation (2020)
- (4) An aggressive subtype of endometrial carcinoma characterized by frequent TP53 mutations (>90%)

# ZN-c3: More Selective for WEE1 in Kinase Screening Panel

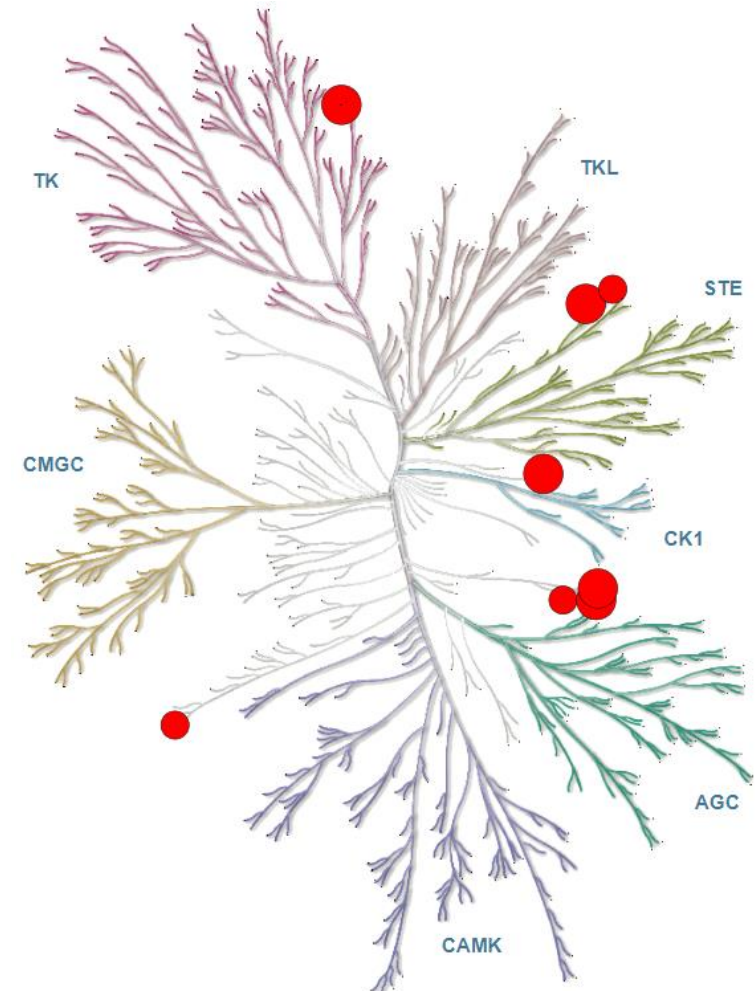
## AZD – 1775 <sup>(1)</sup>



% Inhibition  
(@ 1μM)

- 90+
- 75-89

## ZN-c3



# ZN-c3: Improved Tumor Concentration in Preclinical Models

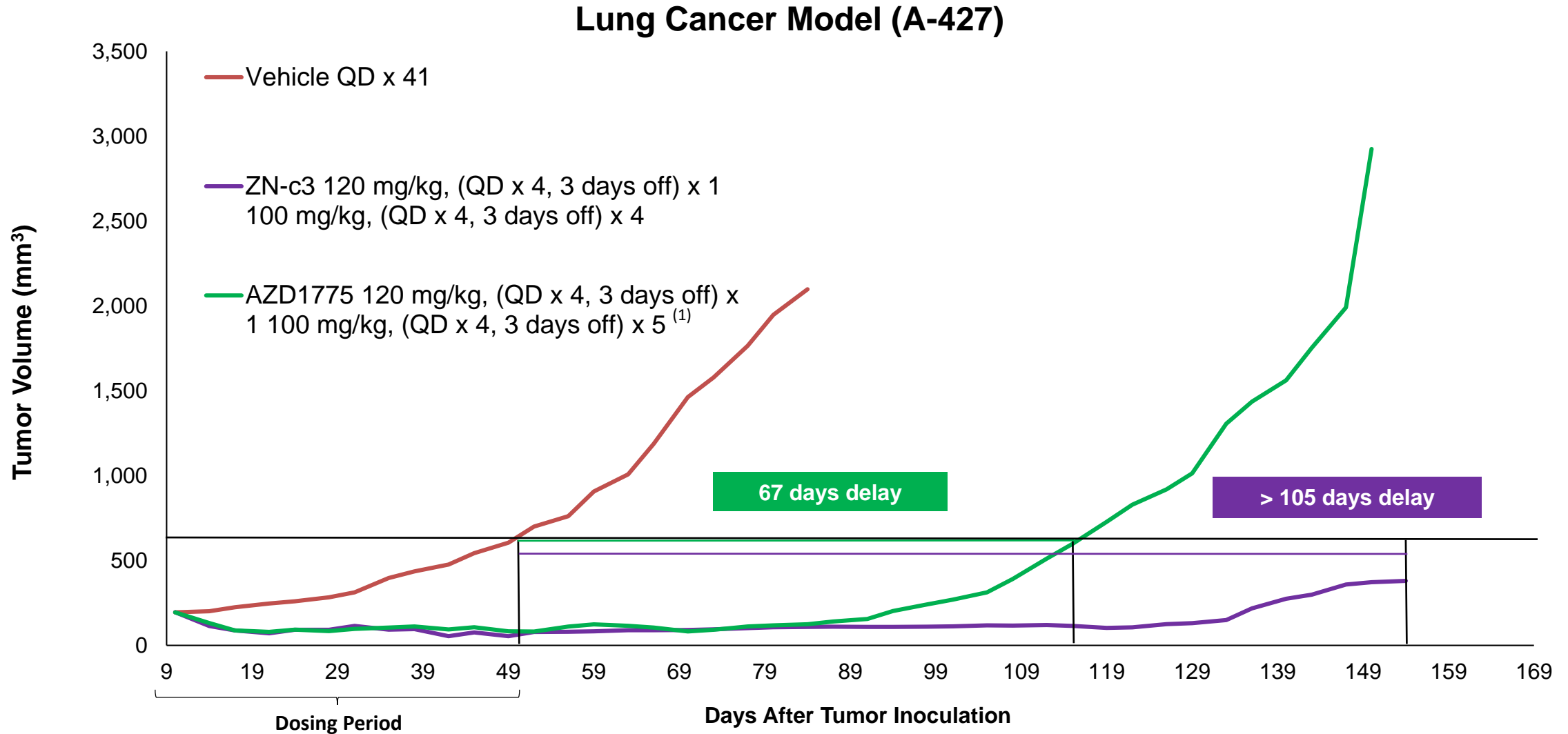
Study (A-427 NSCLC)	ZN-c3			AZD1775		
Dose (mg/kg/day)	20	40	80	20	40	80
C <sub>max</sub> (ng/mL)	1,167	1,997	5,100	635	2,460	4,703
T <sub>max</sub> (hr)	1	1	1	1	1	1
AUC <sub>0-24hr</sub> (ng·hr/mL)	4,863	17,088	39,722	1,494	6,313	13,408
Tumor Conc. (ng/mL)	10.5	48.0	811	BQL	BQL	6.95

