Translating cancer biology into medicines

Cyclacel Pharmaceuticals, Inc. (CYCC) BIOTECH SHOWCASE JANUARY 2024

Disclaimer

This presentation contains certain forward-looking statements that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, the efficacy, safety and intended utilization of Cyclacel's product candidates, the conduct and results of future clinical trials, plans regarding regulatory filings, future research and clinical trials and plans regarding partnering activities. Factors that may cause actual results to differ materially include the risk that product candidates that appeared promising in early research and clinical trials do not demonstrate safety and/or efficacy in larger-scale or later clinical trials, trials may have difficulty enrolling patients, Cyclacel may not obtain approval to market its product candidates, the risks associated with reliance on outside financing to meet capital requirements, and the risks associated with reliance on collaborative partners for further clinical trials, development and commercialization of product candidates. You are urged to consider statements that include the words "may," "will," "would," "could," "should," "believes," "estimates," "projects," "potential," "expects," "plans," "anticipates," "intends," "continues," "forecast," "designed," "goal," or the negative of those words or other comparable words to be uncertain and forward-looking. For a further list and description of the risks and uncertainties the Company faces, please refer to our most recent Annual Report on Form 10-K and other periodic and other filings we file with the Securities and Exchange Commission and are available at www.sec.gov. Such forward-looking statements are current only as of the date they are made, and we assume no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Cyclacel Opportunity

Discovered, optimized, now developing **fadraciclib** & **plogosertib** cell cycle, drug portfolio

Potentially **best-in-class**, 1st or 2nd to market in both drug classes

Both show **single-agent** anticancer activity (CR, PR, SD) with good tolerability

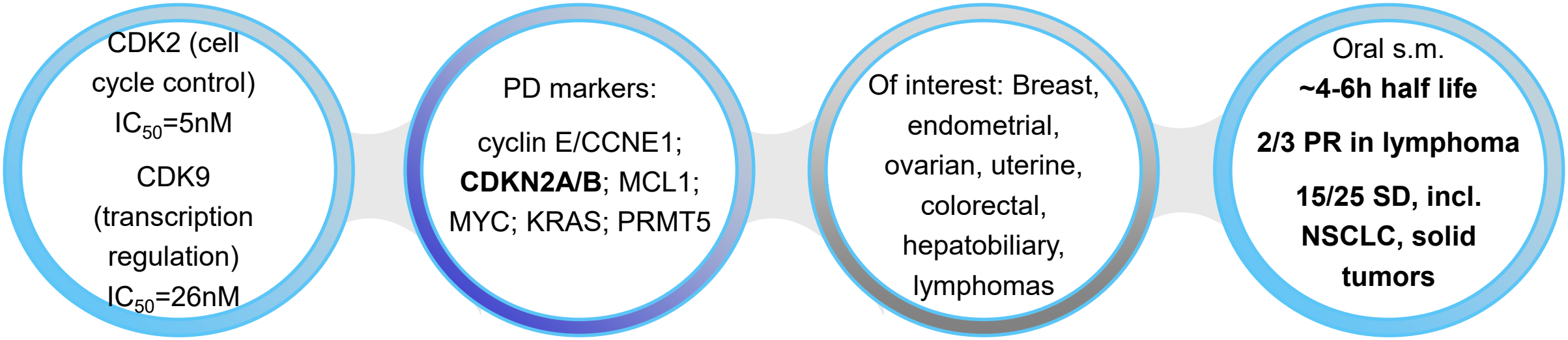
Anticancer activity in NSCLC, GYN endom./ovarian, bile, pancreas, and lymphoma

Mutational profile of responding patients suggests **biomarker** enrichment strategy:
- **CDKN2A/B, MTAP** for **fadra**, **ARID1A** (SWI/SNF), **TP53**, etc. for **plogo**

Multiple 2024 **catalysts** leading to registration pathways; lean operations

CYCLACEL

Fadraciclib (CYC065) Next Gen CDK inhibitor



Ongoing Ph 1/2: 1/1 NSCLC, 4/4 gyn (endometrial, ovarian, cervical); 2/2 cholangio. BTC; 2/2 HCC; 2/2 prostate; 1/2 H&N; 1/1 pancreatic; 1/1 CRC

