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CORPORATE PRESENTATION

March 2022

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This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation.

Data of fulvestrant, RAD1901, abemaciclib, alpelisib, adavosertib, 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.

Company Overview

Lead Program: Wee1i (ZN-c3) potentially first- and best-in-class

- Monotherapy responses in 4 solid tumor types, with 3 Exceptional Responders & an additional 2 confirmed in USC, 1 unconfirmed PR in USC thus far
- Potential accelerated approval paths for USC and biomarker-driven trials
- Fast Track designation granted in USC
- Orphan drug and rare pediatric disease designations granted in osteosarcoma

Oral SERD (ZN-c5): potentially best-in-class profile as monotherapy and in combination, including with ZN-c3

BCL-2 inhibitor (ZN-d5): broad applicability as anti-apoptotic target; potential as monotherapy and in combination, including with ZN-c3

Additional programs targeting fundamental cancer pathways: EGFR inhibitor (ZN-e4) & BCL-xL heterobifunctional degrader

Investigating internal & third-party combinations, including ZN-d5 + ZN-c3 for liquid tumors and ZN-c5 + ZN-c3 for CDK4/6i-resistant tumors

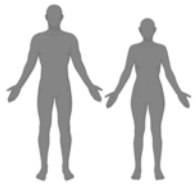
Integrated Discovery Engine: 4 FDA-cleared INDs within the first 5 years

Utilizing the Highly Efficient 'Integrated Discovery Engine' to Generate Best-In-Class Drugs

1. IDENTIFY
2. ANALYZE
3. CREATE
4. GENERATE

1 Patients

Pathways



Genomic features

2 Zentalis Discovery Engine

Functional Screens
- CRISPR screens
- BH3 profiling
- Genomics

Preclinical Models
- 2D
- 3D
- Organoids
- CDX
- PDX

Chemistry
- Enzymatic and allosteric inhibitors
- Heterobifunctional Degraders and Molecular Glues
- Crystallography and SBDD

Machine Learning

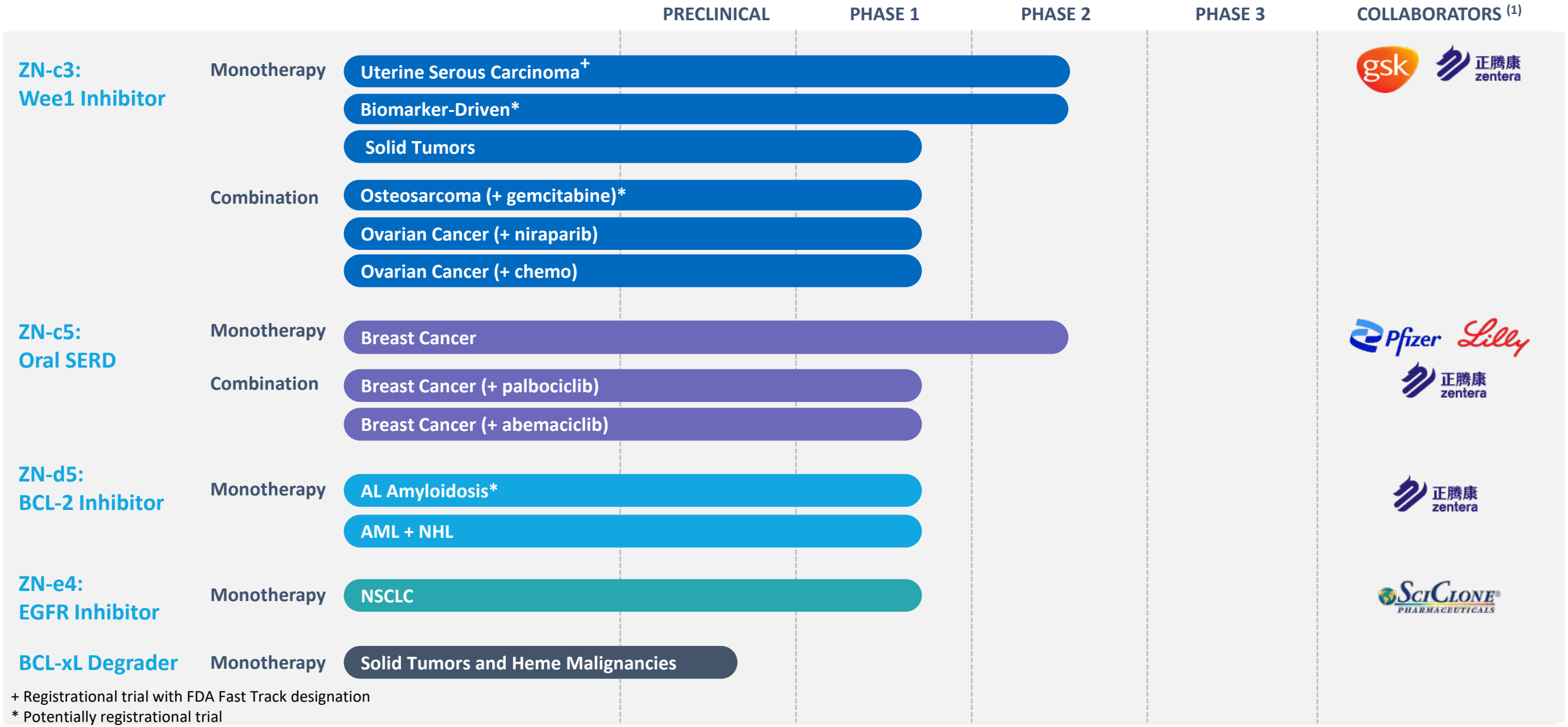
3

4

Zentalis Drugs

Image reproduced from: https://blog.f1000.com/2017/02/01/f1000prime-f1000prime-faculty-launch-bioinformatics-biomedical-informatics-computational-biology/

Broad Oncology Pipeline Designed to Improve Patient Outcomes



+ Registrational trial with FDA Fast Track designation
* Potentially registrational trial

(1) Zentalis is currently evaluating ZN-c5 in combination with palbociclib (Ibrance®), as part of a clinical research collaboration with Pfizer, evaluating ZN-c5 in combination with abemaciclib (Verzenio®), as part of a clinical research collaboration with Lilly. Zentalis intends to evaluate ZN-c3 in combination with niraparib (ZEJULA®), as part of a clinical research collaboration with GlaxoSmithKline. Zentalis maintains full ownership of ZN-c5 and ZN-c3 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 joint venture, has development and commercial rights to ZN-c5, ZN-c3 and ZN-d5 in select Asian countries (including China). Zentera received CTA acceptances in China for ZN-c3, ZN-c3 in combination, ZN-c5 and ZN-d5 and four clinical trials are ongoing.

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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
- **Opportunity: no approved Wee1 inhibitor;** only a few in development e.g., AstraZeneca's adavosertib (AZD1775)

2 ANALYZE: Adavosertib

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

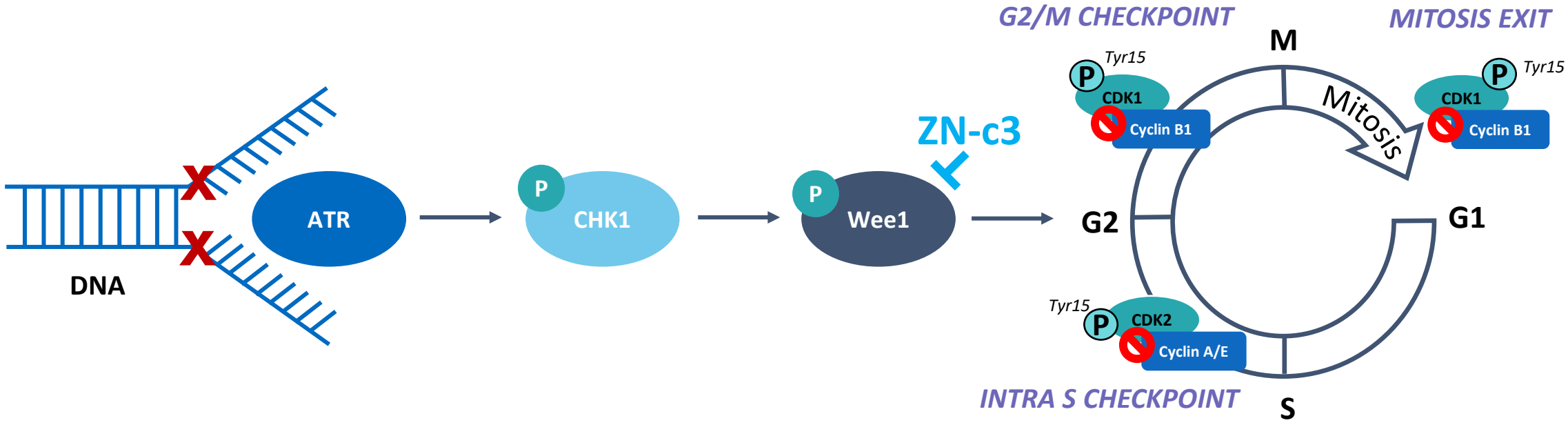
3 CREATE: ZN-c3

- Designed to have improved:
  - Potency
  - Solubility
  - Selectivity
  - PK properties
- **Goal: broader therapeutic window**
- Potential to have broad applicability as monotherapy and in combination

4 GENERATE: Preclinical Evidence

- 117x higher tumor concentration compared to adavosertib
- Greater selectivity for Wee1 compared to adavosertib
- Induced prolonged tumor growth delay in human NSCLC tumor xenograft model

Wee1 Inhibition: Clinically Proven DDR Target for Cancer



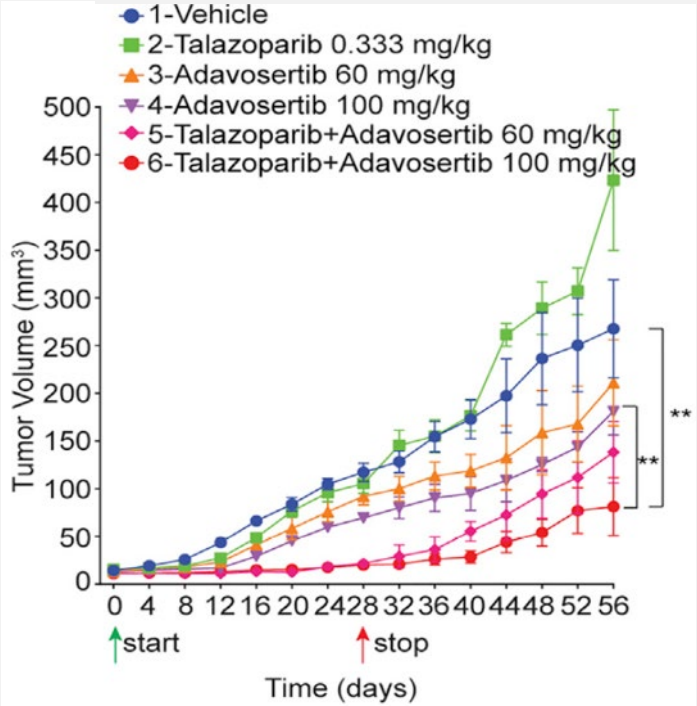
- Wee1 is a protein kinase expressed at high levels in many cancer types that prevents entry into mitosis in response to DNA damage by regulating the G2 checkpoint
- Wee1 inhibition causes cancer cells to proceed to mitosis without repairing DNA damage, resulting in premature mitotic entry and apoptosis
- Wee1 inhibition also causes aberrant origin firing [(1)], depletion of dNTP pools [(2)], and activation of cGAS/STING pathway [(3-5)]
- ZN-c3 has demonstrated significant growth inhibition and induced apoptosis *in vitro* and anti-tumor activity *in vivo*

(1) Di Rora AGL et al. J Hematol Oncol. 2020 Sep 21;13(1):126; (2) Pfister SX et al. Cancer Cell. 2015 Nov 9; 28(5): 557–568; (3) Keenan et al. Clin Canc Res. (2021); (4) Hai J et al. Clin Cancer Res. 2020 Jul 1;26(13):3431-3442; (5) Guo e et al. J. Exp. Med. 2021 Vol. 219 No. 1

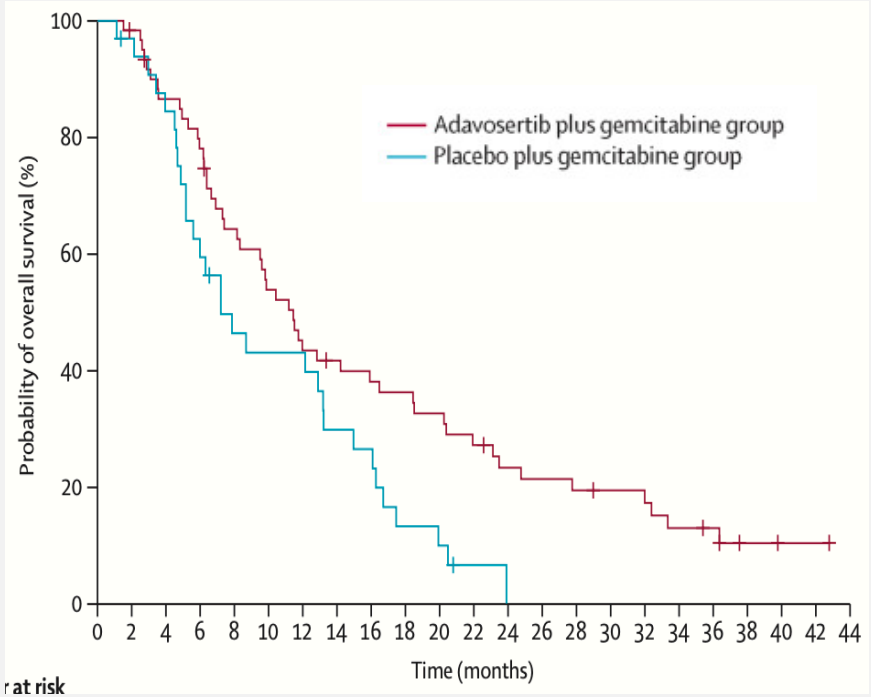
Source: Drawing based on Targeting WEE1 Kinase in Cancer. Matheson CJ, et al. Trends Pharmacol Sci. 2016

Wee1 Inhibitors: Strong Preclinical Activity and Clinical Responses

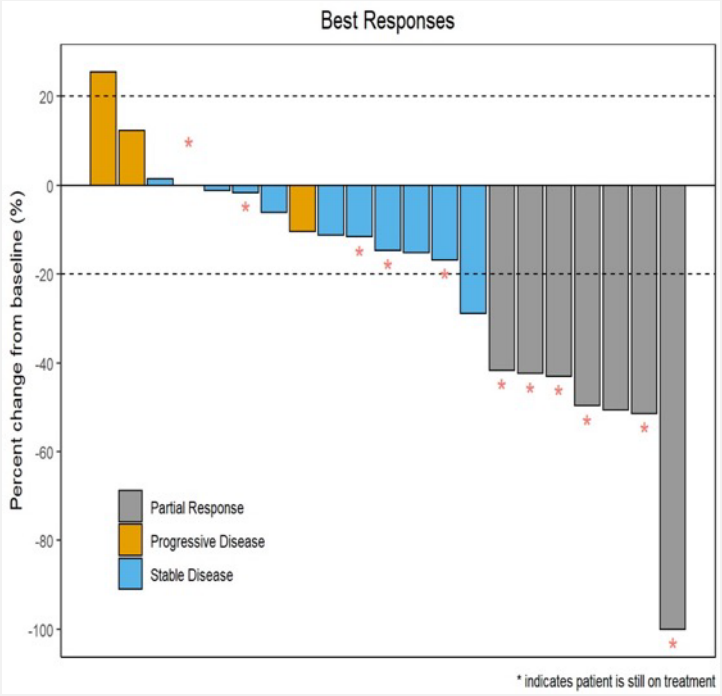
Combination of Wee1 and PARP Inhibitors Showed Improved Anti-Tumor Activity Compared to the Use of Each as Monotherapy (1)



Phase II Study of Wee1 Inhibitor Plus Gemcitabine for Platinum-Refractory Recurrent Ovarian Cancer: Double-Blind, Randomized, Placebo-Controlled (2)



Phase II Trial of Wee1 Inhibitor in Recurrent Uterine Serous Carcinoma (USC) (3,4)



(1) Fang, Y. Cancer Cell (2019). A total of 2 x 10^6 OVCAR8 ovarian cancer cells 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) Lheureux S., Lancet (2021). Addition of a WEE1 to Gemcitabine shows a statistically significant improvement in mOS over Gemcitabine with placebo (HR=0.56, P=0.017)

(3) Liu, J.F. Adavosertib SGO Presentation (2020)

(4) An aggressive subtype of endometrial carcinoma characterized by frequent TP53 mutations (>90%)

ZN-c3: Excellent Potency, PK and Preclinical Activity

ZN-c3 Anti-Proliferative Activity in a Panel of Cell Lines

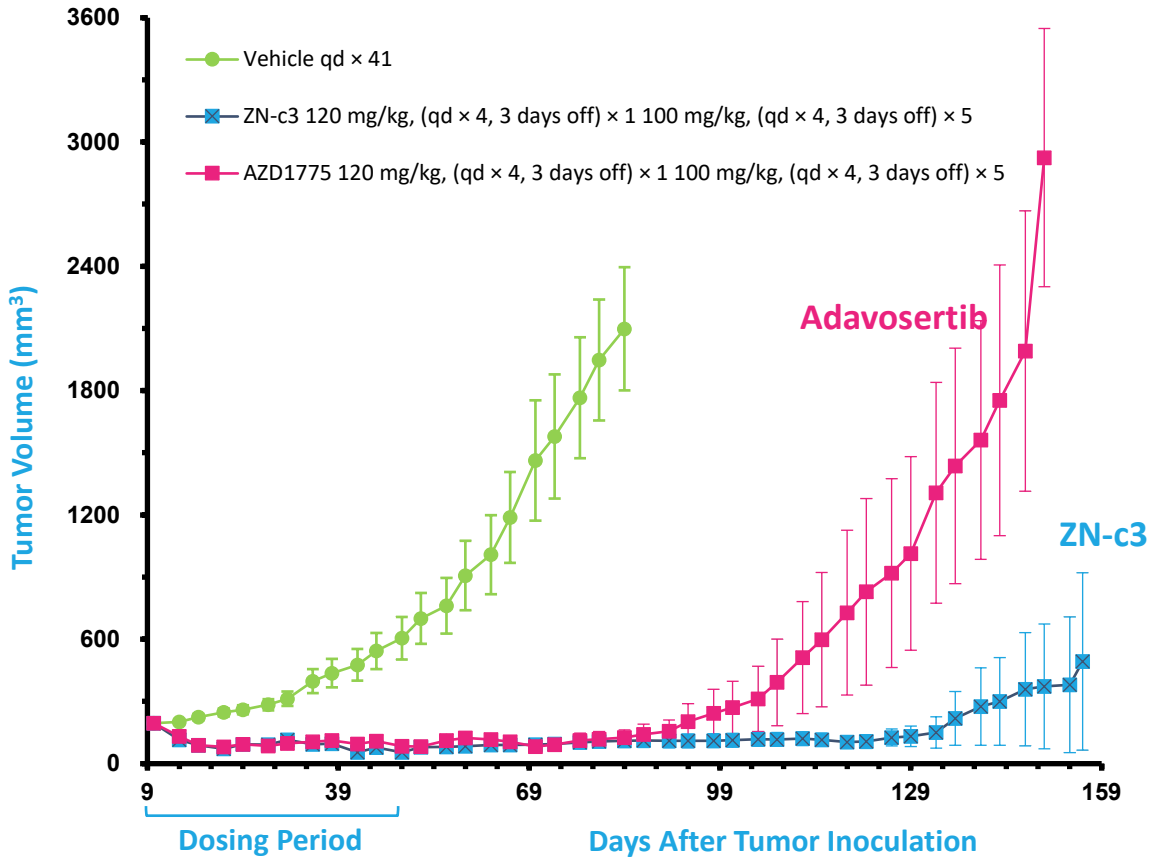
Compound ID	CTG IC_{50}(nM)							
	NSCLC		SCLC		TNBC		Ovarian cancer cells	
	NCI-H23	A-427	DMS-53	NCI-H1048	MDA-MB-231	HCC 1806	OVCAR 3	UWB 1.289
ZN-c3	**124**	**88**	**118**	**92**	**190**	**95**	**69**	**54**
Adavosertib[(1)]	108	94	130	97	233	94	124	57

