



**Translating cancer biology  
into medicines**

**Cyclacel Pharmaceuticals, Inc. (CYCC) NOVEMBER 2024**

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# Cyclacel Opportunity

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Discovered and developing **fadraciclib** & **plogosertib** cell cycle, oncology portfolio

**Fadra** next generation CDK2/9 inhibitor with unique Ph 2 precision medicine strategy

**Single-agent**, Ph 1, anticancer activity (CR, PR, SD) with good tolerability including:

- GYN (breast/endom./ovarian), hepatobiliary, NSCLC, pancreatic, testicular and T-cell lymphoma

Enroll two **Phase 2 cohorts** potentially supporting registration pathways

- patients with solid tumors with CDKN2A/CDKN2B abnormalities (readout 2H 24, n~12)
- T-cell lymphoma (readout 2H 24-1H 25)

# What Problem Are We Trying to Solve?

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Abnormalities in genetic tumor suppression mechanisms enable cancer progression

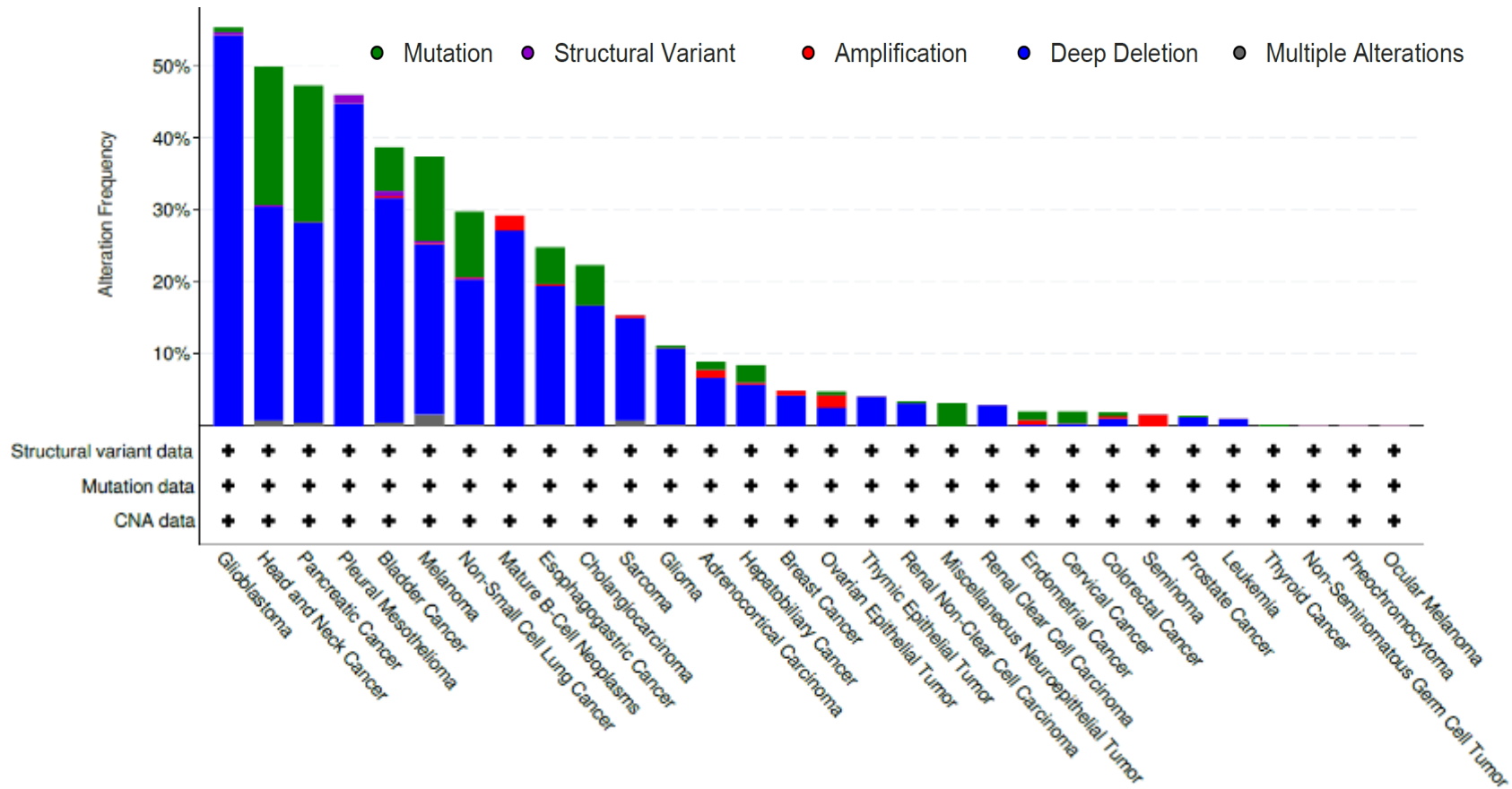
- **CDKN2A** and/or **CDKN2B** abnormalities are widely found in many solid tumors

Use pharmacologic inhibitors acting in the p16 (**CDK2**) and/or p53 (**CDK9**) pathways to restore tumor suppression

Opportunities/Challenges:

- **CDK2** and **CDK9** versus CDK2 versus CDK9
- Single agent and/or combination
- Historical toxicities (mostly hematological) have limited clinical utility

# CDKN2A Alterations

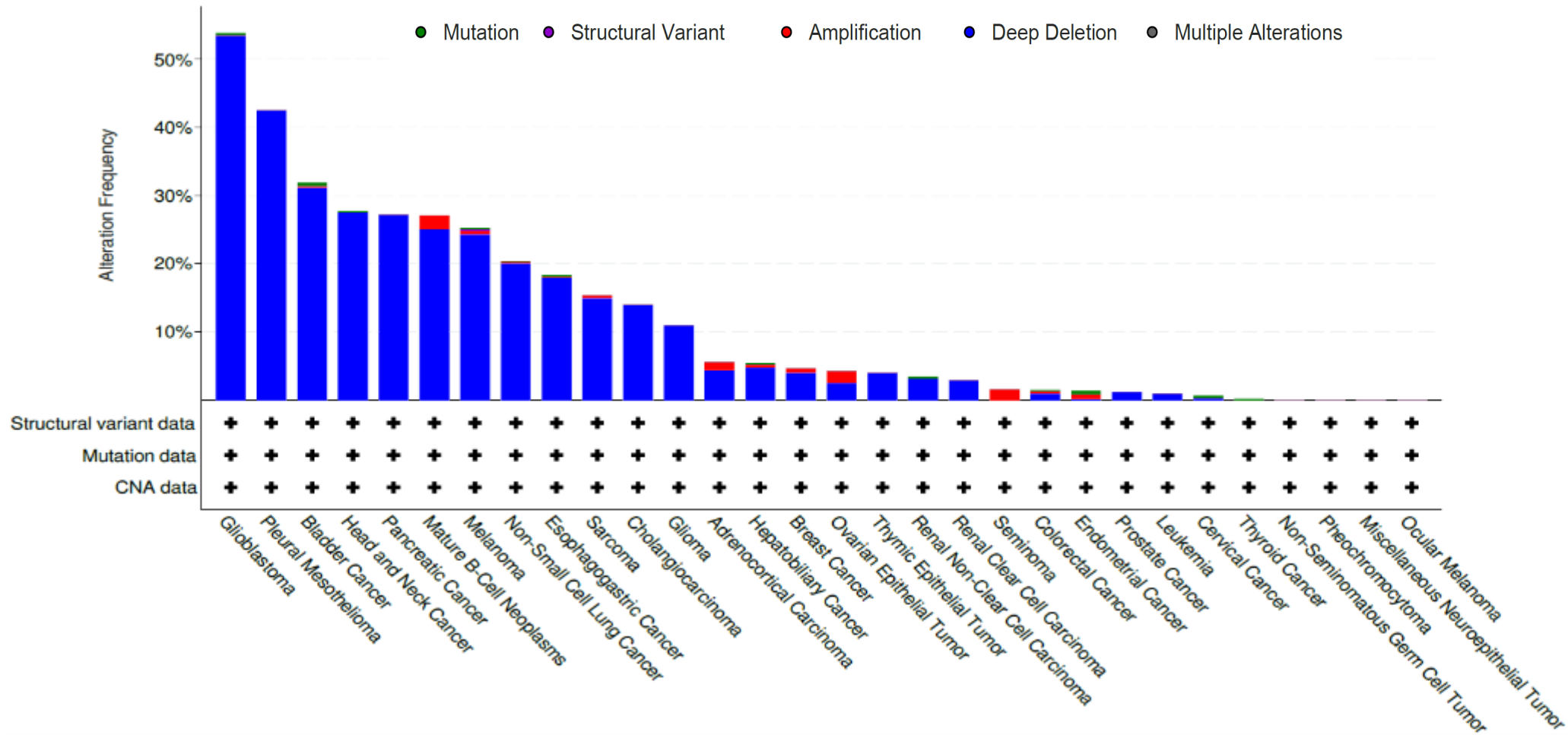


Solid tumors >10%: GBM, H&N, pancreas, esophagus, lung, bladder, HCC/BTC, breast, melanoma, sarcoma

Lymphoma: CDKN2A deletions in 46% of PTCL-NOS patients.



# CDKN2B Alterations



>10%: glioma, lung, bladder, H&N, pancreas, melanoma, esophagus, sarcoma, HCC/BTC, breast, ovarian

# Fadra Phase 1 DE Patient Groups (*n=11 had CDN2A/B abnormalities*)

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- Two **dose escalation** (DE) studies:
  - 065-01 IV (n=52)
    - 20/52 had sequencing data
    - 6/20 had CDKN2A and/or CDKN2B alterations
  - 065-101 oral (n=47)
    - 21/47 had sequencing data
    - 5/21 had CDKN2A and/or CDKN2B alterations

# Ph 1 DE Responder Profiles: CDKN2A/B Alterations *(retrospective review)*

Patient Study	Histology	Best Response (sum of target lesions)	Dose Level	Schedule	Mutation
<b>38</b> iv 065-01	Endometrial	<b>CR</b> (-100%)	213mg QD	2d/wk 2/3 wks	CDKN2A, CDKN2B, MTAP loss, MCL1 amp
<b>14</b> iv 065-01	Ovarian	<b>SD</b> (-2.5%)	192mg/m <sup>2</sup>	1d/3 wks	CDKN2A, CCNE1, MYC gain
<b>11</b> iv 065-01	Salivary gland	<b>SD</b> (0.8%)	128mg/m <sup>2</sup>	1d/3 wks	CDKN2A mutation & gain CDKN2B gain
<b>51</b> oral 065-101	NSCLC squamous	<b>SD</b> (-22%)	125mg BID	5d/wk 4/4 wks	CDKN2B loss
<b>21</b> oral 065-101	PTCL angiimmunoblastic	<b>PR</b> (-16%)	100mg BID	5d/wk 4/4 wks	CDKN2A mutation
<b>16</b> oral 065-101	Cholangio-carcinoma	<b>SD</b> (-5%)	75mg BID	5d/wk 4/4 wks	CDKN2A mutation
<b>55</b> oral 065-101	Pancreatic	<b>SD</b> (4%)	125mg BID	5d/wk 4/4 wks	CDKN2A loss
<b>62</b> oral 065-101	Sertoli germ cell testicular	<b>SD</b> (-12%)	150mg QD	7d/wk 4/4 wks	CDKN2A, CDKN2B, MTAP loss



# Oral Fadra 065-101 Ph 1/2 Solid Tumors & Lymphoma *(ongoing, unselected, late line)*

Enrolled n=47 as of March 26, 2024. No DLT in cohorts 1-5 (n=22). DL5=RP2D. PoC part to start next.