Repeat dosing leads to **continuous** suppression of **transcription** via RNA pol2

CYCLACEL

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

Enrolled n=29; currently evaluating DL6B; No DLT in cohorts 1-5 (n=18); PoC part to start after RP2D

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

	Active
DL6B (n=2 ongoing) *150mg qd tabs 7d (4/4 wk)*	
DL6A (n=6) *125mg bid tabs M to F (4/4 wk)*	✓
DL6 (n=2) *150mg bid caps M to F (4/4 wk)*	✓
DL5 (n=6) *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=3) *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; 2nd /3rd 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)

Cohort 7: mCRC (including KRAS mutated)

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

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

CYCLACEL

Single agent. Single agent; followed by combination. ClinicalTrials.gov Identifier: NCT04983810.*

Fadra Oral 065-101 Related TEAEs *(all ≥2, interim DL6-6A, ongoing)*

Dose level		DL1 (X=3)			DL2 (X=5)			DL3 (X=3)		DL4 (X=3)		DL5 (X=9)			DL6 (X=2)			DL6A (X=10)		
System Organ Class/ Preferred Term	Total (N=35) n/N	G1 (y=2) x/X	G2 (y=1) x/X	G3 (y=2) x/X	G1 (y=4) x/X	G2 (y=2) x/X	G3 (y=4) x/X	G1 (y=2) x/X	G2 (y=2) x/X	G1 (y=2) x/X	G2 (y=1) x/X	G1 (y=7) x/X	G2 (y=6) x/X	G3 (y=2) x/X	G1 (y=2) x/X	G2 (y=2) x/X	G3 (y=2) x/X	G1 (y=8) x/X	G2 (y=6) x/X	G3 (y=1) x/X
Gastrointestinal disorders																				
Constipation	**2 (5.7)**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**2 (20)**	-
Diarrhoea	**9 (25.7)**	-	-	-	-	-	-	-	-	-	-	**3 (33.3)**	-	-	-	-	-	**2 (20)**	-	-
Nausea	**27 (77.1)**	-	-	-	**3 (60)**	-	-	-	-	**2 (66.6)**	-	**4 (44.4)**	**3 (33.3)**	-	-	**2 (100)**	-	**5 (50)**	**4 (40)**	-
Vomiting	**20 (57.1)**	-	-	-	**4 (80)**	-	-	-	-	-	-	**3 (33.3)**	**2 (22.2)**	-	**2 (100)**	-	-	**4 (40)**	**3 (50)**	-
General disorders and admin. site conditions																				
Fatigue	**9 (25.7)**	-	-	-	-	-	-	-	-	-	-	**3 (33.3)**	-	-	-	-	-	**3 (30)**	-	-
Investigations																				
Blood creatinine increased	**5 (14.2)**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**2 (20)**	-
Metabolism and nutrition disorders																				
Decreased appetite	**6 (17.1)**	-	-	-	**2 (40)**	-	-	-	-	-	-	-	-	-	-	-	-	**2 (20)**	-	-
Hyperglycaemia	**8 (22.8)**	-	-	-	-	-	-	-	-	-	-	**2 (22.2)**	-	-	-	-	-	**2 (20)**	-	**2 (20)**

G1 - Mild, G2 - Moderate, G3 - Severe, G4 - Life threatening or disabling.

N = # unique subjects exposed to study drug.

n = # unique subjects who experienced ≥1 episode of a particular AE

x = # unique subjects randomized at a particular dose-level and experienced ≥1 episode of a particular AE

X = # unique subjects randomized at a particular dose level of study drug as of 31-Aug-2023