Improved Tumor Concentration in Preclinical Models

Study (A-427 NSCLC)	ZN-c3			Adavosertib [(1)]		
Dose (mg/kg/day)	**20**	**40**	**80**	20	40	80
C_{max} (ng/mL)	**1,167**	**1,997**	**5,100**	635	2,460	4,703
T_{max} (hr)	**1**	**1**	**1**	1	1	1
$AUC_{0\text{-}24hr}$ (ng·hr/mL)	**4,863**	**17,088**	**39,722**	1,494	6,313	13,408
Tumor Conc. (ng/mL) at 24 h	**10.5**	**48.0**	**811**	**BQL[(2)]**	**BQL**	**6.95**

ZN-c3 Induced Prolonged Tumor Growth Delay

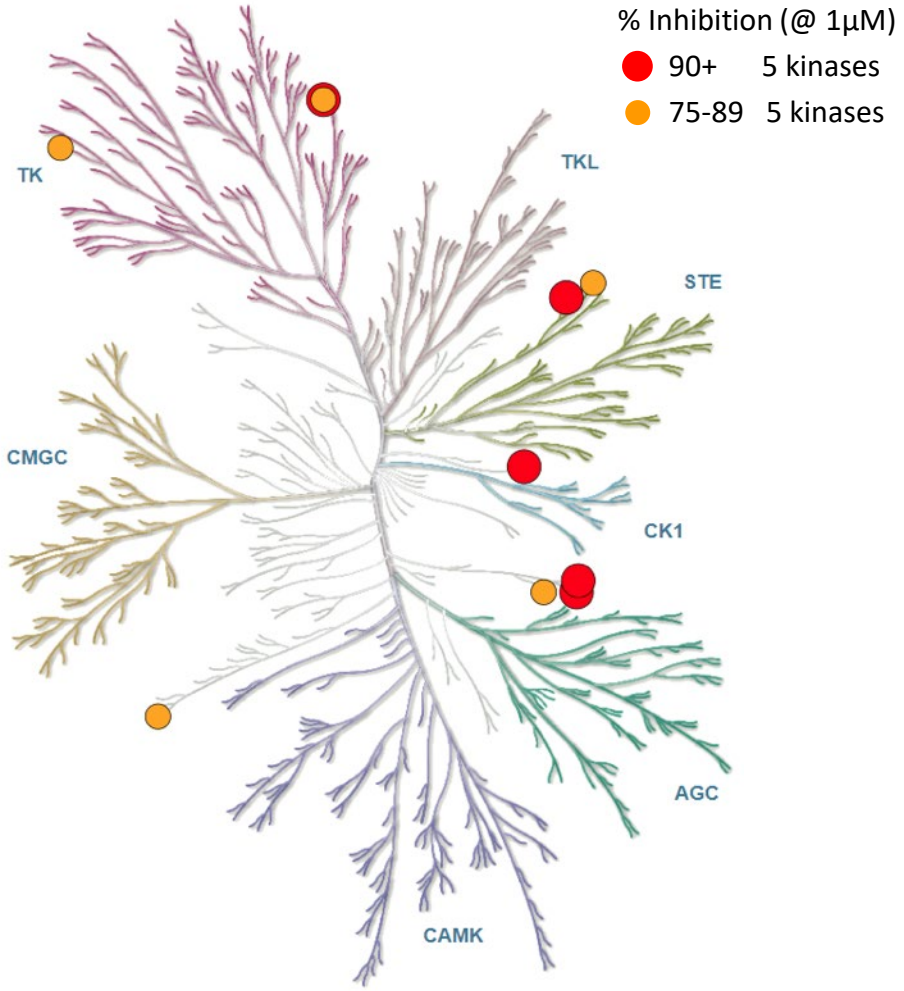
A427 Human NSCLC Tumor Xenograft Model



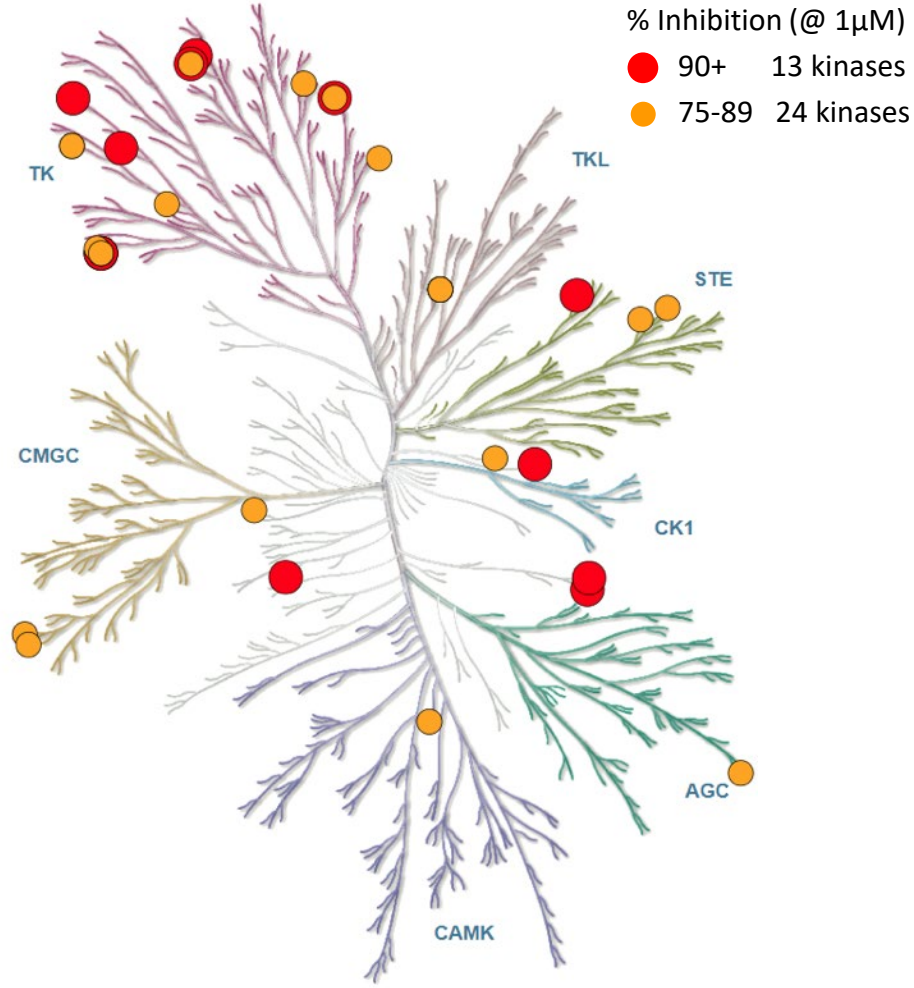
(1) Adavosertib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound.
(2) BQL: Below Quantifiable Level
Note: ZN-c3 has excellent thermodynamic solubility of 2132 µM (vs. 60 µM for Adavosertib) based on internal data

ZN-c3: Differentiated Selectivity Profile

ZN-c3



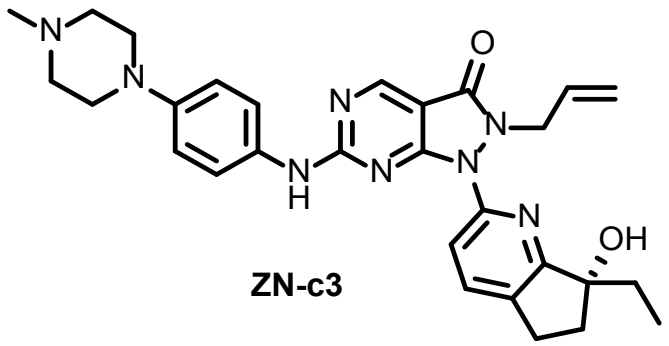
Adavosertib (1)



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

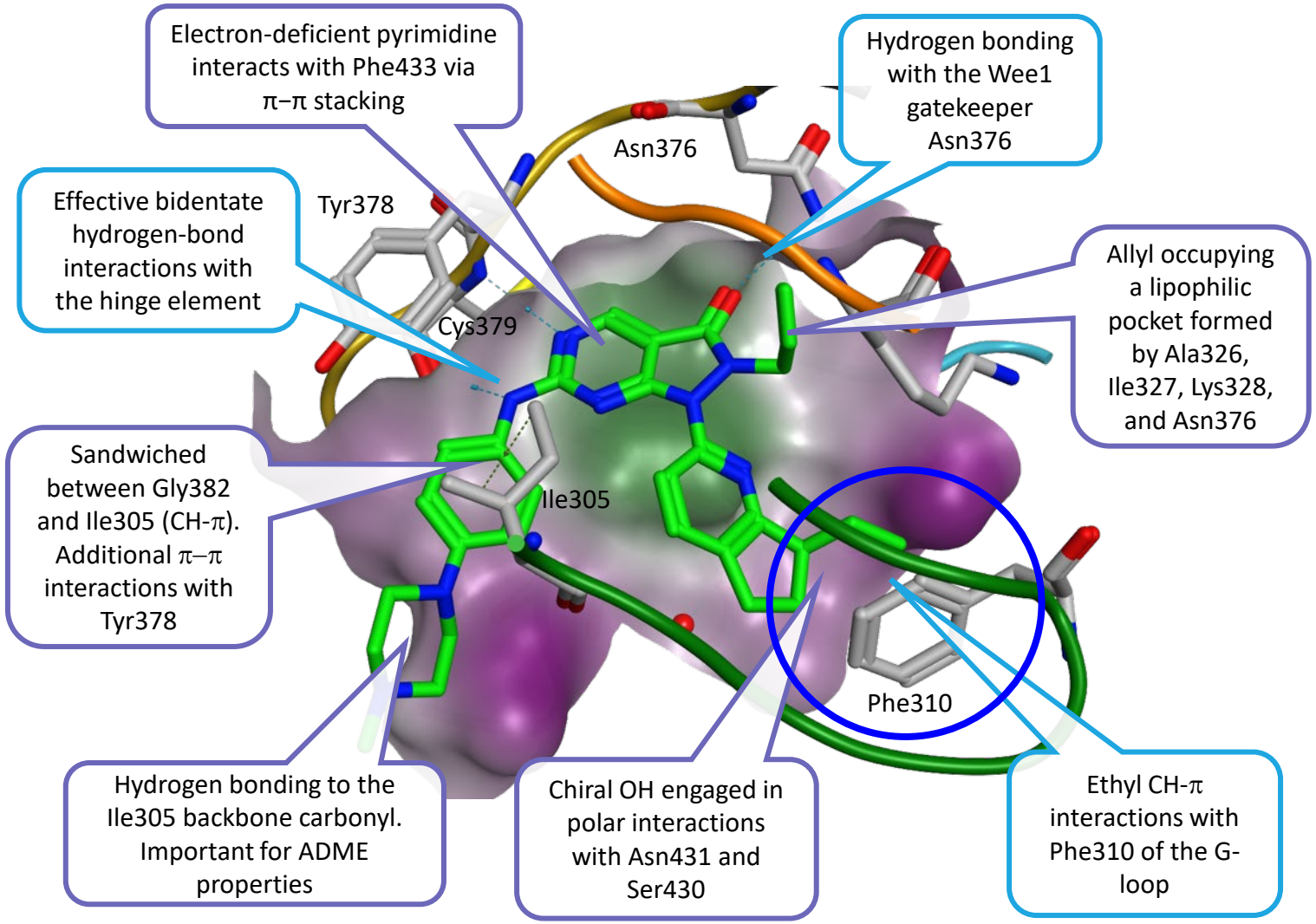
Illustrations reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

Structure-Based Drug Design (SBDD) Led to the Discovery of a Highly Potent and Selective Wee1 Inhibitor ZN-c3 with Improved ADME Properties(1)



ZN-c3

ZN-c3 potency and ADME	
Wee1 IC_{50}	3.8 nM
H23 IC_{50}	103 nM
A427 IC_{50}	75 nM
Log *D*	2.4
*h*PPB	66%
*h*Hep	<18 mL/min/kg
solubility	> 2000 µM
CYP3A4	7 µM
hERG	> 30 µM



(1) Huang, PQ; *et al.* J. Med. Chem. **2021**, *64*, 13004-13024

ZN-c3: Clinical Development Plan

Ongoing and Planned Clinical Programs

Phase 1

Solid Tumors Monotherapy
Dose Escalation and Expansion
Initial data presented at AACR 2021

Ovarian Cancer Combination
Ph 1b Study (+ chemo)
Initiated

ER+/HER2- Breast Cancer Combination
Ph 1b Study (ZN-c5 + ZN-c3)
Initiation Expected in 2H 2022

Phase 1/2

★ **Osteosarcoma Combination**
Ph 1/2 Study (+ gemcitabine)
Initiated

Ovarian Cancer Combination
Ph 1/2 Study (+ niraparib)
Initiated

AML Combination
Ph 1/2 (ZN-d5 + ZN-c3)
Expected Initiation of Phase 1 Portion in 1H 2022

Phase 2

★ **Uterine Serous Carcinoma Monotherapy**
Ph 2 Study
Initiated

★ **Predictive Biomarker Monotherapy**
Ph 2 Study
Initiated

Overview

- **Updated interim Phase 1 monotherapy dose escalation and expansion data** (1)
  - Generated new, deepening and durable tumor responses
  - ZN-c3 was well-tolerated; improved hematological tolerability
- **FDA Fast Track designation for USC**
- **Key FDA designations for osteosarcoma for combo with chemo:**
  - Orphan drug designation
  - Rare pediatric disease designation
- **Planned investigator-initiated trials:**
  - A trial with the Ivy Brain Center in glioblastoma multiforme
  - A trial with immunotherapy with Dana Farber in TNBC

(1) As of May 15, 2021

★ Registrational Study with Potential Accelerated Approval ★ Potentially Registrational Study

ZN-c3: Exceptional Responders with Single Agent Treatment

Who is an Exceptional Responder?

Exceptional Responses are generally observed randomly and the underlying driver of response is often unknown

Exceptional Responses **observed in 3 non-USC patients** who had up to 19 prior lines of treatment and no recent responses

RP2D: 300 mg QD with continuous dosing

Interim Results from Phase 1 Dose Escalation Trial

Overview of Confirmed Exceptional Responders (2)

Patient	Prior lines of therapy	Tumor reduction (%)	Duration on study
CRC, Stage IV	5	51%	169 days
Ovarian cancer, Stage IV	19	68%	221 days and remains on study
NSCLC, Stage IV	5	50%	154 days

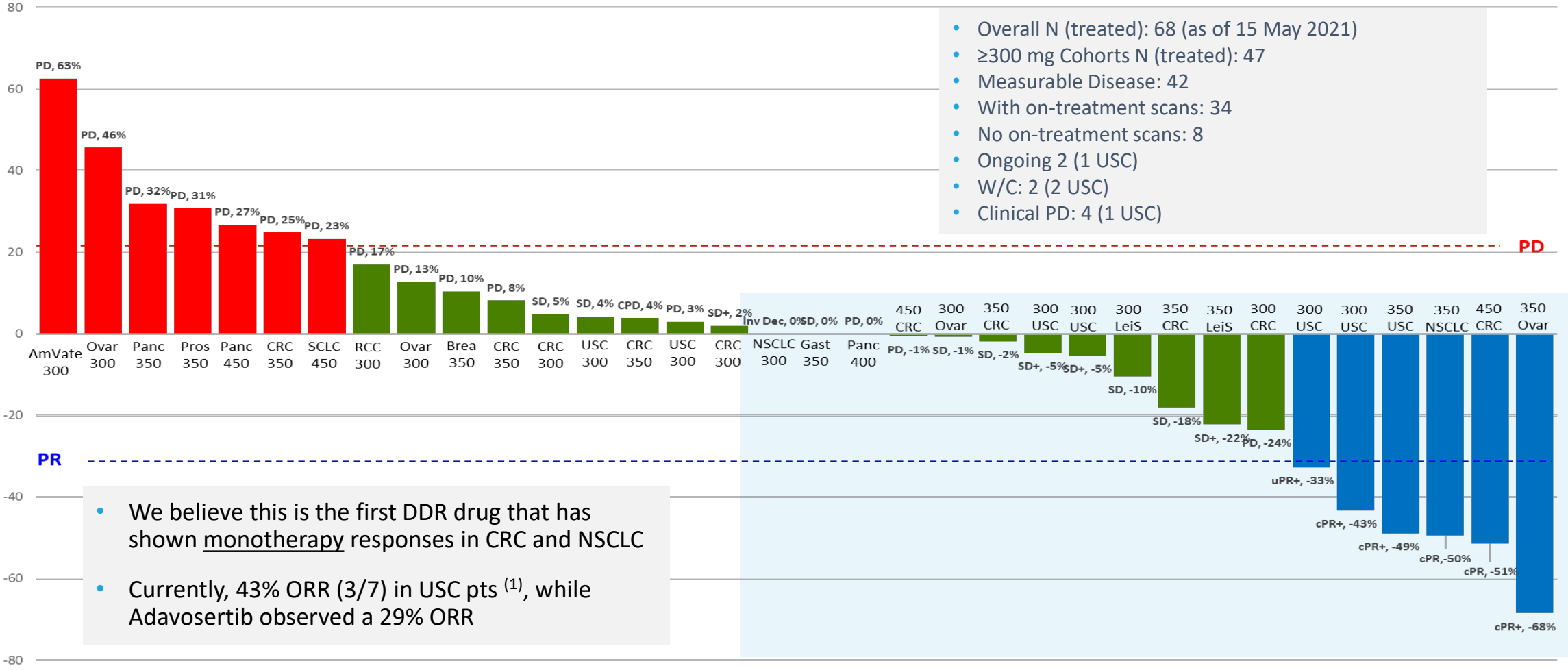
Overview of PRs in USC (2)

Patient	Prior lines of therapy	Tumor reduction (%)	Duration on study
USC, Stage IV (confirmed PR)	2	49%	158 days and remains on study
USC, Stage IV (confirmed PR)	4	43%	123 days and remains on study
USC, Stage IV (unconfirmed PR)	2	33%	31 days and remains on study

(1) *JNCI J* Natl Cancer Inst (2021) 113(1)
(2) As of May 15, 2021

ZN-c3: Displayed Multiple PRs Across Tumor Types

ZN-c3 Dose Escalation and Expansion Study – 300 mg QD and Above Dose Cohorts
Best % Change in Target Lesion Size and Best Overall Response



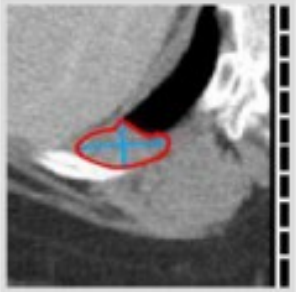
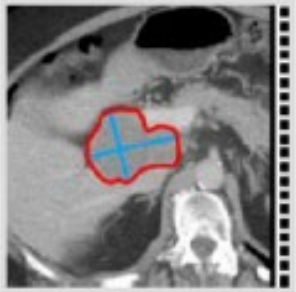
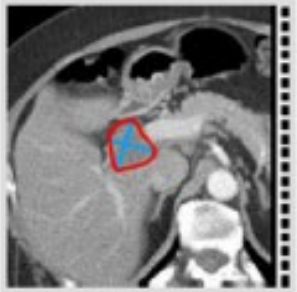
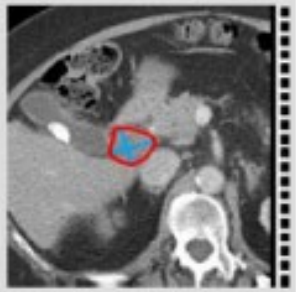
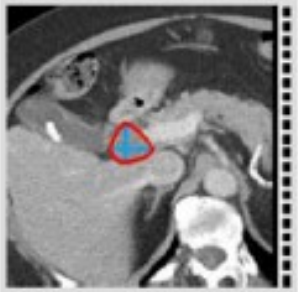
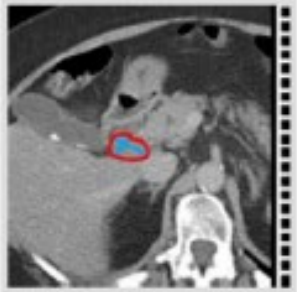
- Overall N (treated): 68 (as of 15 May 2021)
- ≥300 mg Cohorts N (treated): 47
- Measurable Disease: 42
- With on-treatment scans: 34
- No on-treatment scans: 8
- Ongoing 2 (1 USC)
- W/C: 2 (2 USC)
- Clinical PD: 4 (1 USC)

- We believe this is the first DDR drug that has shown <u>monotherapy</u> responses in CRC and NSCLC
- Currently, 43% ORR (3/7) in USC pts [(1)], while Adavosertib observed a 29% ORR

3 subjects with no treatment scans (CRC, USC, Pancreas), and experienced clinical progressive disease (CPD) + denotes treatment ongoing

(1) Waterfall as of 05/15/2021; both uPRs reported at AACR 2021 in USC are confirmed PRs. Newly reported uPR in USC is included. ORR based on radiographic responses.