**Note:** BQL: Below Quantifiable Level

(1) AZD1775 data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.



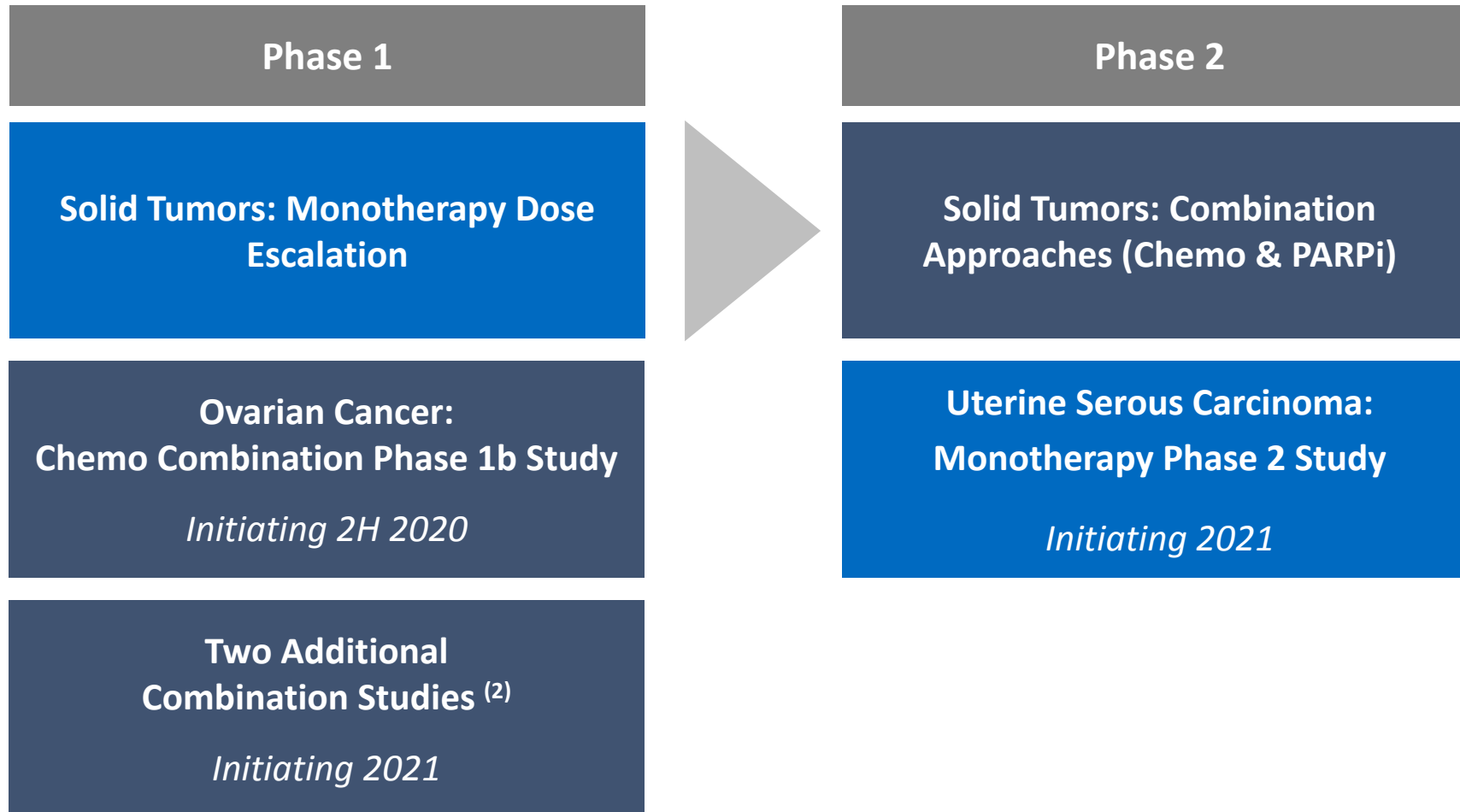
# ZN-c3: Induced Prolonged Tumor Growth Delay at Intermittent Dosing



(1) AZD1775 data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.

# ZN-c3: Clinical Development Plan

## Ongoing and Planned Clinical Programs



## Overview

- Interim and preliminary safety results from Phase 1 monotherapy dose escalation <sup>(1)</sup>
  - Favorable PK profile observed
  - No DLTs observed and well tolerated
  - Enrollment is ongoing; expect to report interim data in 2021

(1) As of the June 19, 2020, in the Phase 1, monotherapy dose escalation portion of the ongoing ZN-c3-001 trial, a total of 22 patients were enrolled and dosed with data available in the electronic data capture system, two patients each at the dose levels of 25 mg, 50 mg, 200 mg and 300 mg, four patients at 100 mg and ten patients at 75 mg/day

(2) Phase 1 combination trials including with chemotherapy and PARP inhibitors in ovarian cancer and other targeted indications

