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CORPORATE PRESENTATION

August 2022

Forward-Looking Statements and Disclaimer

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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.

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Zentalis's product candidates are investigational drugs and have not yet been approved by the U.S. Food and Drug Administration or any other regulatory authority.

Company Overview

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

- Partial responses seen in four tumor types to date
- 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

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 including BCL-xL heterobifunctional degrader

Investigating internal & third-party combinations, including ZN-d5 + ZN-c3 for liquid tumors

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

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

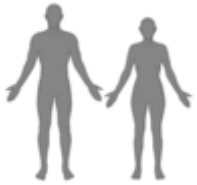
1 IDENTIFY

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

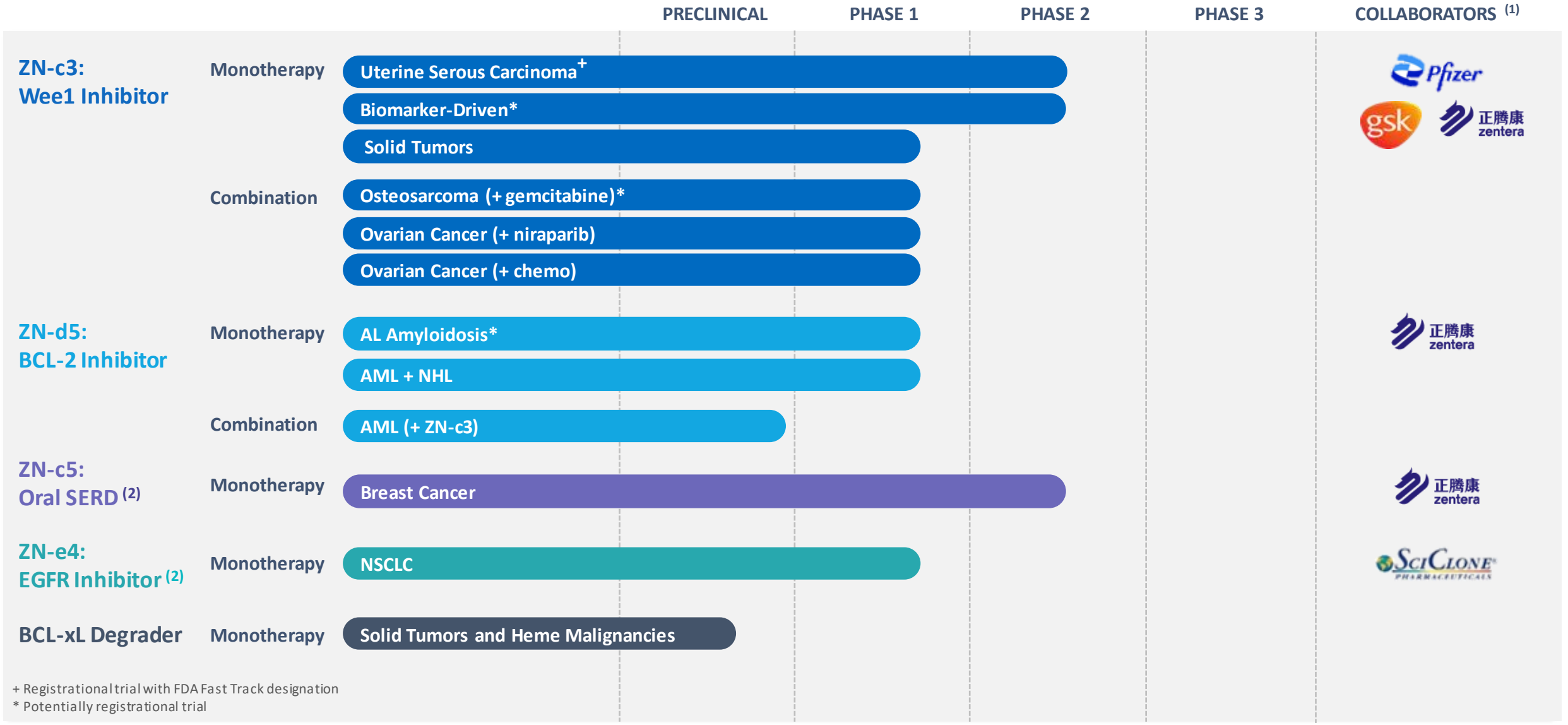
3

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 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 have begun enrollment.

(2) Zentalis will discontinue the clinical development of ZN-c5 and ZN-e4 following completion of its existing clinical trials, which are closed to accrual, in these two programs.

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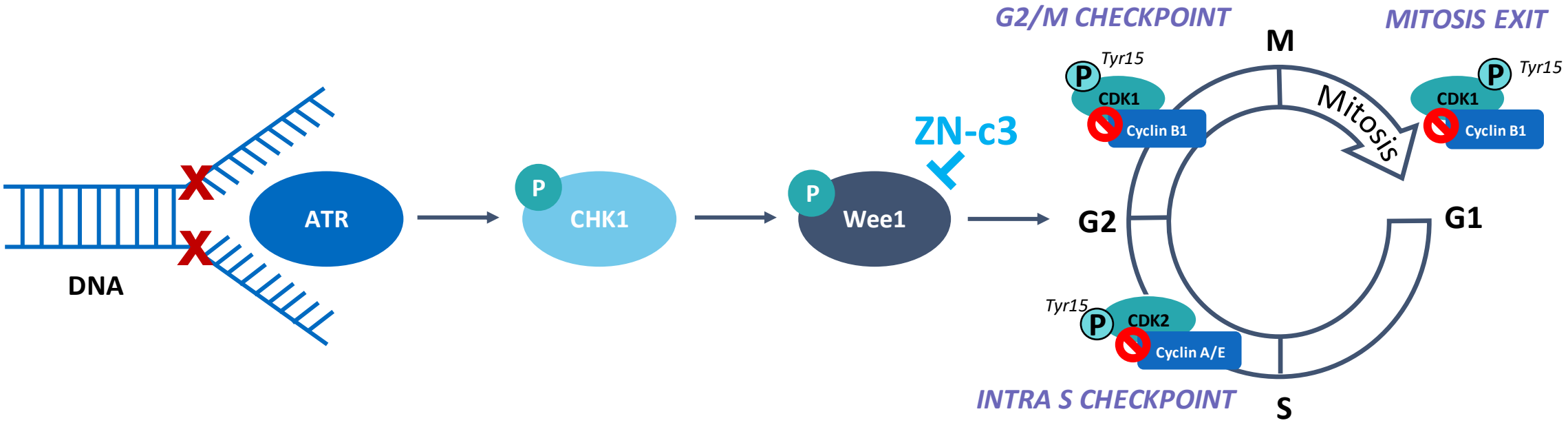
ZN-c3

Wee1 Inhibitor

Wee1 Inhibition: Clinically Proven DDR Target for Cancer

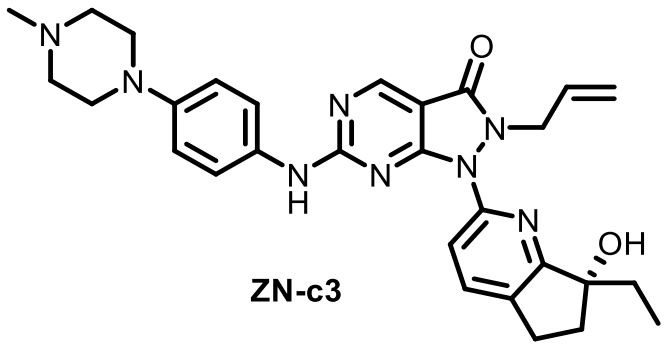


- Wee1 is a protein kinase expressed at high levels in many cancer types that prevents entry into mitosis in response to DNA damage by regulating the G2 checkpoint
- Wee1 inhibition causes cancer cells to proceed to mitosis without repairing DNA damage, resulting in premature mitotic entry and apoptosis
- 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

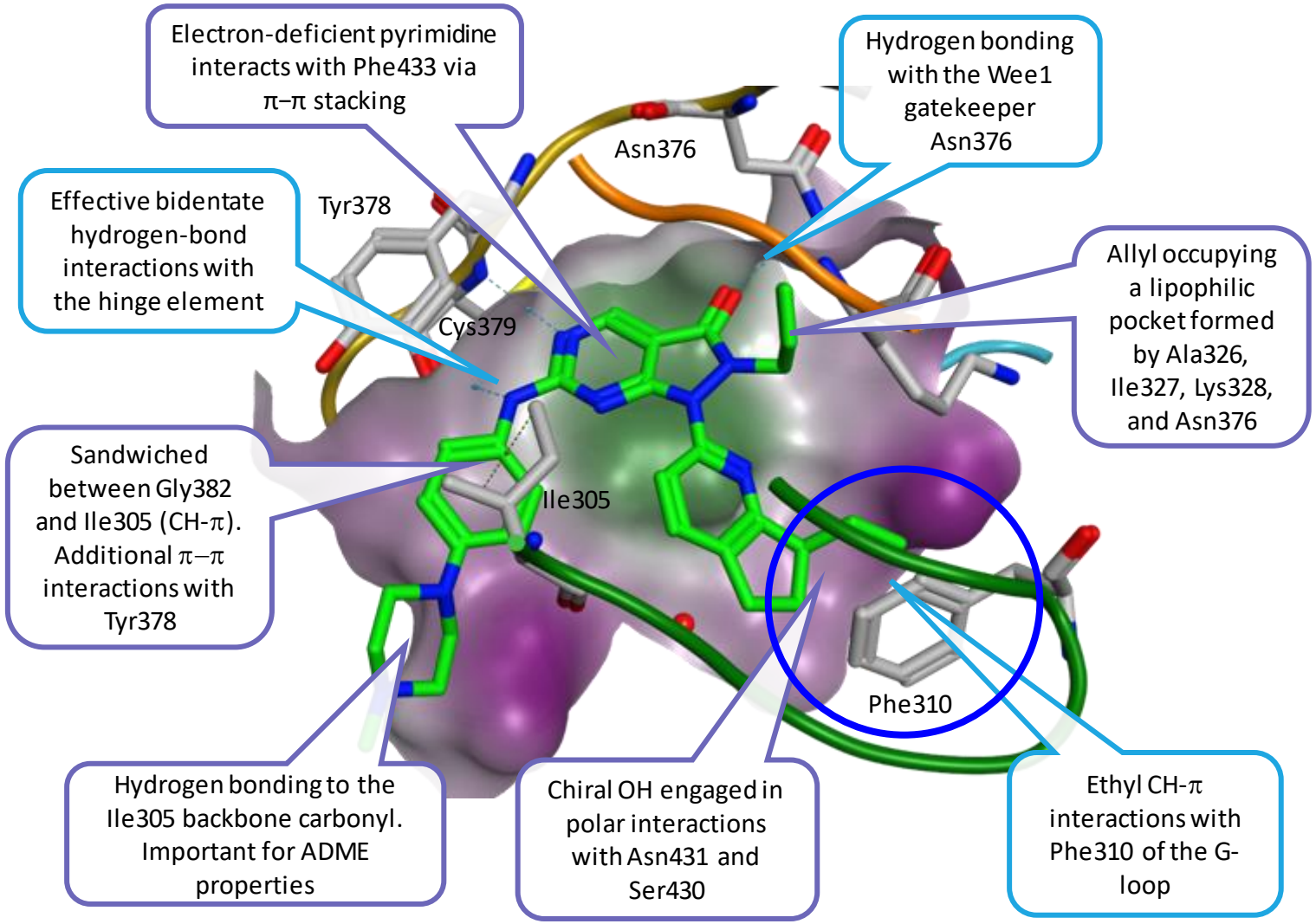
Source: Drawing based on Targeting WEE1 Kinase in Cancer. Matheson CJ, et al. Trends Pharmacol Sci. 2016

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

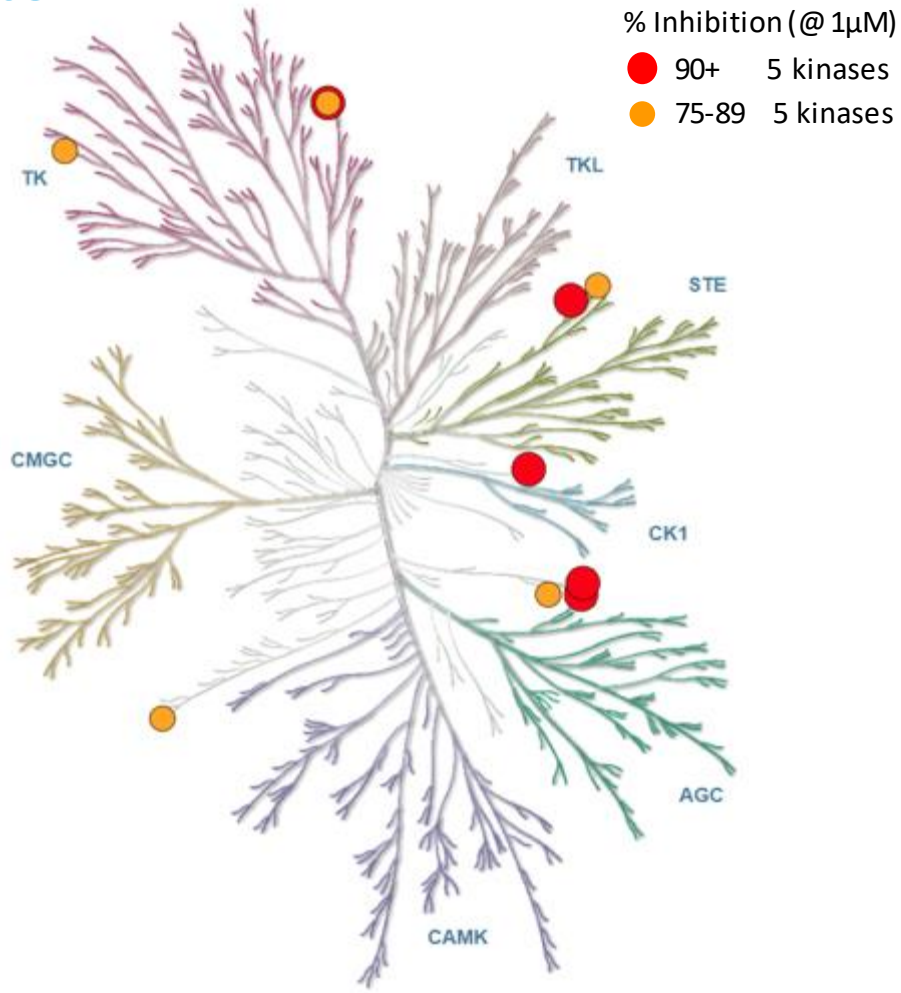
ZN-c3 potency and ADME	
Wee1 IC_{50}	3.8 nM
H23 IC_{50}	103 nM
A427 IC_{50}	75 nM
Log *D*	2.4
*h*PPB	66%
*h*Hep	<18 mL/min/kg
solubility	> 2000 µM
CYP3A4	7 µM
hERG	> 30 µM