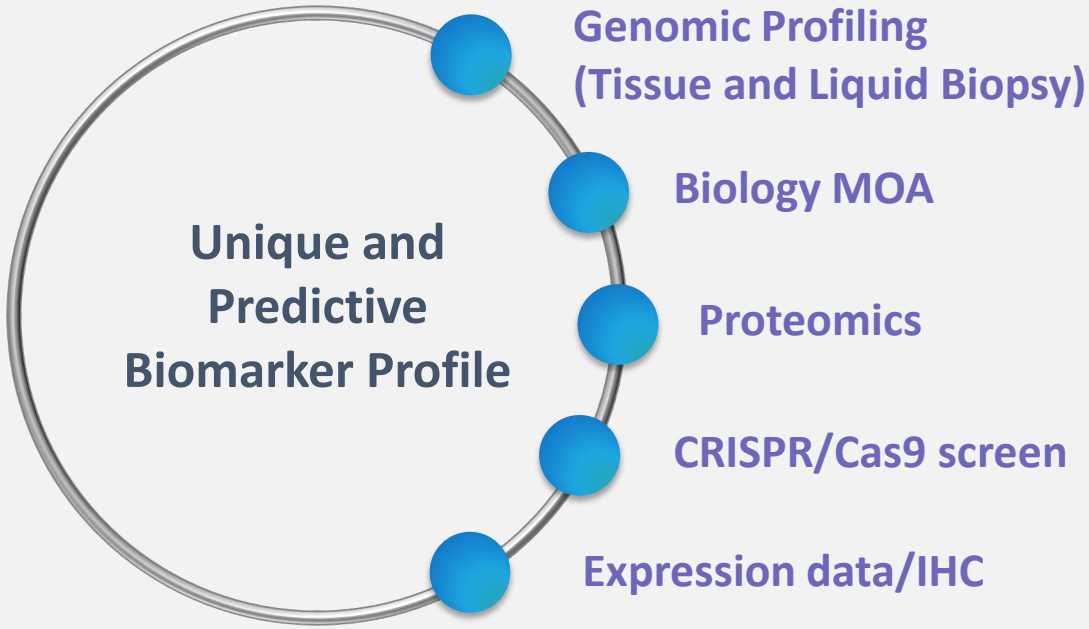
Ovarian Cancer Exceptional Responder Clinical Update

	Baseline (09/22/2020)	Follow-Up 1 (11/24/2020)	Follow-Up 2 (12/28/2020)	Follow-Up 3 (03/01/2021)	Follow-Up 4 (05/17/2021)
Target Lesions					
T01 Pleura Pleura Size	 LA: 32.9 mm SA: 16.6 mm	Disappeared	Disappeared	Disappeared	Disappeared
T02 Peritoneum Pleritoneum Size	 LA: 65.7 mm SA: 51.1 mm	 LA: 36.3 mm (-44.7% ΔP) SA: 34.0 mm (-33.5% ΔP)	 LA: 33.2 mm (-8.5% ΔP) SA: 27.2 mm (-20.0% ΔP)	 LA: 29.7 mm (-10.5% ΔP) SA: 27.6 mm (+1.5% ΔP)	 LA: 27.4 mm (-7.7% ΔP) SA: 18.9 mm (-31.5% ΔP)

All progress values are relative to their previous value (ΔP)

Exceptional Responders Exhibit Unique Biological Features

Zentalis Predictive Biomarker Approach



Confirming Biomarker Profile

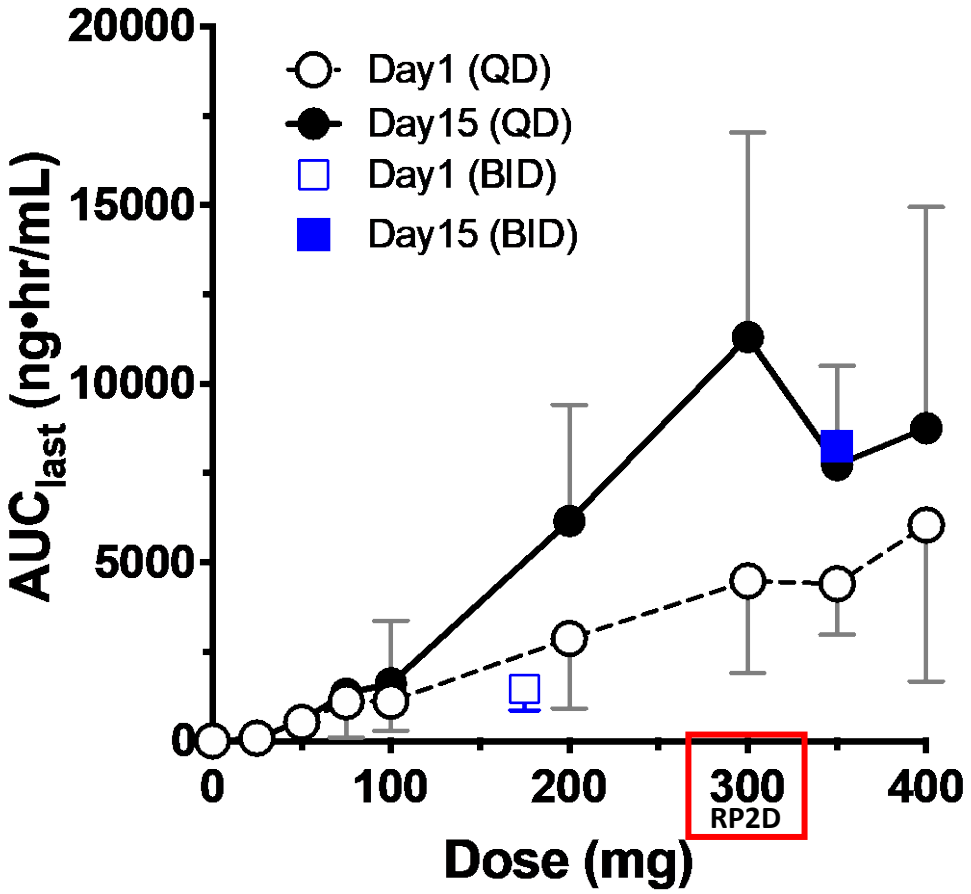
- Observed multiple Exceptional Responses with single agent ZN-c3 (1)
- Activity in tumor types (e.g., CRC) not previously seen by other Wee1i
- Approach to confirm unique, novel and predictive profile
- Clear path for the development of companion diagnostic

Phase 2 predictive biomarker-enabled trial ongoing

(1) Based on data from the ZN-c3 Phase 1 monotherapy trial

ZN-c3: RP2D Shows Highest AUC Across Doses

Interim Plasma Pharmacokinetics



25 & 50 mg: n=2
75 mg: n=10/8
100 mg: n=4

200 mg: n=3
300 mg: n=16/9
350 mg: n=10/9

400 mg: n=3
175 mg BID: n=7/5

ZN-c3 shows ~30% more exposure than Adavosertib at 300 mg dose (RP2D) (1)

- Greater than dose proportional exposure up to 450 mg (not plotted)
- 1.87 to 2.50-fold accumulation at 200-350 mg dose
- No additional increase of exposure occurs beyond Day 15 (up to Cycle 6)
- 300 mg QD exhibited the highest mean AUC between 25-400 mg
- 300 mg QD was well-tolerated without dose reductions in majority of patients

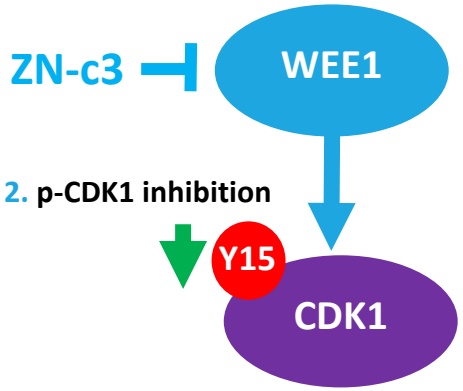
(1) Cancer Chemotherapy and Pharmacology (2020) 86:97–108

Decreases in p-CDK1 Show Target Engagement for Wee1 Inhibition

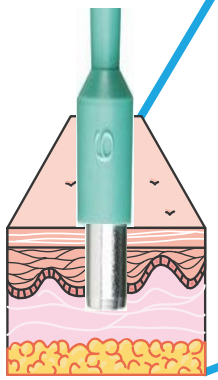
Confirmation of WEE1 Target Engagement in Surrogate Tissue

1. CDK1 phosphorylation (p-CDK1) is mediated by Wee1
2. Inhibition of Wee1 will lead to inhibition of p-CDK1
3. Skin biopsies were performed at baseline and on treatment to verify p-CDK1 levels and level of target engagement of Wee1

1. CDK1 phosphorylation by Wee1

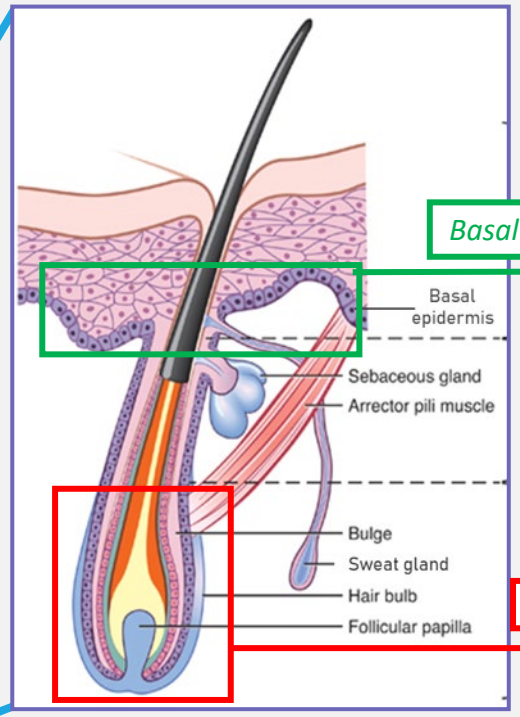


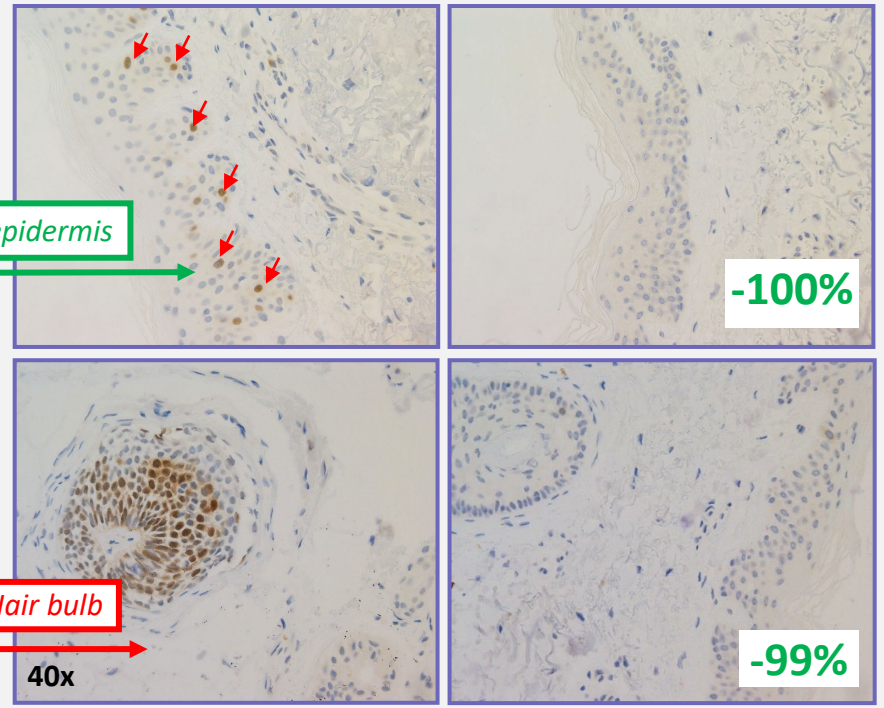
3. Skin Biopsy



Decreases in p-CDK1 at Baseline vs on Treatment

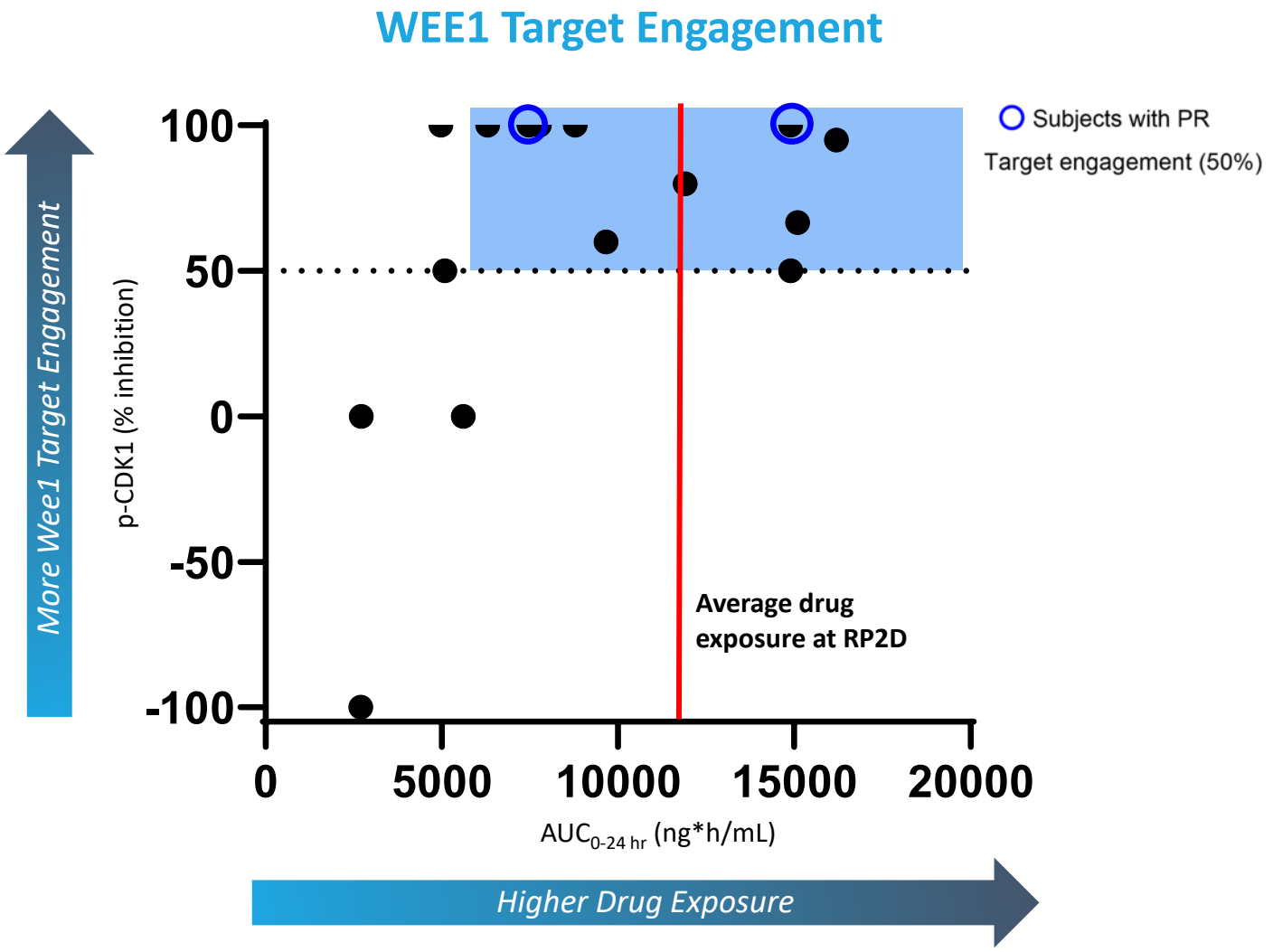
p-CDK1 = Brown Staining (subject with cPR)





Source: Drawing adapted from Servier Medical Art

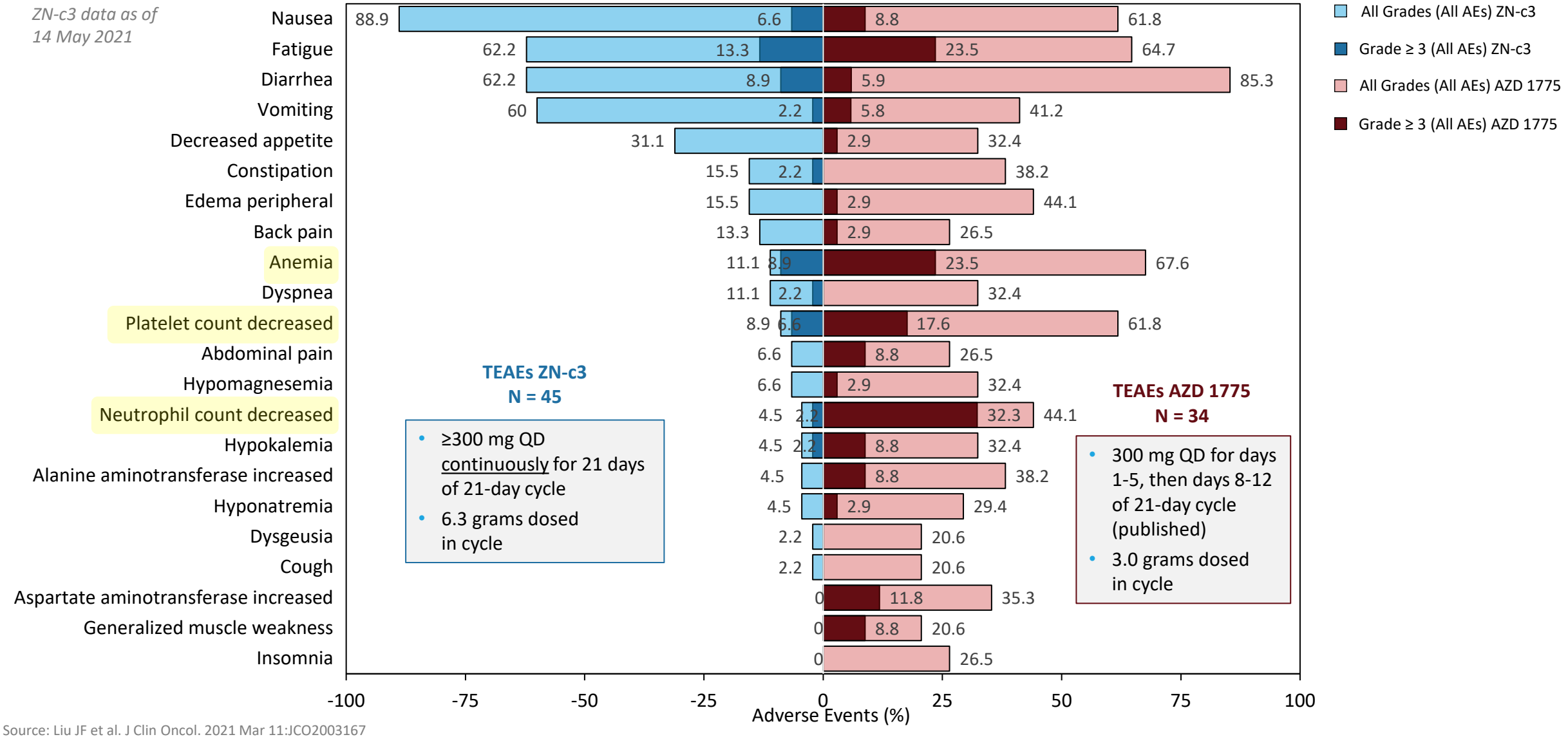
ZN-c3: PK/PD Correlation Shows Active Target Engagement at RP2D