## Dose Escalation\* (3+3; unselected, all comor, late line; DL= dose level)

**DL6B (n=10)**  
150mg qd tabs 7d (4/4 wk) ✓

**DL6A (n=13)**  
125mg bid tabs M to F (4/4 wk) ✓

**DL6 (n=2)**  
150mg bid caps M to F (4/4 wk) ✓

**DL5 (n=9)**  
100mg bid caps M to F (4/4 wk) ✓

**DL4 (n=3)**  
100mg bid caps M to F (3/4 wk) ✓

**DL3 (n=3)**  
75mg bid caps M to F (3/4 wk) ✓

**DL2 (n=4)**  
50mg bid caps M to F (3/4 wk) ✓

**Starting DL (n=3)**  
50mg bid caps MWF (3/4 wk) ✓

## Proof of Concept (PoC)\*\* (Simon 2-stage; 2<sup>nd</sup> /3<sup>rd</sup> line)

**Cohort 1:** Endometrial, Ovarian

**Cohort 2:** Biliary / cholangiocarcinoma

**Cohort 3:** Hepatocellular Carcinoma

**Cohort 4:** Breast (post-CDK4/6i, TNBC, HER-2 refractory)

**Cohorts 5, 6:** Lymphoma (B-cell; T-cell) **N=2**

**Cohort 7:** mCRC (including KRAS mutated)

**Cohort 8 Basket:** biomarker selected  
(related MoA suspected; expand if PR seen) **N=12**

## Pivotal

(if randomized study not needed)

Single-arm, open label, study for n=TBD cancer patients in a histology from PoC

Pivotal indication to be determined based on clinical data from PoC

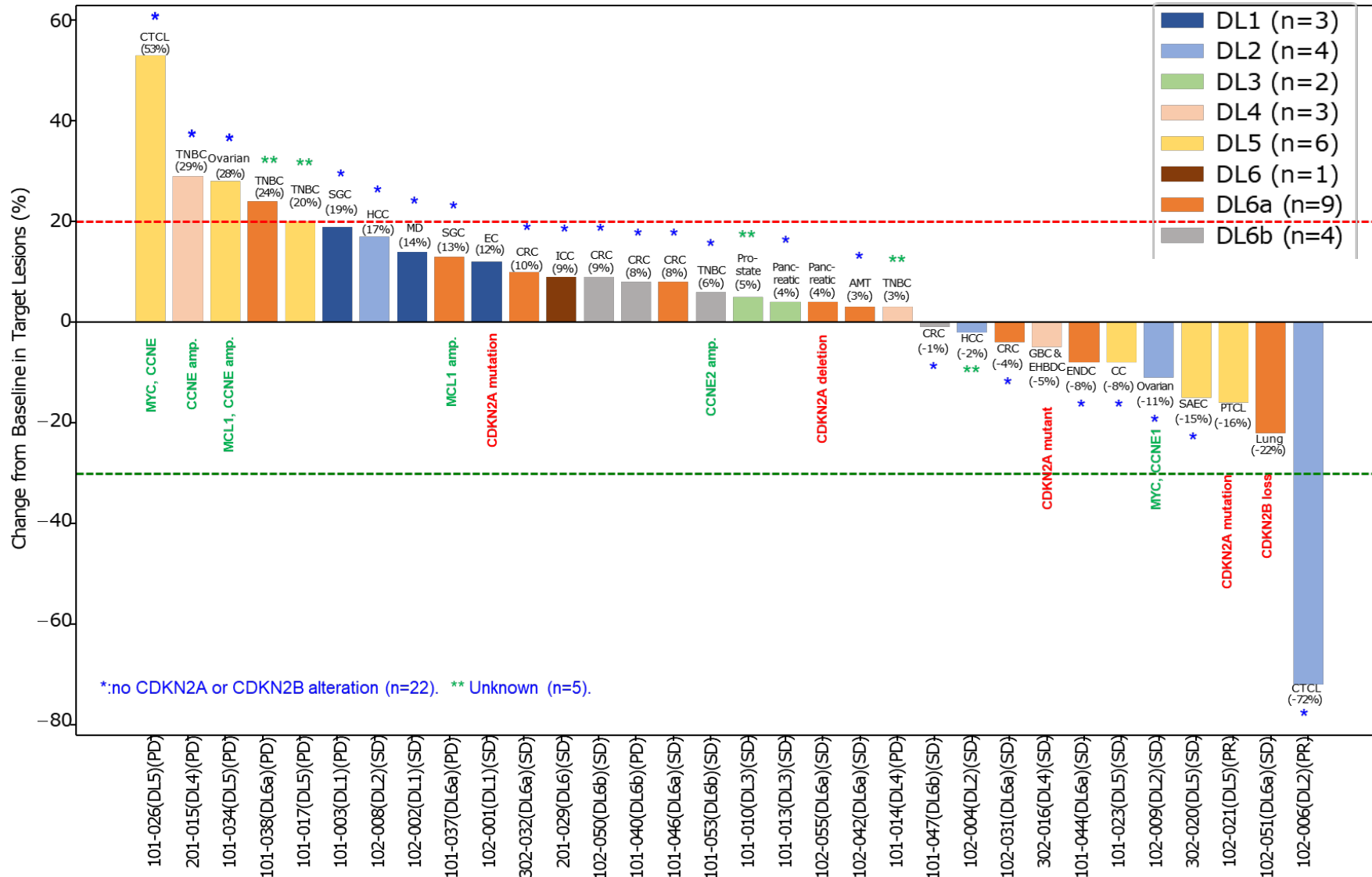
# Oral Fadra Ph 1 DE Safety Summary

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- All dose levels
  - Mostly grade 1 and 2 and reversible
    - Gastrointestinal disorders, including nausea, vomiting, diarrhea, and constipation
    - General, including fatigue
    - Metabolism, including hyperglycemia
    - Hematological, including platelet decrease
- Dose limiting toxicities (DLT) observed at 125mg BID and higher
  - Grade 3 nausea and hyperglycemia; both manageable and reversible
- Dose levels 1-5 were well tolerated with no DLTs reported

# Oral Fadra Ph 1 DE 065-101 Response (all comer, n=32, as of 31JAN24)

AMT = Appendix  
 CC = Cervix  
 CRC = Colon & Rectum  
 CTCL = Cutaneous T Cell Lymphoma  
 EC = Uterus  
 ICC = Intrahepatic bile ducts  
 GBC& EHBDC = Gallbladder and Extrahepatic bile ducts  
 ENDC = Endometrioid  
 MD = Mandible  
 SAEC = Serous Adenocarcinoma of the Endometrium  
 SGC = Salivary glands  
 HCC = Liver  
 TNBC = Triple-Negative Breast Cancer



**Evaluable for response by:**

- RECIST 1.1 (n=29)
- mSWAT (n=1)
- Lugano (n=2)

**PR (n=2)**  
**SD (n=21)**  
**PD (n=9)**

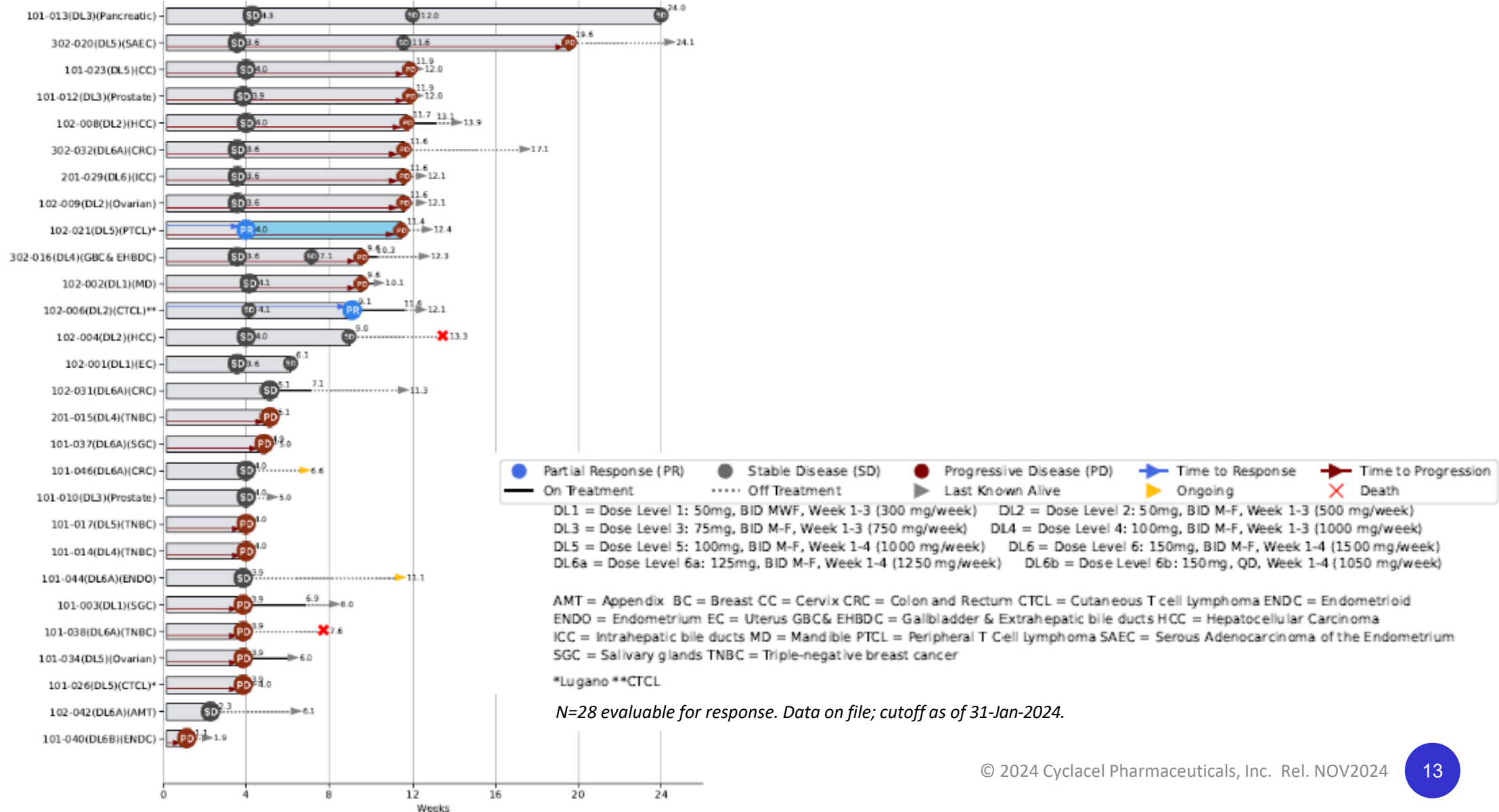
\*:no CDKN2A or CDKN2B alteration (n=22). \*\* Unknown (n=5).



Data on file. Best % change from baseline in target lesions. 101-012 (DL3) no measurable target lesions. \*Tumor assessments at 4 weeks post-treatment and every 8 weeks thereafter.

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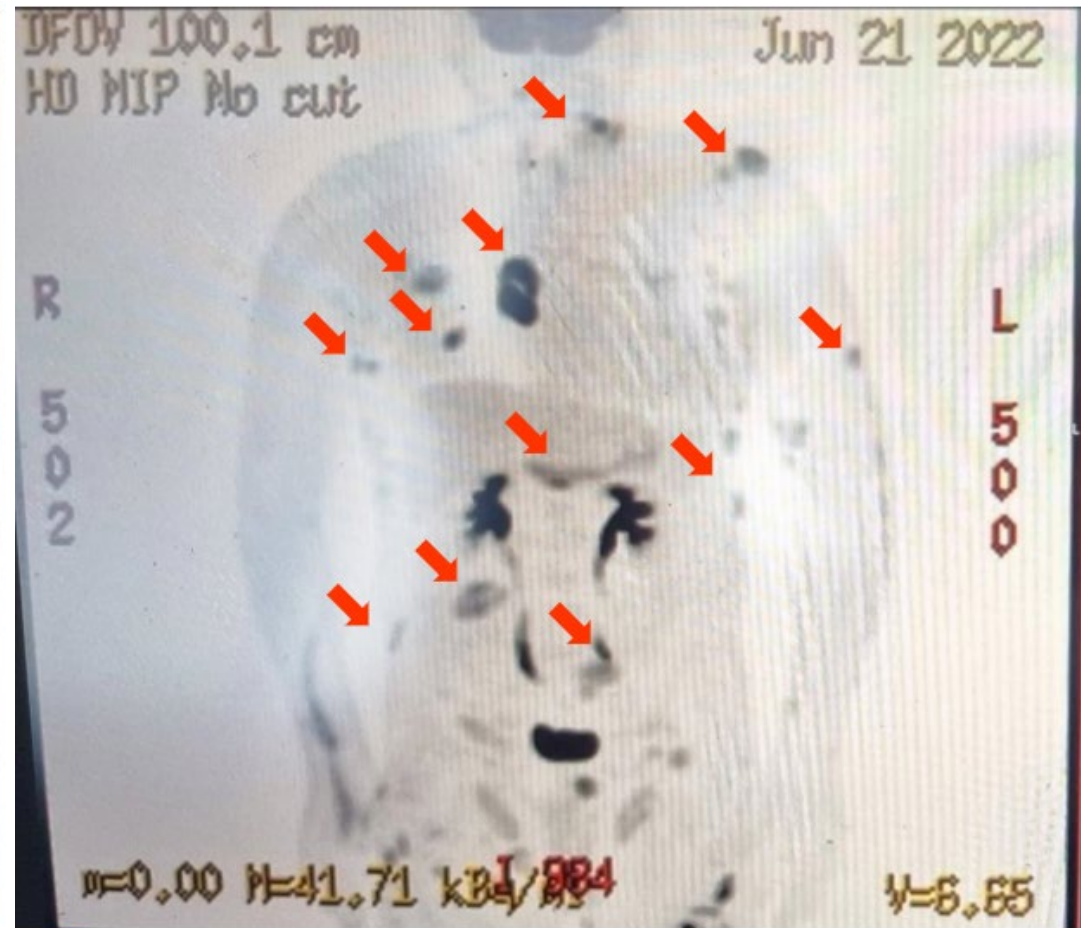
# Oral Fadra Ph 1 DE 065-101 Swimmers Plot (dose escalation part)