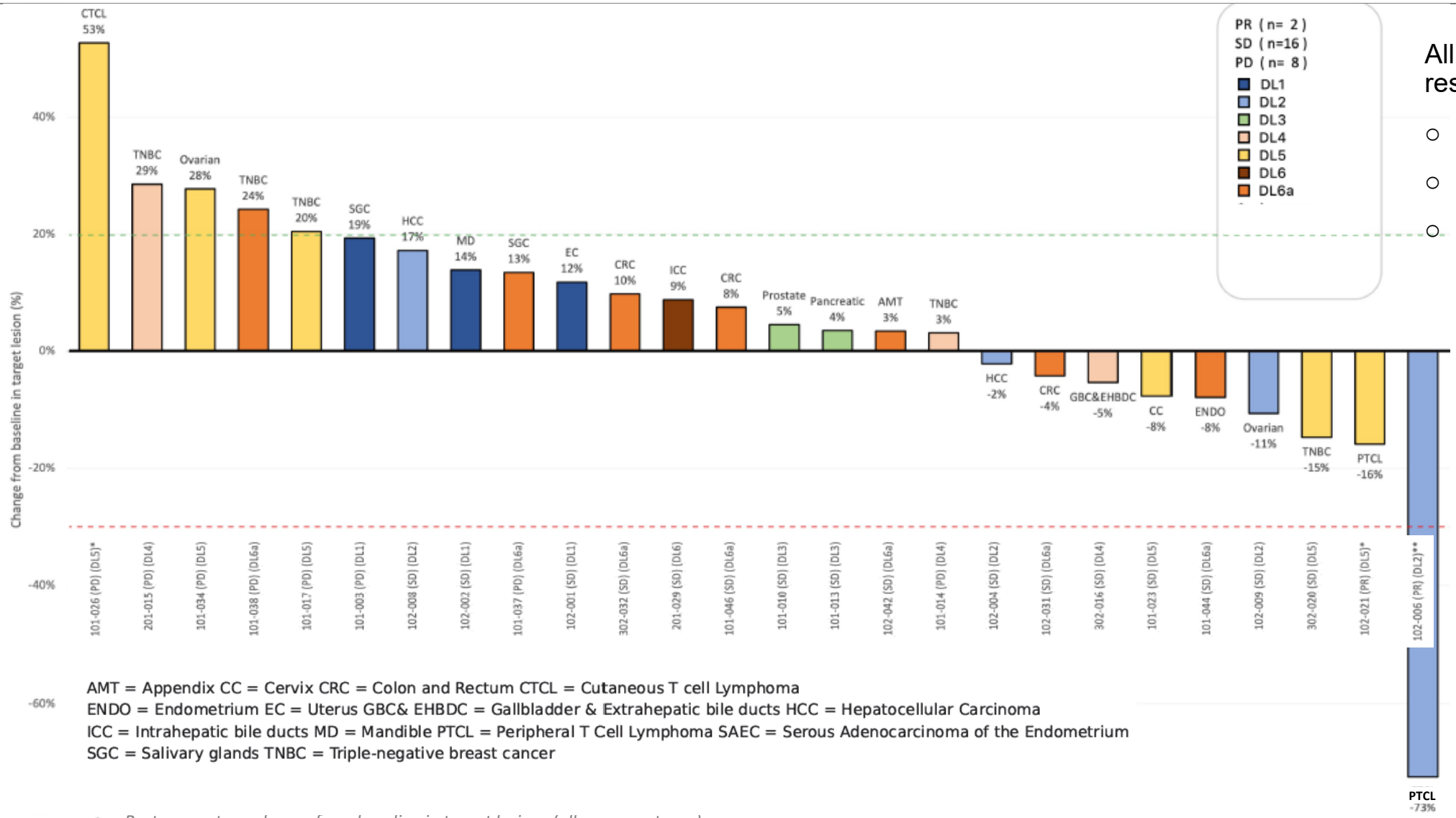
y = # unique subjects randomized at a particular dose-level and experienced ≥1 episode of a particular AE at a particular severity

If a subject has multiple episodes of a particular AE, counted only once for that AE for this presentation.

Data on file.