- Inhibition of p-CDK1 demonstrated Wee1 target engagement
- Increase in dose / drug exposure directly related to Wee1 target engagement
- RP2D showed highest AUC, with excellent target engagement and p-CDK1 levels decreased at least by 50%

ZN-c3: Well Tolerated in Comparison to Adavosertib (1)

ZN-c3 data as of 14 May 2021

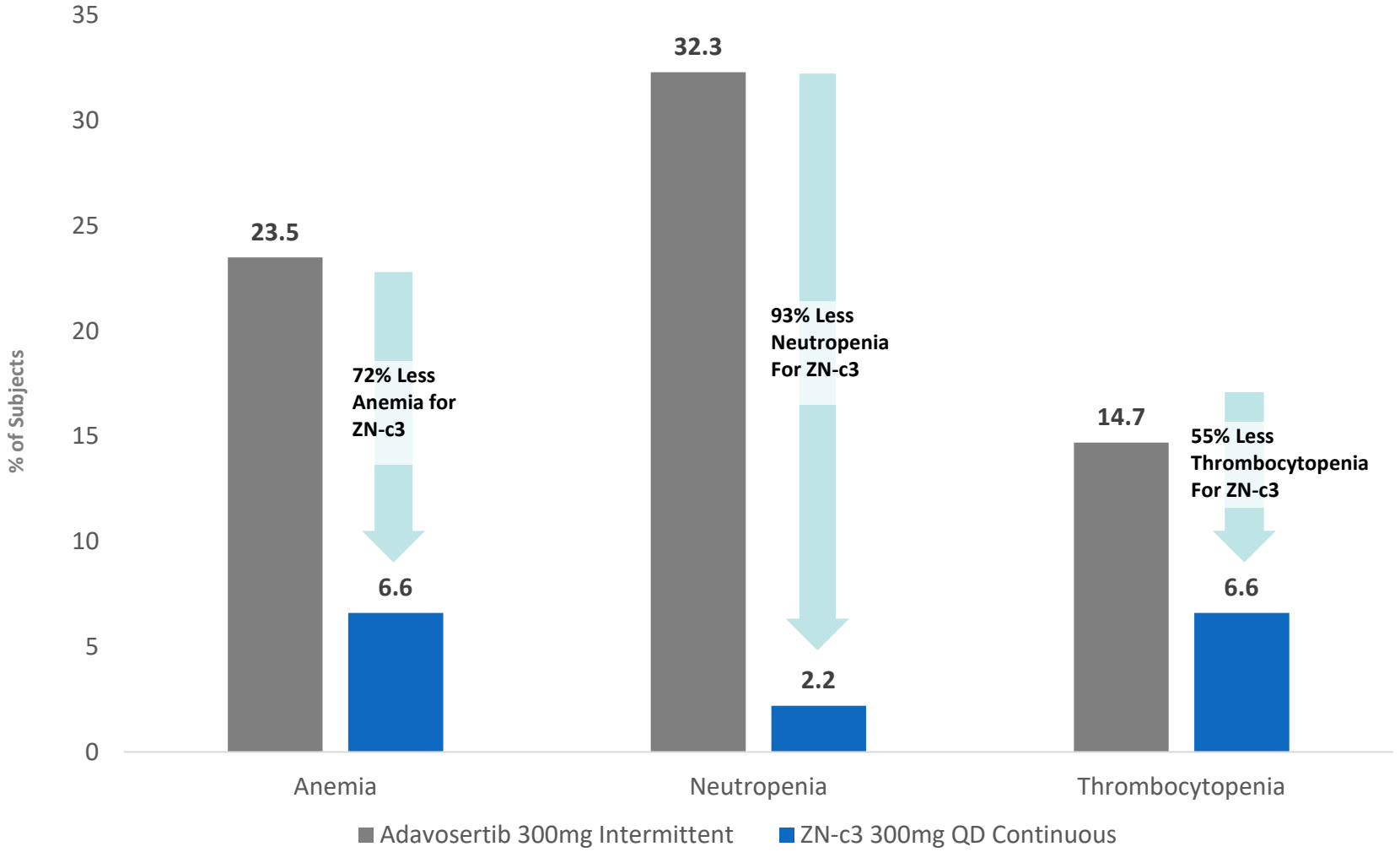


Source: Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167

(1) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful

ZN-c3: Meaningfully Reduced Hematological Toxicities (1)

Interim Grade ≥3 Hematological TEAEs at ≥RP2D



- Significantly lower overall severe hematological AE rate vs Adavosertib
- Despite continuous dosing and delivering 2x the drug load, ZN-c3 induces markedly less hematological toxicity
- Better tolerability unlocks the promise for wide ranging drug combinations with increased efficacy and commercial potential

Source: Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167

(1) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful

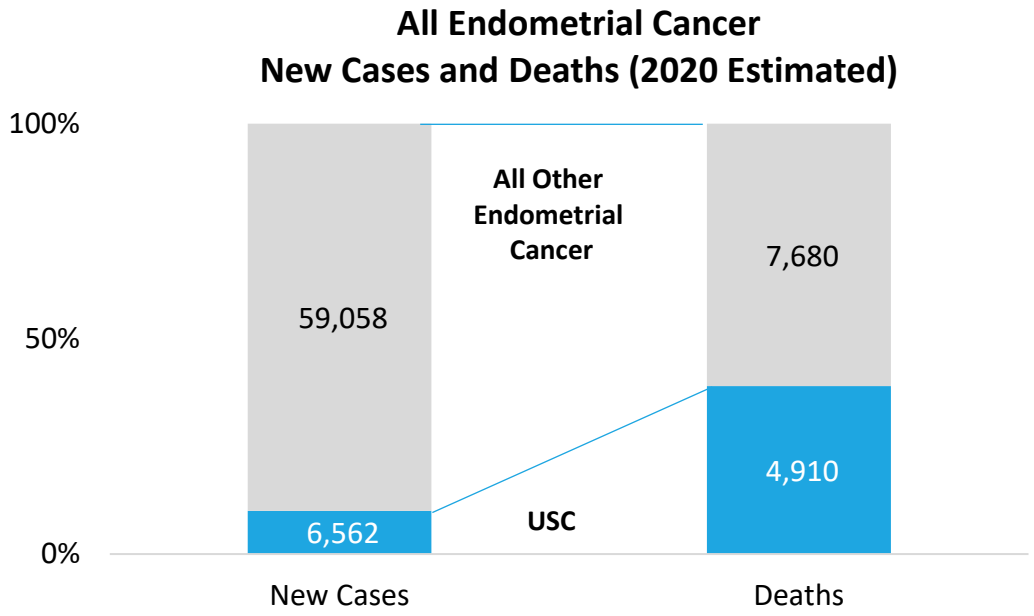
ZN-c3 Uterine Serous Carcinoma Indication Overview

Overview of Uterine Serous Carcinoma (USC)

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

USC Represents High Unmet Medical Need

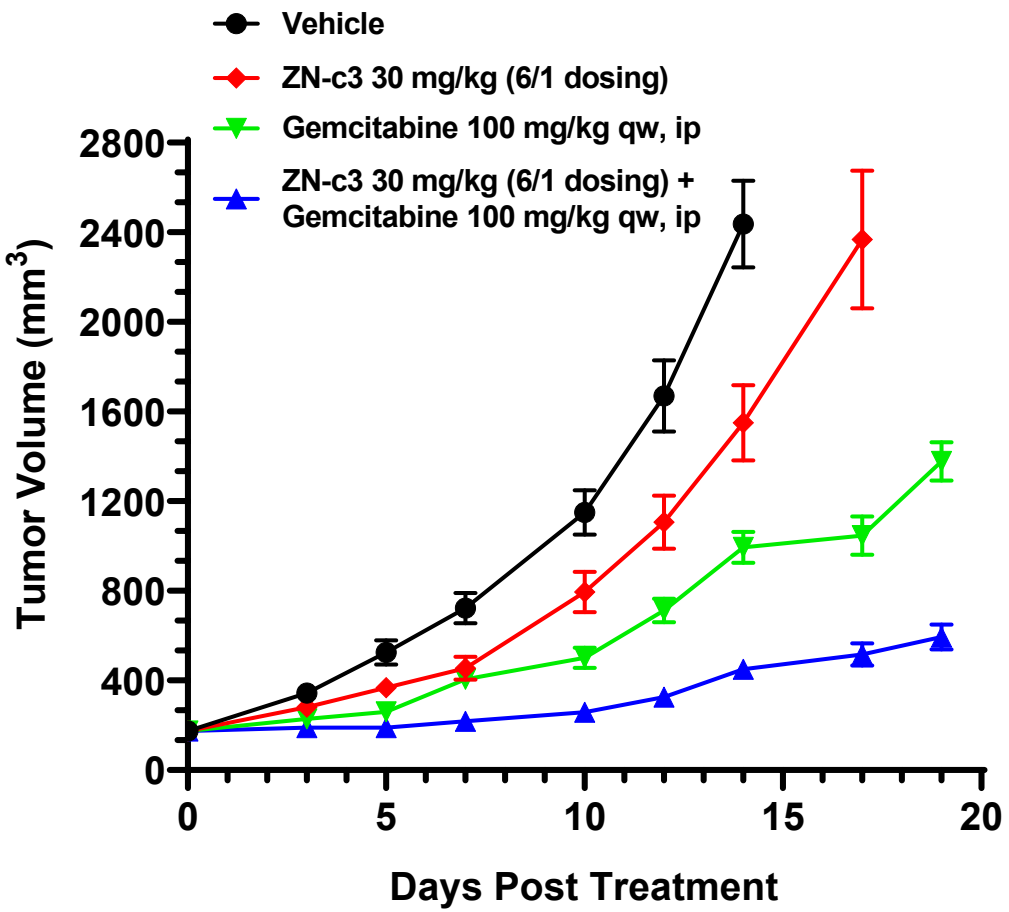
Comprises 10% of Endometrial Cancers with Highest Mortality



Source: Gynecologic Oncology 115 (2009) 142-153, David Boruta et al.; National Cancer Institute, SEER 2020 Data

ZN-c3 in Combination with Gemcitabine Shows Strong Activity in an Osteosarcoma Cancer Model

Osteosarcoma Cancer Model SJSA-1



Clinical Unmet Need in Osteosarcoma

- Approximately 1,000 new cases in the U.S.(1)
- Up to 90% have sequence mutations or structural variants in TP53 and are often enriched in relapsed or refractory cases, portending resistance to chemotherapy(2)
- No significant advances over the last 10 plus years(3)
- Overall survival rate for patients with metastatic or recurrent disease is <20%(4)

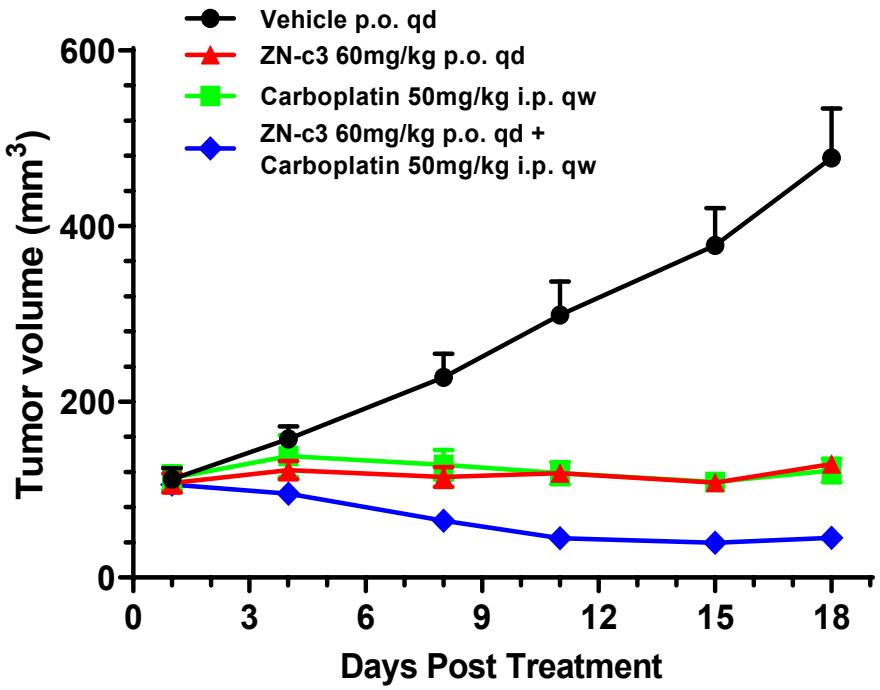
Phase 1/2 Initiated in 3Q 2021

(1) American Cancer Society. Last accessed on April 7th, 2020
(2) Tang et al. J *Orthop Res.* 2019;37(3):789–98
(3) Misaghi A et al. *Sicot-j.* 2018;4:12
(4) Harrison DJ et al. *Expert Rev Anticanc.* 2018;18:1, 39-50

ZN-c3 in Combination Demonstrates Synergistic Activity in Ovarian Cancer Models

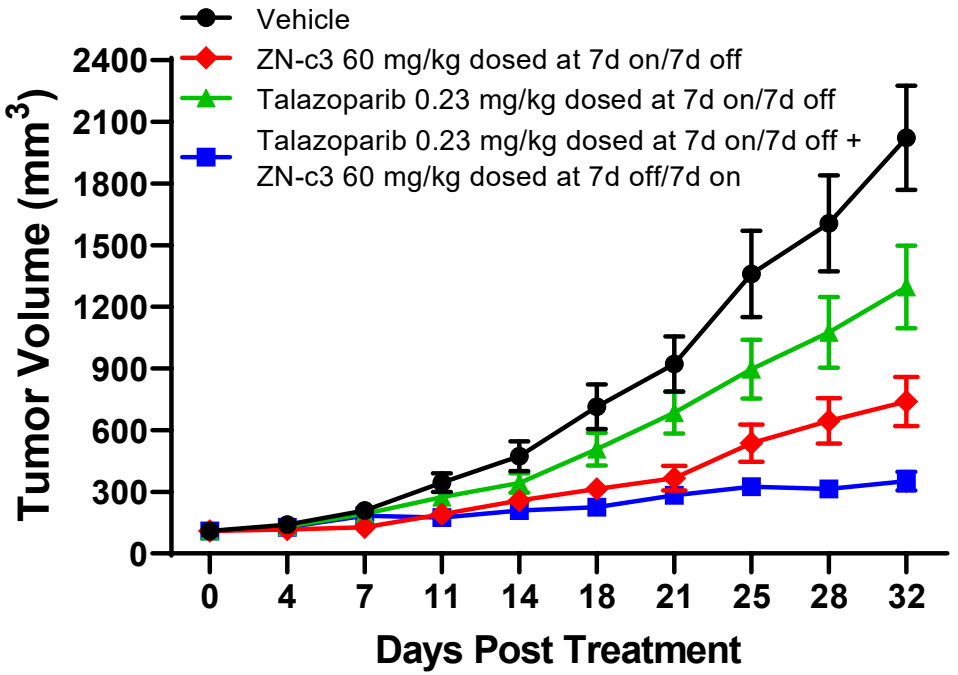
ZN-c3 in combination with carboplatin shows better activity than single agent alone in an ovarian preclinical model

Ovarian Cancer Model TOV21G



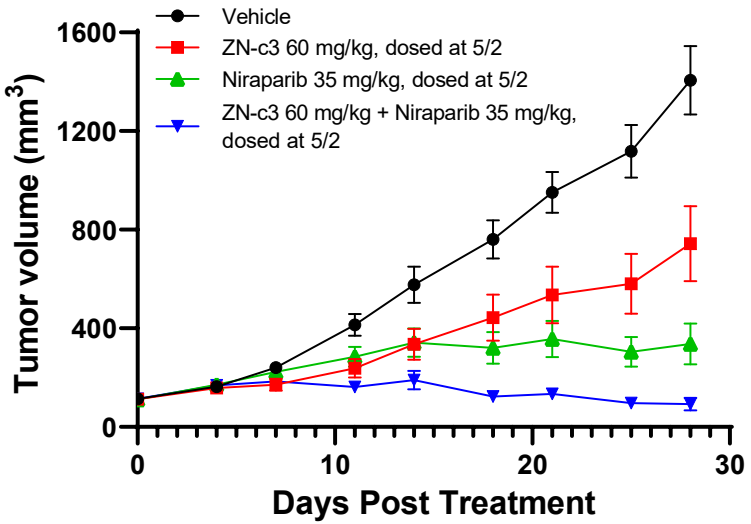
Combination of Wee1 and PARP inhibition has been shown significantly inhibit tumor growth in preclinical models(1)

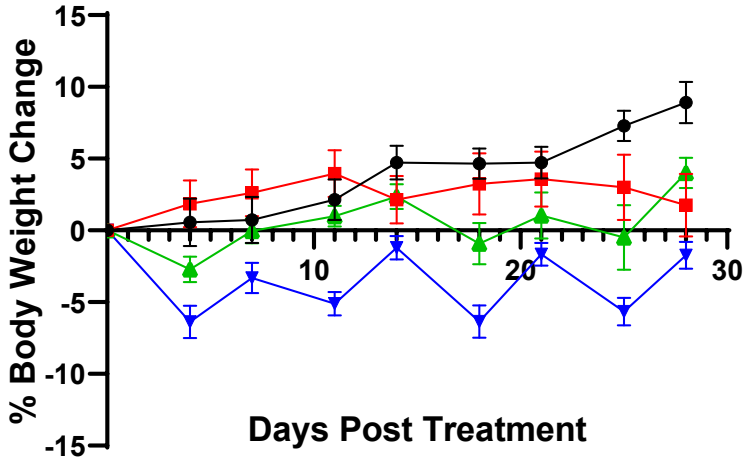
OVCAR3 Tumor Model (sequential dosing)



(1) Fan, Y et al. Cancer Cell. 2019 Jun 10;35(6):851-867

ZN-c3 + PARP Inhibitor Combination Induces Regressions and is Well Tolerated in a TNBC PDX Tumor Model



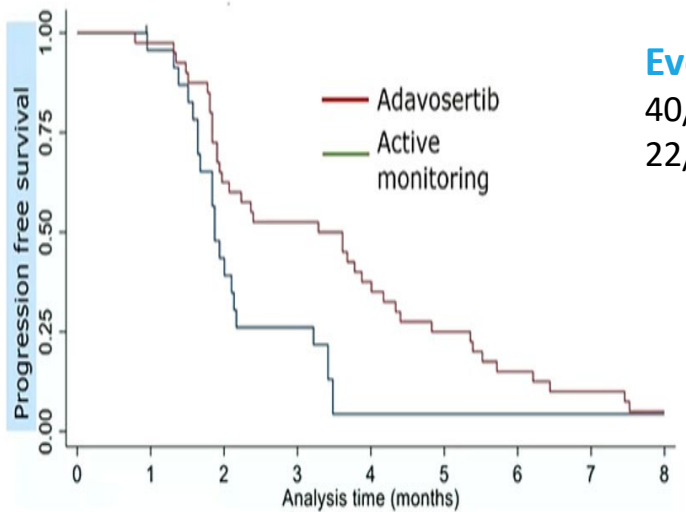


- Tumors with Cyclin E amplification have enhanced sensitivity to Wee1 inhibition (1)
- Combination of PARP and Wee1 inhibitors in TNBC:
  - Results in synergistic cell killing in preclinical models with either BRCA1 mutations or high levels of cyclin E (2)
  - Has shown to induce replication stress, DNA damage and abrogation of the G2 DNA damage check point leading to significant tumor growth inhibition in pre-clinical models (3)
- Wee1 inhibition may broaden the application range of PARP inhibitors in TNBC

(1) Chen X et al Clin Cancer Res. 2018 Dec 15;24(24):6594-6610
(2) Chen X Cancers (Basel). 2021 Apr 1;13(7):1656
(3) Fan, Y et al. Cancer Cell. 2019 Jun 10;35(6):851-867

Wee1 Inhibition Has Shown a Progression-Free Survival Benefit in Patients with Colorectal Cancer

Primary Analysis: Progression Free Survival from Point of Randomization into FOCUS 4-C[1]