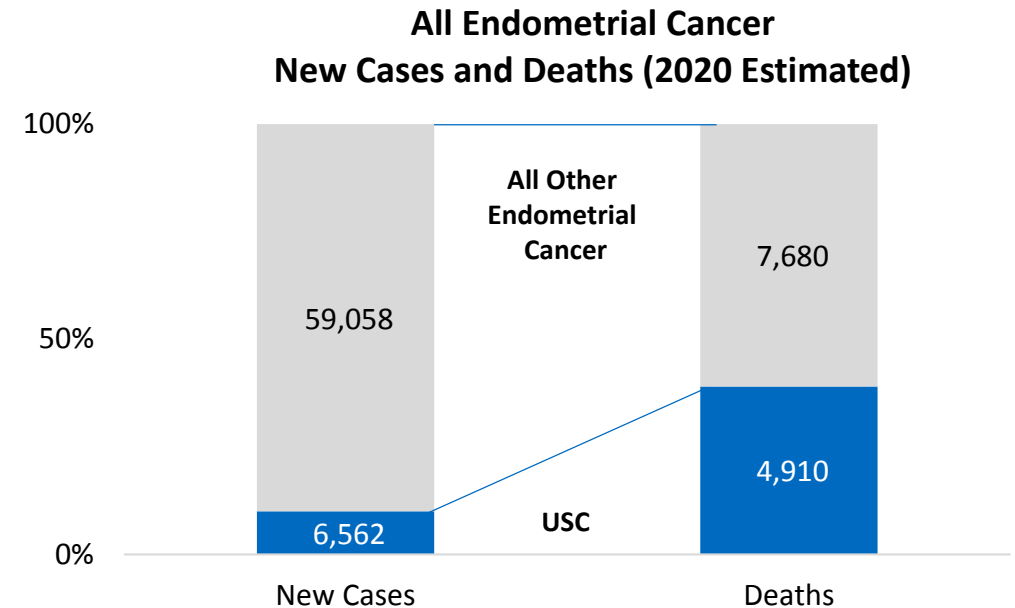
# ZN-c3: Phase 2 Monotherapy Study in USC

## Overview of Uterine Serous Carcinoma (USC)

- Type II endometrial cancer
- Not hormonally mediated
- Approx. 70% of USC present with Stage III or IV disease at diagnosis
- Poor survival rates; only 30-50% even if confined in uterus
- >90% of USCs have TP53 mutation
- Recurrence rates are 29-80% post surgery
- ~6k new cases and ~4.5k deaths in U.S. per year
- Current standard of care include: comprehensive surgery, adjuvant chemotherapy and adjuvant vaginal cuff brachytherapy

## Represents High Unmet Medical Need

*Comprises 10% of Endometrial Cancers with Highest Mortality*



**Will Initiate Phase 2 Monotherapy Trial for Patients with USC in 2021**

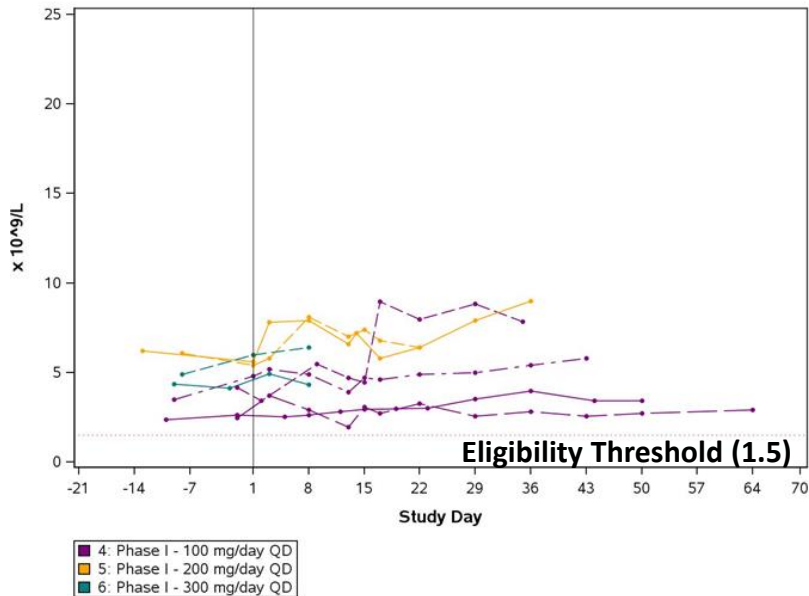
	AZD1775 225mg BID x 1wk/21days N = 3				AZD1775 225mg BID x 2wk/21days N = 19			
Cumulative dose/21 days	1,125 mg				2,250 mg			
Grade (MedDRA)	1	2	3	4	1	2	3	4
Gastrointestinal disorders								
Nausea	1	1			10	4	1	
Vomiting	1	1			10	5		
Diarrhoea					11	3	1	
Abdominal distension/bloating	1				1	2		
Abdominal Pain					4	1		
Flatulence					3			
Oral mucositis					1			
Gastritis						1		
Hematologic AEs								
Anemia	1		2		4	2	1	
Leukopenia	1	1		1	4	4	1	
Neutropenia				1		5	2	
Thrombocytopenia					4	4	1	
Investigations								
Increase in ALT					5			
Increase in AST					3			

[illegible]

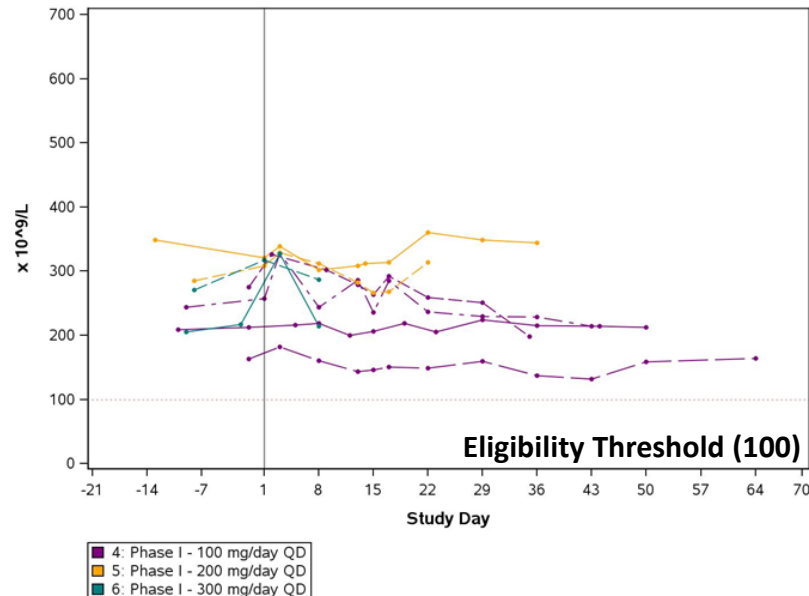
# ZN-c3: Initial Safety Data in Hematological Parameters