CYCLACEL

Fadra Oral 065-101 DL1-6A Response *(dose escalation all comer)*



AMT = Appendix CC = Cervix CRC = Colon and Rectum CTCL = Cutaneous T cell Lymphoma
ENDO = Endometrium EC = Uterus GBC& EHBDC = Gallbladder & Extrahepatic bile ducts HCC = Hepatocellular Carcinoma
ICC = Intrahepatic bile ducts MD = Mandible PTCL = Peripheral T Cell Lymphoma SAEC = Serous Adenocarcinoma of the Endometrium
SGC = Salivary glands TNBC = Triple-negative breast cancer

All evaluable for response by:

- RECIST 1.1 (N=23)
- mSWAT (N=1)
- Lugano (N=2)

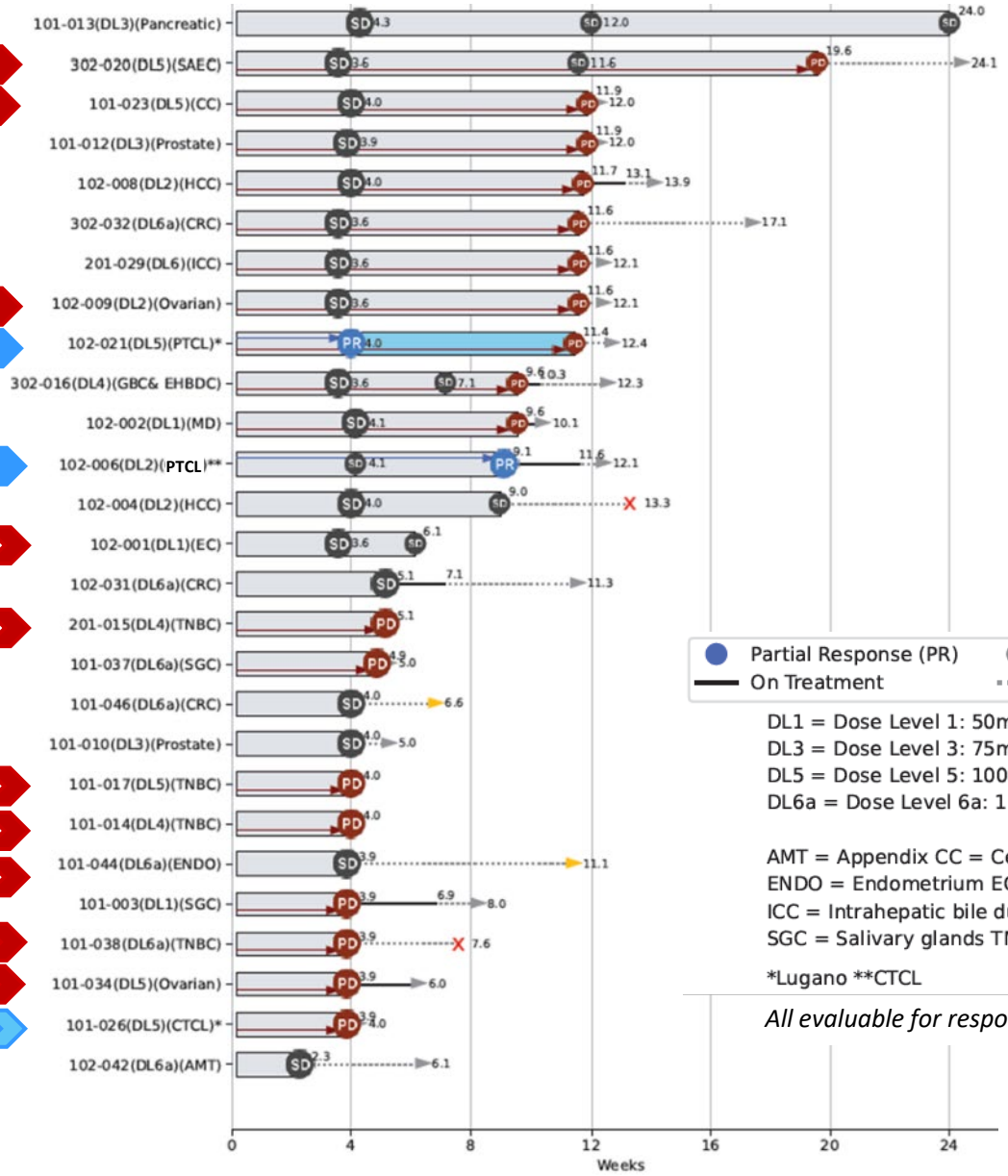
Best percentage change from baseline in target lesions (all response types).
101-012 (SD) (DL3) lesion data not entered. Data on file as of 15SEP23.