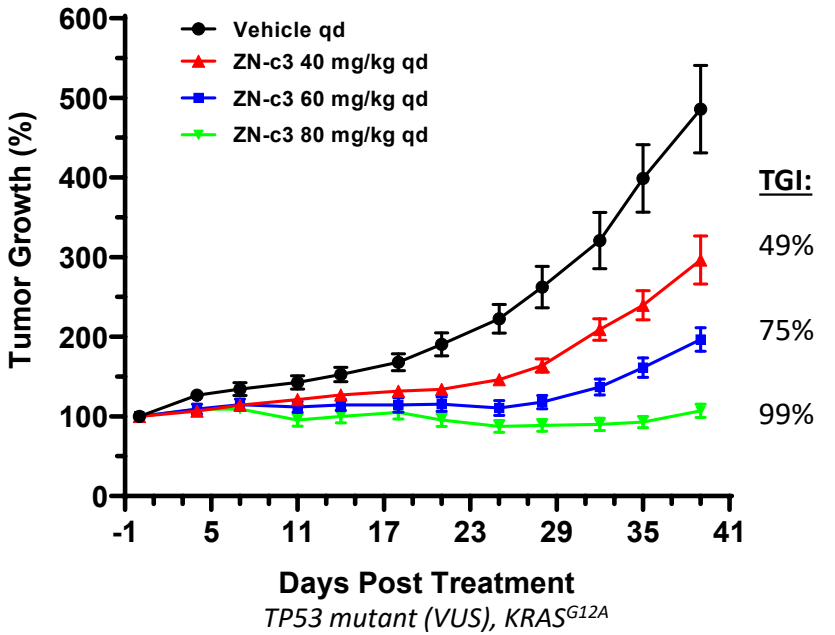


Events/ N	Median PFS (mths)
40/40	3.61
22/24	1.87

HR = 0.35 (0.18 – 0.68), p = 0.0022

Treatment Arm	Numbers at risk (failures)								
	0	1	2	3	4	5	6	7	8
AM	24 (1)	22 (12)	10 (4)	6 (5)	1 (0)	1 (0)	1 (0)	1 (0)	1 (0)
Adavosertib	40 (1)	39 (14)	25 (4)	21 (6)	15 (5)	10 (4)	6 (2)	4 (2)	2 (0)

ZN-c3 is Active in a KRAS/TP53 Mutant Preclinical Colorectal Cancer Model



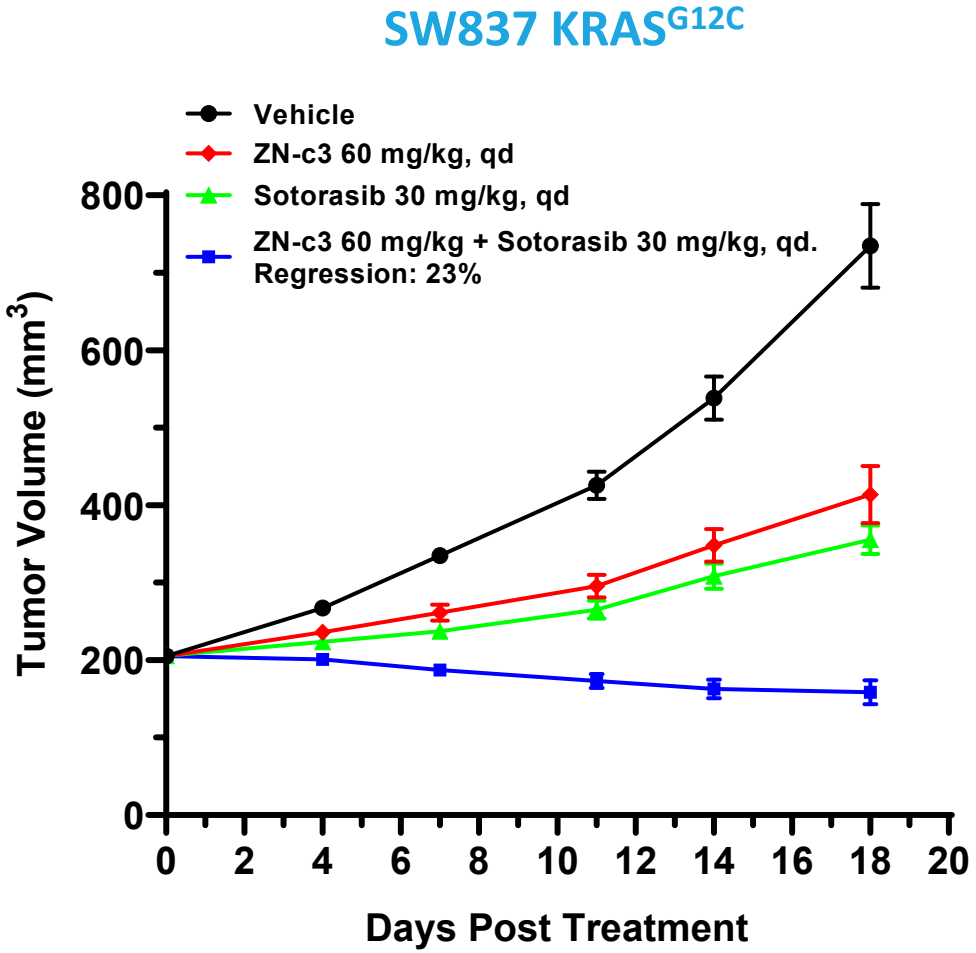
TP53 mutant (VUS), KRAS^{G12A}

- Multiple opportunities for combining ZN-c3 with different agents: 5-FU, irinotecan, anti-PD-1 and others

2021 ESMO congress

(1) Seligmann JF et al. J Clin Oncol. 2021 Sep 18

ZN-c3 in Combination with Sotorasib(1) Induces Regressions in a KRAS/TP53 Mutant Preclinical Colorectal Cancer Model



- Wee1 inhibition has been shown to improved PFS compared with active monitoring in patients with KRAS/TP53 mutated CRC (FOCUS4C trial)(2)
- These data support combining ZN-c3 with KRASG12C inhibitors in this population

(1) Sotorasib (AMG510, KRAS G12C inhibitor)
(2) Seligmann JF et al. J Clin Oncol. 2021 Sep 18

ZN-c3: Cornerstone of Multiple Treatments in Many Indications

- Potentially registrational trials underway
- Superior selectivity and tolerability profile supports combination therapies across multiple indications
- Efficacy observed in hematologic tumors in addition to solid tumors

ZN-c3 Development Program			
Indication	Treatment	Status	Addressable Patient Population[1]
USC*	ZN-c3 monotherapy	Enrolling	~12,000[2]
Solid Tumors	ZN-c3 monotherapy	Enrolling	N/A
Ovarian	ZN-c3 and chemotherapy	Enrolling	~14,000[3]
Osteosarcoma*	ZN-c3 and gemcitabine	Enrolling	~1,000[4] (US incidence)
Predictive Biomarker*	ZN-c3 monotherapy	Initiated Dec 2021	~55,000[5]
Ovarian	ZN-c3 and niraparib (PARPi)	Initiated Dec 2021	~18,000[6]
Breast (ER+/HER2-)	ZN-c5 (SERD) and ZN-c3	Initiate 2022	>1,500,000[7] (total); ~450,000 (CDK4/6i r/r)[8]
Breast (HER2+)	ZN-c3 and trastuzumab	-	~400,000[9] (total); ~60,000 (trastuzumab resistant)[10]
Colorectal	ZN-c3 monotherapy	-	>2,000,000[11] (total); ~500,000 (TP53/KRAS mutant)[12]
AML	ZN-d5 (BCL-2i) and ZN-c3	Initiate 1H 2022	~68,000[13] (US prevalence)

* Potentially registrational trial

(1) North America, Western Europe, and Japan prevalence unless otherwise stated.
(2) Gynecologic Oncology 115 (2009) 142-153, David Boruta et al.; National Cancer Institute, SEER 2020 Data.
(3) Informa Pharma Intelligence. Ovarian Cancer November 2020; Platinum resistant/refractory.
(4) Cancer.org; SEER database.
(5) Observed predictive biomarker frequency data across solid tumor types; biomarker not disclosed.
(6) Informa Pharma Intelligence. Ovarian Cancer November 2020; estimated PARP treated patients.
(7) Informa Pharma Intelligence. ER+/HER2- BC December 2020; All stages.
(8) Li et al. Mechanisms of CDK4/6 Inhibitor Resistance in Luminal Breast Cancer. Front Pharmacol (2020).
(9) Informa Pharma Intelligence. HER2+ BC March 2021; All stages.
(10) Olson & Mullins. When Standard Therapy Fails in Breast Cancer: Current and Future Options for HER2-Positive Disease. J Clin Trials (2013).
(11) Globocan 2020 https://gco.iarc.fr/today/data/factsheets/cancers/10_8_9 Colorectum fact sheet.pdf
(12) American Cancer Society Facts & Figures 2020; Based on flowchart of patients from Seligmann JF et al. J Clin Oncol. 2021. US population.
(13) Cancer.org; SEER database (2018).

zentalis

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**
- **Opportunity to combine with ZN-c3 in CDK4/6 inhibitor-resistant population**

2

ANALYZE:
Fulvestrant

- Fulvestrant limitations:
  - 2 painful monthly intramuscular injections (insoluble)
  - Capped efficacy at approved dose
  - Low convenience and high resource utilization

3

CREATE:
ZN-c5

- Designed 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**

4

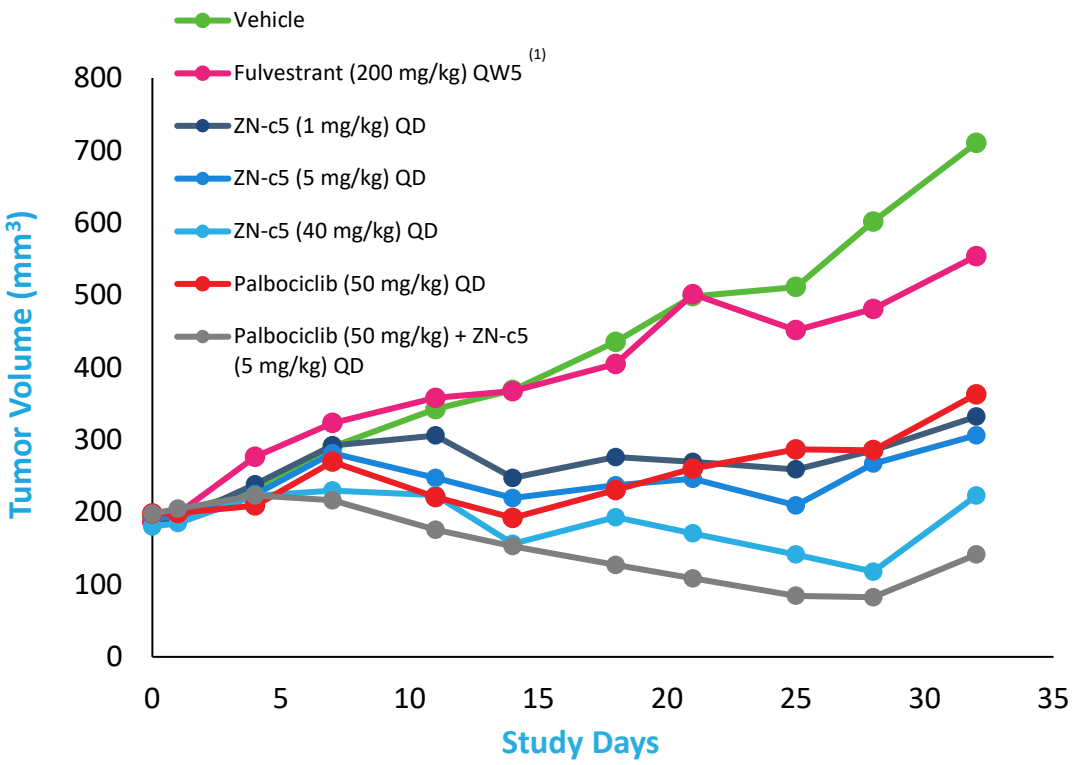
GENERATE:
Preclinical Evidence

- Dose proportional responses and meaningful tumor shrinkage in combination with CDK4/6 inhibitor
- Anti-tumor activity in ESR1 mutant models as monotherapy and in combination with CDK4/6 inhibitors
- No agonist activity in uterus
- Bone protective activity in mouse model of osteoporosis

ZN-c5: Demonstrated Strong Preclinical Anti-Tumor Activity

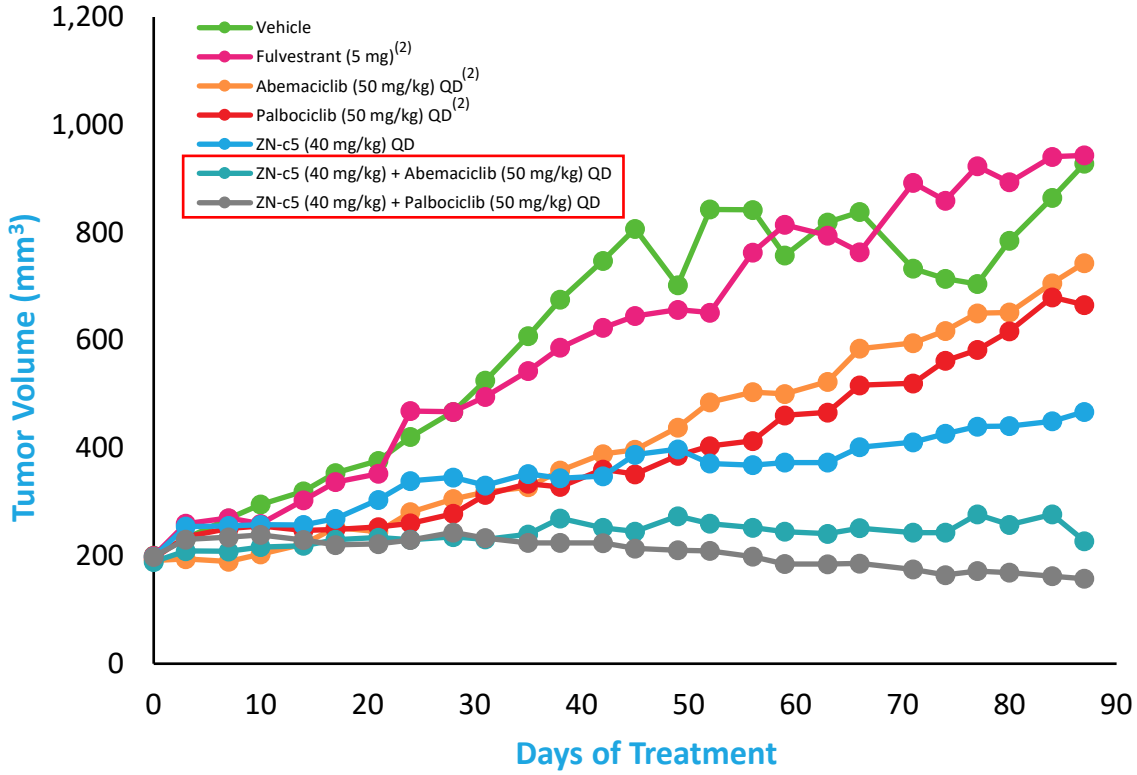
Exhibited Dose Proportional Response and Meaningful Tumor Shrinkage

Breast Cancer Model (MCF7)



Robust Anti-Tumor Activity in ESR1 Models as Monotherapy and in Combination

ESR1 Mutant Breast Cancer Model (WHIM20)



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

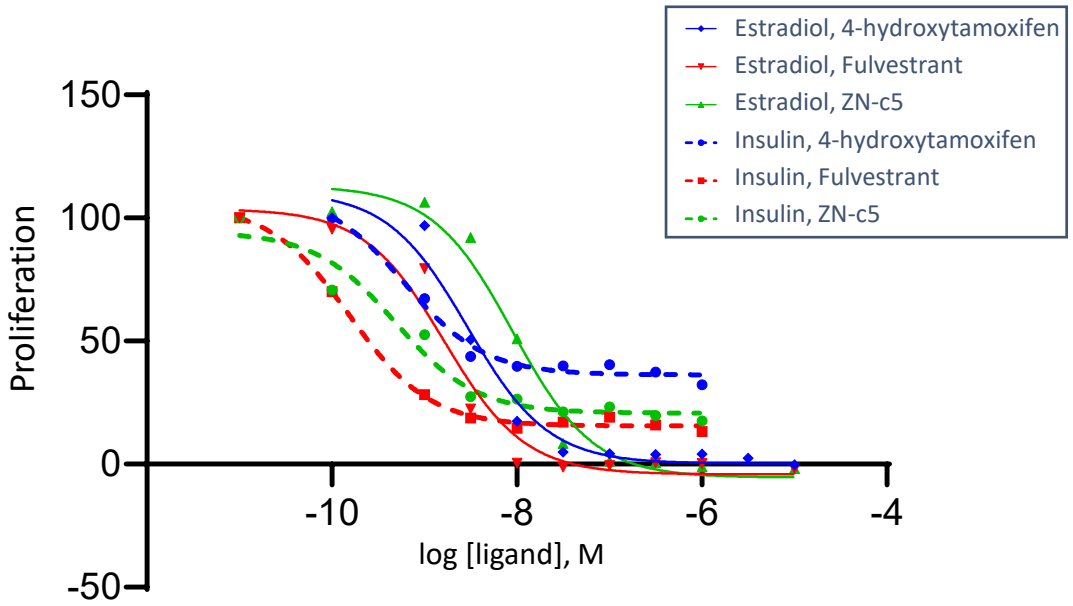
(1) Fulvestrant based on evaluation of comparable proxy chemical compounds purchased from commercial sources rather than the pharmaceutical companies commercializing the compound.
(2) Data based on evaluation of comparable proxy chemical compounds purchased from commercial sources rather than the pharmaceutical companies commercializing the compound.