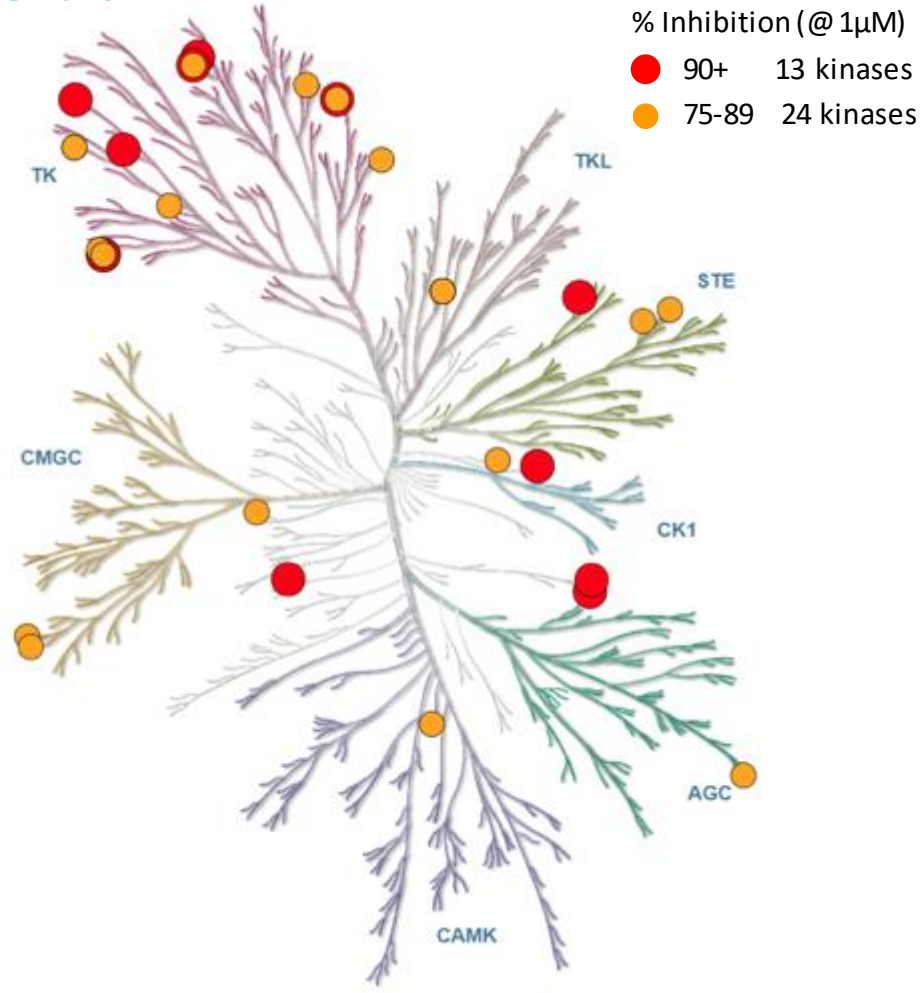
(1) Huang, PQ; *et al*. J. Med. Chem. **2021**, *64*, 13004-13024

ZN-c3: 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)

ZN-c3 Clinical Development Plan: Cornerstone of Multiple Treatments in Many Indications

- Potentially best-in-class/first-in-class profile; efficacy observed in hematologic and solid tumors
- Targeting superior selectivity and tolerability profile supports combination therapies across multiple indications
- Potentially registrational trials underway; planning for a Phase 3 trial in combination with chemo in ovarian cancer
- Significant market opportunity across a broad range of solid and liquid tumors

Ongoing and Planned Clinical Programs

Indication	Treatment	Status	Addressable Patient Population[1]	Trial Updates#
USC*	ZN-c3	Phase 2 enrolling	~12,000[2]	Initial enrollment/safety update – 2H 2022
Solid Tumors	ZN-c3	Phase 1 enrolling	N/A	Initial USC cohort data presented at AACR 2022
Ovarian	ZN-c3 & chemotherapy	Phase 1b enrolling	~14,000[3]	Initial readout presented at AACR 2022
Osteosarcoma+	ZN-c3 & gemcitabine	Phase 1/2 enrolling	~1,000[4] (U.S. incidence)	Initial readout – 2H 2022
Predictive Biomarker+	ZN-c3	Phase 2 initiated	~55,000[5]	-
Ovarian (gsk)	ZN-c3 & niraparib (PARPi)	Phase 1/2 initiated	~18,000[6]	-
AML	ZN-c3 & ZN-d5 (BCL-2i)	Phase 1/2 planned	~68,000[7] (U.S. prevalence)	Trial to initiate in 2022
Colorectal	ZN-c3	-	>2,000,000[8] (total); ~500,000 (TP53/KRAS mutant)[9]	-

*Registrational Study with Potential Accelerated Approval; +Potentially Registrational Study

(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) Cancer.org; SEER database (2018).
(8) Globocan 2020 https://gco.iarc.fr/today/data/factsheets/cancers/10_8_9 Colorectum fact sheet.pdf
(9) American Cancer Society Facts & Figures 2020; Based on flowchart of patients from Seligmann JF et al. J Clin Oncol. 2021. US population.
Expected

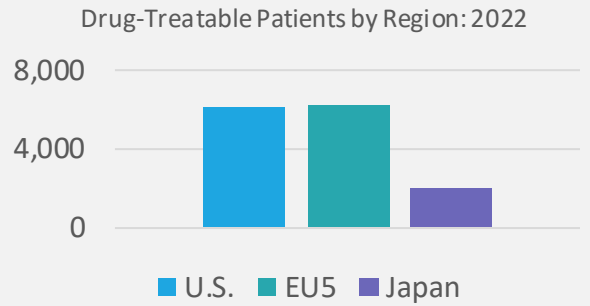
Platinum-Resistant/Refractory Ovarian Cancer Remains an Unmet Need

UNMET NEED

- Platinum-resistant and -refractory ovarian cancer represents a **high unmet need**
- It is associated with a poor prognosis and limited treatment options
  - **ORR of 11.8% with SOC[1] for platinum resistant patients**
- **Improvement in efficacy with acceptable safety profile** would make a meaningful difference for patients

PATIENT POPULATION

- In 2022, the total number of drug-treatable second line platinum-resistant ovarian cancer patients is estimated to be **>14,000 in the United States, EU5 and Japan[2]**



COMPETITIVE LANDSCAPE

- Current standard of care for second line platinum-resistant ovarian patients is single-agent chemotherapy ± bevacizumab[3]
- Ongoing pivotal trials focus on novel MOAs, including ADCs, and combinations with either PARPi or chemotherapy.[3] Of note, ADCs only work in a sub-population of patients
- ZN-c3 is potentially a first-in-class treatment option that works synergistically with other anticancer therapies

ZN-c3's efficacy and tolerability profile are well-positioned for the platinum-resistant/refractory ovarian population

(1) Pujade-Lauraine et al. J Clin Oncol 2014; 32:1302-1308; AURELIA study (2) Decision Resources Group; data on file. (3) CancerMPact Treatment Architecture Ovarian cancer July 2021; data on file.

Expectations for Efficacy in Recurrent Ovarian Cancer Patients

Study Name / Author	Drug	Platinum Refractory	Prior Bevacizumab Treatment	ORR	Overall Survival for Wee1 Inhibitor
AURELIA (Phase 3, Randomized Trial) (1)	Chemotherapy (PLD, paclitaxel, topotecan) in control arm	Not included	None	11.8%	N/A
Moore KM, CCR (Phase 2, Open Label) (2)	Adavosertib + chemotherapy	Not included	34% overall	11-33% range (High dose C2 arm not tolerated)	N/A
Lheureux S, Lancet (Phase 2, DB, PC, Randomized Trial) (3)	Adavosertib + gemcitabine	Included Plat Refractory (10%)	Unknown	23% (6% chemo alone)	**mOS = 11.4 mos; HR = 0.56 vs gemcitabine alone (p=0.017)**
ZN-c3-002	ZN-c3 + chemotherapy	Included Plat Refractory (7%)(4)	46% overall		

A response rate >20% may lead to significant PFS and OS advantages in larger trials

(1) Pujade-Lauraine E et al. [AURELIA study] *J Clin Oncol* 2014; 32:1302-1308.
(2) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(3) Lheureux S et al. *Lancet* 2021; 397: 281–92
(4) Platinum refractory population of 7% in evaluable population

ZN-c3-002: Summary of Clinical Activity

Summary of Clinical Activity (All Cohorts)

Group	N	Evaluable* (n)	PR/uPR+ (n)	SD/SD+ (n)	PD (n)	DCR (%)	ORR (%)
Total	56	43	13	24	6	86.0	30.2
ZN-c3 + PLD	30	24	3	17	4	83.3	12.5
ZN-c3 + Carboplatin	17	11	5	4	2	81.8	45.5
ZN-c3 + Paclitaxel	9	8	5	3	–	100	62.5

Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1

* Patients with measurable disease and at least one post-baseline scan

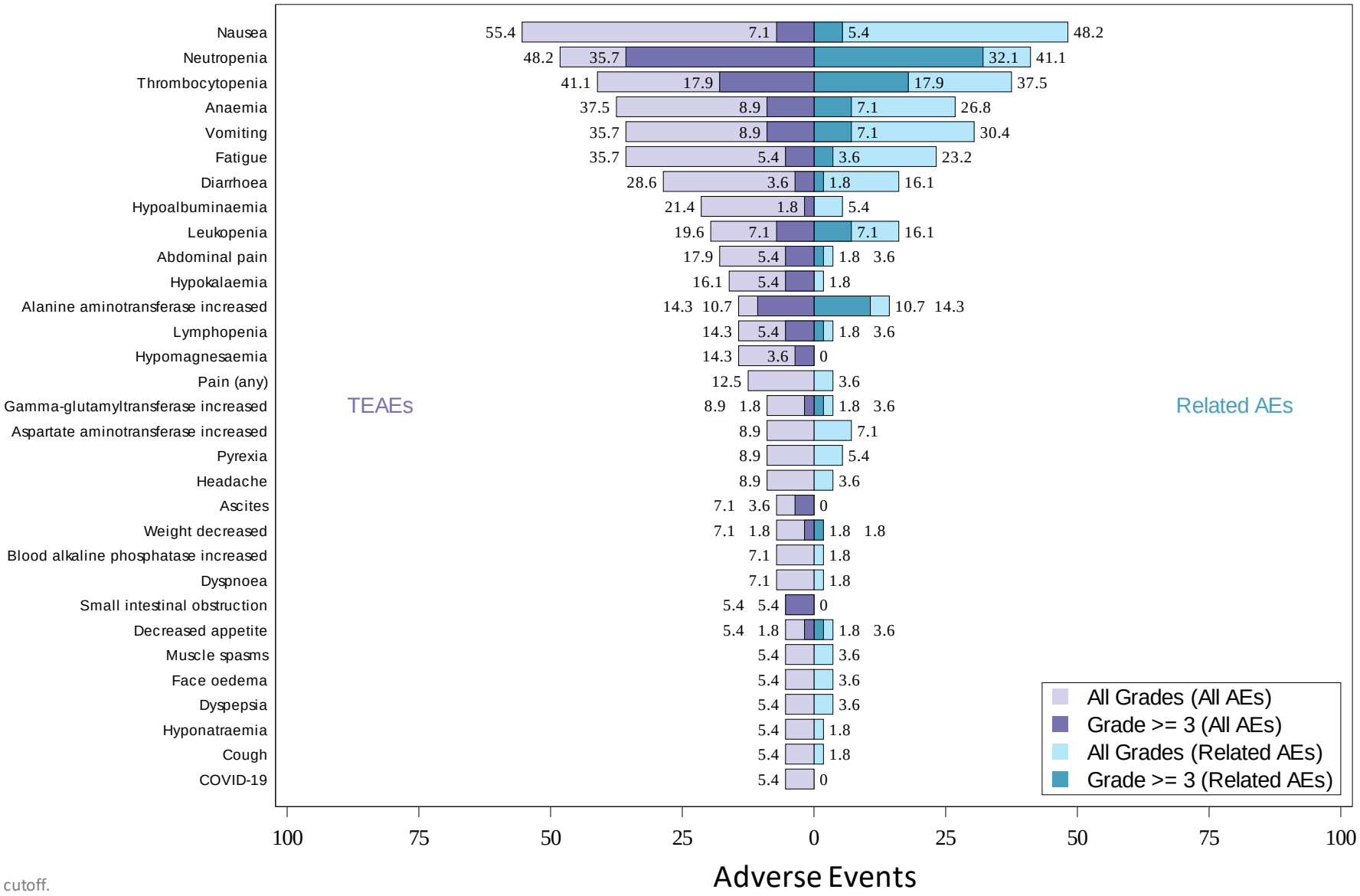
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+

+ Indicates treatment is ongoing for this subject

PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progress ive disease

Data cutoff January 28, 2022

ZN-c3-002: TEAEs ≥5% for All Patients (N=56)(1)

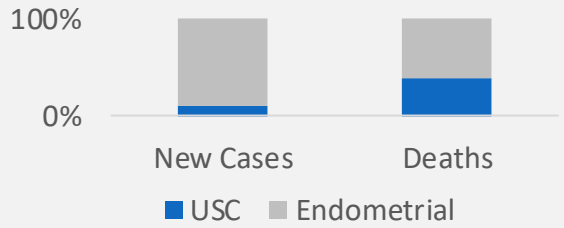


(1) January 28, 2022 data cutoff.