# PR in angioimmunoblastic PTCL pt. (oral 065-101 DE, 1<sup>st</sup> cycle, CDKN2A loss)



Baseline scan



Cycle 2 scan



# CDKN2A deletion in T Cell Lymphoma

ARTICLE

Non-Hodgkin Lymphoma



Ferrata Storti Foundation

## CDKN2A deletion is a frequent event associated with poor outcome in patients with peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)

Incidence of CDKN2A deletions was 46%.<sup>1</sup>

**Haematologica** 2021  
Volume 106(11):2918-2926

Francesco Maura,<sup>1,4</sup> Anna Doderò,<sup>5</sup> Cristiana Carniti,<sup>5</sup> Niccolò Bolli,<sup>2,5</sup> Martina Magni,<sup>5</sup> Valentina Monti,<sup>6</sup> Antonello Cabras,<sup>6</sup> Daniel Leongamornlert,<sup>3</sup> Federico Abascal,<sup>3</sup> Benjamin Diamond,<sup>1</sup> Bernardo Rodriguez-Martin,<sup>7</sup> Jorge Zamora,<sup>7</sup> Adam Butler,<sup>3</sup> Inigo Martincorena,<sup>3</sup> Jose M. C. Tubio,<sup>7</sup> Peter J. Campbell,<sup>3</sup> Annalisa Chiappella,<sup>8\*</sup> Giancarlo Pruneri<sup>2,6</sup> and Paolo Corradini<sup>2,5</sup>

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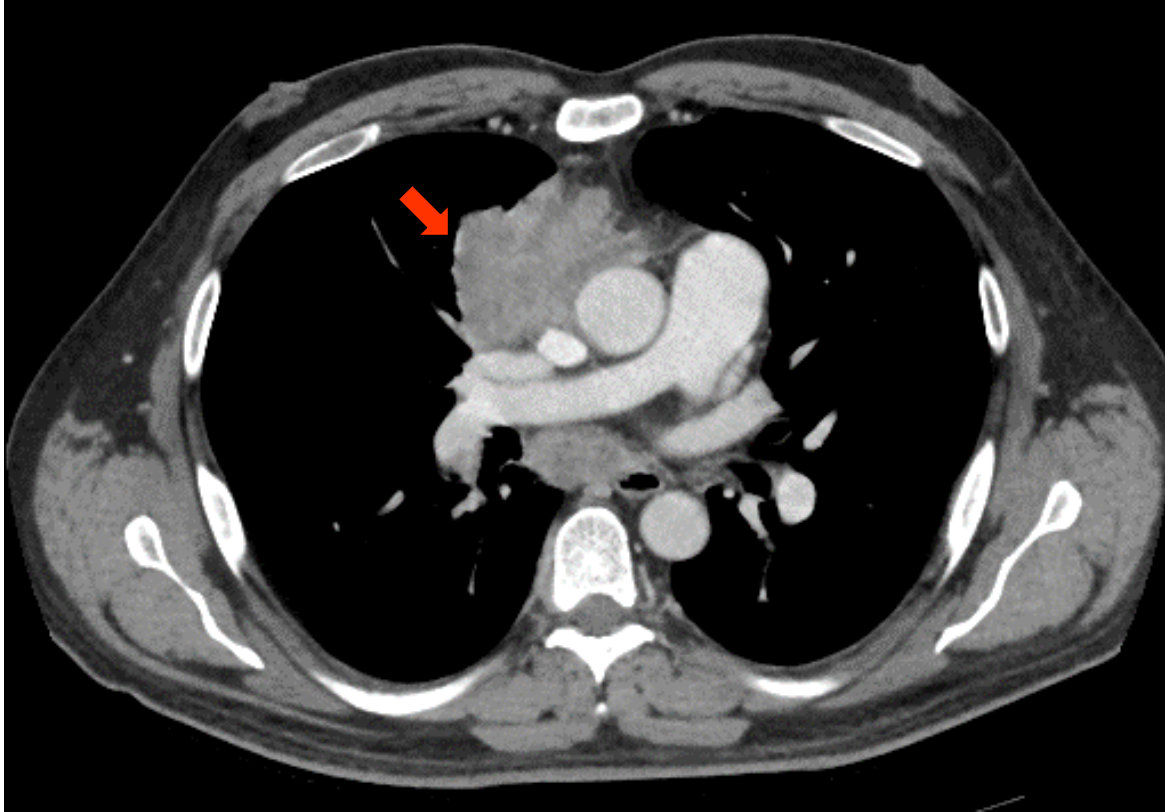
<sup>1</sup> Maura F et al *Haematologica*. 2021 Nov 1 106 11 2918.

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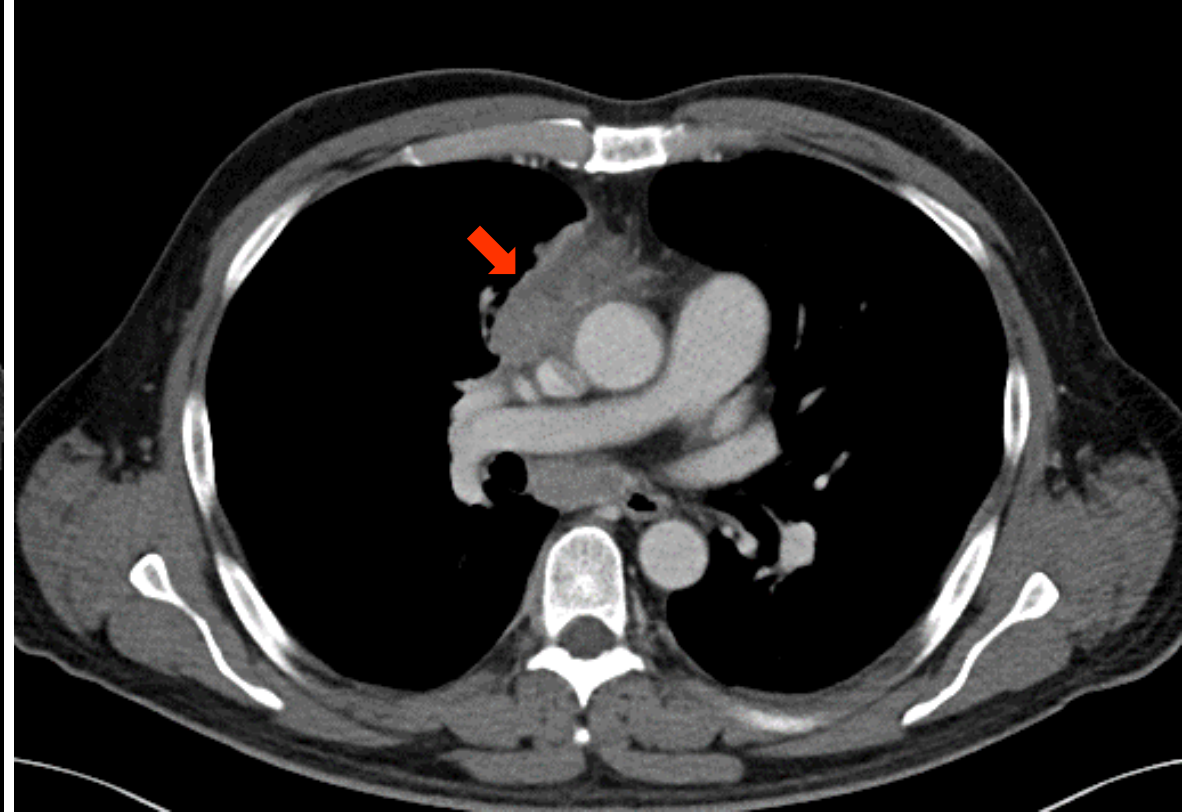


# Squamous NSCLC patient (oral 065-101, DE, 1 cycle DL6a)



Baseline scan 7-SEP-23

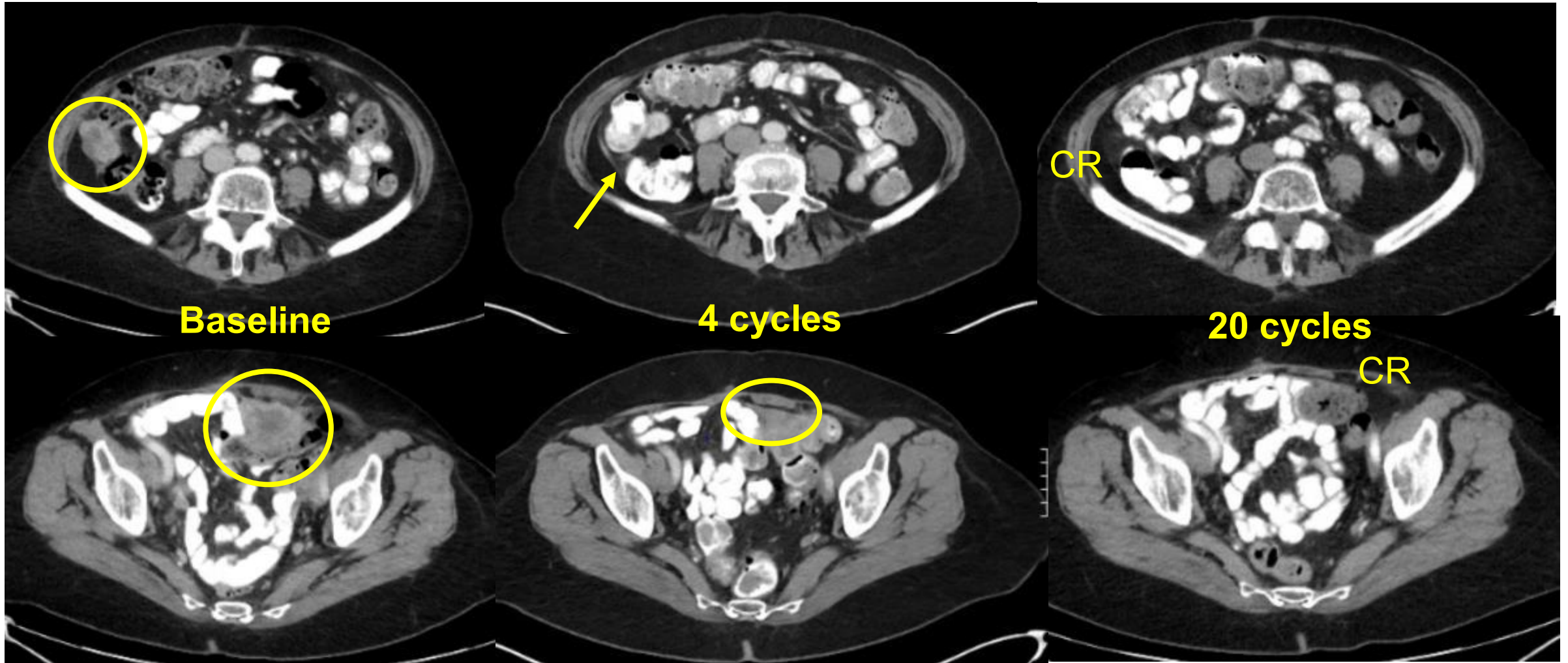
50y old, NOV22-APR23 carboplatin+paclitaxel;  
MAY23 atezolizumab+docetaxel, progressed