ZN-c5: An ER Antagonist with No Agonist Activity

- Two Activation Function domains (AF-1 and AF-2) are involved in ER transcriptional activity
- ZN-c5 is an **estrogen receptor antagonist**, blocking both AF-1 and AF-2 activity

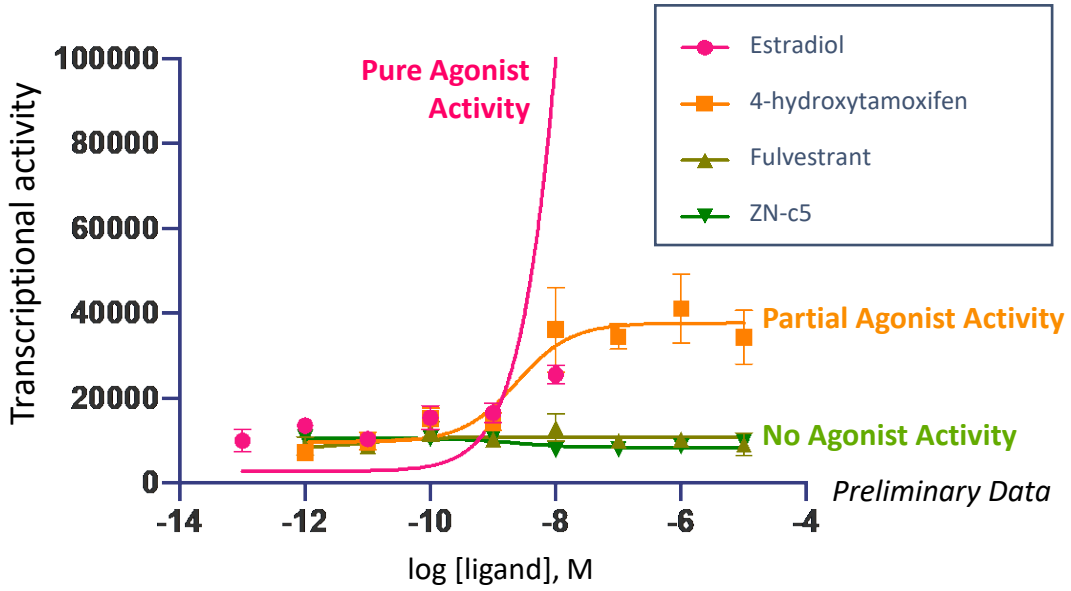
ZN-c5 Inhibits AF-1- and AF-2-Mediated Proliferation

MCF-7 cells treated with Insulin (AF-1 activation) or Estradiol (AF-2 activation) (1)



ZN-c5 has No ER Agonist Activity

Transcriptional activity of ERa AF1 construct (Nonfunctional AF-2) (1)



(1) Suzanne Wardell, John Norris, Duke School of Medicine

ZN-c5: Clinical Development Plan

Ongoing and Planned Clinical Programs

Phase 1/2	Phase 1b
Monotherapy Dose Escalation/Expansion Ph 1/2 Study *Initiated Ph 2*	**Combination** Lilly Dose Escalation Ph 1b Study (+ abemaciclib) *Initiated*
Combination Pfizer Ph 1/2 Study (2) (+ palbociclib) *Enrolling*	**Combination** Ph 1b Study (ZN-c5 + ZN-c3) in CDK4/6i resistant breast cancer *Initiation Expected in 2H 2022*

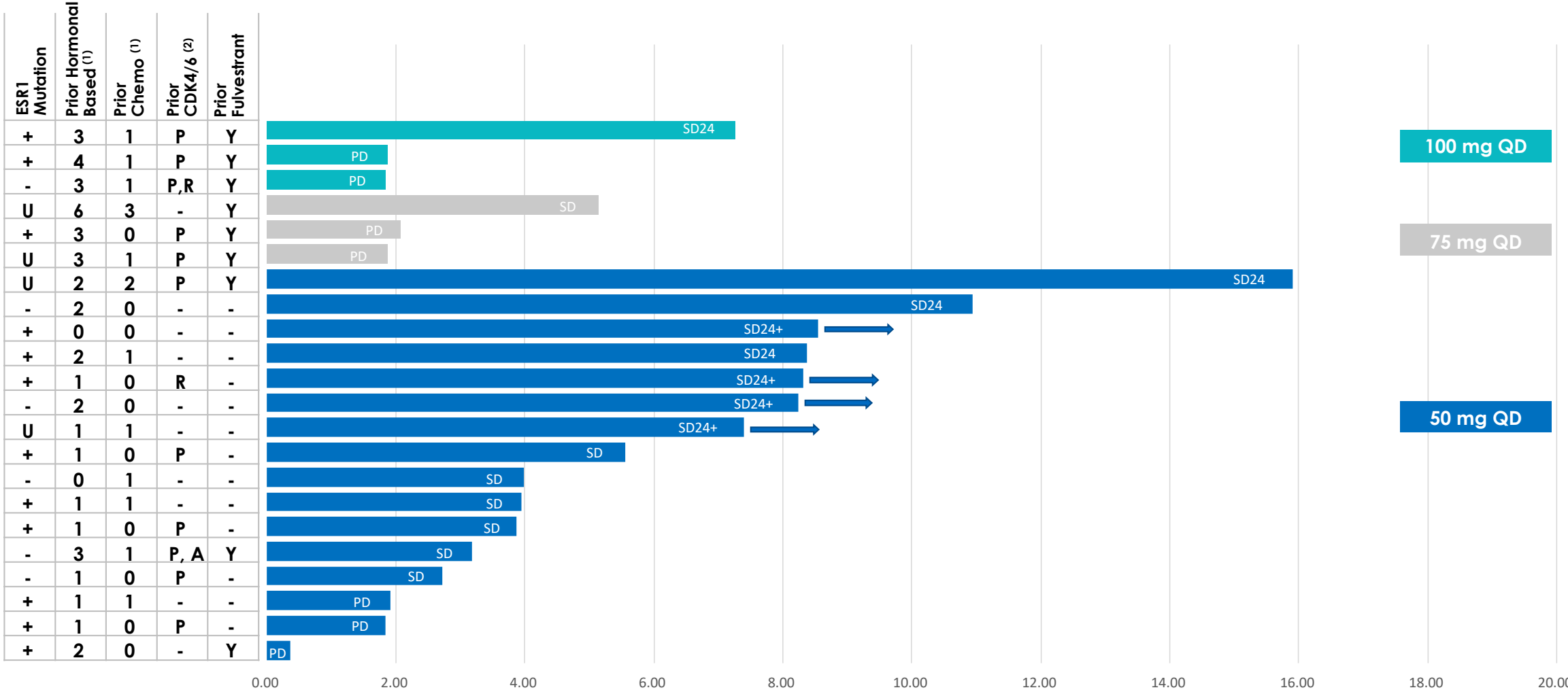
Overview

- **Updated interim Phase 1/2 monotherapy data (1,2)**
  - Patients at 50 mg: CBR 44% (PR + SD ≥ 24 weeks), PFS 3.9 months
  - Patients at 50 mg without prior CDK4/6i: CBR 56%, PFS 8.3 months
  - Phase 2 ongoing, with ZN-c5 dosed at 50 mg QD and possibly at 25 mg QD
  - No dose-limiting toxicities at any dose level
- **Window of Opportunity study has completed enrollment (n=35)**
- **ZN-c5 can be administered with or without food**

(1) The cut off-date for this analysis was 15 September 2021.
(2) A total of 56 patients are included

Updated Interim Clinical Data: ZN-c5-001 Monotherapy 50-100 mg

Treatment Duration (months) and Response by Dose as of 15 September 2021



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

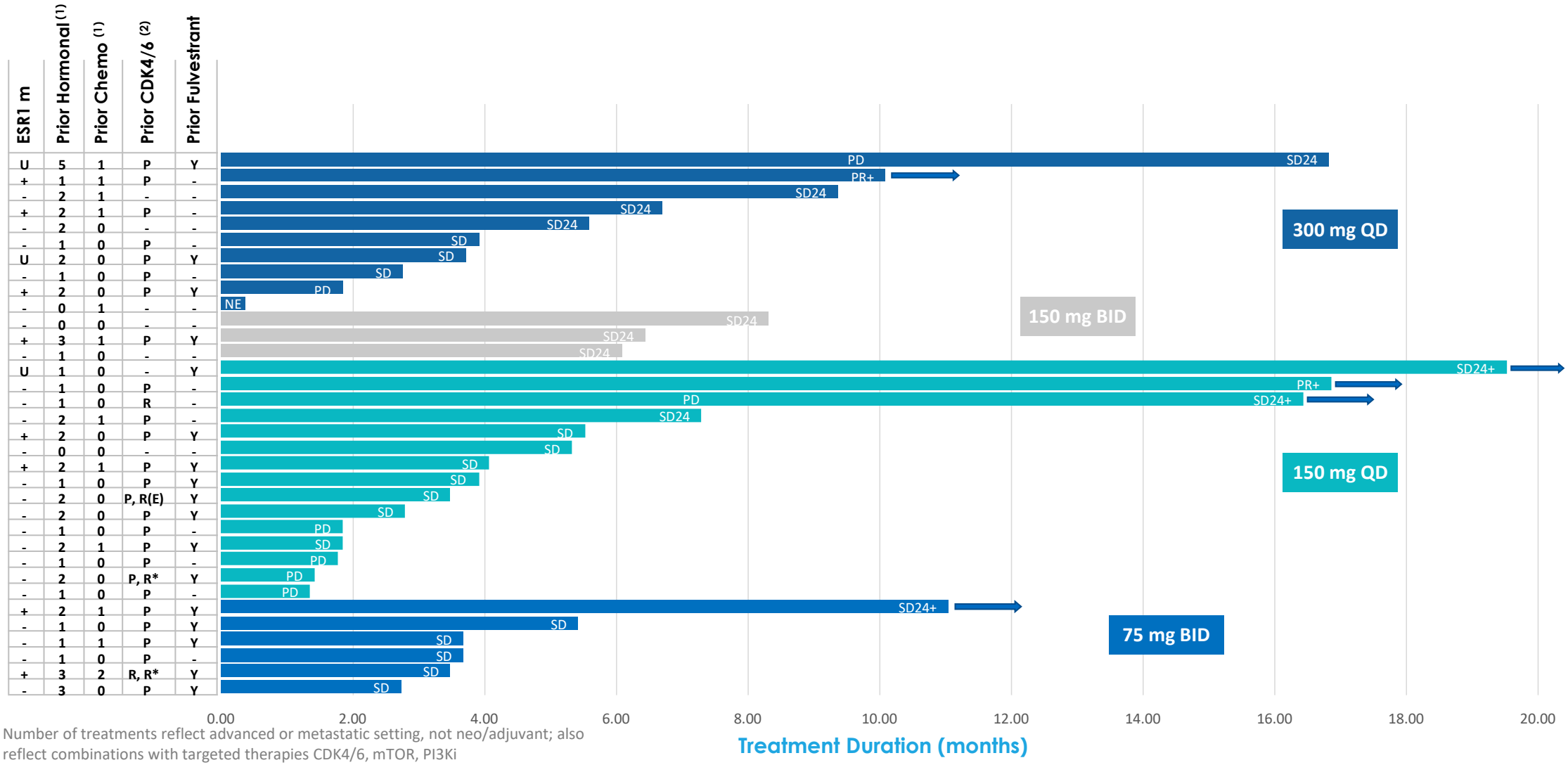
(2) P-palbociclib, A-abemaciclib, R-ribociclib, E-experimental treatment (could be placebo)

\+ ESR1 mutation detected

U Unknown

Updated Interim Clinical Data: ZN-c5-001 Monotherapy 150-300 mg

Treatment Duration (months) and Response by Dose as of 15 September 2021



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

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

\+ ESR1 mutation detected

U Unknown

ZN-c5-001 Monotherapy Efficacy Summary by Dose

Interim Monotherapy Efficacy Results

Data cut-off 15 September 2021

Dose (mg)	50		75	100	150	300	Overall
	No prior CDK	Prior CDK					
N (enrolled)	9	7	3	3	21	13	56
CBR	5/9 (56%)	2/7 (29%)	0/3 (0%)	1/3 (33%)	5/21 (24%)	8/13 (62%)	21/56 (38%)
ORR	0/7	0/7	0/2	0/3	1/14	1/8	2/41

ZN-c5-001: ZN-c5 is Differentiated from Competition on Safety

	AZD-9833 (AstraZeneca)	GDC-9545 (Roche)	Amcenestrant (Sanofi)	LSZ102 (Novartis)	G1T48 (G1 Therap.)	OP-1250[4] (Olema)	ARV-471 (Arvinas)	ZN-c5 [1] (Zentalis)
Dose	75 mg QD *(Initial Reported Data)*	30 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)*	60 mg QD *(60, 90 and 120 mg as potential RP2D)*	360 mg QD *(Initial Reported Data)*	50 mg QD *(Likely R2PD)*
AUC (ng*hr/mL)	683	5,070	~36,600 [2]	25,600	2,690	5,046	~34,000	63,700
Treatment-Related AEs: % Patients Treated with Drug (All Doses Tested)								
Diarrhea	0-10% [3]	17%	8%	62%	27%	N/A[5]	0-10% [3]	3.6%
Nausea	18%	21%	8%	56%	15%	51%	24%	10%
Bradycardia	45%	10%	N/A	N/A	N/A	11%[6]	0-10% [3]	0%
Visual Disturbances	53%	0-10% [3]	N/A	N/A	N/A	14%[6]	0-10% [3]	0%
Other Notable Adverse Events: All Doses Tested								
Other Notable Adverse Events	QTcF DLT; Dizziness	Hot Flush; Dizziness Reported; Fatigue; Arthralgia; QTc Reported	Hot Flush	N/A	Hot Flush; Fatigue	Neutropenia, Fatigue, Vomiting, Headache	Vomiting, Arthralgia, Fatigue, Decreased Appetite	Hot Flush (14%), Fatigue (13%)

Sources: AZD9833 ASCO 2020 Poster; GDC-9545 SABCS 2019 Poster; LSZ102 Poster SABCS 2017; amcenestrant ASCO 2020 Poster; G1T48 ESMO 2019 Poster; OP-1250 SABCS 2021 poster; ARV-471 2020 Presentation

(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 AZD9833, GDC-9545, amcenestrant, LSZ102, G1T48 and ARV-471 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 AZD9833, GDC-9545, amcenestrant, LSZ102, G1T48 and ARV-471 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 AZD9833, GDC-9545, amcenestrant, LSZ102, G1T48 and ARV-471 clinical trials may not be statistically or clinically meaningful. For these reasons, you should not place undue weight on the table.

(2) Visual estimation based on graph

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

(4) OP-1250 is an oral CERAN/SERD. (5) Only TRAEs >15% listed. (6) Listed under TEAEs.

ZN-c5: Well-Tolerated as a Monotherapy

Treatment-Related AEs in ≥ 10% of Subject per Cohort and Total; Total Treatment-Emergent AEs

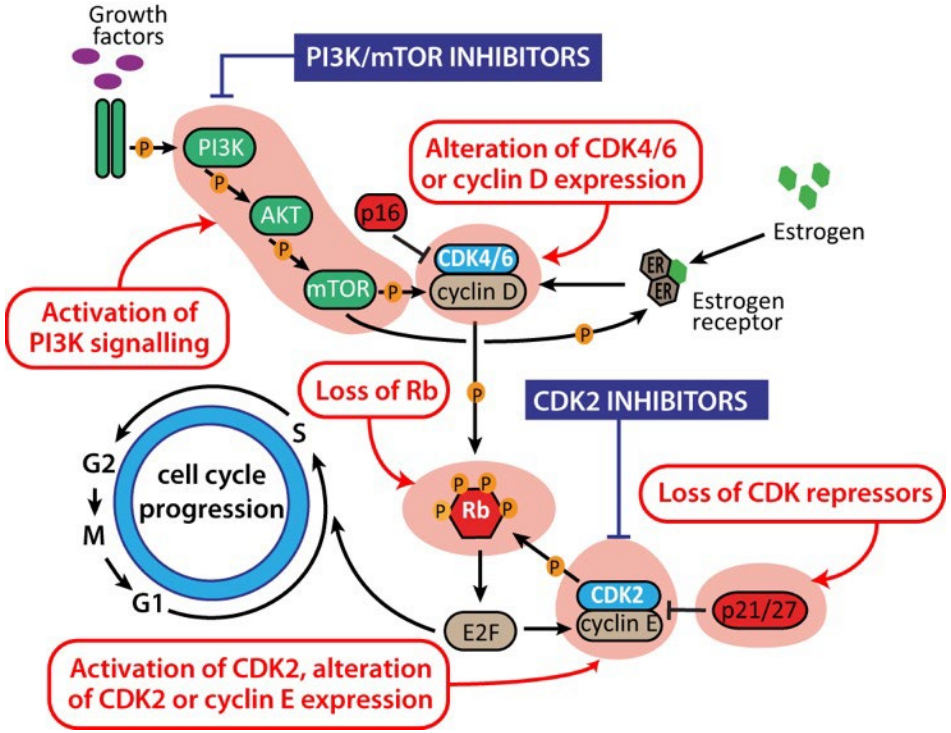
Data cut-off 15 September 2021

Preferred Term	50 mg QD (N = 16)		75 mg QD (N = 3)		100 mg QD (N = 3)		75 mg BID (N = 6)		150 mg QD (N = 15)		150 mg BID (N = 3)			300 mg QD (N = 10)			Total TRAEs (N = 56)				Total TEAEs (N = 56)			
NCI CTCAE Grade	1	2	1	2	1	2	1	2	1	2	1	2	3	1	2	3	1	2	3	All	1	2	3	All
Any AE, n (%)	6	2	1	0	0	0	2	2	5	4	1	1	1	4	3	1	19 (34%)	12 (21%)	2 (4%)	33 (59%)	13 (23%)	27 (48%)	14 (25%)	54 (96%)
Hot flush, n (%)	0	0	0	0	0	0	2	0	3	0	0	0	0	1	2	0	6 (11%)	2 (4%)	0	8 (14%)	6 (11%)	2 (4%)	0	8 (14%)
Nausea, n (%)	1	0	0	0	0	0	1	0	1	1	0	1	0	1	2	0	4 (7%)	4 (7%)	0	8 (14%)	12 (21%)	5 (9%)	0	17 (30%)
Fatigue, n (%)	1	0	0	0	0	0	1	0	2	0	1	0	0	1	1	0	6 (11%)	1 (2%)	0	7 (13%)	12 (21%)	3 (5%)	0	15 (27%)

Diarrhea events: 2 out of 56 subjects (3.6%), only grade 1 or 2 events observed
Grade 3 events: n=1 hypersensitivity (300 mg qd); n=1 γGT increase (150 mg bid)

No observed bradycardia, no visual disturbances, no QTC, no dizziness

Unmet Need for CDK4/6i-Resistant Patients

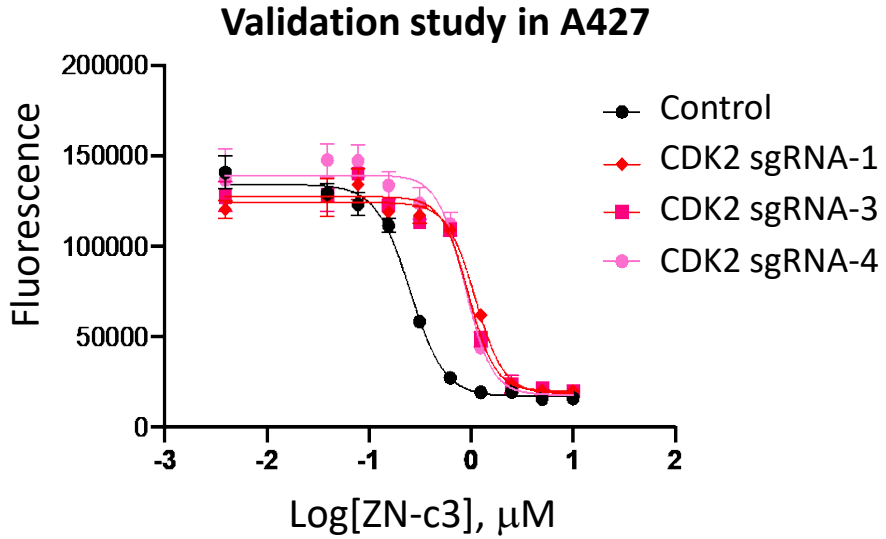


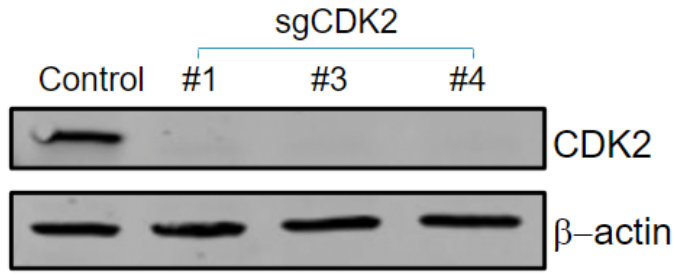
CDK4/6i resistance mechanisms[1,2]

- CCNE1 amplification / CDK2 activation
- Loss of Rb1
- CDK7 overexpression
- MDM2 overexpression
- Wee1 overexpression

Increased dependence on G2/M checkpoint

Internal CRISPR screen shows CDK2 is associated with increased sensitivity to ZN-c3