The Unmet Need in Uterine Serous Carcinoma is Significant

UNMET NEED

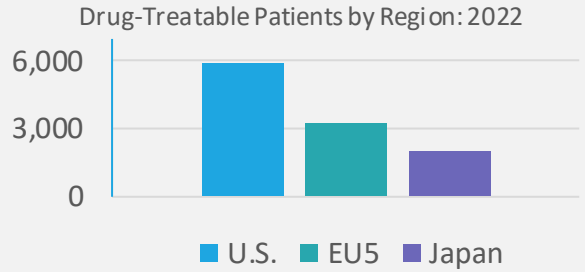
- USC results in **~40% of endometrial cancer deaths** despite comprising only 10% of cases



  - **Prior to pembro+len approval, ORR of 9.5% with PLD was chemo SOC for third-line USC**(1)
  - The 5-year survival rate for late-stage USC is 33% (2)
- >90% of USC patients have TP53 mutations(3)

PATIENT POPULATION

- In 2022, the total number of drug treatable **third line** advanced or recurrent endometrial cancer patients is approximately **10,000 in the United States, EU5 and Japan**(4)



- **Improvement in efficacy while limiting toxicities** would make a meaningful difference for patients

COMPETITIVE LANDSCAPE

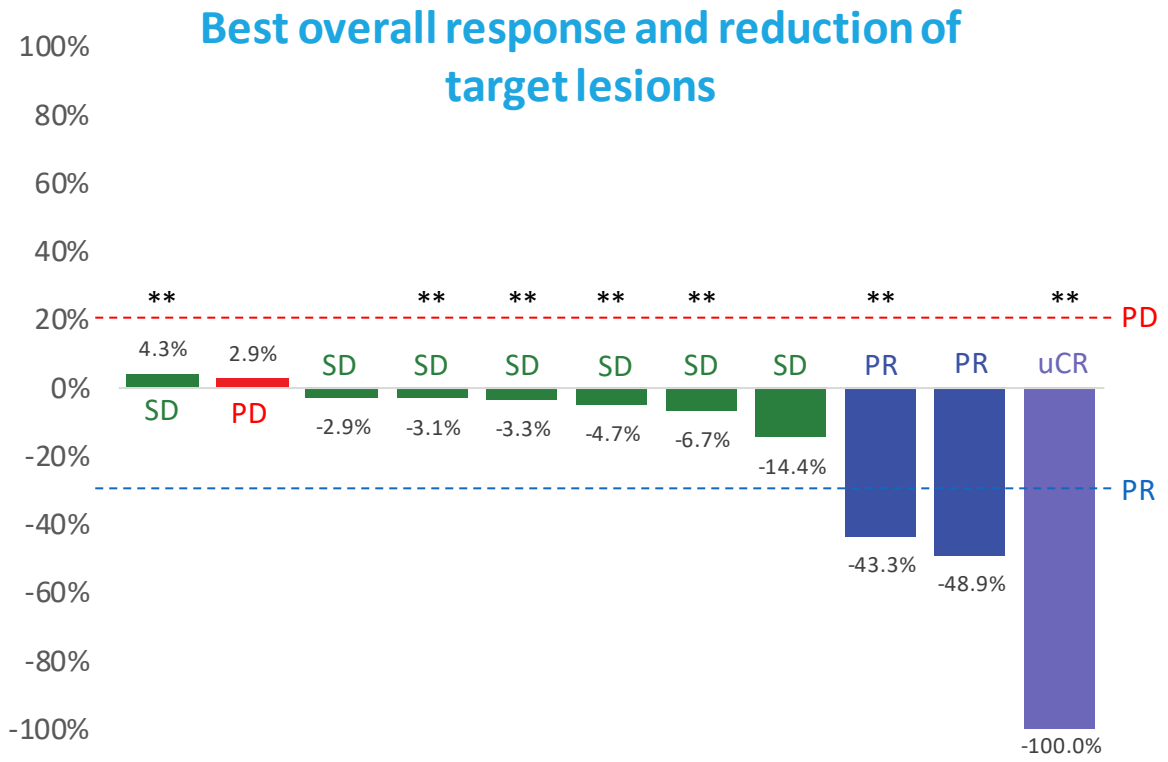
- Current standard of care for third line, USC is single-agent chemotherapy, with some limited use of bevacizumab and pembrolizumab monotherapies(5)
- There is a **high need** for a therapeutic option in later line patients **after prior platinum containing chemotherapy and pembrolizumab + lenvatinib treatment**(1)
  - Another Wee1 inhibitor (adavosertib) is also in late-stage clinical evaluation
- ZN-c3 is potentially a best in-class treatment option for USC

ZN-c3's efficacy and tolerability profile are well positioned for the USC population

(1) Muggia, J Clin Oncol, 2002 (2) Hamilton CA et al. Br J Cancer. 2006 Mar 13;94(5):642-6. (3) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167. (4) Decision Resources Group; data on file. (5) CancerMPact, Future Trends and Insights Endometrial cancer June 2021; data on file.

ZN-c3-001: Summary of Clinical Activity – Complete Response Seen

Best Overall Response	N = 11; n (%)
Complete Response (unconfirmed)*	1 (9)
Partial Response (confirmed)	2 (18)
Stable Disease	7 (63.6)
≥ 12 weeks	4 (36.3)
< 12 weeks	3 (27.3)
Progressive Disease	1 (9)
Overall Response Rate (95% CI = 6.0%, 61.0%)	3 (27.3)
DCR‡ (CR + PR + SD) (95% CI = 58.7%, 99.8%)	10 (90.9)
Duration of Response	5.6 months
mPFS	4.2 months



** Prior pembrolizumab + Lenvatinib use

*The BOR for this subject is cPR.
†N=11 subjects with measurable disease and at least 1 postbaseline tumor assessment.
‡Includes 3 subjects with cPR and 7 with SD.
Median duration of response for 3 responders = 5.55 months (95% CI, 4.11 – not available).
BOR, best overall response; cPR, confirmed partial response; DCR, disease control rate; PD, progressive disease; PR, partial response; SD, stable disease; uCR, unconfirmed complete response.
Data cutoff January 21, 2022.

ZN-c3 Compares Favorably in Efficacy and Tolerability to Adavosertib

Trial	Dosing Schedule	Prior Pem/Len Use (%)	ORR (%)	DCR (%)	Grade ≥3 Heme Tox (Neutropenia/Anemia/ Thrombocytopenia)
ZN-c3-001	300 mg QD continuously; 21-day cycle	57.1	27.3	90.9	0.0/9.4/3.1[1]
Liu et al[2]	300 mg QD D1-5, 8-12; 21-day cycle	Very low[3]	29.4	78.8	32.3/23.5/17.6

- ZN-c3 demonstrated a higher DCR and on par ORR to adavosertib in a sicker patient population
- ZN-c3-001 USC cohort had 57% prior pembrolizumab + lenvatinib use
- Oral continuous dosing regimen for ZN-c3 is enabled by its best-in-class tolerability profile

(1) AE profile for 32 ZN-c3 patients at 300mg QD continuous dosing from ZN-c3-001 study.
(2) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167
(3) Exact number of patients receiving TKI/IO combi not available.

Not a head-a-head comparison

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

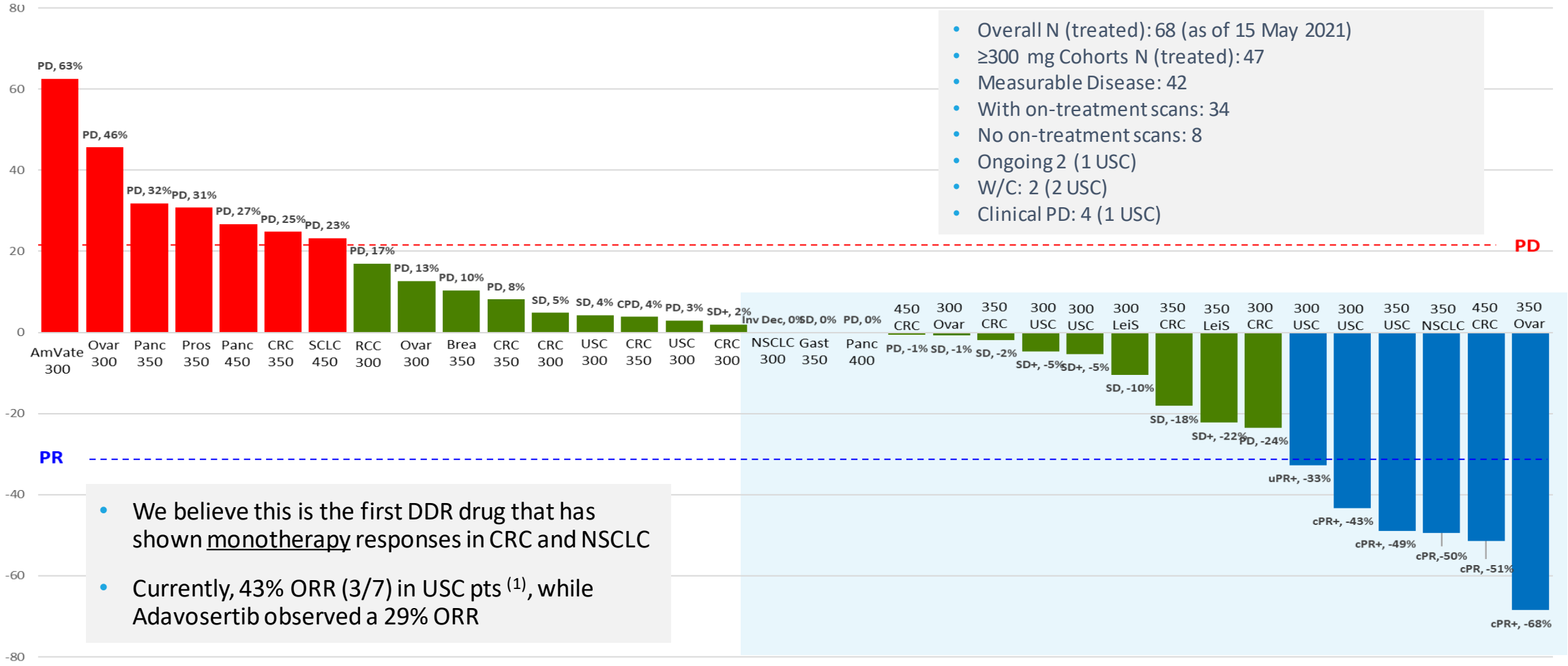
Overview of PRs in USC (2)

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; USC update on slide 16

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)

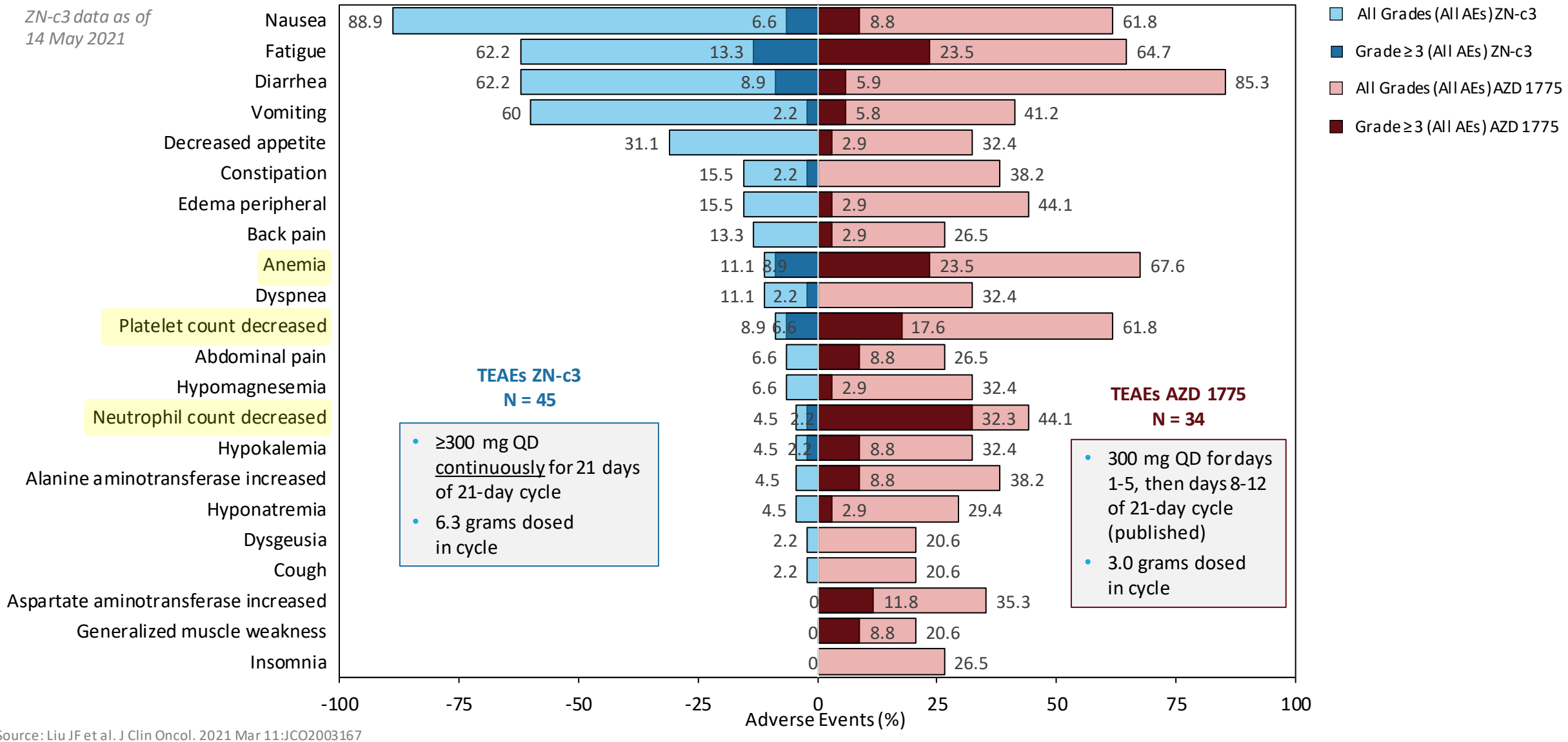
- We believe this is the first DDR drug that has shown <u>monotherapy</u> responses in CRC and NSCLC
- Currently, 43% ORR (3/7) in USC pts (1), while Adavosertib observed a 29% ORR

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.