Cycle 1 scan 9-OCT-23

SD sum of all target lesions **-22%**. D1C1 14-SEP-23  
**NGS: CDKN2B loss**

# PR then CR Endometrial Pt (065-01 Part 2 IV with CDKN2A, CDKN2B and MTAP loss)



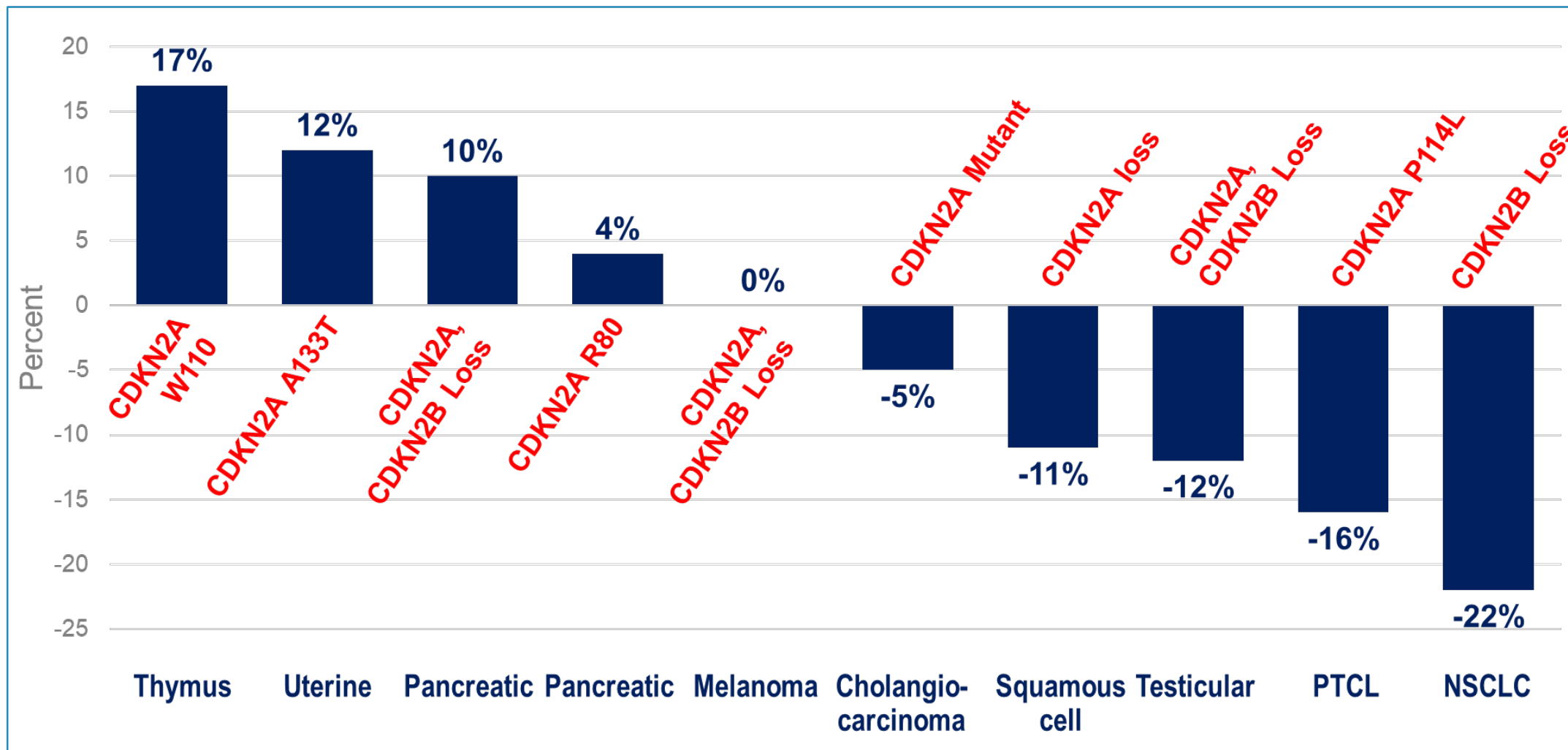
# Oral Fadra Expansion Cohort 8: RELATED TEAE (N=12)

System Organ Class (SOC)/Preferred Term (PT)	n (%)	Any G	G1	G2	G≥3
<b>Patients with at least 1 related TEAE</b>		<b>7 (58.3)</b>	<b>3 (25.0)</b>	<b>4 (33.3)</b>	<b>0</b>
Gastrointestinal disorders	5 (41.7)	3 (25.0)	2 (16.7)	2 (16.7)	0
Diarrhoea	2 (16.7)	0	0	2 (16.7)	0
Nausea	2 (16.7)	2 (16.7)	0	0	0
Vomiting	2 (16.7)	2 (16.7)	0	0	0
Investigations	2 (16.7)	1 (8.3)	1 (8.3)	0	0
Blood creatinine increased	1 (8.3)	0	0	1 (8.3)	0
Platelet count decreased	1 (8.3)	1 (8.3)	0	0	0
Metabolism and nutrition disorders	2 (16.7)	1 (8.3)	1 (8.3)	0	0
Hypocalcaemia	2 (16.7)	1 (8.3)	0	1 (8.3)	0
Hyperglycaemia	1 (8.3)	0	0	1 (8.3)	0
Hypokalaemia	1 (8.3)	0	0	1 (8.3)	0
General disorders & administration site conditions	1 (8.3)	0	0	1 (8.3)	0
Asthenia	1 (8.3)	0	0	1 (8.3)	0
Nervous system disorders	1 (8.3)	1 (8.3)	0	0	0
Dysgeusia	1 (8.3)	1 (8.3)	0	0	0
Psychiatric disorders	1 (8.3)	1 (8.3)	0	0	0
Insomnia	1 (8.3)	1 (8.3)	0	0	0
Renal and urinary disorders	1 (8.3)	1 (8.3)	0	0	0
Renal failure	1 (8.3)	1 (8.3)	0	0	0
Vascular disorders	1 (8.3)	1 (8.3)	0	0	0
Hypotension	1 (8.3)	1 (8.3)	0	0	0

## Oral Fadra Expansion Anticancer Activity *(interim data; ongoing)*

	<b>N</b>	<b>PR</b>	<b>SD</b>	<b>PD</b>	<b>ORR</b>	<b>DCR</b>
<b>Dose Escalation</b>	<b>6</b>	<b>1</b>	<b>5</b>	<b>-</b>	<b>17%</b>	<b>100%</b>
<b>Expansion <i>(interim data, ongoing)</i></b>	<b>6</b>	<b>-</b>	<b>2</b>	<b>4</b>	<b>0%</b>	<b>33%</b>
<b>Total <i>(interim data, ongoing)</i></b>	<b>12</b>	<b>1</b>	<b>7</b>	<b>4</b>	<b>8%</b>	<b>67%</b>

# Oral Fadra Expansion Cohorts: Best % Change in Target Lesions (from baseline, all response types)





# Potential for Oral Fadra as Precision Medicine

Single agent responses and broad activity in liquid and solid cancers

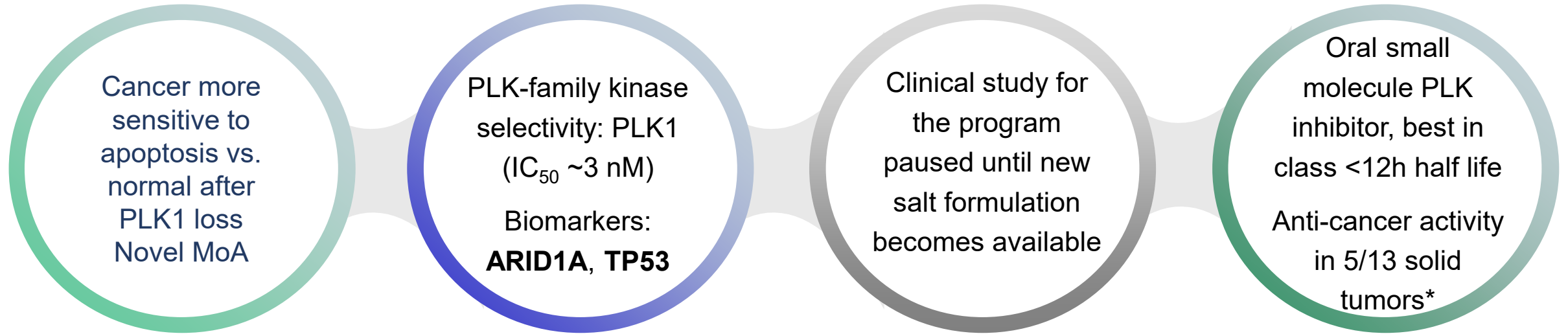
CDK2 + CDK9 inhibition may be superior to either CDK2 or CDK9

- Cancer cells adapt to CDK2i; CDK2i work better if CDK9i silences MYC
- Exploiting CDKN2A/B vulnerability for precision medicine strategy
- **Fadra** unusual next gen CDKi; has threaded the needle of transient suppression of anti-apoptosis proteins without broad hematological toxicity





# Plogosertib (CYC140) Next Gen PLK1 inhibitor

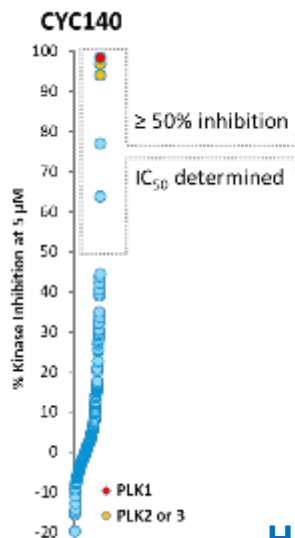


Novel mechanism with a unique **mutational** strategy  
**Targeting ARID1A and TP53 Mutated Cancers**

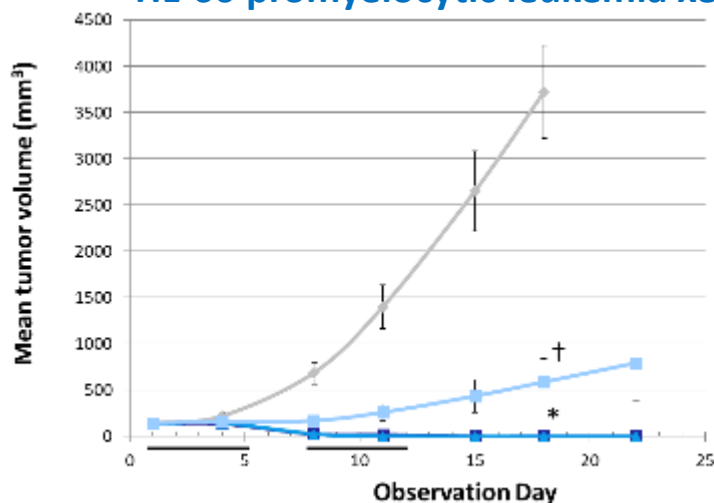
# Plogo Preclinical Activity

## Kinase Profile

Kinase	CYC140 IC <sub>50</sub> (nM)	PLK1 Selectivity (fold)
PLK1	2.7	1
PLK2	155	58
EIF2AK3	292	109
PLK3	297	112
CaMK2δ	1630	612
DAPK1	2860	1074



## HL-60 promyelocytic leukemia xenograft

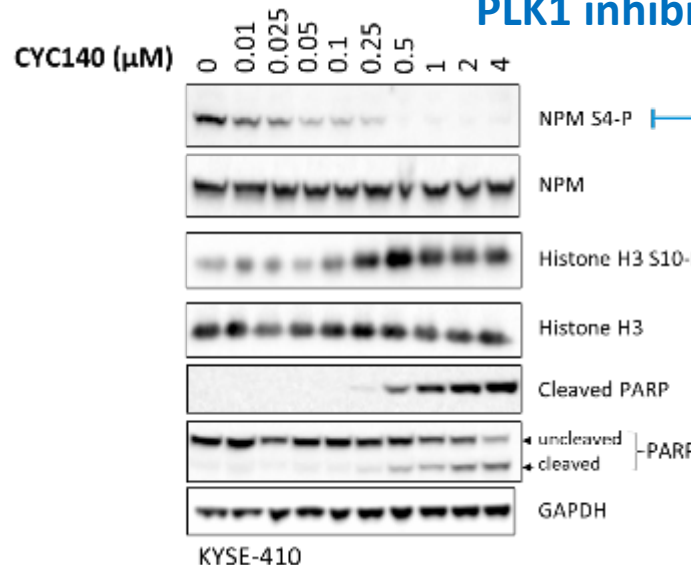


- Vehicle
- CYC140 67 mpk po qd 5/2/5
- ▲ CYC140 54 mpk po qd 5/2/5
- ◆ CYC140 40 mpk po qd 5/2/5

† 13% T/C (4/10 CR)  
P < 0.0001

\* 0% T/C (10/10 CR)  
P < 0.000001

## PLK1 inhibition



CYC140 treatment

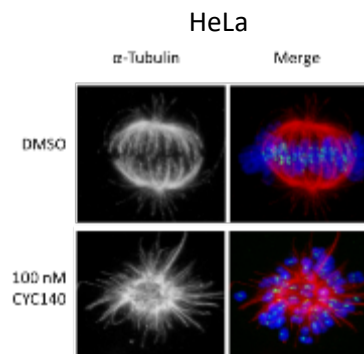
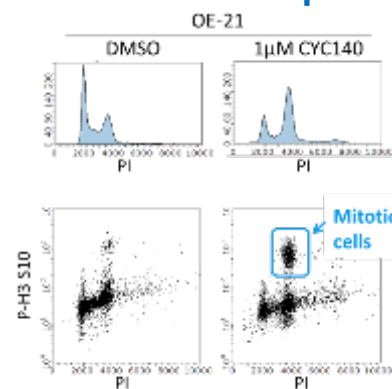
PLK1 inhibition

Mitotic arrest

Inhibition of cell proliferation and induction of cell death

NPM: 2 h CYC140, assay at 2 h.  
H3: 6 h CYC140, assay at 24 h.  
PARP & GAPDH: 6 h CYC140, assay at 72 h.