No observed effects on hematological parameters for dose levels ranging from 25 mg/day up to 300 mg/day

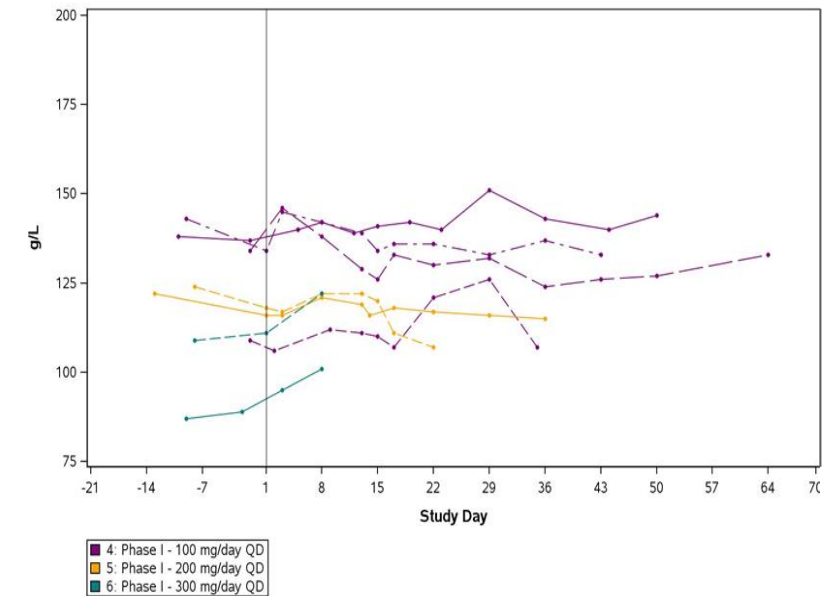
## Neutrophils <sup>(1)</sup>



## Platelets <sup>(1)</sup>



## Hemoglobin <sup>(1)</sup>



**Note: Each Line Represents An Individual Patient**

(1) Data as of June 19, 2020; Dose levels <100 mg: no effect on ANC, platelets and Hgb

# ZN-c3: Favorable Initial Pharmacokinetics Profile

	Day 1 <sup>(1)</sup>					Day 15 <sup>(1)</sup>				
	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr) <sup>(2)</sup>	AUC <sub>0-8hr</sub> (ng*h/mL)	AUC <sub>0-24hr</sub> (ng*h/mL)	t <sub>1/2</sub> (hr)	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr) <sup>(2)</sup>	AUC <sub>0-8hr</sub> (ng*h/mL)	AUC <sub>0-24hr</sub> (ng*h/mL)	t <sub>1/2</sub> (hr)
<b>25 mg</b>	14	2	62	87	10	9	2	41	63	11
<b>50 mg</b>	55	2.5	246	533	8	48	4	255	594	15
<b>75 mg</b>	122	2	620	1,100	7	152	1	842	1,330	9
<b>100 mg</b>	124	1	822	1,120	8	199	3	822	1,620	9
<b>200 mg</b>	353	2	1,550	2,870	7	712	2	3,480	6,160	7

(1) 25 and 50 mg: n=2; 75 mg: n=10 on Day 1 and n=8 on Day 15; 100 mg: n=4; 200 mg: n=3

(2) Median are listed for T<sub>max</sub>

# ZN-c3: Favorable Initial Pharmacokinetics Profile (Cont'd)

	ZN-c3: Day 1 <sup>(1)</sup>				
	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr) <sup>(2)</sup>	AUC <sub>0-8hr</sub> (ng*h/mL)	AUC <sub>0-24hr</sub> (ng*h/mL)	t <sub>1/2</sub> (hr)
25 mg	14	2	62	87	10
50 mg	55	2.5	246	533	8
75 mg	122	2	620	1,100	7
100 mg	124	1	822	1,120	8
200 mg	353	2	1,550	2,870	7

25 and 50 mg: n=2; 75 mg: n=10; 100 mg: n=4; 200 mg: n=3

	AZD1775: Day 1 <sup>(3)</sup>		
	C <sub>max</sub> (ng/mL)	T <sub>max</sub> (hr) <sup>(2)</sup>	AUC <sub>0-8hr</sub> (ng*h/mL)
25 mg	21***	3***	100***
50 mg	78* 67***	2* 3***	371* 329***
75 mg	112**	1**	550**
100 mg	104* 162** 157***	3* 2** 2***	570* 720** 730***
200 mg	236* 232** 239***	4* 3** 3***	1,260* 1,205** 1,165***

AZD1775 data based on Part 2A (100 mg, 200 mg) and Part 2B (25 mg, 50 mg, 75 mg) of Phase 1 AZD1775 combination study since data at above doses not available from monotherapy data: \* With Cisplatin; \*\* With Carboplatin; \*\*\* With Gemcitabine <sup>(3)</sup>

(1) 25 and 50 mg: n=2; 75 mg: n=10 on Day 1 and n=8 on Day 15; 100 mg: n=4; 200 mg: n=3

(2) Median are listed for T<sub>max</sub>

(3) AZD1775 data from Leijen, et al (2016) J Clin Oncol 34:4371-4380

# ZN-d5: BCL-2 Inhibitor



# ZN-d5: Oral BCL-2 Inhibitor for Hematologic Malignancies

1

## IDENTIFY: BCL-2

- Broad applicability as anti-apoptotic target
- Difficult target given intracellular location
- Potential for use in combination
- **Venetoclax: only approved BCL-2 inhibitor**
- Small number of agents in development

2

## ANALYZE: Venetoclax

- Demonstrated clinical efficacy in hematologic malignancies
- Approvals in CLL/SLL and AML
- Addresses side effects of previous BCL-2 inhibitors
- Thrombocytopenia still observed in 29% of patients, attributed to BCL-xL inhibition

3

## CREATE: ZN-d5

- ZN-d5 designed as an oral BCL-2 inhibitor to optimize:
  - Potency
  - Selectivity
  - PK properties
- Plan to explore in combination with ZN-c5 for breast cancer