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

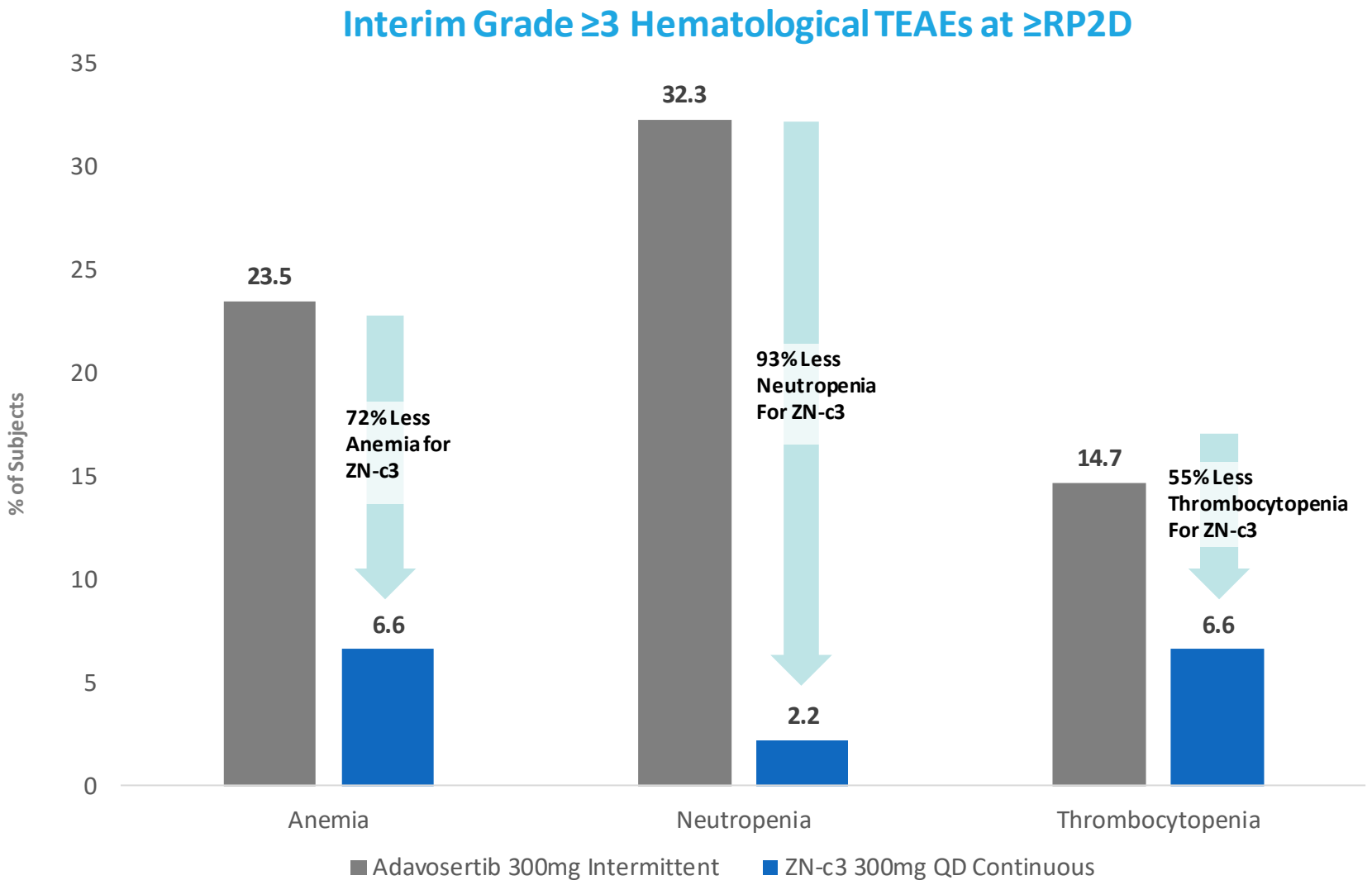
ZN-c3 data as of 14 May 2021



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)



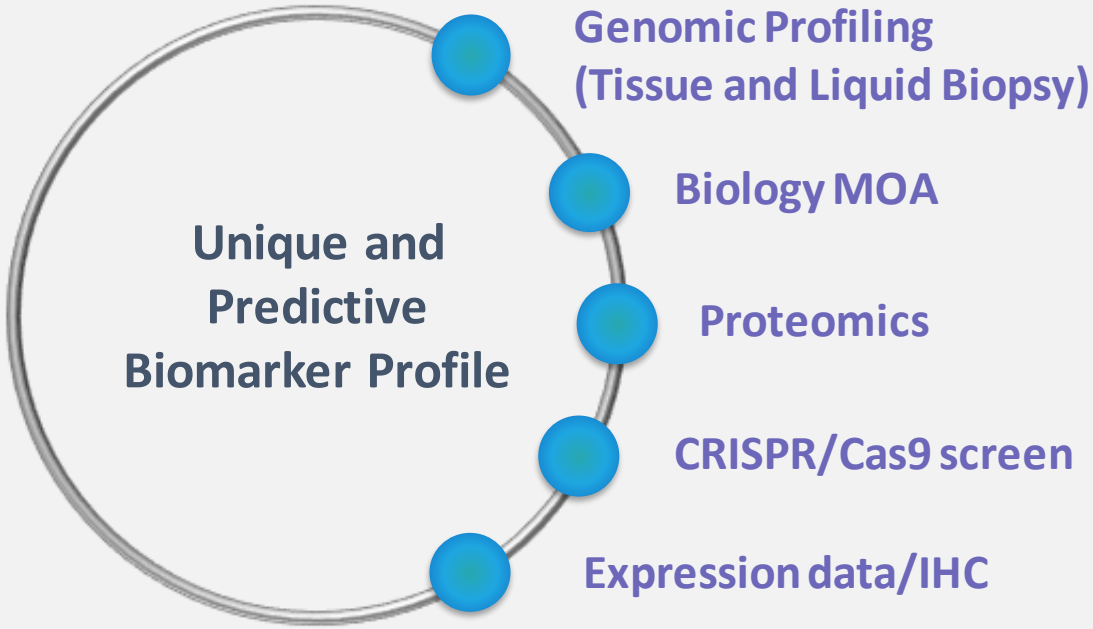
- Significantly lower overall severe hematological AE rate vs Adavosertib
- Despite continuous dosing and delivering 2x the drug load, ZN-c3 induces markedly less hematological toxicity
- Better tolerability unlocks the promise for wide ranging drug combinations with increased efficacy and commercial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

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

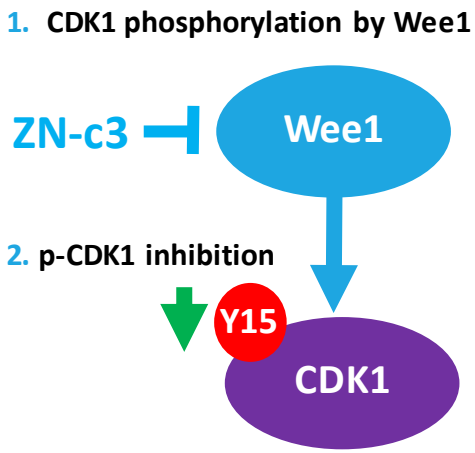
Phase 2 predictive biomarker-enabled trial ongoing

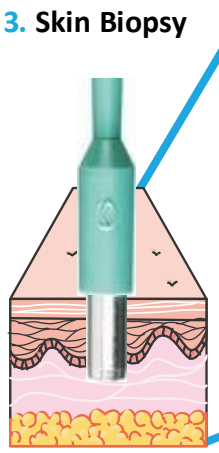
(1) Based on data from the ZN-c3 Phase 1 monotherapy trial

Decreases in p-CDK1 Show Target Engagement for Wee1 Inhibition

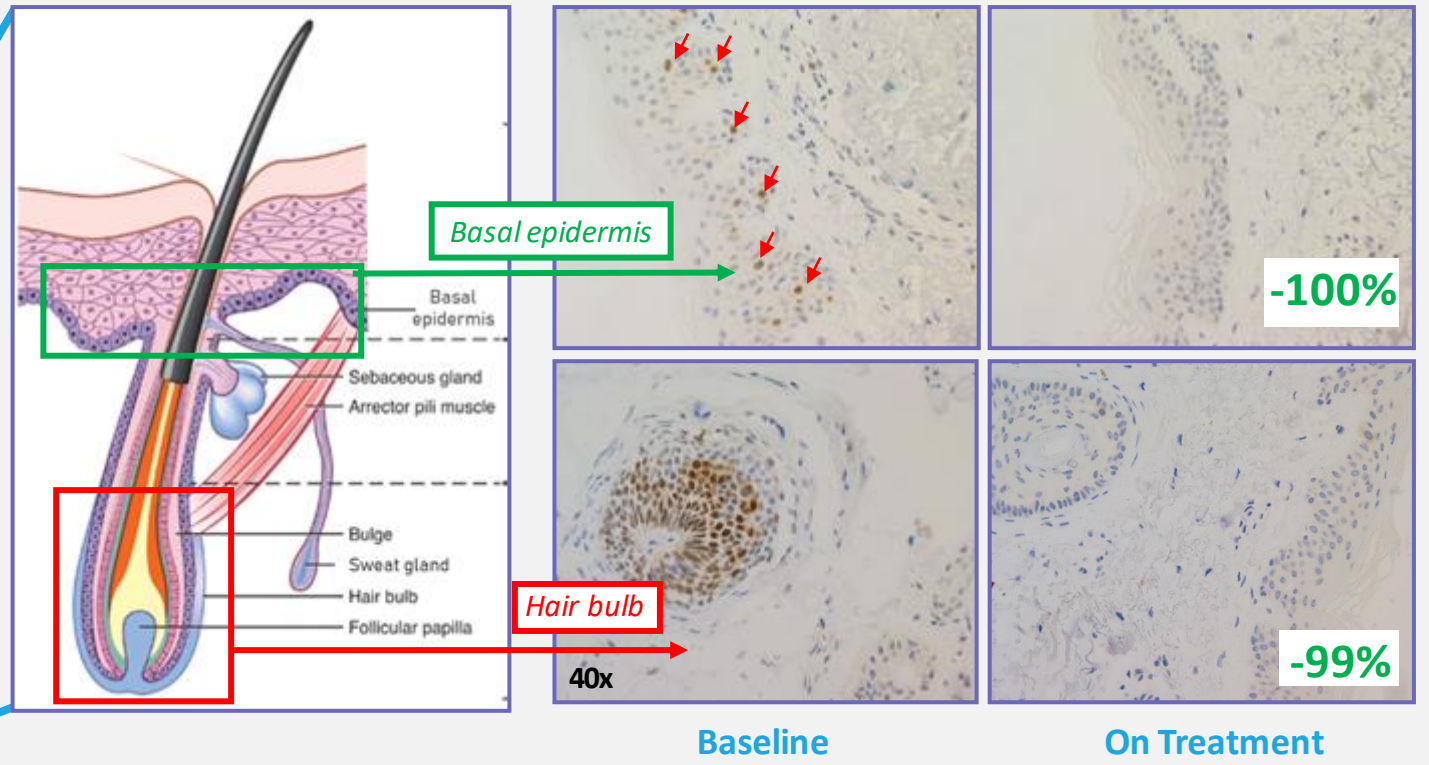
Confirmation of Wee1 Target Engagement in Surrogate Tissue