## CYC140 increases mitotic cell number and induces monopolar spindle formation



# PLK Inhibitors in Clinical Development

## Volasertib

(Boehringer Ingelheim;  
i.v. BI-6727 discontinued)

- BTD in AML Ph2 data; but Ph 3 POLO-1 in AML failed; imbalance of deaths likely due to myelosuppression; long terminal half-life ~110h
- Dose intensity led to single agent activity
- Epigenetic activity incl. BRD4 inhibition

## Onvansertib

(Cardiff; p.o., selectivity primarily PLK1, secondarily CDK9, etc.\*)

- Signal in KRASmut mCRC with bevacizumab/FOLFIRI; terminal  $t_{1/2}$  ~24h
- Ph 1b: *AML w/chemo; prostate w/ abiraterone*; mPDAC w/chemo; SCLC
- Ph 2: mCRC 3 arm RCT 2 doses triplet therapy vs control bevacizumab/chemo (n=90)

## Plogosertib

(Cyclacel; p.o., selectivity primarily PLK1, secondarily PLK2, PLK3)

- Preclinical activity in multiple solid tumors and leukemias; terminal  $t_{1/2}$  ~11h
- Single agent anticancer activity in NSCLC, ovarian, biliary, ACC, etc. (4 dose levels)
- Epigenetic MoA incl. BRD4 inhibition: modulating novel cancer pathways

# Plogo 140-101 Oral Ph1/2 Ongoing in Solid Tumors & Lymphoma

## Dose Escalation\* (3+3; all comer, late line; DL=dose level)

**DL7 (n=3)**  
20mg qd M to F (wk 1 to 3)

**DL6 (n=3)**  
20mg qd M to F (wk 1 & 3)

**DL5 (n=3)**  
15mg qd M to F (wk 1 to 3)

**DL4 (n=3)**  
15mg qd M to F (wk 1 & 3)

**DL3 (n=3)**  
10mg qd M to F (wk 1 to 3)

**DL2 (n=3)**  
10mg qd M to F (wk 1 & 3)

**Starting DL (n=3)**  
5mg qd M to F (wk 1 to 3)

Active



**Schedule:** 3 out of 4 wk per cycle.

## Proof of Concept (PoC)\*\* (Simon 2-stage; 2<sup>nd</sup> /3<sup>rd</sup> line)

**Cohort 1:** Bladder cancer

**Cohort 2:** Breast cancer (TNBC)

**Cohort 3:** Lung cancer (NSCLC and SCLC)

**Cohort 4:** Hepatocellular carcinoma (HCC) and biliary tract cancer

**Cohort 5:** Metastatic colorectal cancer (mCRC) including KRAS-mutated

**Cohort 6:** B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL)

**Cohort 7:** T-cell lymphoma (CTCL/PTCL)

**Cohort 8 Basket:** tumors suspected to have related MoA (expand if responses)

## Pivotal (if randomized study not needed)

Single-arm, open label, study for n=TBD cancer patients

Indication in pivotal study to be determined based on clinical data from PoC

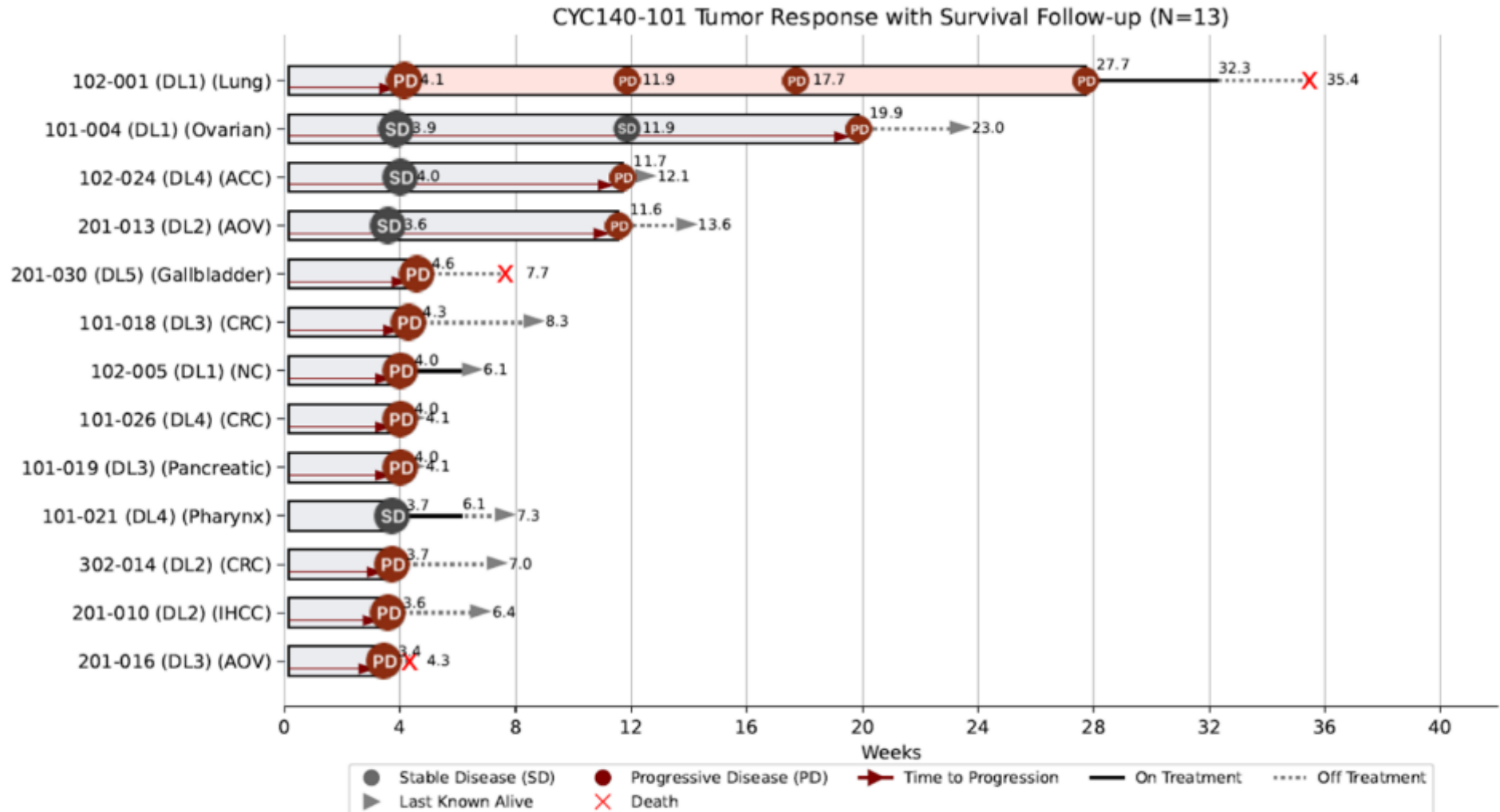


# Oral Plogo Well Tolerated up to Dose Level 5

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- Drug-related adverse events reported, mostly grade 1 and 2 and reversible
  - General including fatigue
  - Hematological: anemia
  - Investigations: mild transaminase increase
- No dose limiting toxicities observed to date

# Plogo Oral 140-101 DL1-4 Swimmers Plot (*dose escalation ongoing*)

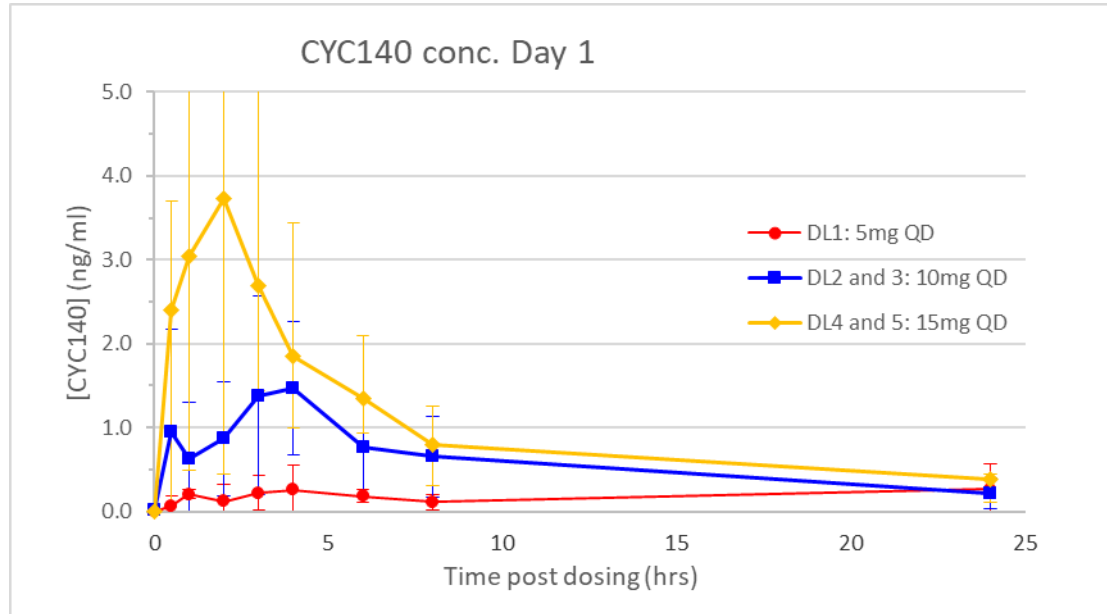


DL1 = Dose Level 1: 50mg, BID MWF, Week 1-3 (300 mg/week) DL2 = Dose Level 2: 50mg, BID M-F, Week 1-3 (500 mg/week) DL3 = Dose Level 3: 75mg, BID M-F, Week 1-3 (750 mg/week)  
 DL4 = Dose Level 4: 100mg, BID M-F, Week 1-3 (1000 mg/week) DL5 = Dose Level 5: 100mg, BID M-F, Week 1-4 (1000 mg/week)  
 ACC = Adenoid Cystic Carcinoma (Salivary glands) AOV = Ampulla of Vater CRC = Colon and Rectum IHCC = Intrahepatic cholangiocarcinoma NC = NUT carcinoma (Paranasal sinuses)  
 Data cutoff date: 2023-10-02

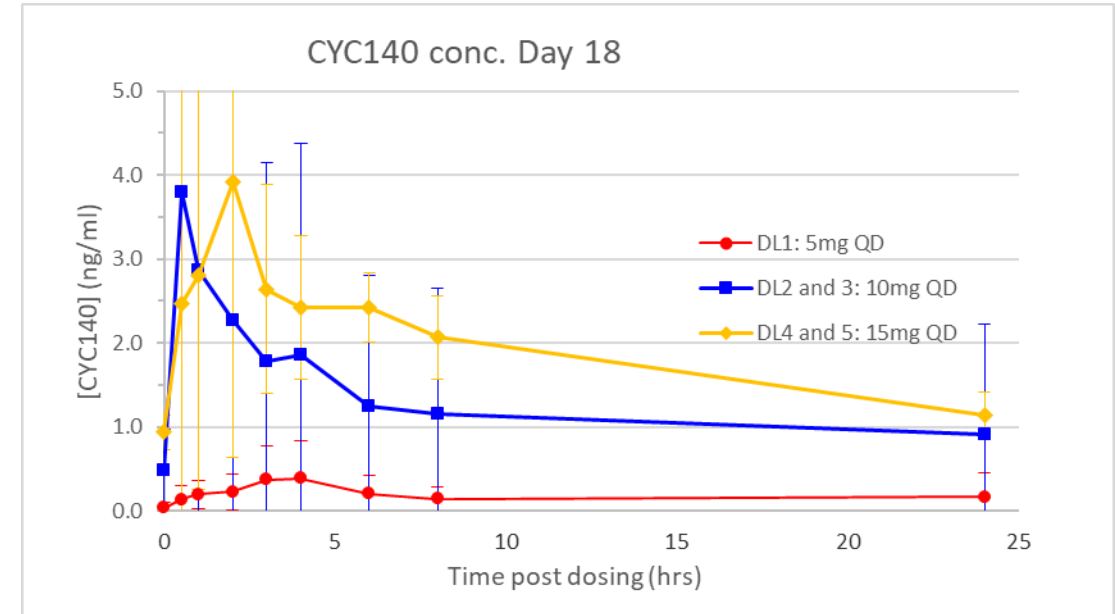


# Mean ( $\pm$ SD) Plasma Plogo Concentration-Time Plot C1D1 & C1D18

Day 1



Day 18



Based on preclinical modeling data, efficacious doses yet to be achieved.