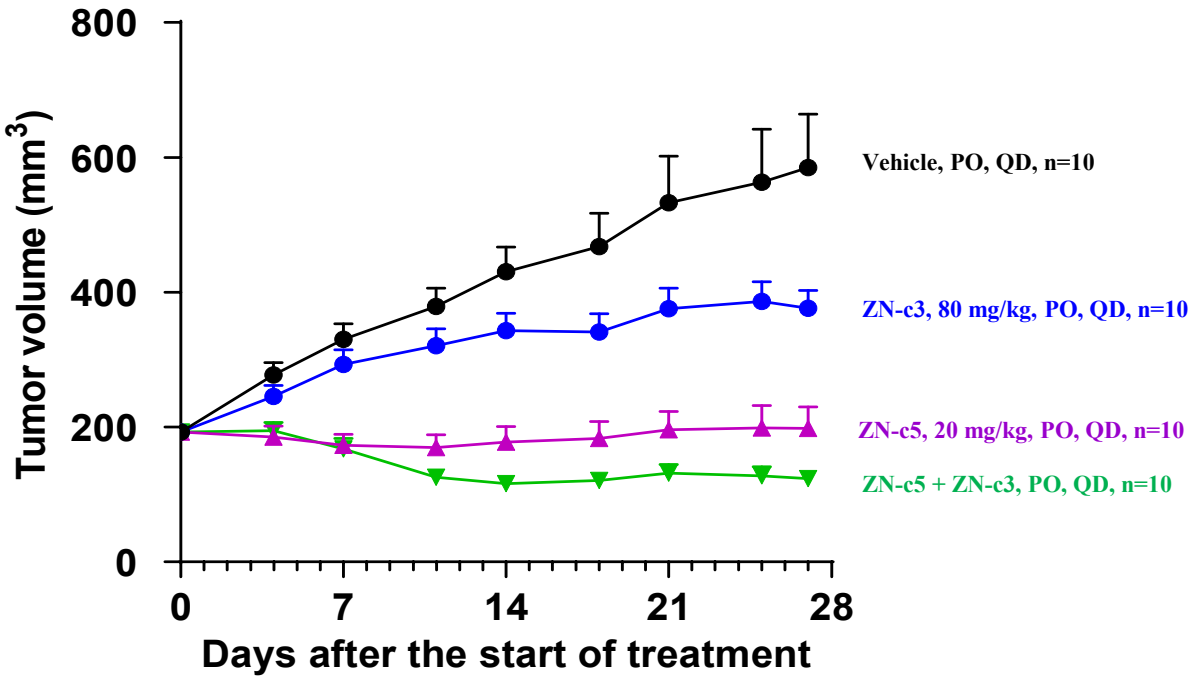




(1) Portman N. et al., Endocrine-Related Cancer (2019) 26, R15–R30
(2) McCartney A. et al. Front Oncol. (2019) Jul 23;9:666

Combining ZN-c5 with ZN-c3 in ER+/HER2- Breast Cancers R/R to CDK4/6i

T47D xenograft model



* Currently assessing ZN-c3 + ZN-c5 in palbociclib-resistant ER+/HER2- Breast PDX models

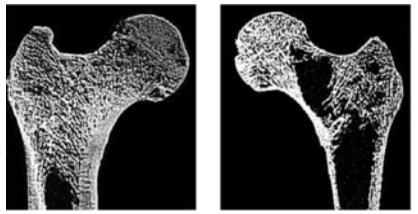
- ER+/HER2- is the largest breast cancer subtype with a prevalence >1,500,000(1)
- In the PALOMA-2 trial (palbociclib + letrozole), 30% of patients developed CDK4/6 inhibitor resistance within 2 years(2), leaving limited treatment options for such a large patient population
- Addressable patient population ~450,000

Study Initiation 2022

(1) Informa Pharma Intelligence. ER+/HER2- BC December 2020; All stages. North America, Western Europe, and Japan.
(2) Li et al. Front Pharmacol (2020)

ZN-c5 Safety Profile and Bone Protective Activity Supports Use in Adjuvant Settings

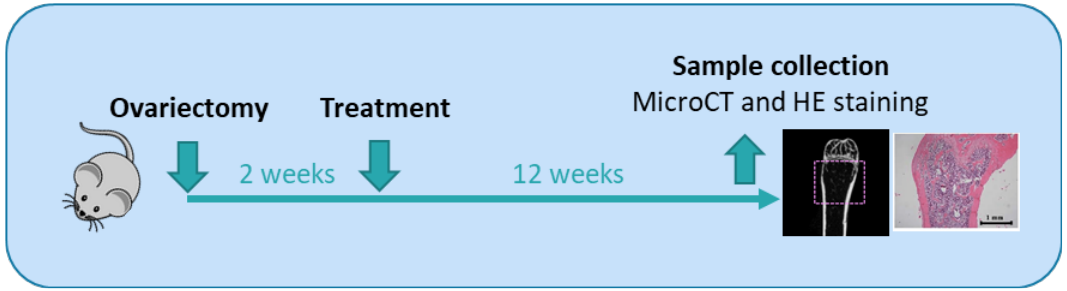
- Loss of estrogen associated with osteoporosis in post-menopausal women



ResearchGate / Thesis / Ehsan Basafa (2013)

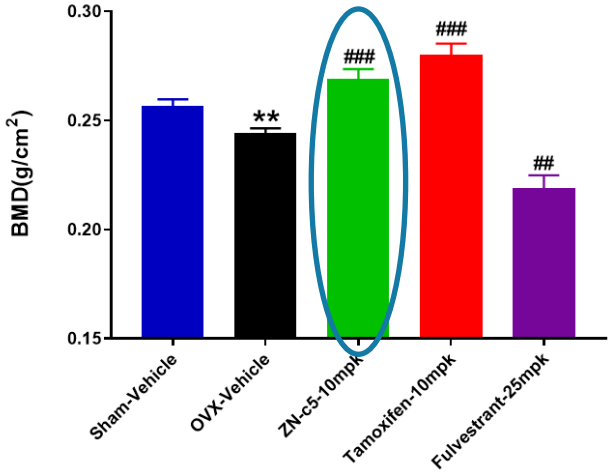
- Advanced breast cancer patients suffer from osteolytic bone metastasis
- Treatment with Fulvestrant is associated with osteolysis
- ZN-c5 opportunity:
  - **ZN-c5 combines anti-tumor effect with bone-protective effect**

Assessment of ZN-c5 on bone density in ovariectomized mice



Bone Mineral Density

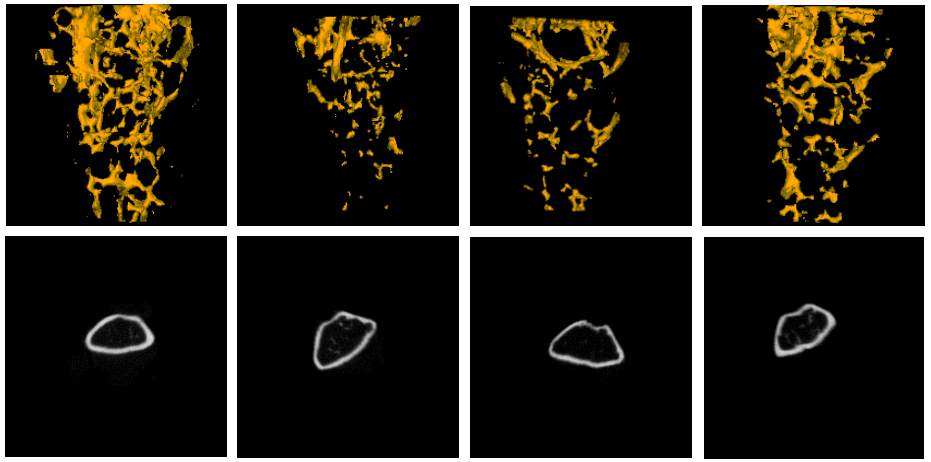
9 weeks; Femur



***p < 0.05, **p < 0.01, ***p < 0.001,* analyzed by unpaired t-test. All data are presented as mean ± SEM.
** Compared with sham-vehicle group; # Compared with OVX-vehicle group*

Micro-CT of Trabecular Bone

12 weeks; Femur

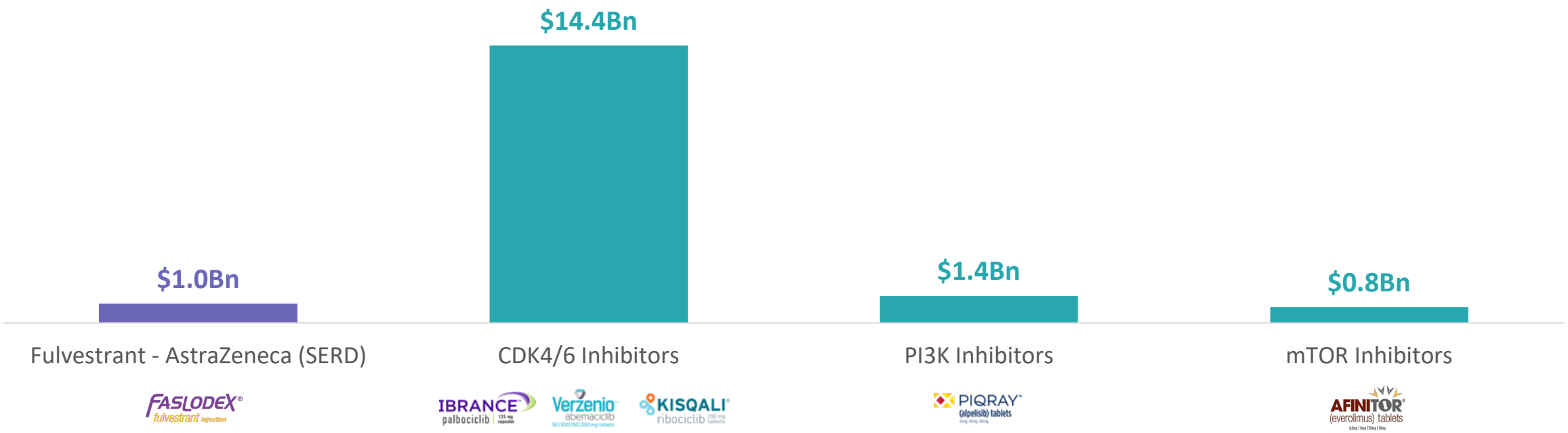


Sham Vehicle | OVX Vehicle | OVX Fulvestrant | OVX ZN-c5 10mpk

Note: Fulvestrant was dosed sc QW, ZN-c5 was dosed po QD

Vast Market Opportunity for Oral SERDs

~$1Bn+ Markets in Various Classes Treating ER+ Breast Cancer(1)



Faslodex Sales of ~$1.0Bn Reflect Only Part of Significant Market Potential for an Oral SERD and does not include the much larger adjuvant opportunity

(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

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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

- Designed to optimize:
  - Potency
  - Selectivity
  - PK properties

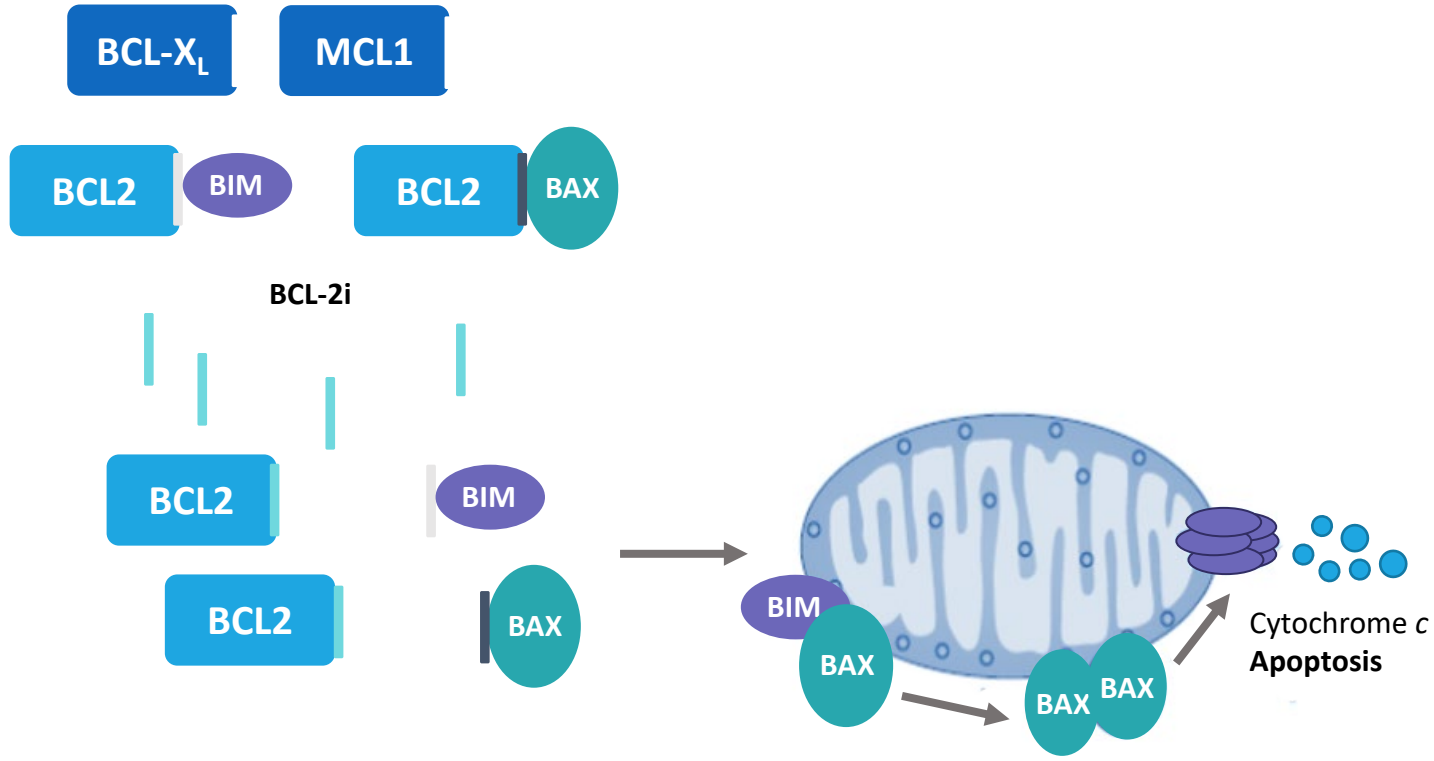
4 GENERATE: Preclinical Evidence

- Improved *in vitro* potency and has 10x improved selectivity for BCL-2 vs BCL-xL compared to venetoclax
- 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
- Strong anti-tumor activity consistent with venetoclax in leukemia model

BCL-2: A Clinically Validated Oncology Target

- BCL-2 is an anti-apoptotic protein involved in tumor survival and chemo resistance (1)
- The intrinsic apoptotic pathway is controlled by the BCL-2 protein family on the mitochondrial outer membrane (2, 3)
- BCL-2 inhibitors may restore the normal apoptosis process, making it an important target for cancer treatments

Mechanism of action of BCL-2 inhibitors (1)



(1) Konopleva M et al. Cancer Discov. 2016 Oct;6(10):1106-1117
(2) Konopleva M and Letai A. Blood. 2018 Sep 6;132(10):1007-1012
(3) Bhola PD and Letai A. Mol Cell. 2016;61(5):695-704

ZN-d5: A Potent BCL-2 Inhibitor with Improved Selectivity for BCL-2

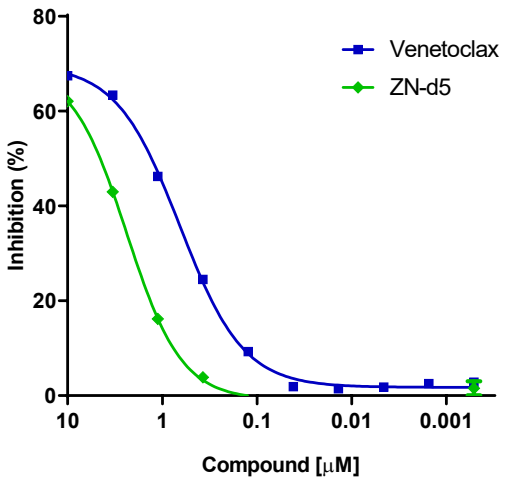
ZN-d5 has >14x Improved Selectivity for BCL-2 vs BCL-x_L and Binds With Higher Affinity to BCL-2 Mutants than Venetoclax

Compound ID	Affinity (Kd, nM)			IC_{50} (nM) BCL-2 Type			
	BCL-2	BCL-x_L	MCL-1	WT	G101V	F104L	D103Y
Venetoclax	0.41	28	>30000	1.3	7.3	8.4	18.3
ZN-d5	0.29	190	>30000	1.4	3.7	1.4	5.0

ZN-d5 Exhibits Potent *In Vitro* Activity Across Multiple Tumor Cell Lines

Compound ID	CTG IC_{50} (nM)							
	ALL	MCL		DLBCL		AML		
	RS4;11	Mino-1	Granta-519	DOHH-2	Toledo	HL-60	Molm-13	MV4-11
Venetoclax	2.9	1.1	161	43	191	26	18	3.8
ZN-d5	5.1	0.1	89	50	92	21	39	5.1

ZN-d5: Less Human Platelet Toxicity Compared to Venetoclax in an *In Vitro* Assay



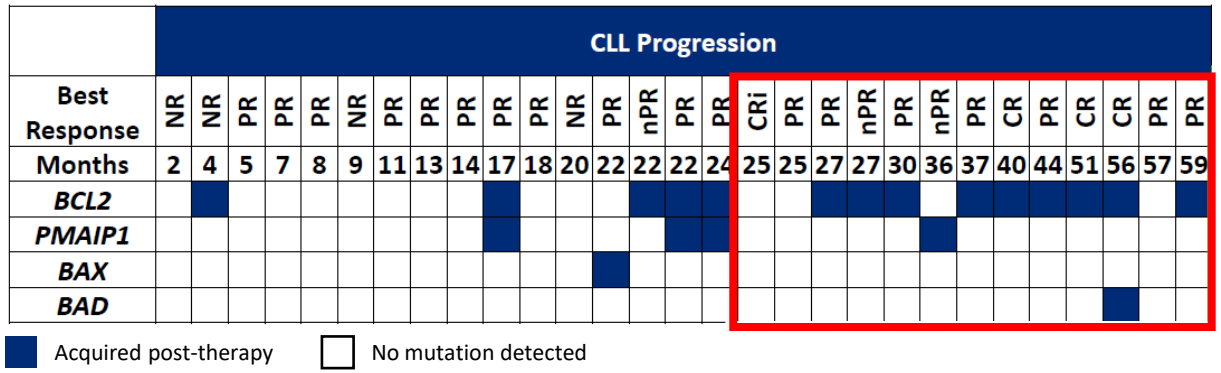
Compound ID	CTG (24 h) IC_{50} (μM)
Venetoclax	0.6
ZN-d5	2.4

ZN-d5 shows activity in preclinical models of ALL, NHL and AML

ZN-d5: May Bind with Higher Affinity to BCL-2 Mutants than Venetoclax

Mutations in BCL-2 May be Driving Sub-Clonal Pockets of Resistance to Venetoclax in CLL

CLL Progression on Venetoclax



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

- % (16/29) of patients with CLL progression

Compound	IC_{50} (nM) BCL-2 Type			
	WT	G101V	F104L	D103Y
Venetoclax	1.3	7.3	8.4	18.3
ZN-d5	1.4	3.7	1.4	5.0

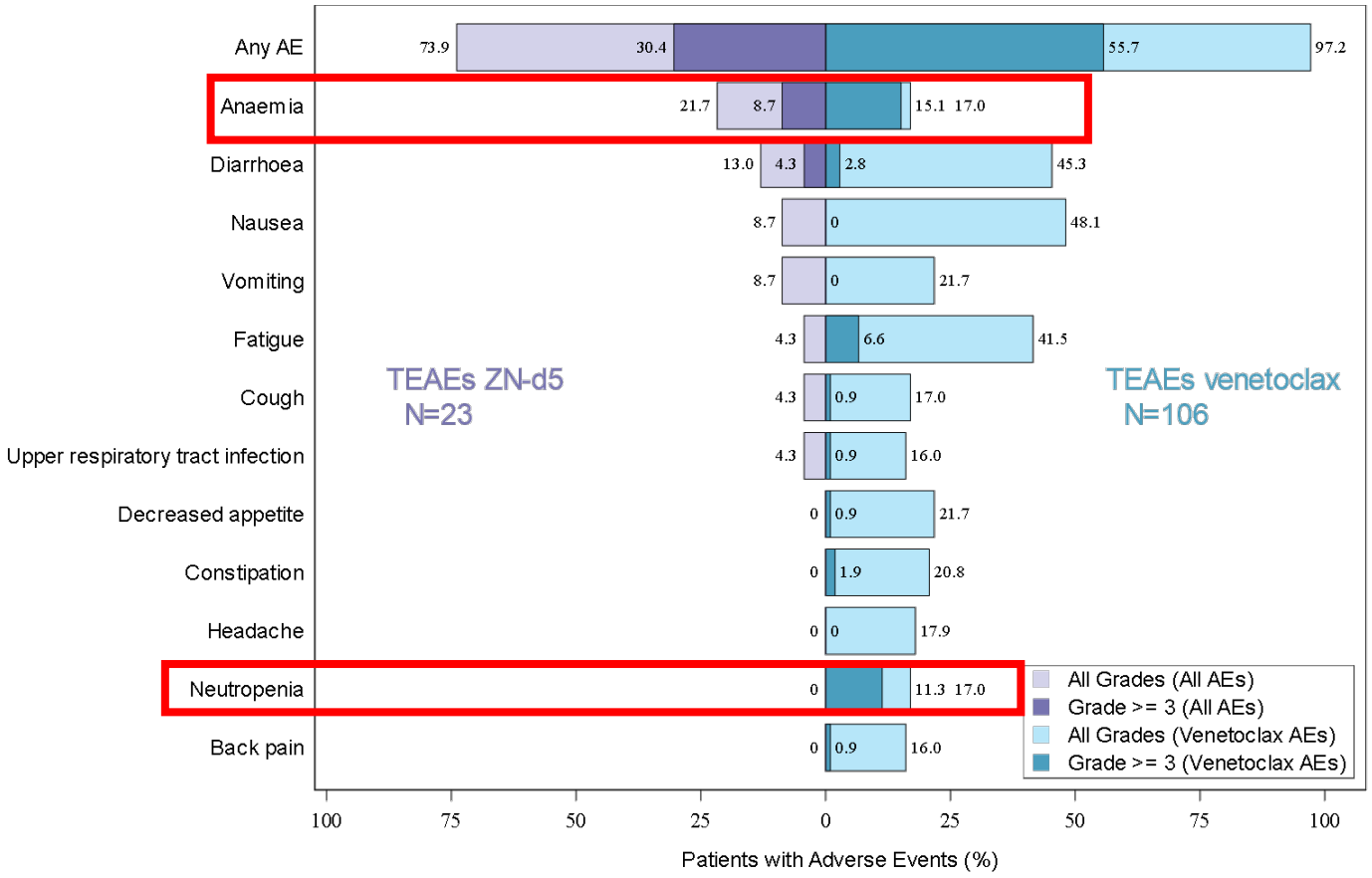
Note: Competition assay for displacing BAK peptide bound to BCL-2