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



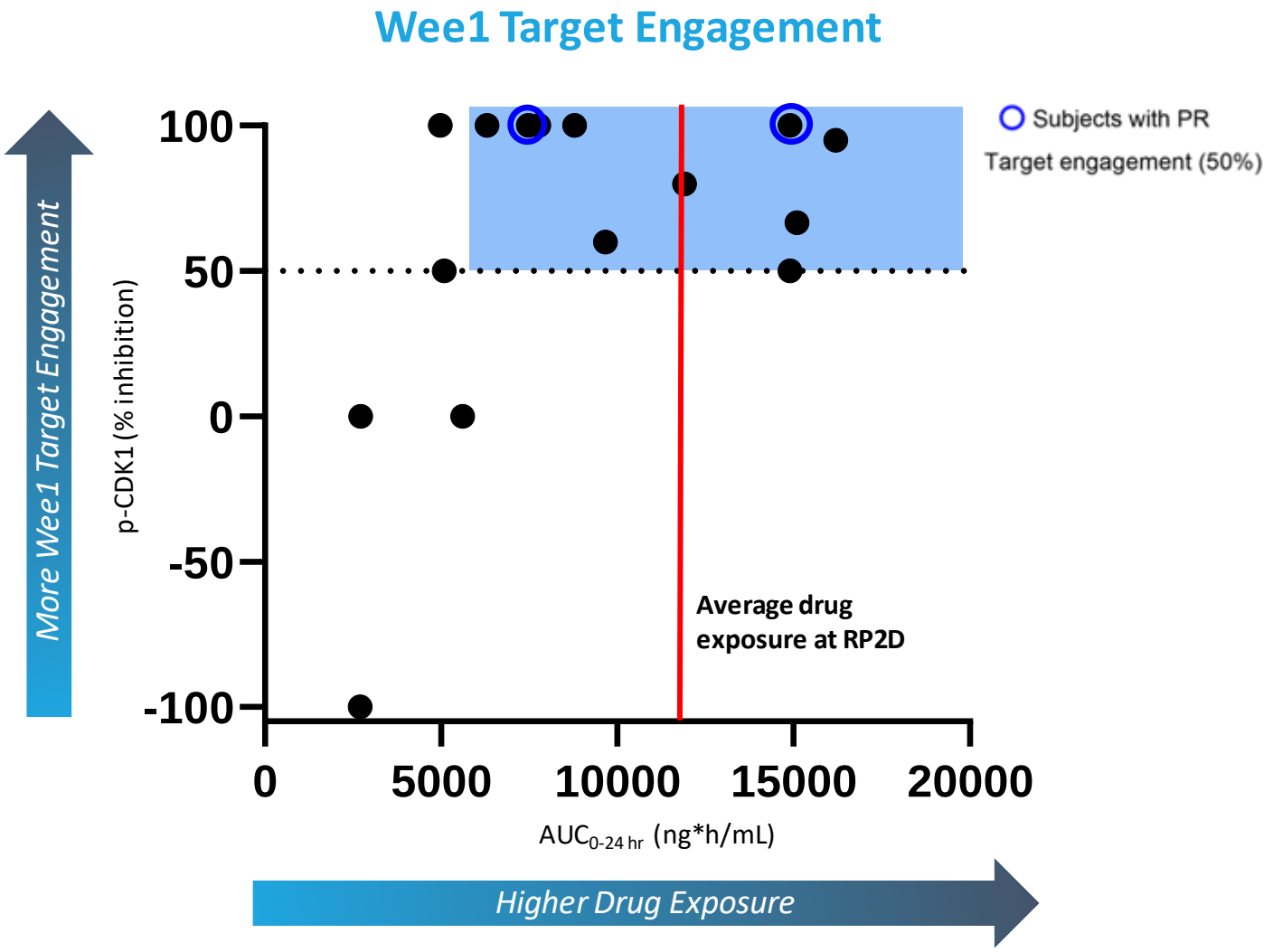


Decreases in p-CDK1 at Baseline vs on Treatment



Source: Drawing adapted from Servier Medical Art

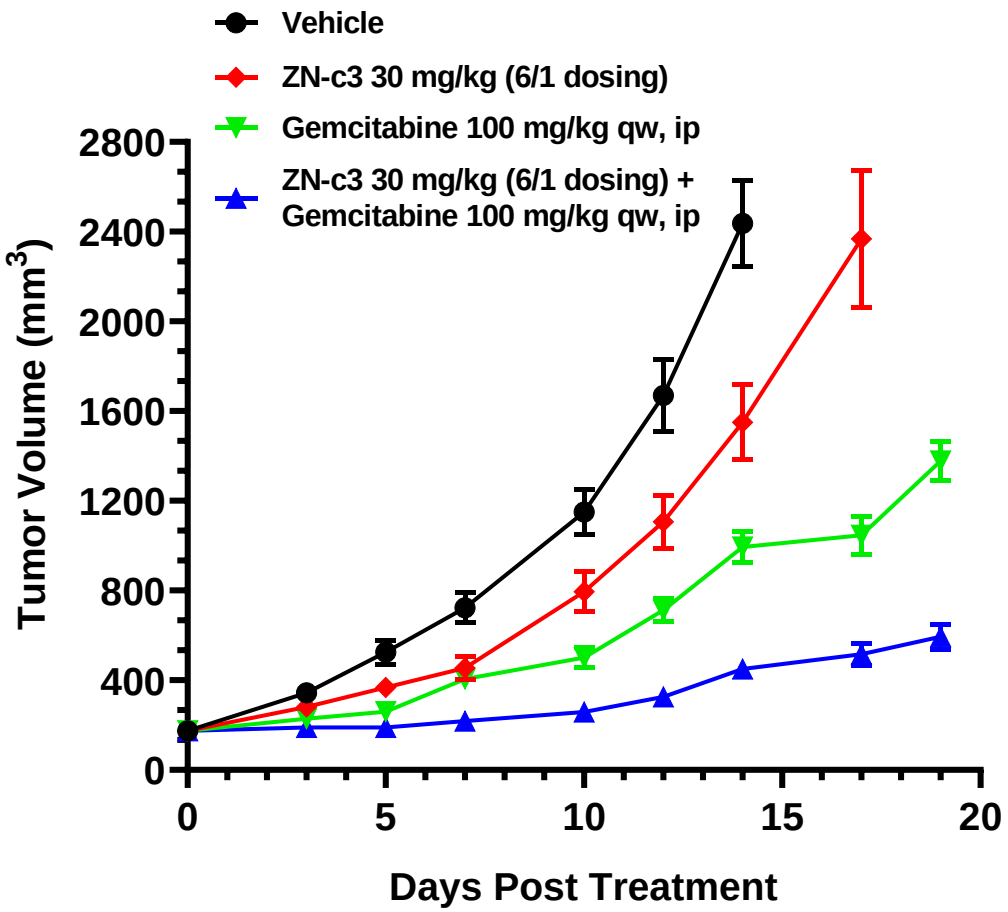
ZN-c3: PK/PD Correlation Shows Active Target Engagement at RP2D



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

Osteosarcoma Cancer Model SJSA-1



Clinical Unmet Need in Osteosarcoma

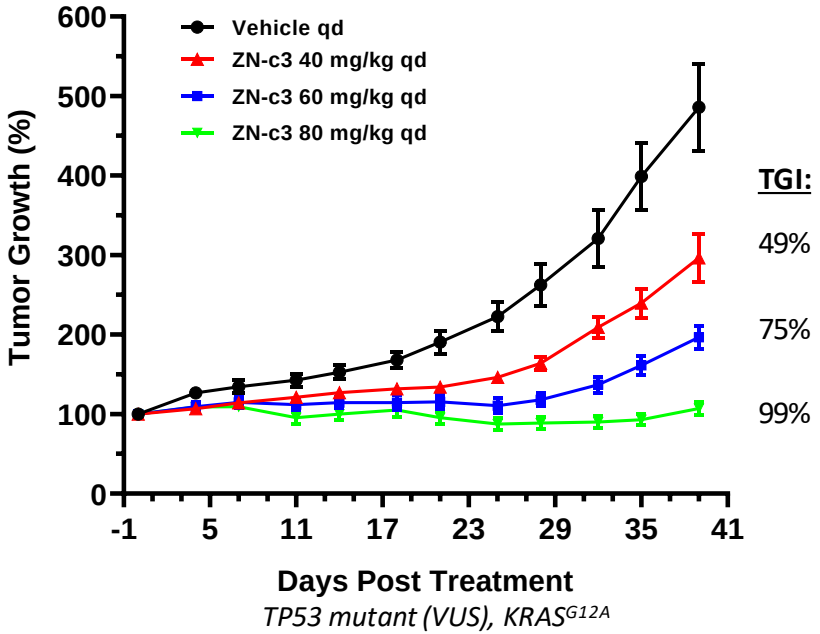
- Approximately 1,000 new cases in the U.S.(1)
- Up to 90% have sequence mutations or structural variants in TP53 and are often enriched in relapsed or refractory cases, portending resistance to chemotherapy(2)
- No significant advances over the last 10 plus years(3)
- Overall survival rate for patients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

Phase 1/2 initial readout expected 2H 2022

(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

Wee1 Inhibition as a Monotherapy and in Combination Shows Strong Preclinical Activity in Colorectal Cancer

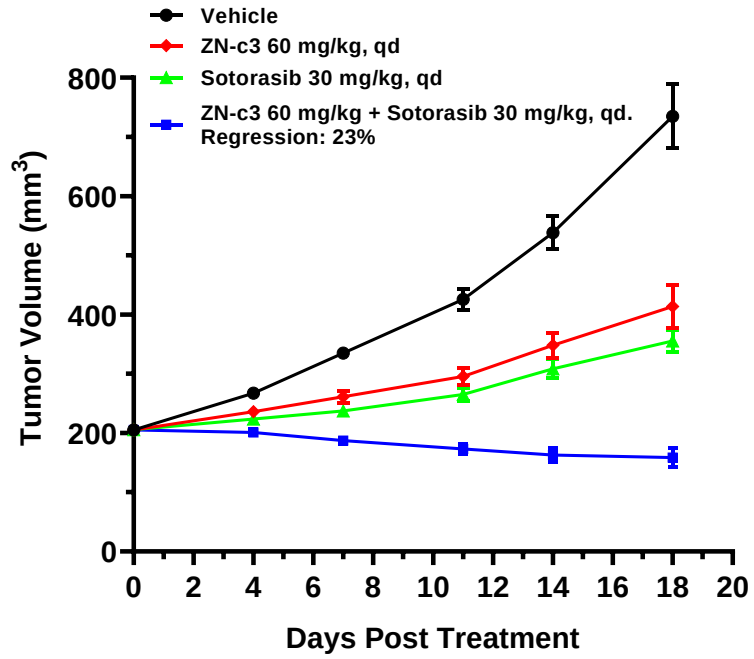
ZN-c3 is Active in a KRAS/TP53 Mutant Preclinical Colorectal Cancer Model



TP53 mutant (VUS), KRAS^{G12A}

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

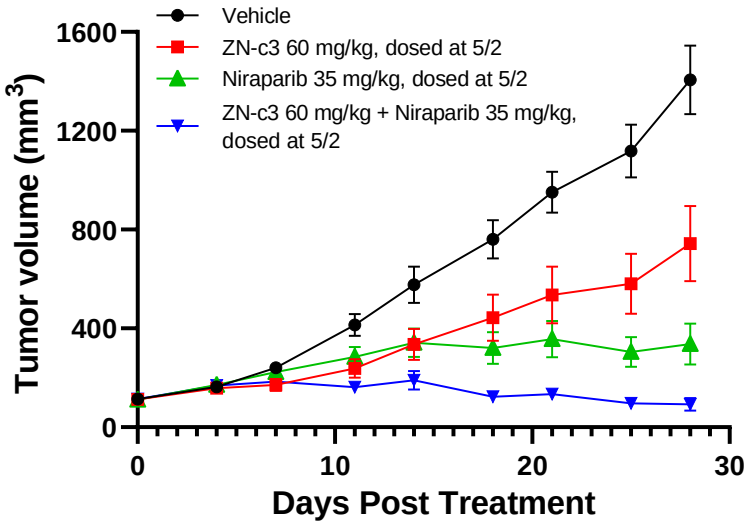
ZN-c3 in Combination with Sotorasib(1) Induces Regressions in a KRAS/TP53 Mutant Preclinical Colorectal Cancer Model

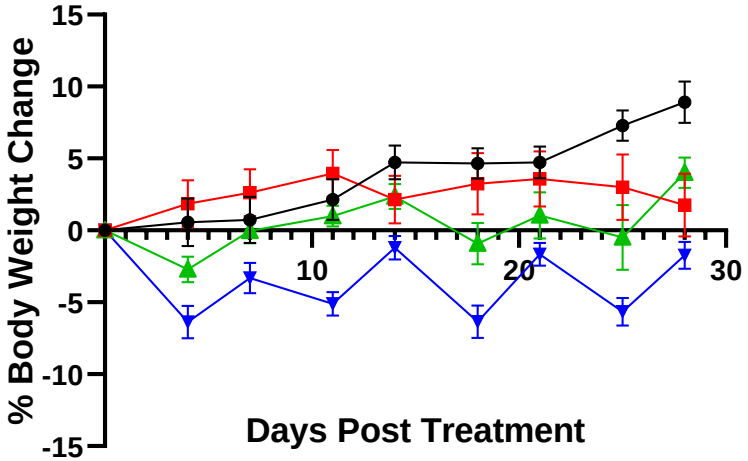


- Wee1 inhibition has been shown to improved PFS compared with active monitoring in patients with KRAS/TP53 mutated CRC (FOCUS4C trial)(2)
- These data support combining ZN-c3 with KRAS^{G12C} inhibitors in this population

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

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

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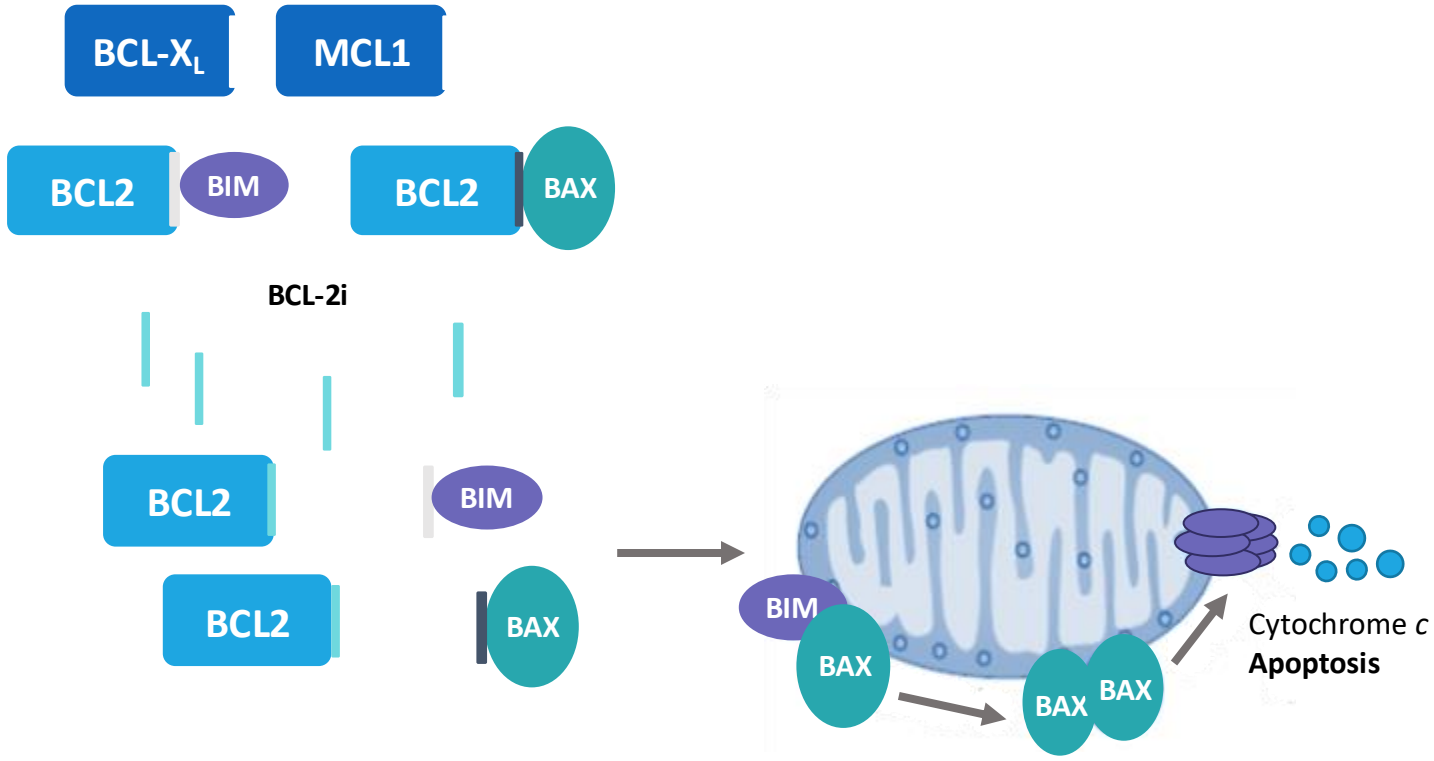
ZN-d5

BCL-2 Inhibitor

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 Designed with Improved Selectivity for BCL-2

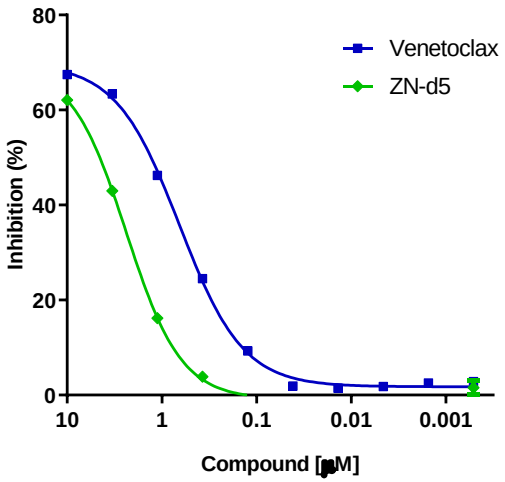
ZN-d5 has >14x Improved Selectivity for BCL-2 vs BCL-x_L and Binds With Higher Affinity to BCL-2 Mutants than Venetoclax