# Plogo Conventional Dose Escalation Strategy

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## Potential activity across mechanistically relevant tumors

- Specific mutations in SWI/SNF complex subunit proteins, incl. ARID1A, SMARCA, etc.
- Novel targets in molecular pathways with unmet medical need
- Could lead to patient selected, biomarker driven Ph1 expansion group

Preclinical sensitivity data from world-class laboratories in CRC, lymphoma, melanoma, ovarian, SCLC.

Requires updated formulation to increase exposure levels

Increased patent exclusivity to 2040

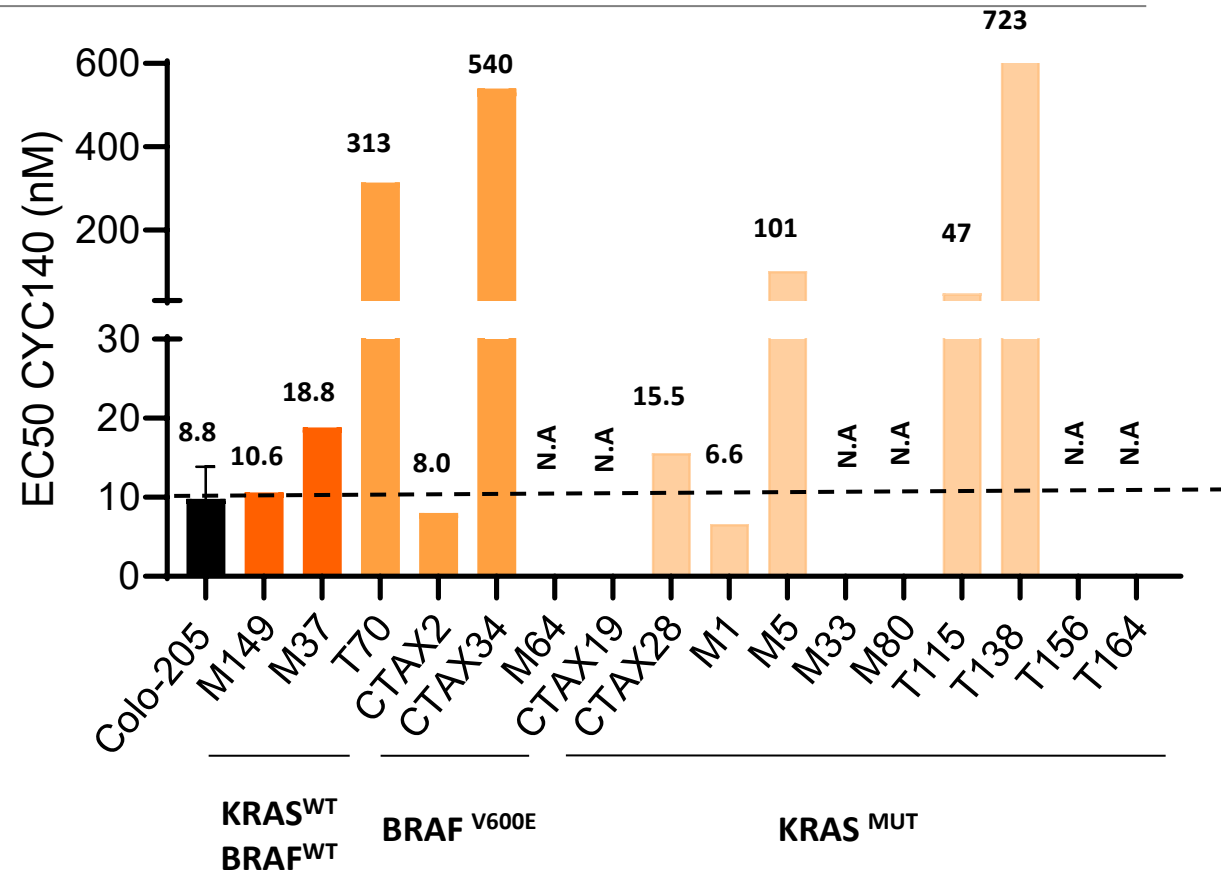
# Colorectal PDX Organoid Sensitivity to Plogo

*In vitro* 3D models from 16 CRC PDX

- 10 KRAS<sup>mut</sup>, 3 BRAF<sup>V600E</sup>, 3 KRAS<sup>WT</sup>/BRAF<sup>WT</sup>
- Completed EC<sub>50</sub> by cell viability (19-point dose curve: 0.038 nM – 10 μM)

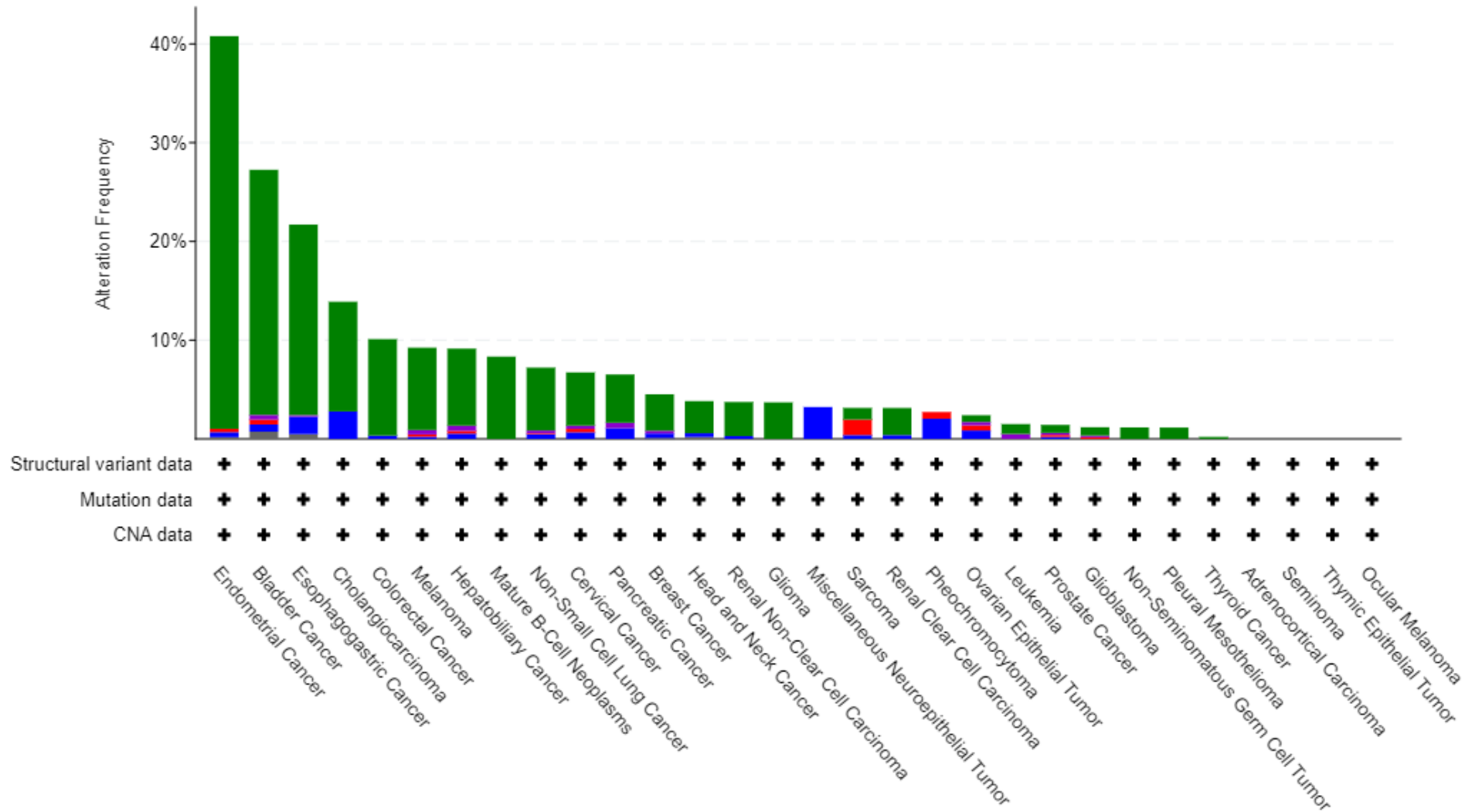
Sensitivity to plogo:

- 5 models with EC<sub>50</sub> < 30 nM
- Does not appear BRAF or KRAS dependent
- None of resistant are ARID1A mut
- **3/5 sensitives are ARID1A mutant**
- **5/5 sensitives are TP53 mutant**



	KRAS <sup>WT</sup> BRAF <sup>WT</sup>		BRAF <sup>V600E</sup>		KRAS <sup>MUT</sup>					
<b>PDXO</b>	CTAX 19	CTAX 28	M1	M5	M33	M80	T115	T138	T156	T164
<b>KRAS</b>	G12D	G12D	G12D	G13D	G12D	G12C	G12V	G12V	G12C	G12V

# ARID1A Modifications



Solid tumors >15%:  
 endometrial, bladder,  
 esophagus, bile duct,  
 colorectal

# Plogo Low Dose Strategy

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Epigenetic hypothesis

**Plogo** enables **chromatin accessibility** at low concentrations

Combination strategy with other epigenetic modulators

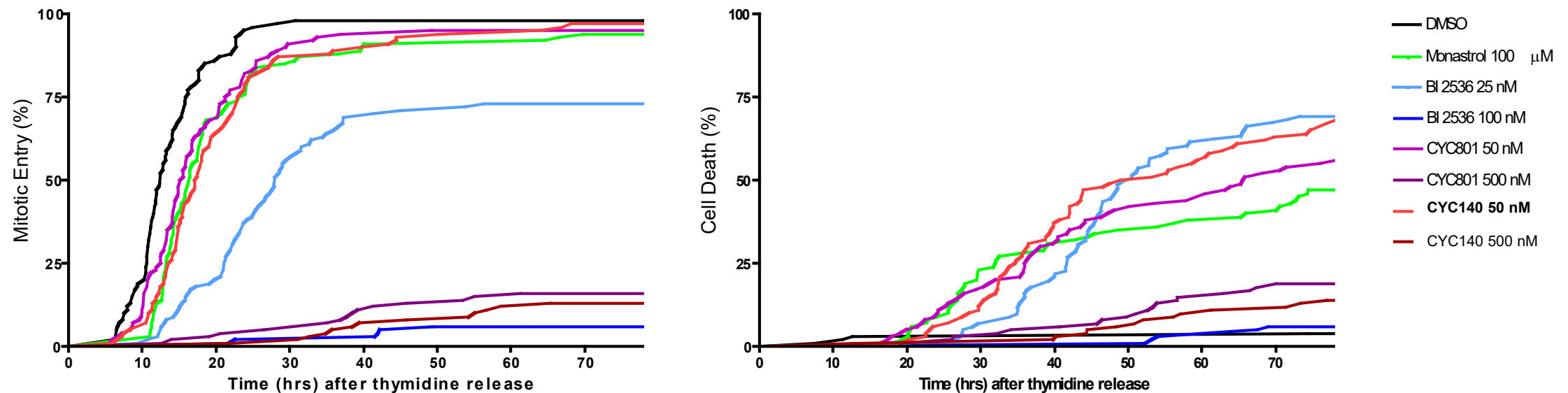
- Hypomethylating agents or HDAC Inhibitors