**Current Status: IND cleared and plan to initiate Phase 1 trial in hematological malignancies in 1H 2021**

# ZN-d5: Excellent *In Vitro* Potency and Better BCL-xL Selectivity

ZN-d5 has >14x improved selectivity for BCL-2 vs BCL-xL compared to venetoclax



Compound	Affinity (nM)		CTG IC <sub>50</sub> (nM)						
			ALL	MCL	DLBCL		AML		
	BCL-2 Kd	BCL-xL Kd	RS4;11	Granta-519	DOHH-2	Toledo	HL-60	Molm-13	MV4-11
Venetoclax	0.41	28	2.9	161	43	191	26	18	3.8
ZN-d5	0.29	190	5.1	89	50	92	21	39	5.1

# ZN-d5: Observed to Bind with Higher Affinity to BCL-2 Mutants than Venetoclax in *In Vitro* Assay

## Mutations in BCL-2 may be driving sub-clonal pockets of resistance to Venetoclax in CLL

### CLL Progression on Venetoclax

	CLL Progression																												
Best Response	NR	NR	PR	PR	PR	NR	PR	PR	PR	PR	PR	NR	PR	nPR	PR	PR	Cri	PR	PR	nPR	PR	nPR	PR	CR	PR	CR	CR	PR	PR
Months	2	4	5	7	8	9	11	13	14	17	18	20	22	22	22	24	25	25	27	27	30	36	37	40	44	51	56	57	59
<i>BCL2</i>																													
<i>PMAIP1</i>																													
<i>BAX</i>																													
<i>BAD</i>																													

 Acquired post-therapy  
 No mutation detected

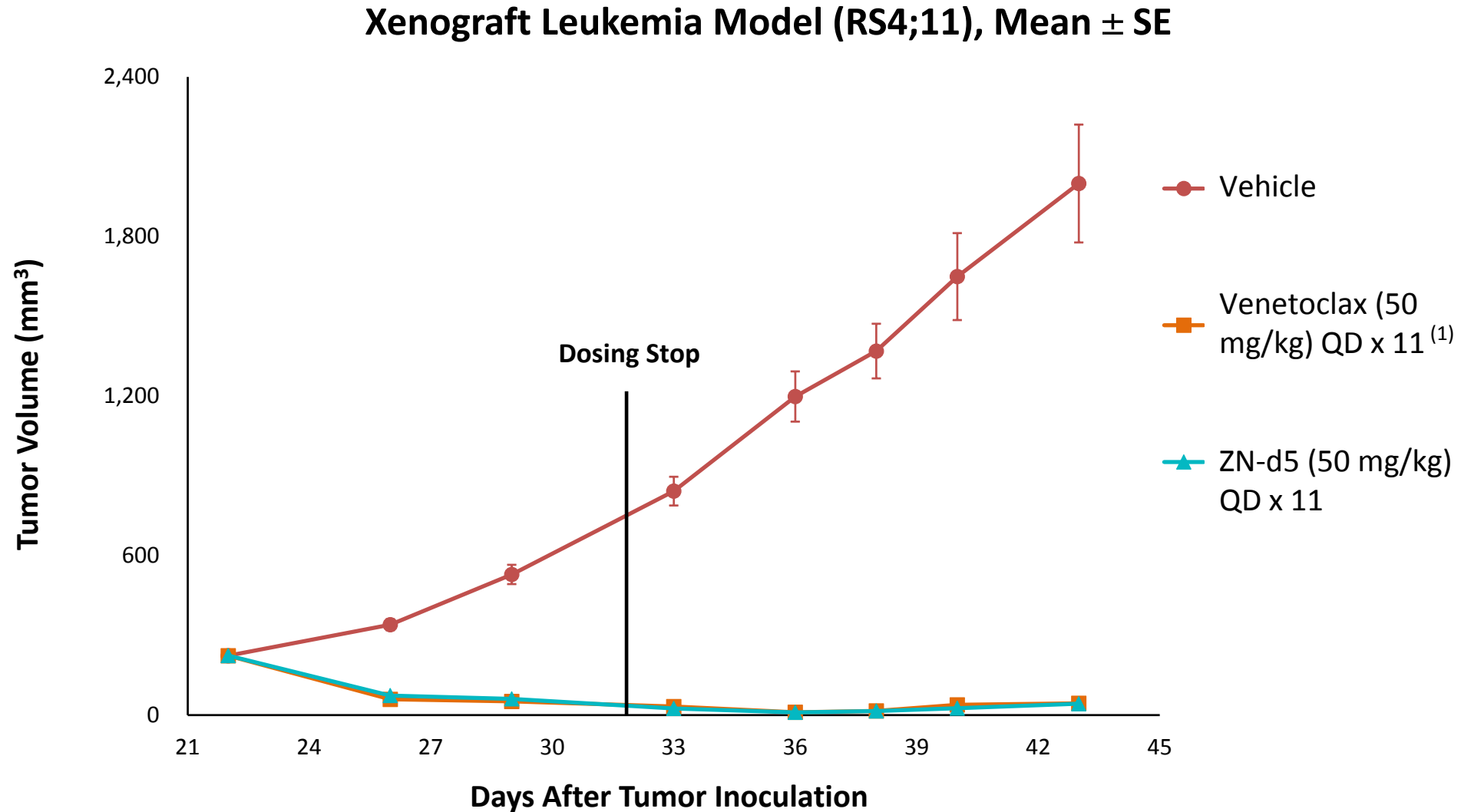
- 55% (16/29) patients acquired mutations in *BCL2* family members
  - 48% (14/29) with mutations in *BCL2*
  - 21% (6/29) with mutations in *PMAIP1* (NOXA), *BAX* or *BAD*
- Majority (9/14) were detected with *BCL2* mutations after 24 months on venetoclax
  - 55 % (16/29) of patients with CLL progression

Source: Chyla, B. ASH Presentation (2019)

Compound	IC <sub>50</sub> (nM) BCL-2 Type			
	WT	G101V	F104L	D103Y
Venetoclax	1.3	7.3	8.4	18.3
<b>ZN-d5</b>	<b>1.4</b>	<b>3.7</b>	<b>1.4</b>	<b>5.0</b>