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



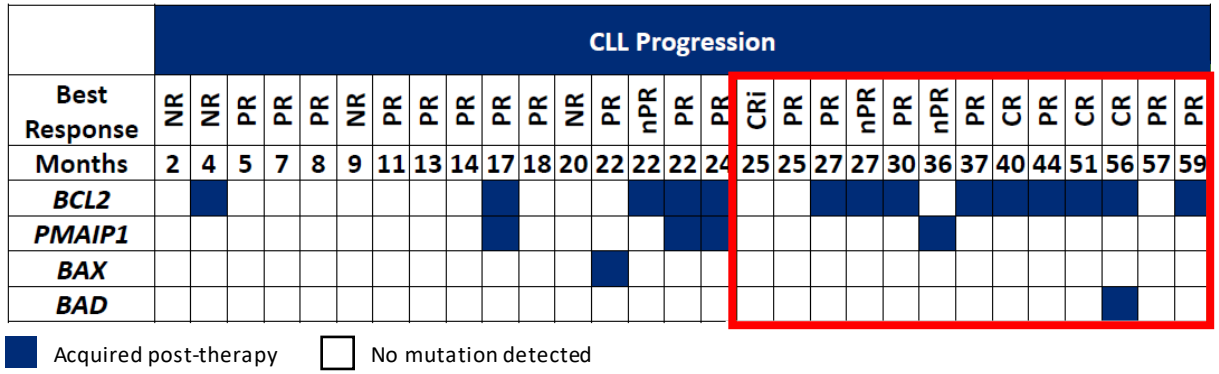
Compound ID	CTG (24 h) IC_{50} (µM)
Venetoclax	0.6
ZN-d5	2.4

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

- 55% (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 Clinical Development Plan

- 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
- Preclinical combination data of ZN-d5 + ZN-c3 utilizing novel biology showed synergistic and additive activity across multiple indications in both solid and liquid tumors, often at subtherapeutic doses

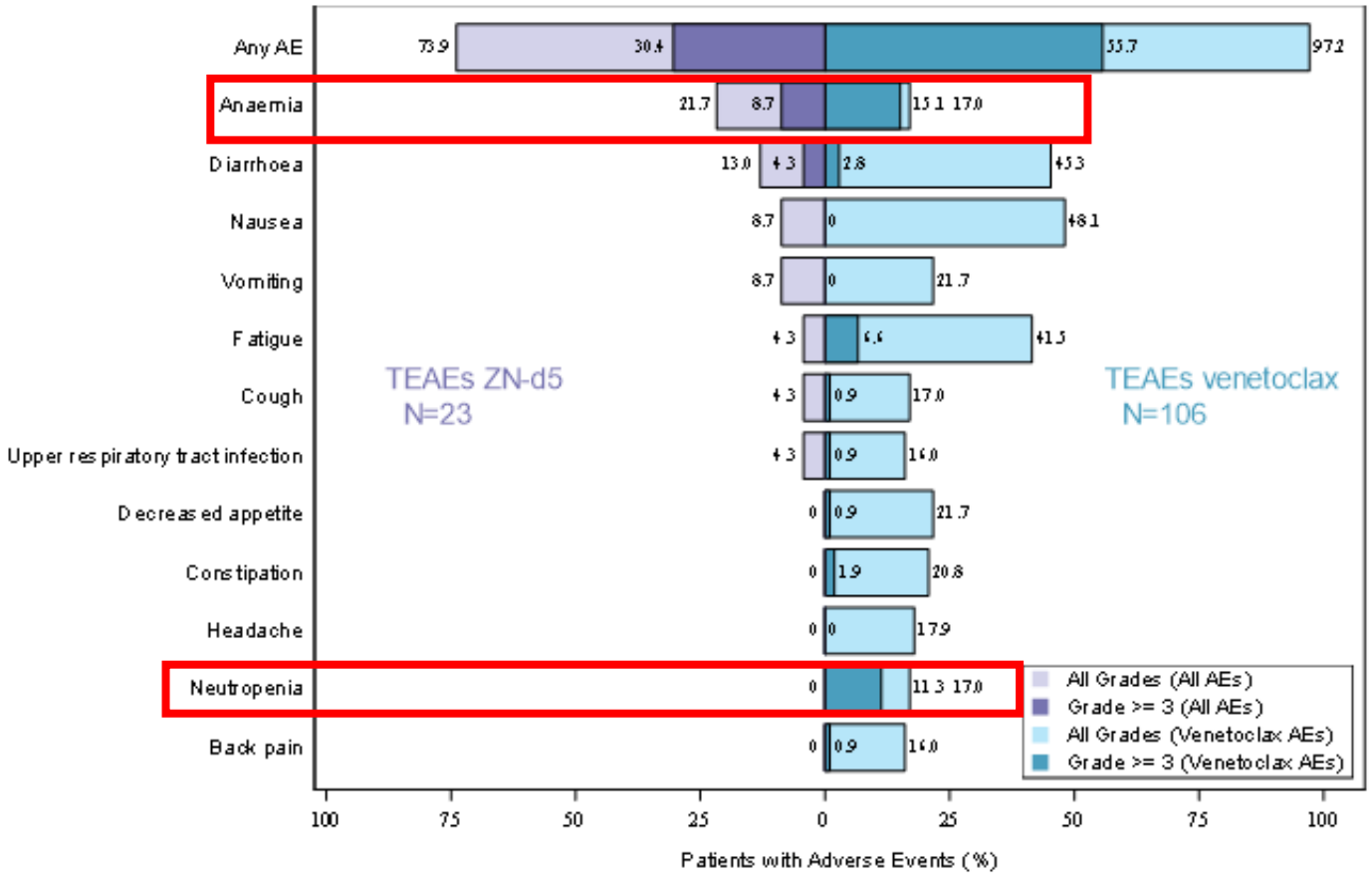
Ongoing and Planned Clinical Programs			
Indication	Treatment	Status	Trial Updates
AML and Non-Hodgkin's Lymphoma	ZN-d5	Phase 1 enrolling	Updated results in 2H 2022
AL Amyloidosis[+]	ZN-d5	Phase 1/2 enrolling	-
AML	ZN-d5 & ZN-c3 (Wee1i)	Phase 1/2 planned	Trial to initiate in 2H 2022

[+]Potentially Registrational Study

ZN-d5: Favorable Early Comparison to Venetoclax in NHL

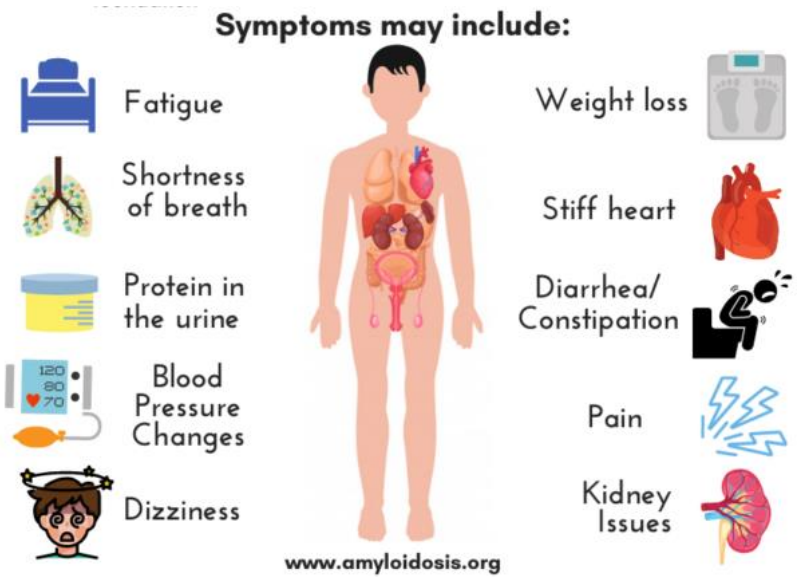
- ZN-d5 100-1200 mg, empty stomach
- Venetoclax 200-1200 mg with food
- Early toxicity profile in NHL favorable vs. published venetoclax data(1)
  - Fewer AEs of any Grade, Grade ≥3
  - No TLS observed
  - Venetoclax AEs not dose-dependent

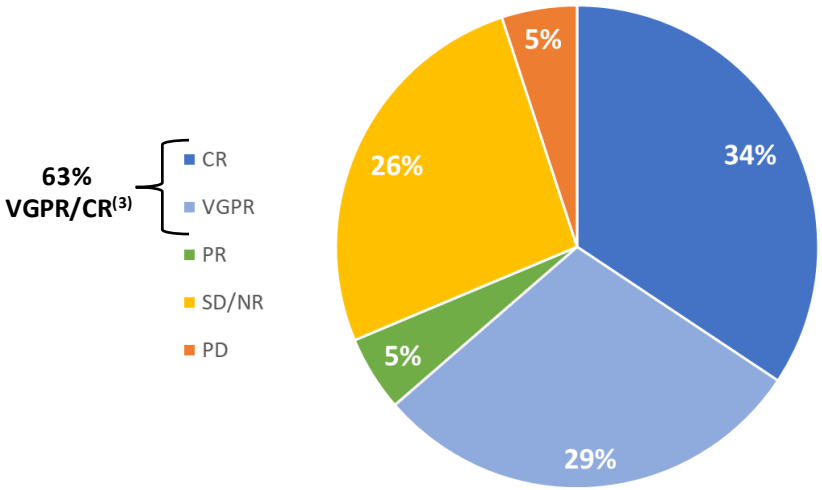
Adverse Event	Any Grade			
	All Doses (N = 106)	≤ 400 mg (n = 22)	600 to 900 mg (n = 33)	1,200 mg (n = 51)
Emergent*				
Any event	103 (97)	21 (96)	33 (100)	49 (96)
Nausea	51 (48)	9 (41)	15 (45)	27 (53)
Diarrhea	48 (45)	7 (32)	14 (42)	27 (53)
Fatigue	44 (42)	10 (45)	9 (27)	25 (49)
Decreased appetite	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 in AL (Primary) Amyloidosis





- AL Amyloidosis: Deposition of immunoglobulin light chains
  - Clonal plasma cell population secretes misfolding light chain
  - Progressive systemic amyloid accumulation causes widespread organ damage
  - **High morbidity and mortality**
- Orphan disease
  - Estimated worldwide prevalence is 75,000(1)
  - About 4k new cases/year in the US(2)
- Not a cancer, but treated like one
  - Agents active in multiple myeloma used in first-line and relapsed/refractory settings
  - Daratumumab only approved therapy, for first-line use with CyBorD
- **Relapsed/refractory setting is a high unmet medical need**

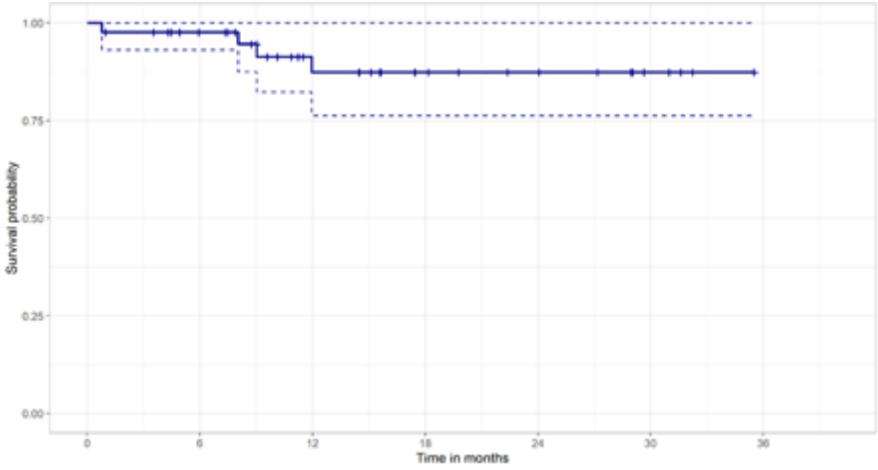
AL Amyloidosis study is currently enrolling patients

(1) Zhang et al. Clin Lymphoma Myeloma Leuk. 2019;19(suppl 10):e339
(2) Kyle et al, Mayo Clin Proc. 2019;94:465-471
(3) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

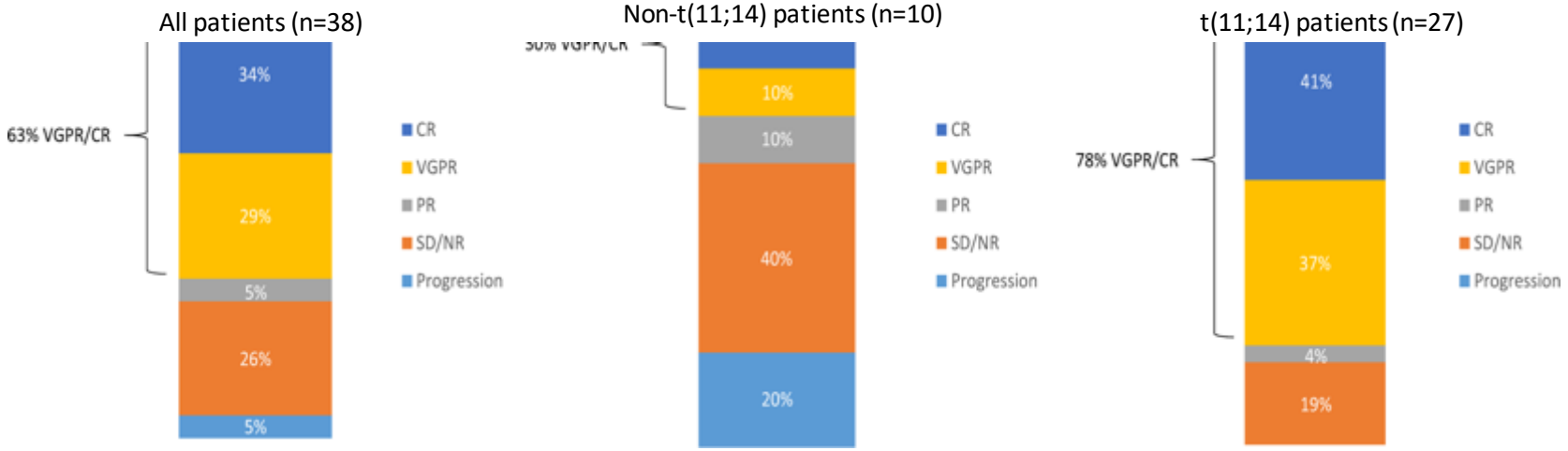
BCL-2 Inhibition has Shown Robust Clinical Activity in AL Amyloidosis