Fadra Oral 065-101 DL1-6A Swimmers Plot *(dose escalation part)*

GYN

T Cell Lymphoma

NB Now on 5th cycle



Partial Response (PR) | Stable Disease (SD) | Progressive Disease (PD) | Time to Response | Time to Progression
On Treatment | Off Treatment | Last Known Alive | Ongoing | Death

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) DL6 = Dose Level 6: 150mg, BID M-F, Week 1-4 (1500 mg/week)
DL6a = Dose Level 6a: 125mg, BID M-F, Week 1-4 (1250 mg/week)

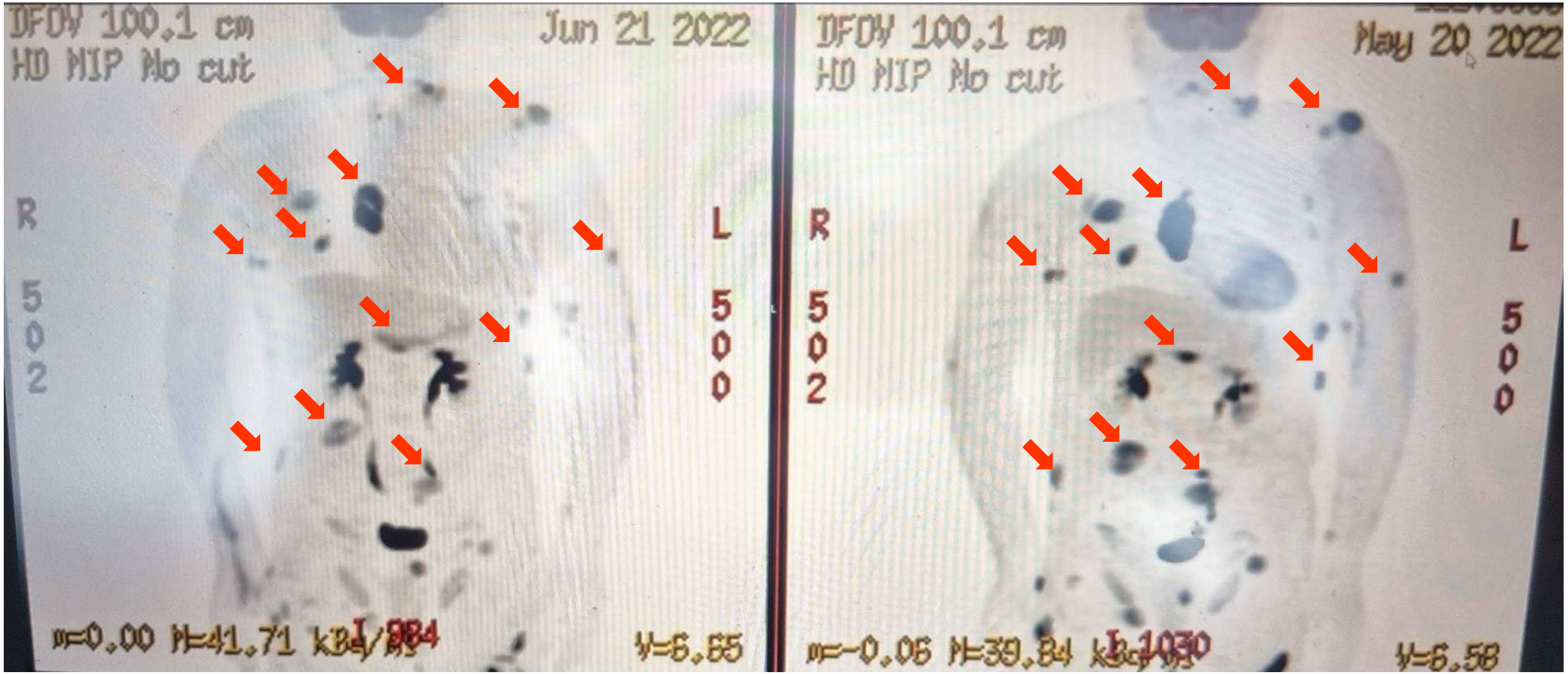
AMT = Appendix CC = Cervix CRC = Colon and Rectum CTCL = Cutaneous T cell Lymphoma
ENDO = Endometrium EC = Uterus GBC& EHBDC = Gallbladder & Extrahepatic bile ducts HCC = Hepatocellular Carcinoma
ICC = Intrahepatic bile ducts MD = Mandible PTCL = Peripheral T Cell Lymphoma SAEC = Serous Adenocarcinoma of the Endometrium
SGC = Salivary glands TNBC = Triple-negative breast cancer