Note: Competition assay for displacing BAK peptide bound to BCL-2

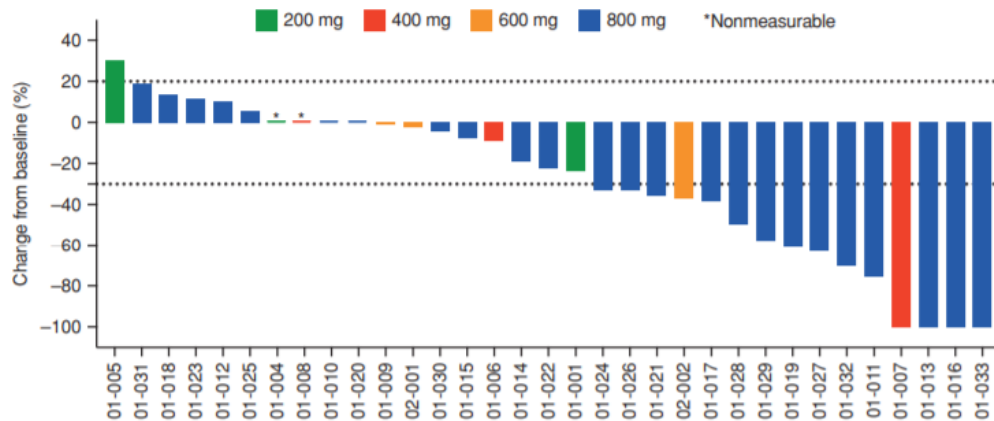
# ZN-d5: Strong Anti-Tumor Activity Consistent with Venetoclax in Preclinical Leukemia Model



(1) Venetoclax data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.

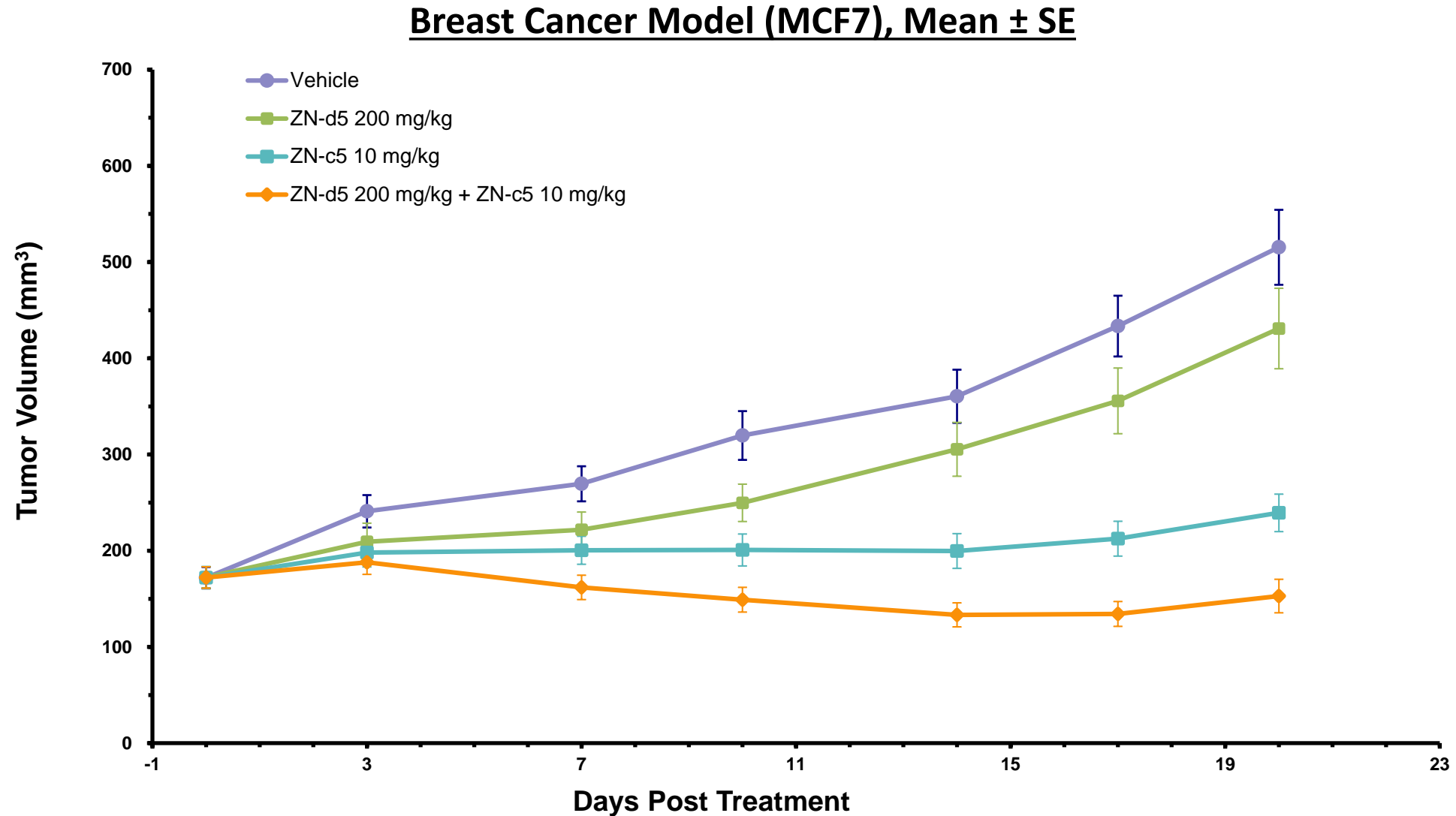
# Initial Venetoclax + Tamoxifen Clinical Data is Compelling (Presented at 2018 SABCS)

## A Phase Ib Dose-Escalation and Expansion Study of the BCL2 Inhibitor Venetoclax Combined with Tamoxifen in ER and BCL2-Positive Metastatic Breast Cancer



Venetoclax, a potent and selective BCL2 inhibitor, synergizes with endocrine therapy in preclinical models of ER-positive breast cancer. Using a phase Ib 3 + 3 dose-escalation and expansion study design, 33 patients with ER and BCL2-positive metastatic disease (mean prior regimens, 2; range, 0–8) were treated with daily tamoxifen (20 mg) and venetoclax (200–800 mg). Apart from uncomplicated “on-target” lymphopenia, no dose-limiting toxicities or high-grade adverse events were observed in the escalation phase (15 patients), and 800 mg was selected as the recommended phase II dose (RP2D). In the expansion phase (18 patients), few high-grade treatment-related adverse events were observed. For 24 patients treated at the RP2D, the confirmed radiologic response rate was 54% and the clinical benefit rate was 75%. Treatment responses were preempted by metabolic responses (FDG-PET) at 4 weeks and correlated with serial changes in circulating tumor DNA. Radiologic responses (40%) and clinical benefit (70%) were observed in 10 patients with plasma-detected *ESR1* mutations.