- Patients with the t(11;14) translocation have a worse prognosis than the general AL amyloidosis community [1]
- BCL-2 inhibition showed an improved response rate in the t(11;14) cohort with a trend towards better survival

OS for All Patients



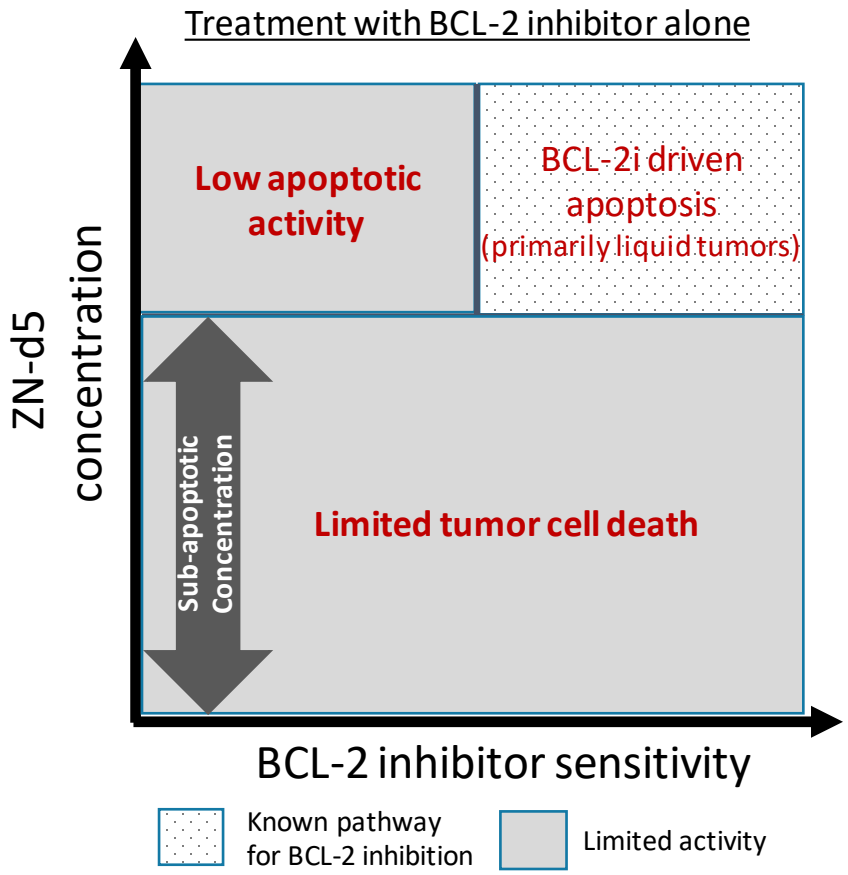
Best Response in Evaluable Patients

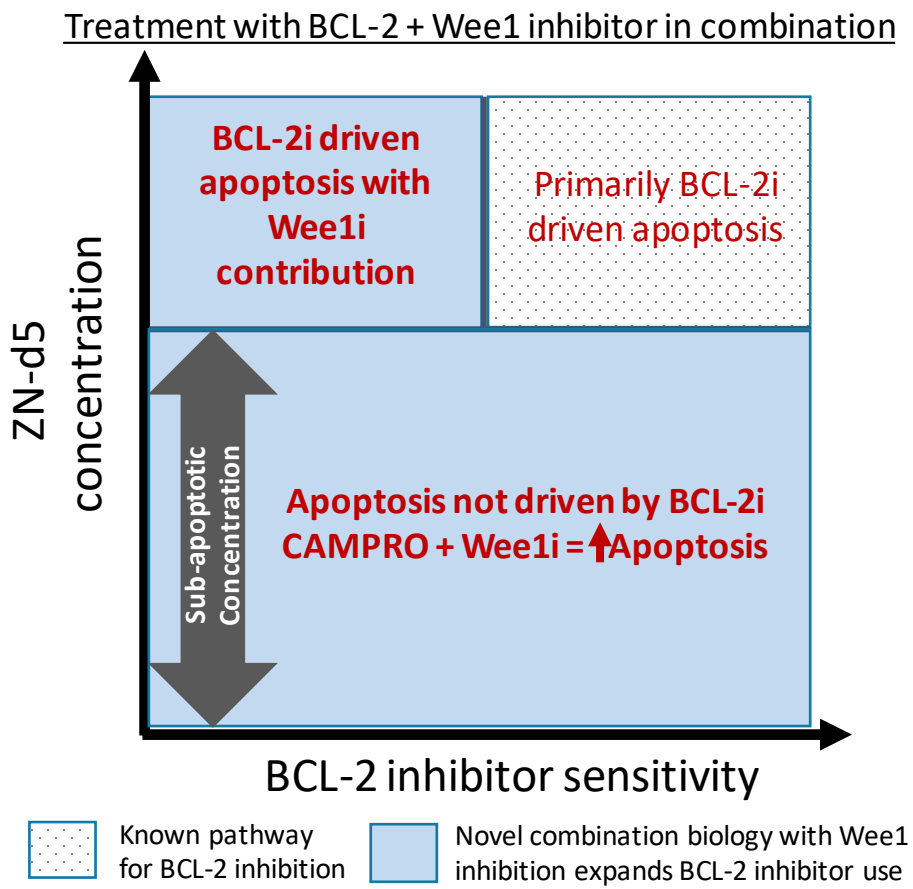


(1) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

Novel Biology Supports Synergy of BCL-2 and Wee1 Inhibition – *CAMPRO (CAspase Mediated PROteolysis)*

BCL-2 inhibition (BCL-2i) induces CAMPRO of multiple proteins, including DNA damage repair (DDR) proteins

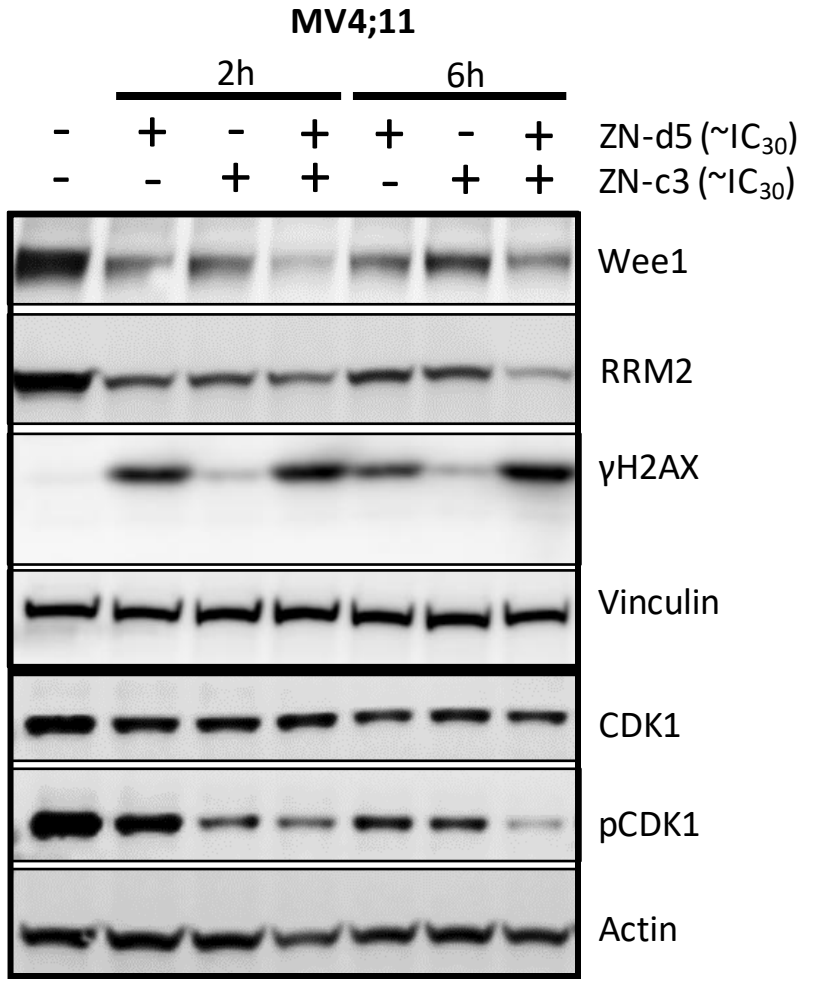




This novel synergistic finding supports the use of ZN-d5 + ZN-c3 in both sensitive and less sensitive tumor cells, opening a large market opportunity across both solid and liquid tumors

ZN-d5 + ZN-c3 Combination Treatment Also Results in Decreased Levels of DDR Proteins

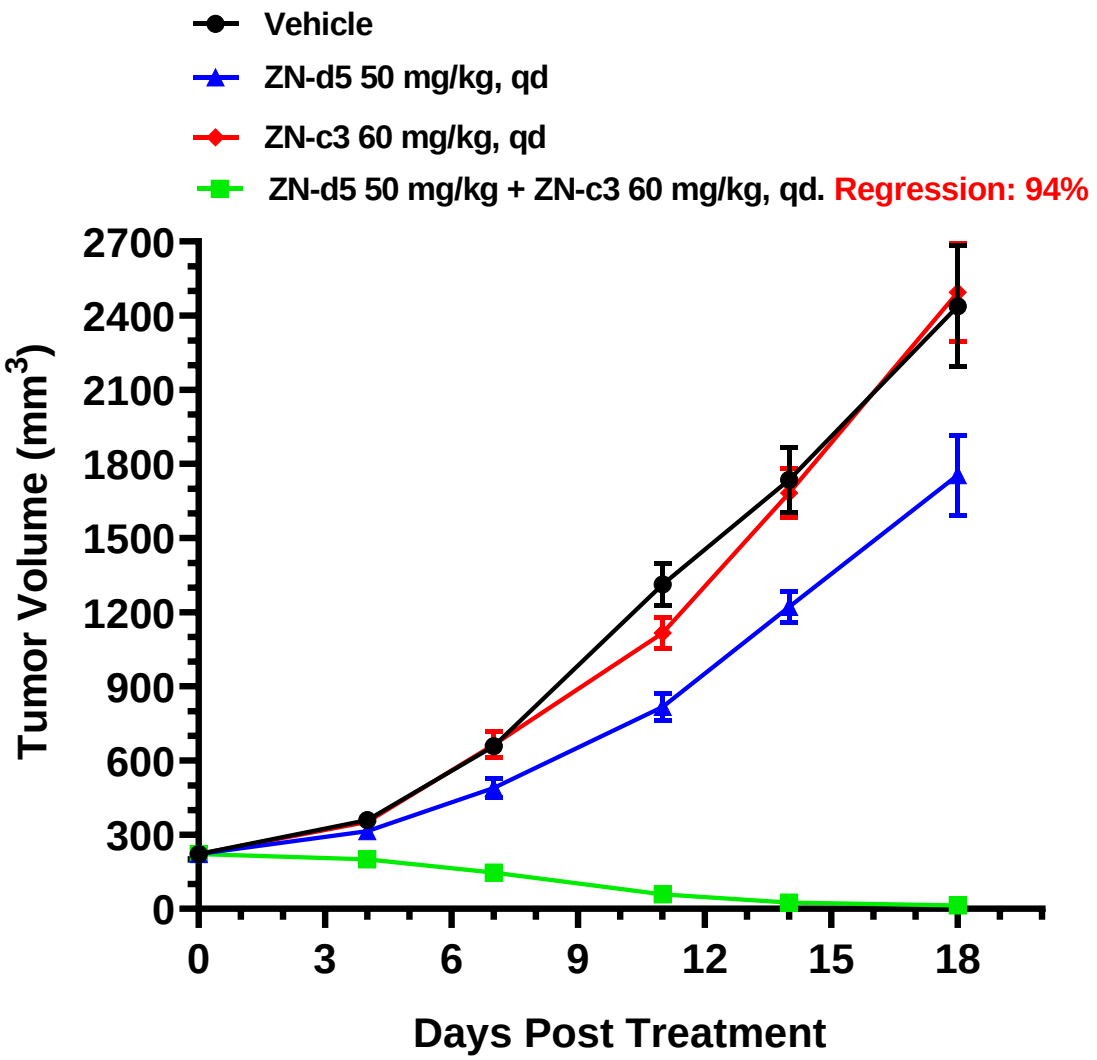
- **ZN-d5 at subtherapeutic doses activates caspases leading to:**
  - DNA damage (increased in γH2AX)
  - Degradation or decrease of DDR related proteins (Wee1 and RRM2)
  - **These effects are increased when combined with ZN-c3**
- **This, in turn, results in inhibition of multiple relevant pathways (e.g. pCDK1) and synergistic anti-tumor activity when combined with ZN-c3**



Based on preclinical data

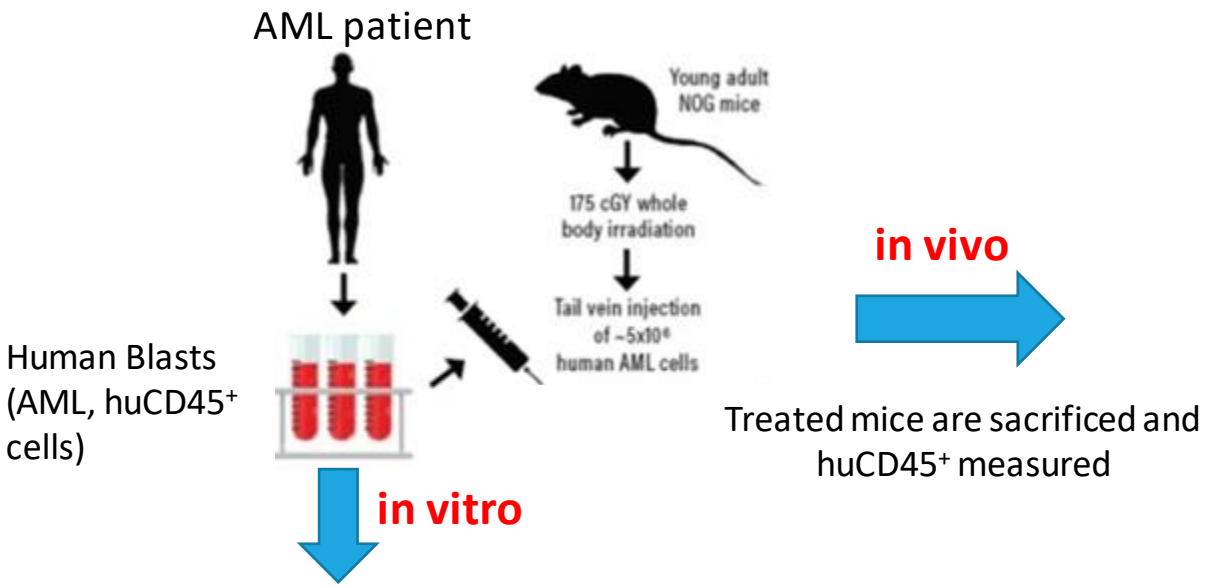
The Combination of BCL-2 and Wee1 Inhibitors Results in Synergism in Several Tumor Models Including AML