Can use current formulation

Front line opportunity in TP53 mutated AML

# Optimizing PLK1i Exposure May Enhance Cell Death Induction – Rationale for Lower, Prolonged Dosing

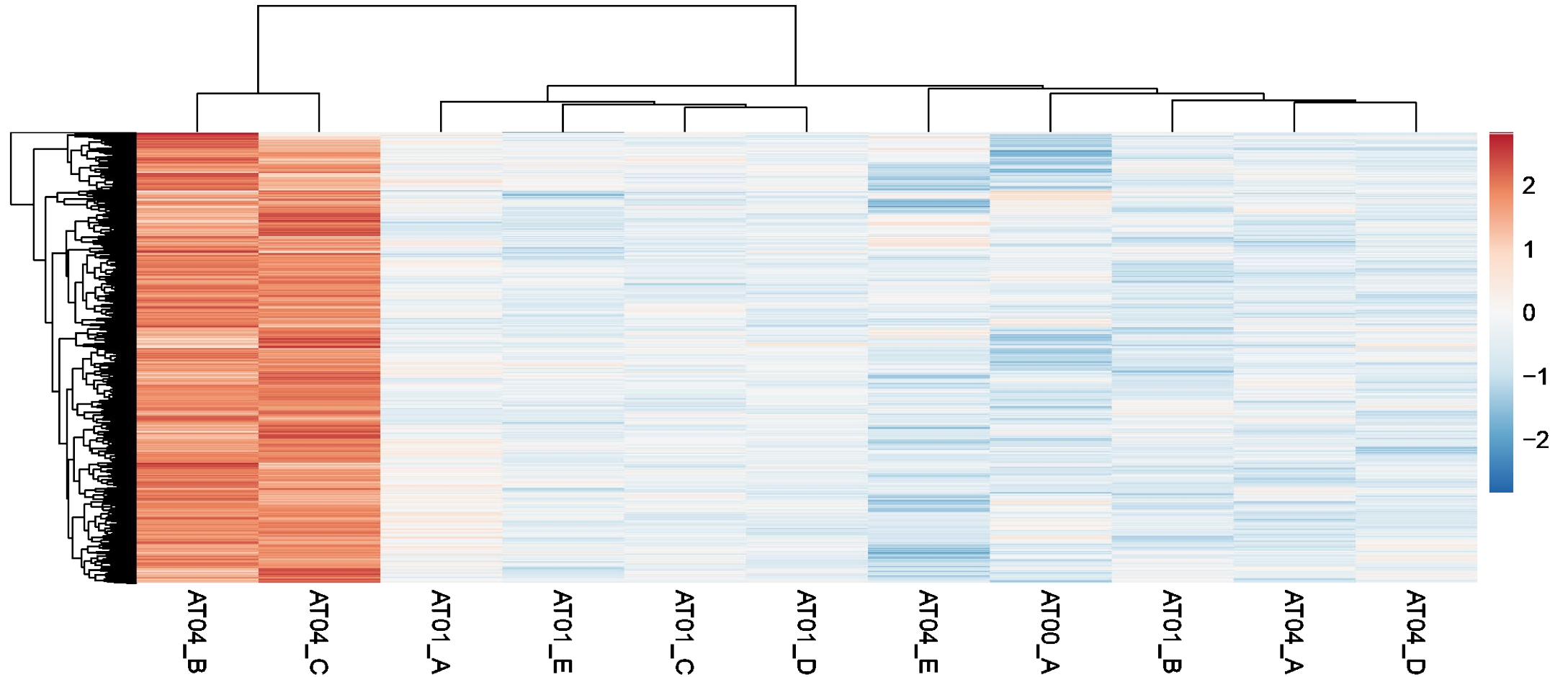
## RKO colon carcinoma cell line - Single thymidine block and release prior to treatment



At high doses, PLK1i treatment stops growth; at lower doses PLK1i starts cell cycle and then more tumor cells die.

# Low Dose Plogo has Dramatic Effect on Chromatin Access

ATAC-Seq to Discover Enhancers  
and Transcription Factor Motifs  
A=0, B=1, C=5, D=10, E=200nM



**Red: open & transcribing segments. Blue: closed chromatin segments**



# TP53 Mutated AML Unmet Need

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TP53 mutated patients do not benefit from 1L AML Standard of Care:

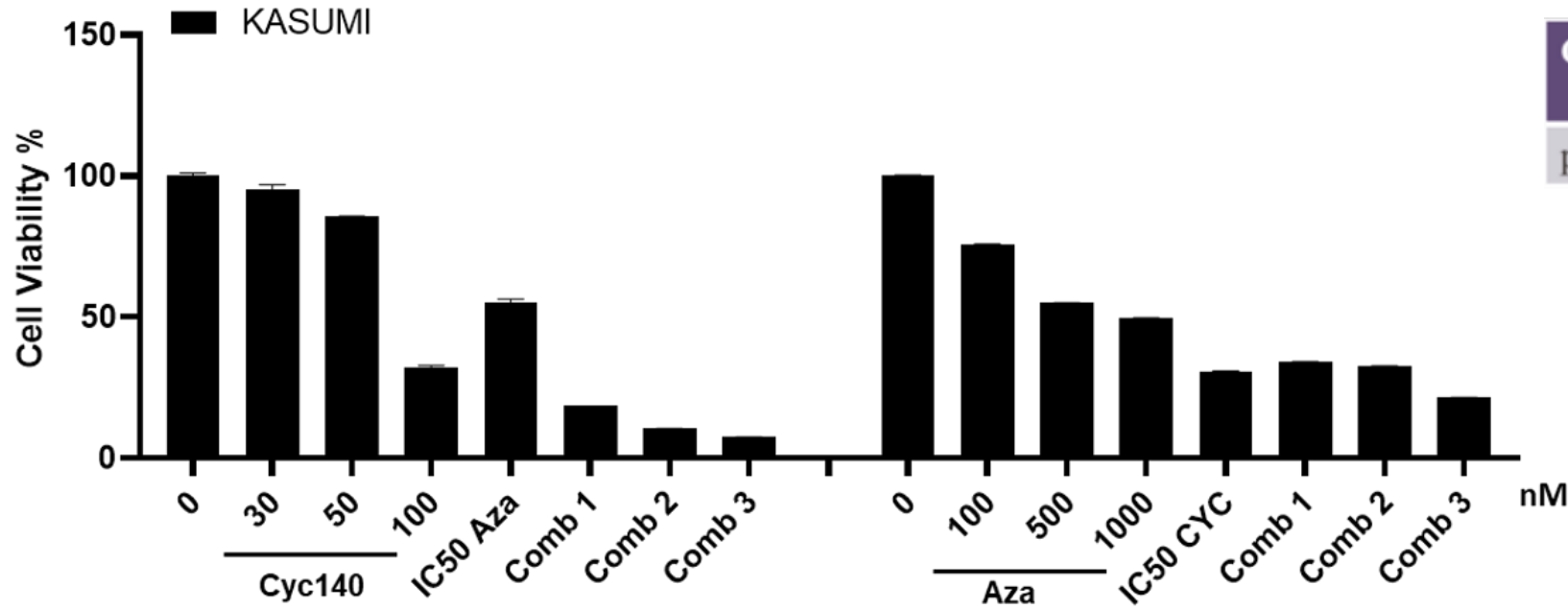
- venetoclax + azacitidine; poor OS

Ethical to test as 1L treatment in a single arm study

Large unmet medical need

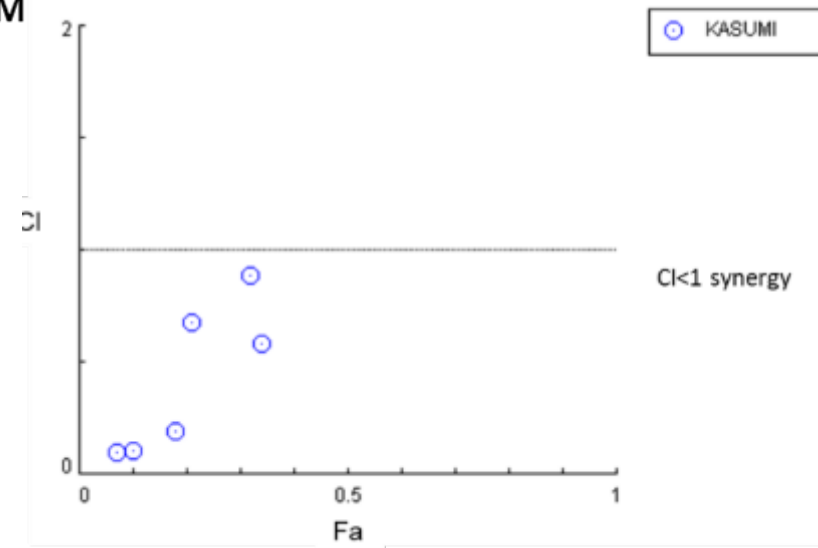
Excellent opportunity for disease modifying treatment

# Preclinical Plogo (aka CYC140) + Aza Activity in AML



Cell lines	CYC IC50	AZA IC50
p53 mut KASUMI	112 nM	415 nM

Dose cyc (nM)	Dose aza (nM)	Effect	CI
112.0	100.0	0.34	0.58177
112.0	500.0	0.32	0.88934
112.0	1000.0	0.21	0.67775
30.0	415.0	0.18	0.19355
50.0	415.0	0.1	0.10447
100.0	415.0	0.07	0.09959



# Financial Position & Capitalization

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Cash equivalents: **\$6.0 million** (as of June 30, 2024)<sup>1</sup>

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Operating cash burn (excludes non-cash items):

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- ✓ 2023 Annual: \$16.1 million<sup>1</sup>
  - ✓ 6 months ended June 30, 2024: \$4.3 million<sup>1</sup>
- 

Fully diluted shares: 18.1 million<sup>1</sup>

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Estimated capital into Q4 2024<sup>1</sup>

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Nasdaq compliance with stockholder equity rule; extension granted to December 24, 2024<sup>2</sup>

# Milestone Momentum \*

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- ✓ **Fadra** initial Phase 2 data in cohort with CDKN2A/B abnormalities 2H 24
- **Fadra** initial lymphoma cohort data 1H 25
- **Fadra** final Phase 2 data in cohort with CDKN2A/B abnormalities 2H 24
- **Fadra** complete tablet manufacture and validation 1H 25
- **Plogo** alternative salt formulation clinical supply availability



**Thank You**

**Cyclacel Pharmaceuticals, Inc.**

200 Connell Drive #1500  
Berkeley Heights, NJ 07922

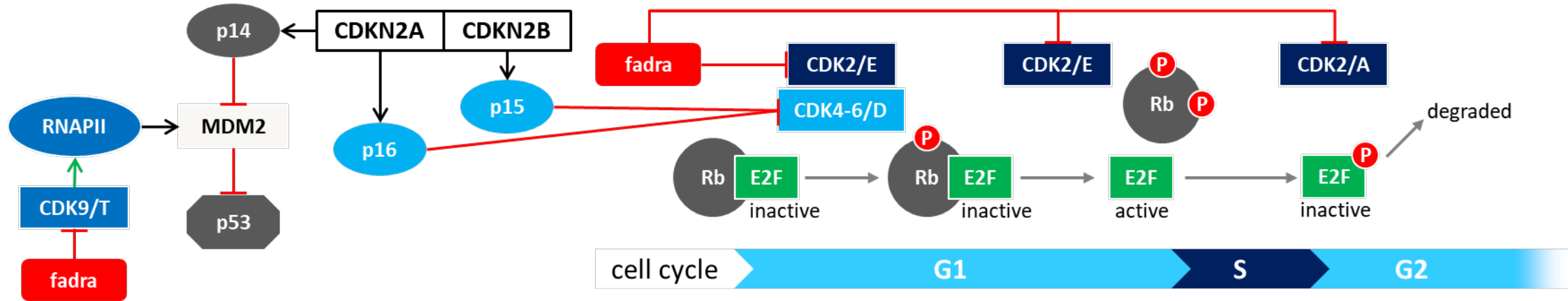
**Contact:** [ir@cyclacel.com](mailto:ir@cyclacel.com)  
+1 (908) 517 7330