# All Oral Internal Combination of ZN-c5 + ZN-d5 Shows Promising Potential in MCF7 Model



# ZN-e4: EGFR Inhibitor

# ZN-e4: Third-Generation EGFR Inhibitor for NSCLC

1

## IDENTIFY: EGFR

- Regulator of proliferation and survival in lung cancer
- Third generation inhibitors targeting T790M mutation have produced clinically meaningful benefits
- **Osimertinib: only approved third-generation EGFR inhibitor**
- Broad combination potential

2

## ANALYZE: Osimertinib

- Addresses the T790M-mediated acquired resistance and improving efficacy
- ~60% of patients reported rashes
- **AZ5104, a major metabolite of osimertinib, may be responsible for these toxicities**

3

## CREATE: ZN-e4

- ZN-e4 designed to achieve similar potency, but:
  - Improved selectivity for mutant EGFR
  - No production of potent metabolite for wild-type EGFR
  - Better solubility
- **Actively evaluating potential combinations**

**Current Status: Phase 1/2 Trial (Monotherapy Dose Escalation)**



# ZN-e4: Improved Selectivity and Tolerability in Preclinical Models

## ZN-e4 is More Selective than Osimertinib...

	Double Mutant Cell IC <sub>50</sub> (nM)	Single Mutant Cell IC <sub>50</sub> (nM)	Wild-Type Cell IC <sub>50</sub> (nM)
Osimertinib: Core Drug	15	29	294
ZN-e4: Core Drug	20	38	839

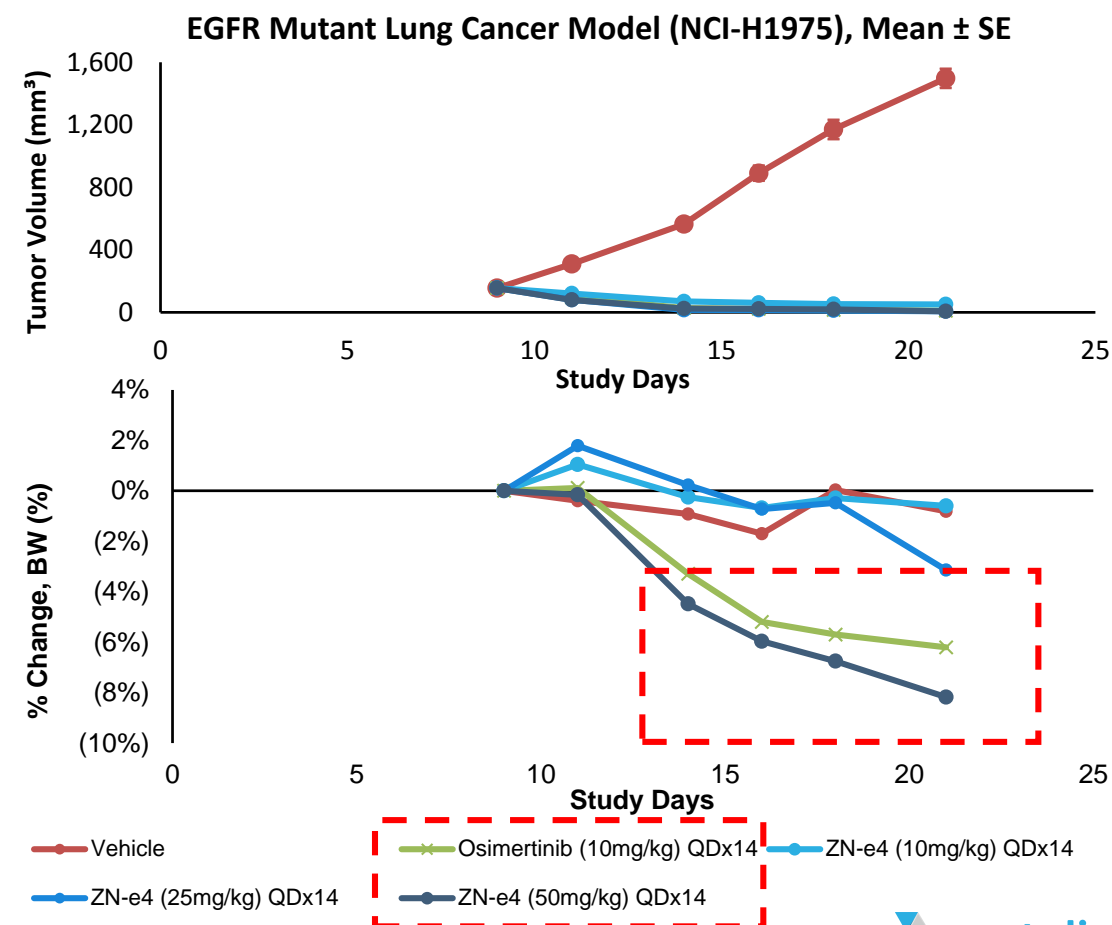
## ...And Does Not Form a Potent Metabolite for Wild-Type EGFR

	Double Mutant Cell IC <sub>50</sub> (nM)	Single Mutant Cell IC <sub>50</sub> (nM)	Wild-Type Cell IC <sub>50</sub> (nM)
Osimertinib: AZ5104	2 <sup>(2)</sup>	2 <sup>(2)</sup>	33 <sup>(2)</sup>
ZN-e4	No Potent Metabolite for Wild-Type EGFR Formed		

(1) Osimertinib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.