Source: Chyla, B. ASH Presentation (2019)

ZN-d5: Favorable Early Comparison to Venetoclax in NHL

- ZN-d5 100-1200 mg, empty stomach
- Venetoclax 200-1200 mg with food
- Early toxicity profile in NHL favorable vs. published venetoclax data(1)
  - Fewer AEs of any Grade, Grade ≥3
  - No TLS observed
  - Venetoclax AEs not dose-dependent

Adverse Event	Any Grade			
	All Doses (N = 106)	≤ 400 mg (n = 22)	600 to 900 mg (n = 33)	1,200 mg (n = 51)
Emergent*				
Any event	103 (97)	21 (96)	33 (100)	49 (96)
Nausea	51 (48)	9 (41)	15 (45)	27 (53)
Diarrhea	48 (45)	7 (32)	14 (42)	27 (53)
Fatigue	44 (42)	10 (45)	9 (27)	25 (49)
Decreased appetite	23 (22)	4 (18)	4 (12)	15 (29)
Vomiting	23 (22)	5 (23)	6 (18)	12 (24)
Constipation	22 (21)	6 (27)	7 (21)	9 (18)
Headache	19 (18)	2 (9)	7 (21)	10 (20)
Anemia	18 (17)	7 (32)	6 (18)	5 (10)
Cough	18 (17)	7 (32)	6 (18)	5 (10)
Neutropenia	18 (17)	4 (18)	8 (24)	6 (12)
Back pain	17 (16)	3 (14)	6 (18)	8 (16)
Upper RTI	17 (16)	5 (23)	8 (24)	4 (8)



(1) Davids et al, J Clin Oncol 2017;35:826-833; emergent AEs reported in ≥15% of subjects. ZN-d5 results as of 03 Nov 2021 data cutoff.

ZN-d5: Preliminary Cross-Trial Data Comparison to Venetoclax

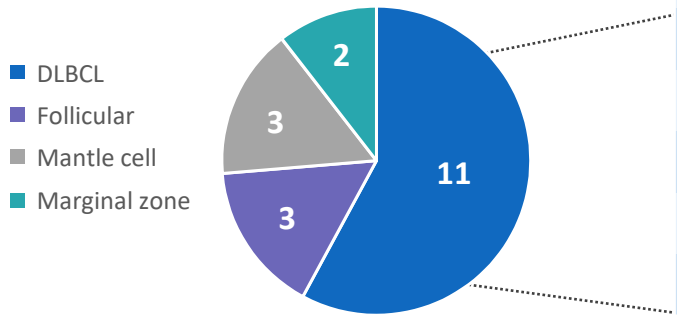
Pharmacology Data Comparison

	ZN-d5	Venetoclax
Dosing state	empty stomach	with food
Mean AUC (µg·hr/mL) @ 400 mg	8.7	32.8 [2]
Unbound drug fraction (%)[1]	0.12	0.06

- Higher AUCs expected for ZN-d5 when dosing commences with food in 2022

Clinical Data Comparison

ZN-d5 All Evaluable Subjects [3]



		ZN-d5	Venetoclax
DLBCL	n	11	34
	ORR	2 (18%)	6 (18%)
	CR	1 (9%)	4 (12%)
	cPR	1 (9%)	2 (6%)
	SD	2 (18%)	8 (24%)
	PD	7 (64%)	19 (56%)

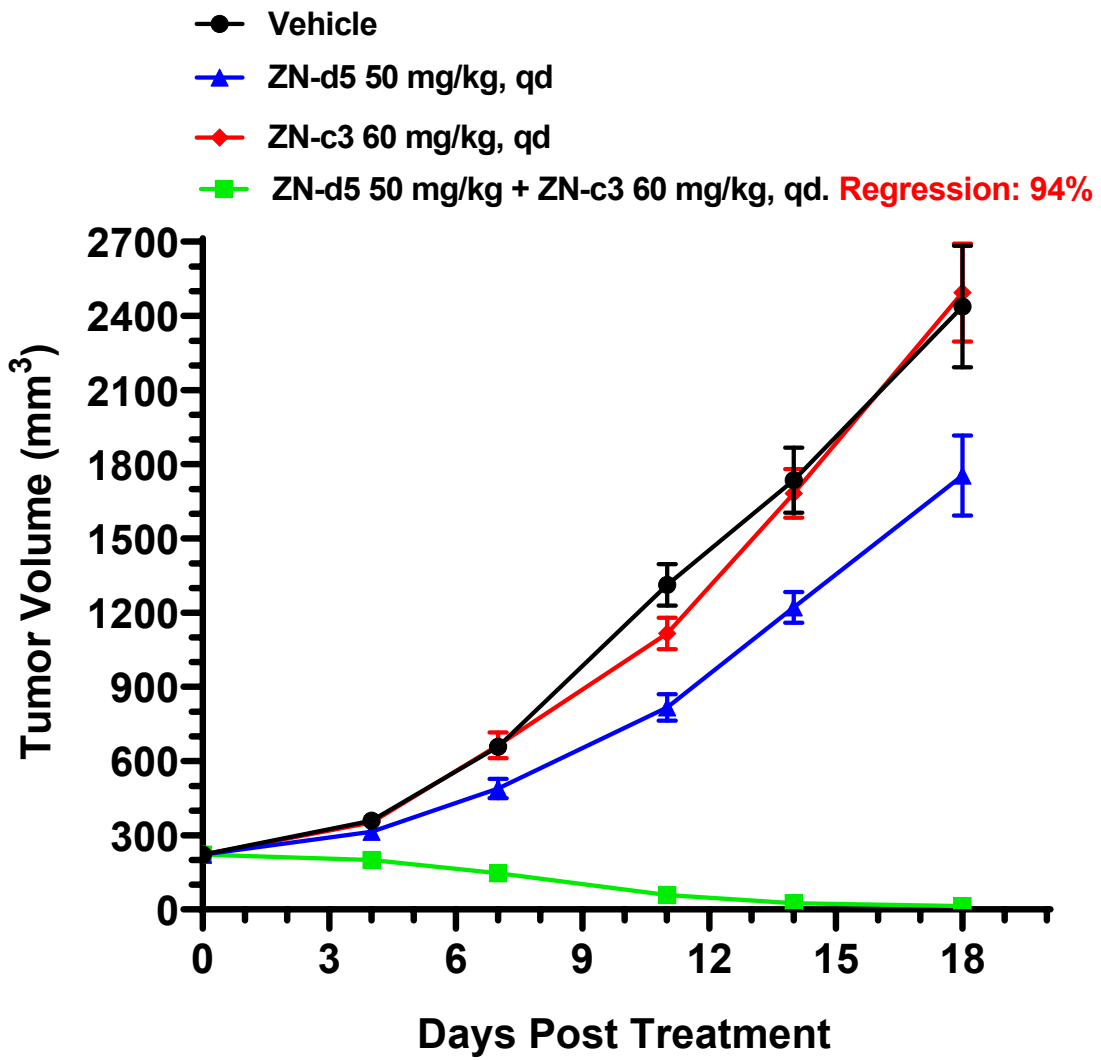
Caveat: Small number of evaluable NHL subjects for cross-study comparison

- Clinical activity (18% ORR, 36% DCR) in DLBCL is promising at this early stage and on par with venetoclax activity
- An additional unconfirmed PR in follicular lymphoma at 800 mg ZN-d5 (w/o food) observed after Nov 3, 2021 data cut

(1) Human plasma protein binding comparison was run multiple times in 10% plasma and calculated to 100% plasma.
(2) Salem et al. J Clin Pharmacol 2017;57:484-492
(3) N=19 response-evaluable NHL subjects dosed with ZN-d5

The Combination of BCL-2 and Wee1 Inhibitors Results in Synergism in Several Tumor Models Including AML

HL-60 AML model



- ZN-d5 and ZN-c3 combination represents a novel therapeutic approach
- Significant enhancement of activity than single agent in several indications, including AML
- Combination regimen was well-tolerated in mice
- **Zentalis is the only company known to have both inhibitors in clinical development**

ZN-d5: Clinical Development Plan

Ongoing and Planned Clinical Programs

Phase 1

Monotherapy
AML and Non-Hodgkin's Lymphoma Dose Escalation (1)
Initiated

Phase 1/2 (2)

★ **Monotherapy**
Amyloidosis
Initiated

Combination
AML
ZN-d5 + ZN-c3
Expected Initiation of Phase 1 Portion in 1H 2022

Overview (2)

- **Interim monotherapy dose-escalation study update**
  - 27 treated (23 NHL including 13 DLBCL)
  - Escalated doses through 1200 mg daily in the fasting state currently and will transition to the fed state in 2022
  - No unexpected safety findings

(1) As of November 3, 2021
(2) Trial designs will be based off data generated from Phase 1 trials

★ Potentially Registrational Study

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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

- Designed to achieve similar potency with:
  - Improved selectivity for mutant EGFR
  - No production of potent metabolite for wild-type EGFR
  - Better solubility
- **Actively evaluating potential combinations**

4 GENERATE: Preclinical Evidence

- Improved selectivity in comparison to osimertinib across single mutant, double mutant and wild-type cells
- Confirmed no potent metabolite for wild-type EGFR formed
- Favorable tolerability observed, similar weight loss to osimertinib at 5x efficacious dose

Source: Osimertinib data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound

ZN-e4: Improved Selectivity and Tolerability in Preclinical Models

ZN-e4 is More Selective than Osimertinib…

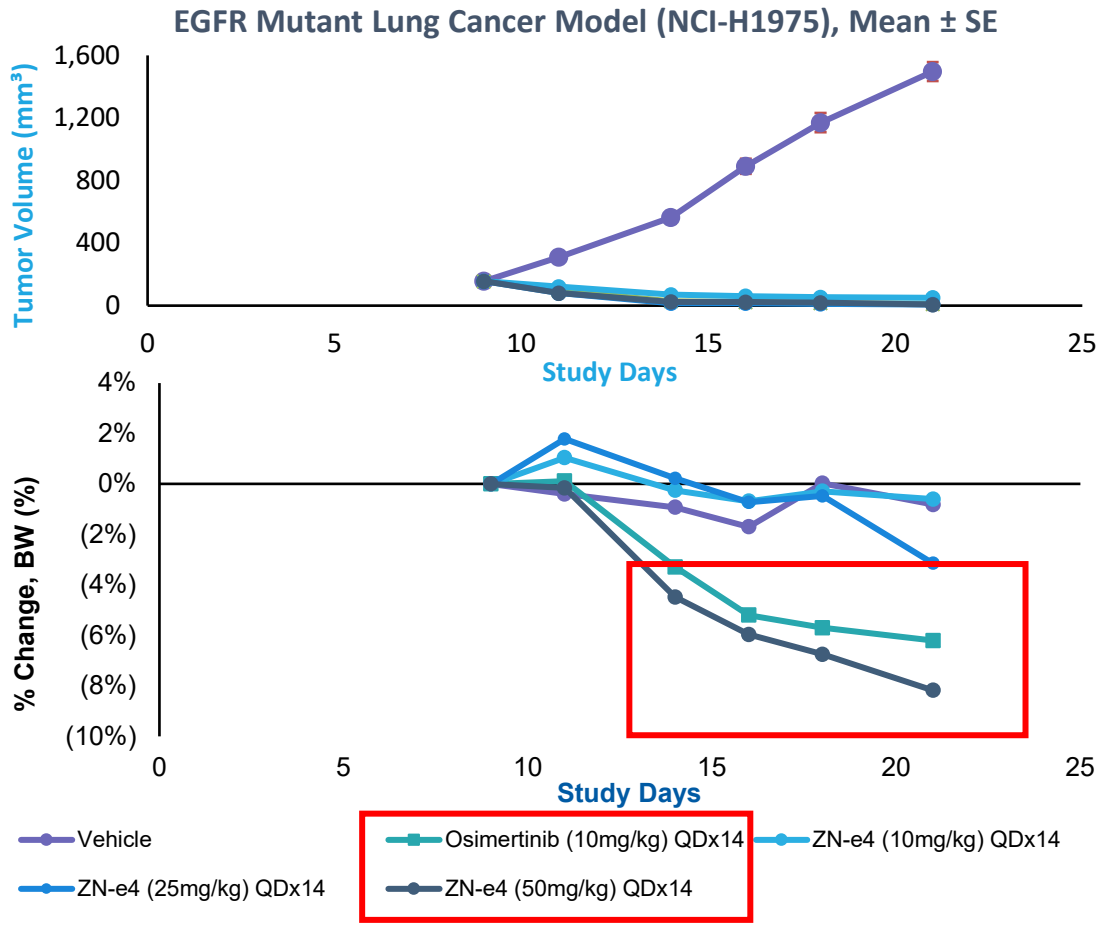
	Double Mutant Cell IC_{50} (nM)	Single Mutant Cell IC_{50} (nM)	Wild-Type Cell IC_{50} (nM)
Osimertinib: Core Drug	15	29	294
ZN-e4: Core Drug	**20**	**38**	**839**

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

	Double Mutant Cell IC_{50} (nM)	Single Mutant Cell IC_{50} (nM)	Wild-Type Cell IC_{50} (nM)
Osimertinib: AZ5104	2 (2)	2 (2)	33 (2)
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)

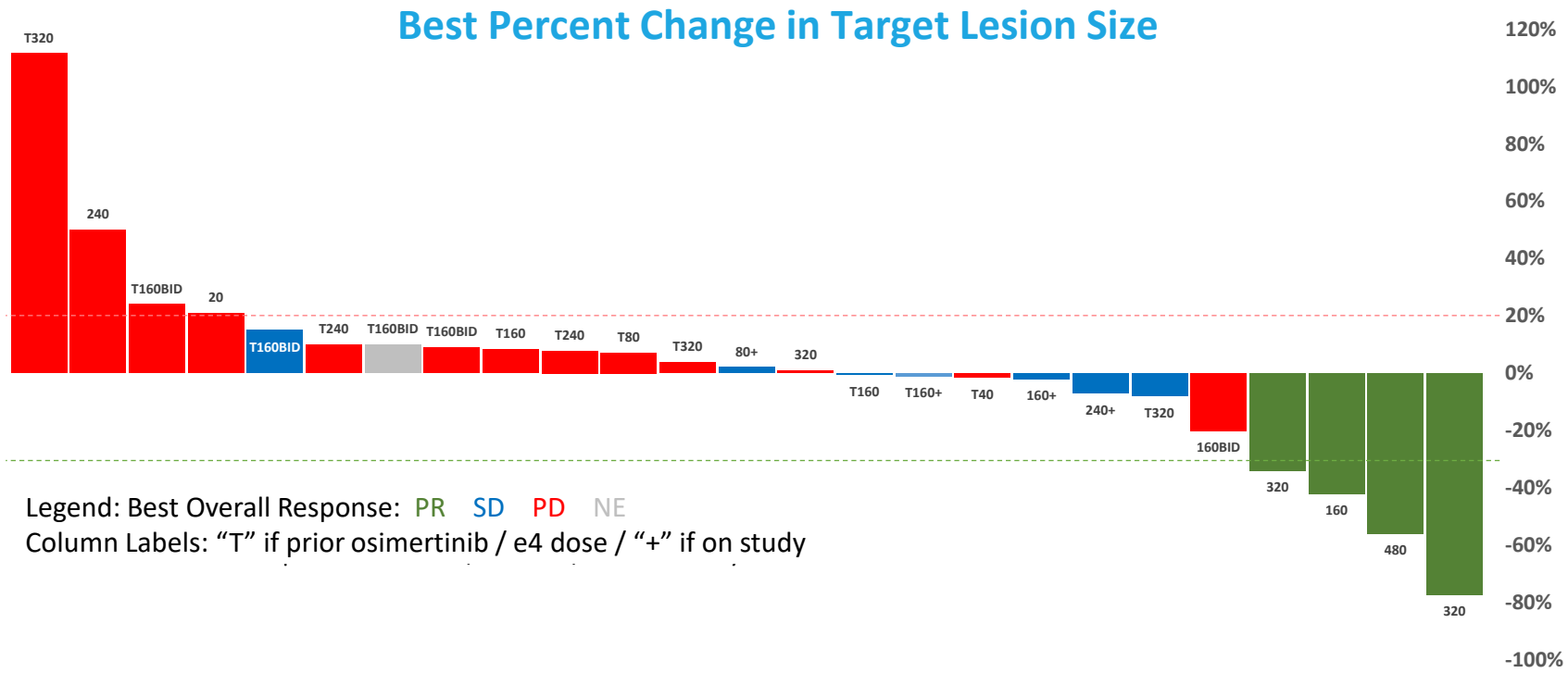
Favorable Tolerability Observed: ZN-e4 Similar Weight Loss to Osimertinib at 5x Efficacious Dose (1)



ZN-e4: Clinical Update

ZN-e4 shows clear efficacy and excellent safety in osimertinib-naïve NSCLC (1)

- Enrolled 32 subjects total
- Skin toxicity appears substantially better
- ORR 36% (4/11) in relapsed, osimertinib-naïve subjects
  - All failed prior EGFRi and 1-2 lines of chemo
  - Only one subject with T790M positive
- Phase 2 dose will be 240 mg



(1) As of November 1, 2021

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Conclusions

Key Milestones

ZN-c3: Wee1 Inhibitor

1H 2022	Initial readout on Phase 1 USC expansion cohort
1H 2022	Initial readout on Phase 1b ovarian chemotherapy combo
2H 2022	Initial enrollment/safety update on Phase 2 USC trial+
2H 2022	Initial readout on Phase 1/2 chemotherapy combo in osteosarcoma*

ZN-c5: Oral SERD

1H 2022	Phase 1b combination study topline results with Pfizer's palbociclib
1H 2022	Phase 1b combination study topline results with Lilly's abemaciclib
2H 2022	Initiate Phase 1b combination study of ZN-c5 + ZN-c3 in CDK4/6i resistant breast cancer

ZN-d5: BCL-2 Inhibitor

1Q 2022 ✓	Initiate Phase 1/2 monotherapy study in amyloidosis*
1H 2022	Initiate Phase 1/2 combination study of ZN-d5 + ZN-c3 in AML
2H 2022	Updated results from Phase 1 dose escalation study in AML and NHL

ZN-e4: EGFR Inhibitor

2H 2022	Report results on Phase 1 NSCLC trial

Integrated Discovery Engine

2022	Initiate IND enabling studies for an internal program

Zentera

2022	Maximize value from investment in and partnership with Zentera

+ Registrational trial with FDA Fast Track designation
* Potentially registrational trial

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