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# Appendix



# CDKN2A/B Genetic Abnormalities and Fadra MoA



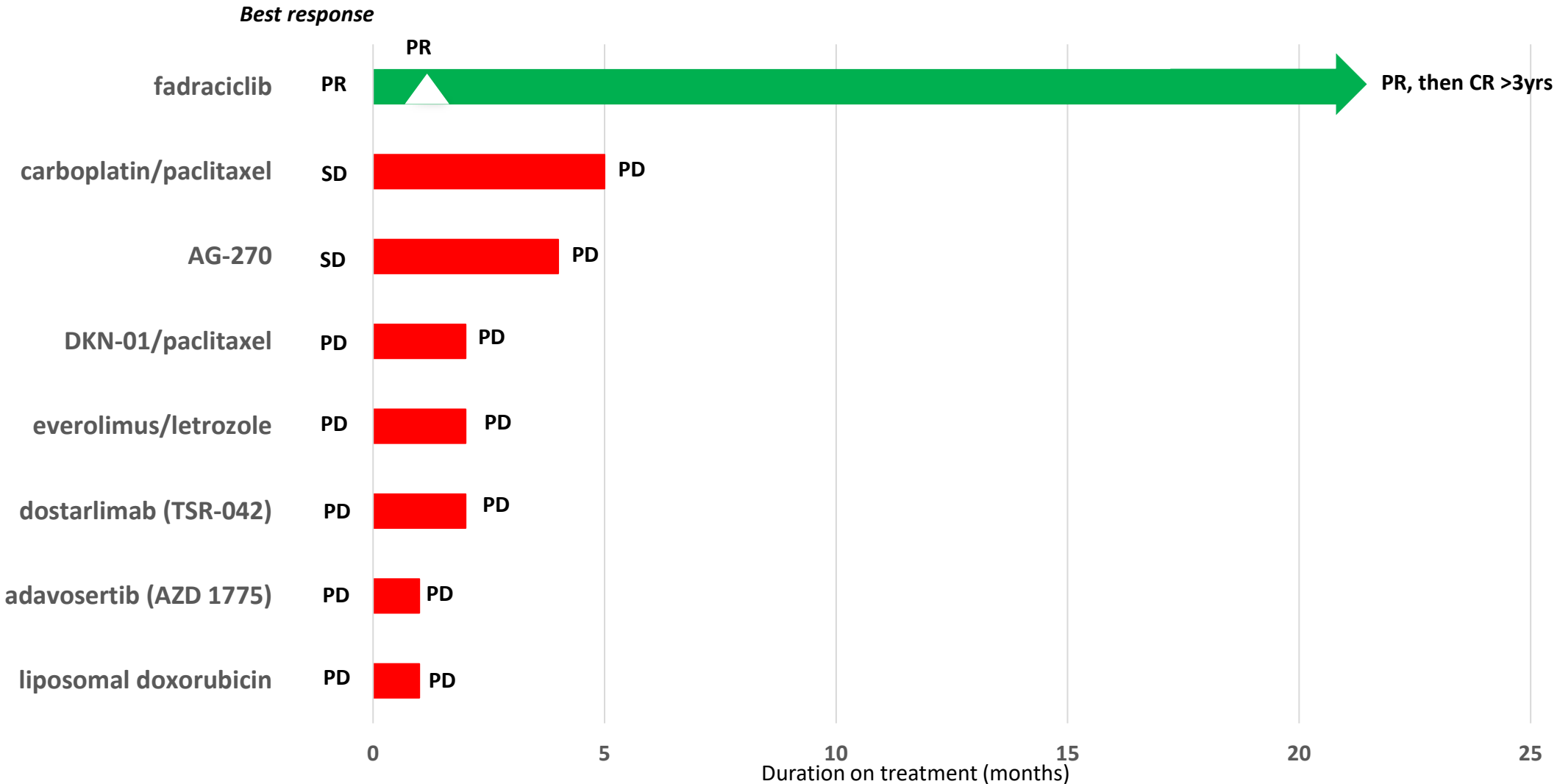
*CDKN2A* encodes p16<sup>INK4a</sup>, *CDKN2B* p15<sup>INK4b</sup> which inhibit D-type cyclin complexes w/ CDK4 & CDK6

- Dysregulated CDK4/6 drive cancer progression, proliferation in G1, suggesting a role for CDK4/6 inhibition
- Abemaciclib (CDK4/6i) activity in *CDKN2A* mutant cells is limited by **CDK2 bypass** of CDK4/6 inhibition <sup>1</sup>

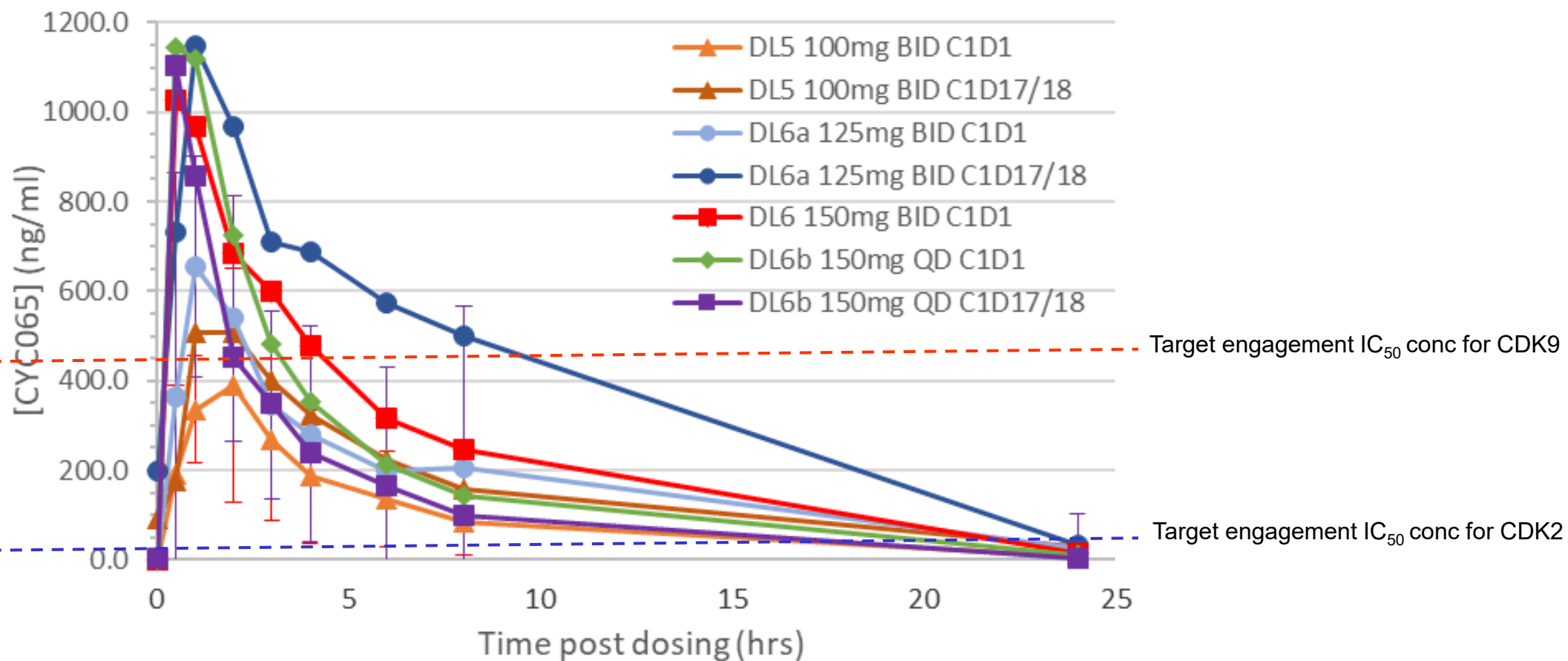
*CDKN2A* also encodes p14<sup>ARF</sup>, which disrupts MDM2-directed degradation of p53; suppression of MDM2 expression by **CDK9i** may compensate for loss of this activity

No approved drugs for patients with *CDKN2A*/ *CDKN2B* abnormalities

# Endometrial Patient History 065-01 Part 2 IV

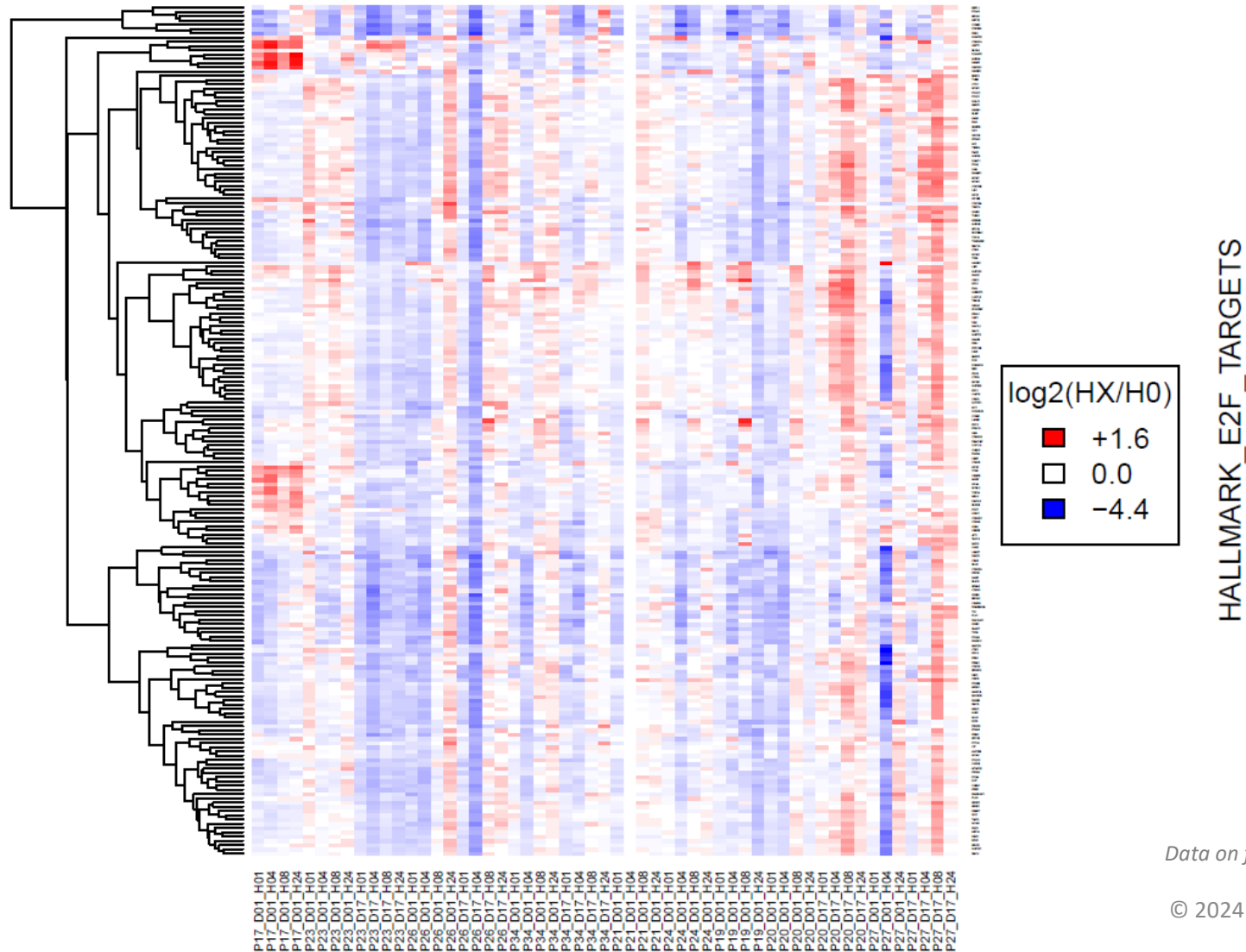


# Dose Proportional PK with CDK2 and 9 Coverage at Higher Dose Levels



# Fadra Suppresses E2F (CDK2 dependent) DL5 Phase 1 Patients

## Gene expression levels CYC065-101 DL5



Data on file. Blue=suppression, Red=overexpression.