(2) Finlay, M.J. of Med. Chem. (2014)

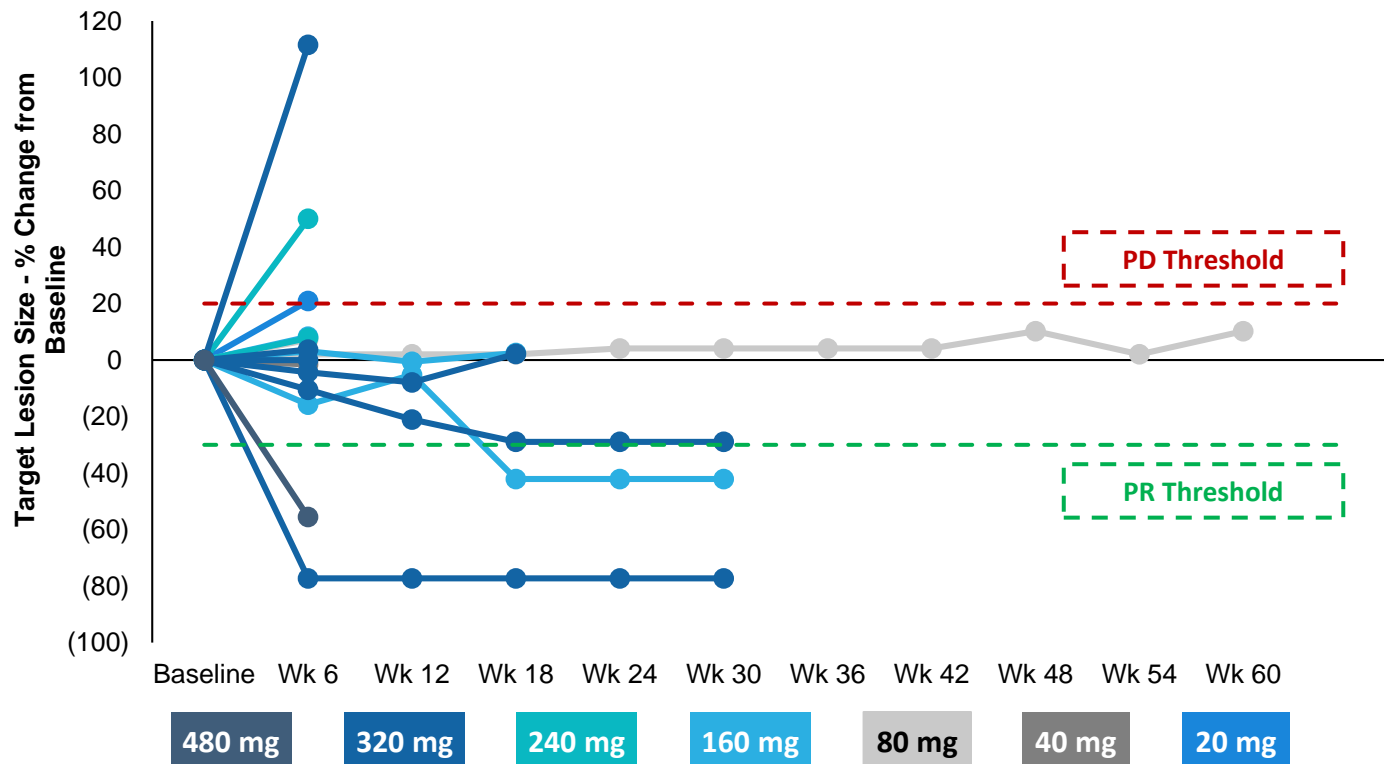
## Favorable Tolerability Observed: ZN-e4 Similar Weight Loss to Osimertinib at 5x Efficacious Dose <sup>(1)</sup>



# ZN-e4: Clinical Development Overview

Focused on completion of Phase 1 trial and will evaluate whether to initiate Phase 2 portion of upon its completion

## Interim & Preliminary Efficacy: Change In Target Lesion Size <sup>(1)</sup>



## Current Status

- As of Feb. 5, 2020, 19 patients had been dosed in this trial in seven dose level cohorts <sup>(2)</sup>
  - 11 of 19 patients treated with osimertinib
- 3 partial responses (2 confirmed, 1 unconfirmed) in osimertinib-naïve patients at 160, 320 and 480 mg
- One other patient currently with stable disease has a reduction in target lesion size of approximately 29%.
- Generally well tolerated, 1 DLT at the 320 mg dose level; trial is currently ongoing at a higher dose level

# Conclusion

# Key Milestones

Event	Expected Timing
<b>ZN-c5 (Oral SERD)</b>	
✓ Phase 1 topline results from monotherapy dose escalation study	■ Achieved July '20
★ Initiating Phase 1b combination study with abemaciclib	■ 2H 2020
■ Phase 1 topline results from Window of Opportunity study	■ 1H 2021
■ Initiate Phase 2 monotherapy study	■ 1H 2021
■ Initiate Phase 2 combination study with palbociclib	■ 1H 2021
★ Initiate Phase 1b combination study with ZN-d5	■ 2021
★ Initiate Phase 2/3 monotherapy in earlier-stage patients	■ 2021 <sup>(1)</sup>
<b>ZN-c3 (WEE1 Inhibitor)</b>	
■ Initiate Phase 1 combination dose escalation study	■ 2H 2020
■ Phase 1 initial results from dose escalation study in advanced solid tumors	■ 2021
★ Initiate Phase 2 monotherapy in uterine serous carcinoma	■ 2021
★ Initiate two additional Phase 1 combination studies	■ 2021 <sup>(1)</sup>

Event	Expected Timing
<b>ZN-d5 (BCL-2 Inhibitor)</b>	
✓ IND Clearance	■ April '20
■ Initiate Phase 1 trial in AML and B cell lymphoma	■ 1H 2021
<b>ZN-e4 (EGFR Inhibitor)</b>	
■ Initial results from dose escalation study	■ 2021
■ Evaluate potential for use in combinations for treatment of lung cancer	■ 2021+
<b>Integrated Discovery Engine</b>	
■ Submit 5 <sup>th</sup> IND	■ 2021
<b>Zentera</b>	
★ Submit ZN-c5, ZN-c3, ZN-d5 INDs in China	■ 2021

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