HL-60 AML model



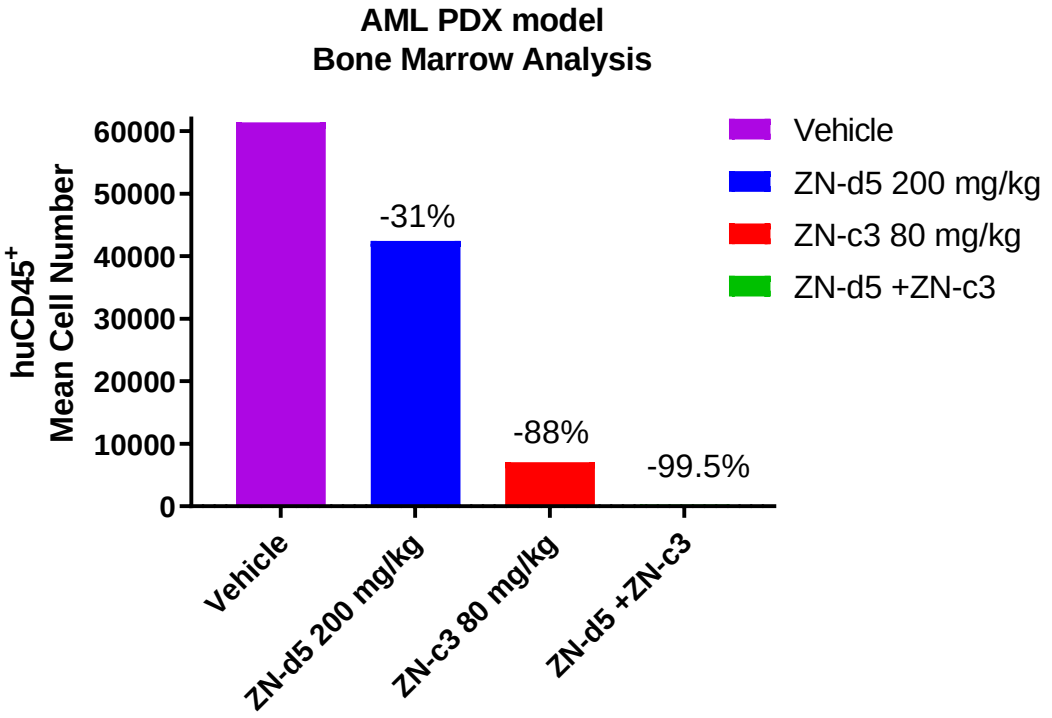
- ZN-d5 and ZN-c3 combination represents a novel therapeutic approach
- Significant enhancement of activity than single agent in several indications, including AML
- Combination regimen was well-tolerated in mice
- **Zentalis is the only company known to have both inhibitors in clinical development**

ZN-d5 Combined with ZN-c3 is Active in Patient-Derived AML Samples



Clinical				In vitro (ZN-d5+ZN-c3)	
Patient	Blasts % (before treatment)	Post- Collection Treatment	Blasts % (After Treatment)	ZN-d5/ZN-c3 Treatment (nM)	Blasts % (After Treatment)
3930	93.4	Vidaza/Venetoclax	Residual AML (33% blast) (~2 months post-treatment)	120/500	4.6
3977	62.1	Vidaza/Venetoclax	Residual AML (68% blast) (~2 months post-treatment)	65/100	0
3978	41.1	Gilteritinib/Venetoclax	Residual AML (32% blast) (~1 month post-treatment)	65/500	3.6

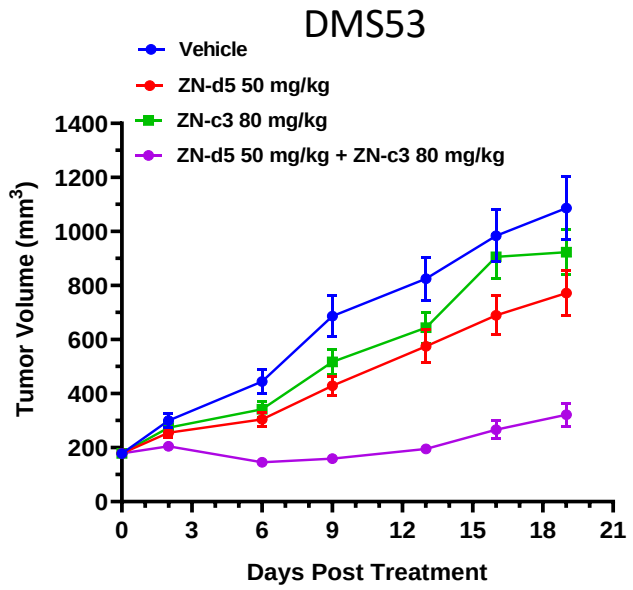
- The combination of ZN-d5+ ZN-c3 is active *in vitro* in **3/3 samples from patients who progressed on venetoclax**
- The combination of ZN-d5 + ZN-c3 is active *in vitro* in 29 patient's derived AML samples independently of TP53 mutation

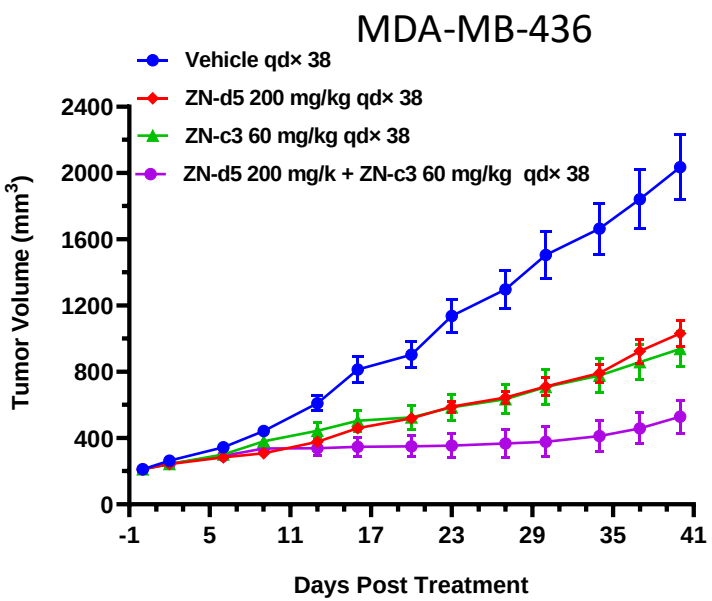


n= 6 or 10, qd x 17 treatment

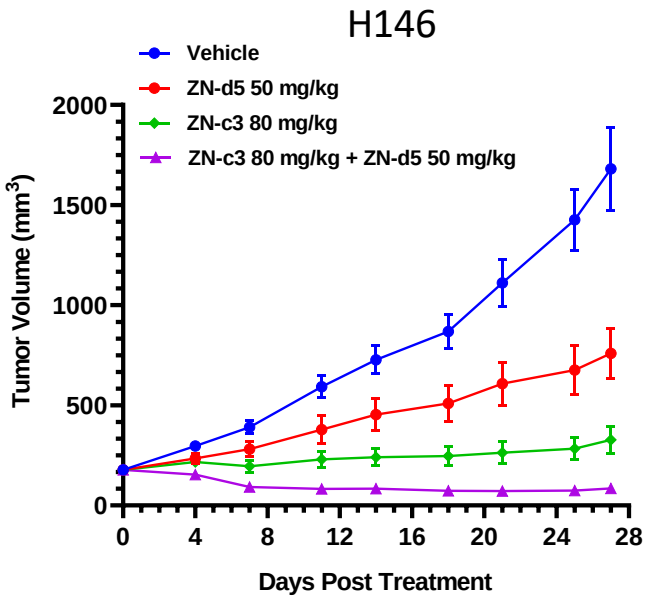
ZN-d5 + ZN-c3 shows promising activity in samples from AML patients progressing on venetoclax

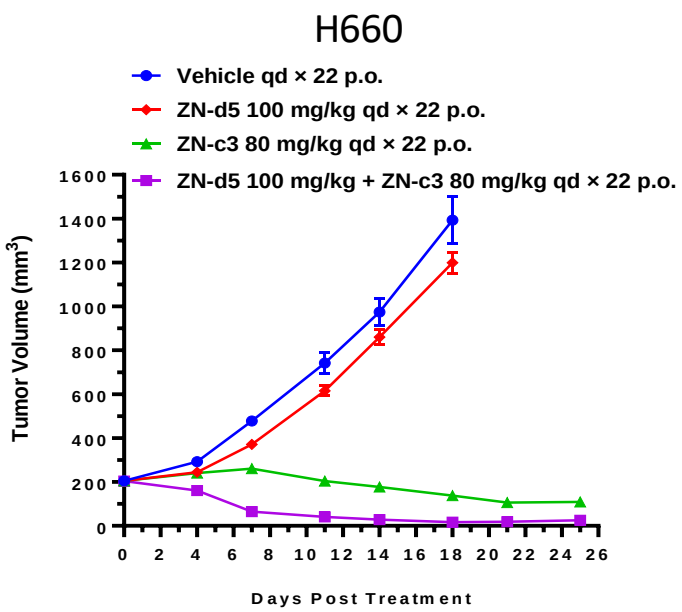
Antitumor Activity in Solid Tumor Models with the ZN-d5 + ZN-c3 Combination Represents Market Expansion Opportunities





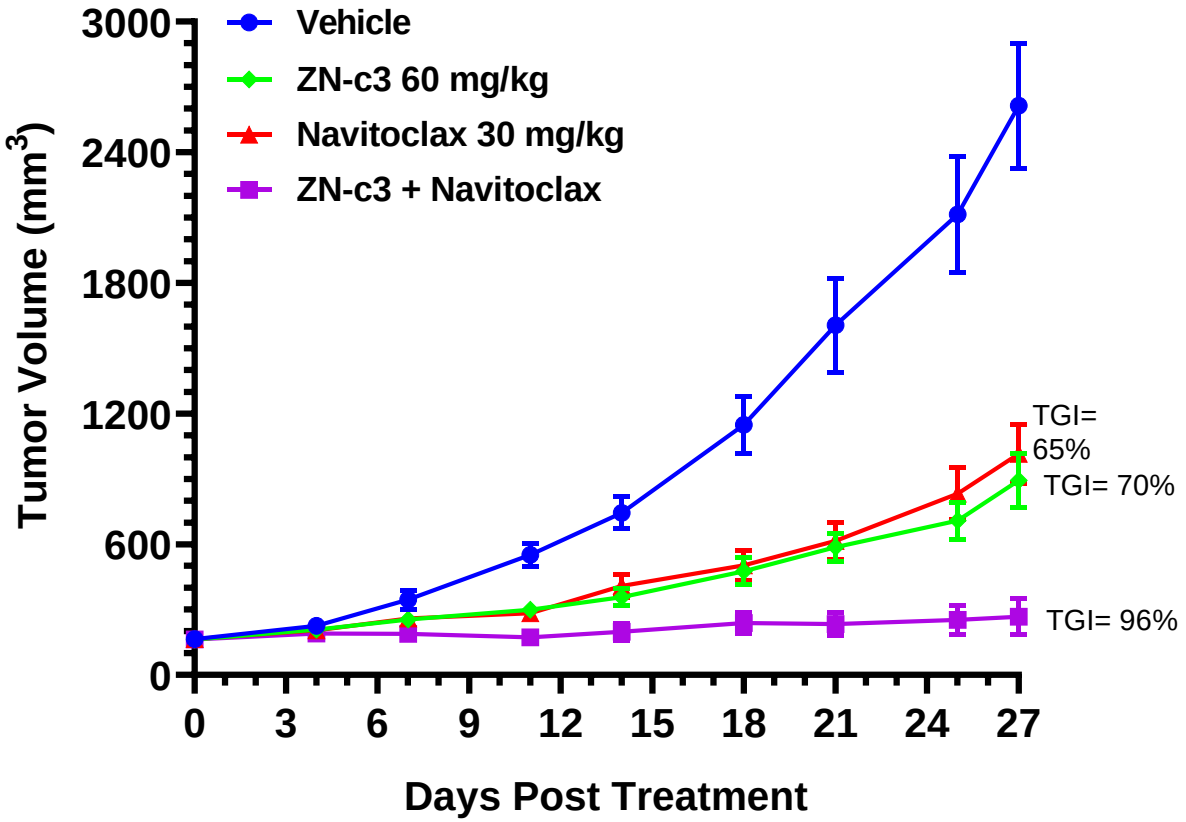
Cell Line	Indication
DMS53	SCLC
MDA-MB-436	TNBC





Cell Line	Indication
H146	NSCLC
H660	Neuroendocrine Prostate

ZN-c3 Combined with a Low Dose of Navitoclax (BCL-xL Inhibitor) Results in Enhanced Anti-tumor Activity in the ALL model MOLT-4



The MOA of the combination of ZN-d5 and ZN-c3 represents a novel therapeutic approach which also applies to combinations of ZN-c3 with other inhibitors of anti-apoptotic proteins

- Navitoclax enhances the anti-tumor activity of ZN-c3 at one-third of the active dose used as a single agent in xenografts (30 versus 100 mg/kg)
- Opportunity to overcome the toxicity observed with navitoclax

TGI: Tumor Growth Inhibition
ALL: Acute Lymphoblastic Leukemia
MOLT-4 model is BCL-xL dependent, but is not on BCL-2

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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[1]
2H 2022		Initial readout on Phase 1/2 chemotherapy combo in osteosarcoma[2]

ZN-d5: BCL-2 Inhibitor

1Q 2022	✓	Initiate Phase 1/2 monotherapy study in amyloidosis[2]
2H 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

Integrated Discovery Engine

2022	Initiate IND enabling studies for an internal program

Zentera

2022	Maximize value from investment in and partnership with Zentera

[1] Registrational trial with FDA Fast Track designation
[2] Potentially registrational trial

zentalis

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