*Lugano **CTCL

All evaluable for response. Data on file; cutoff as of 15-Sep-2023.

CYCLACEL

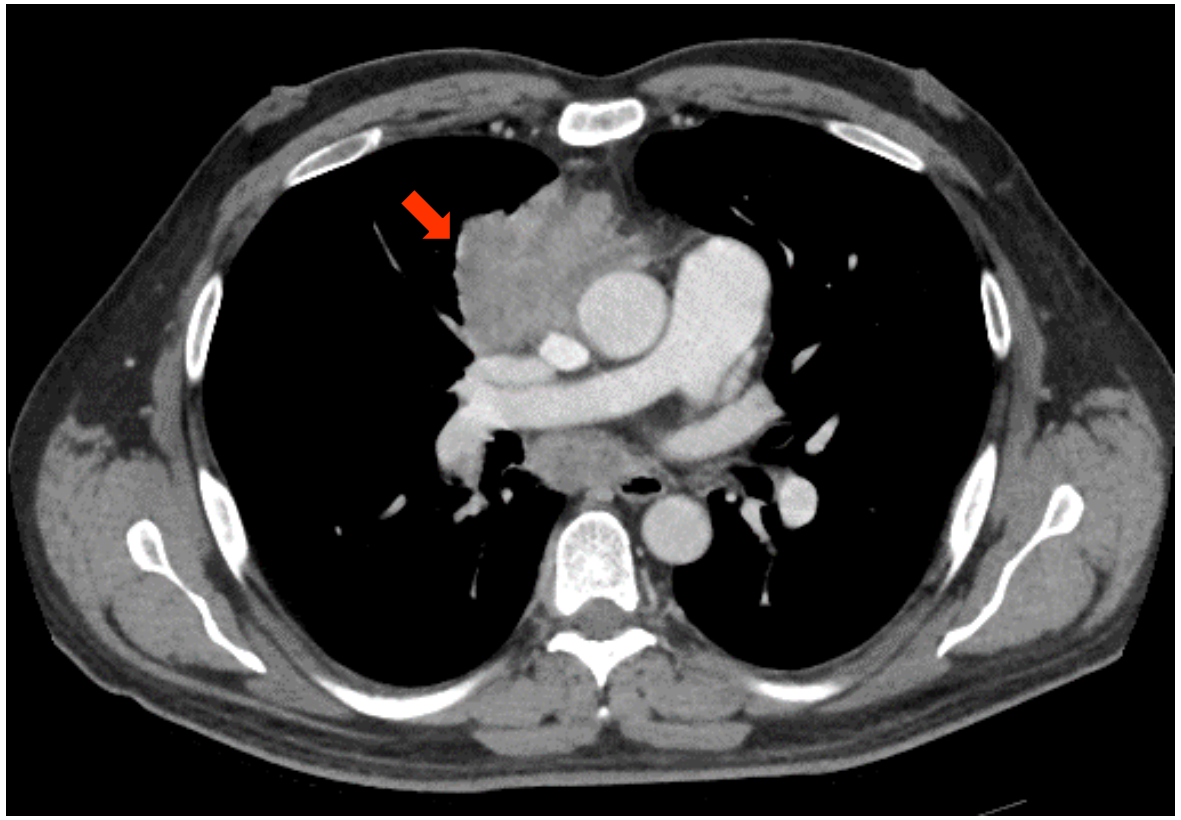
PR in angioimmunoblastic PTCL pt. *(oral 065-101, 1st cycle DL5)*



Cycle 2 scan *Baseline scan*

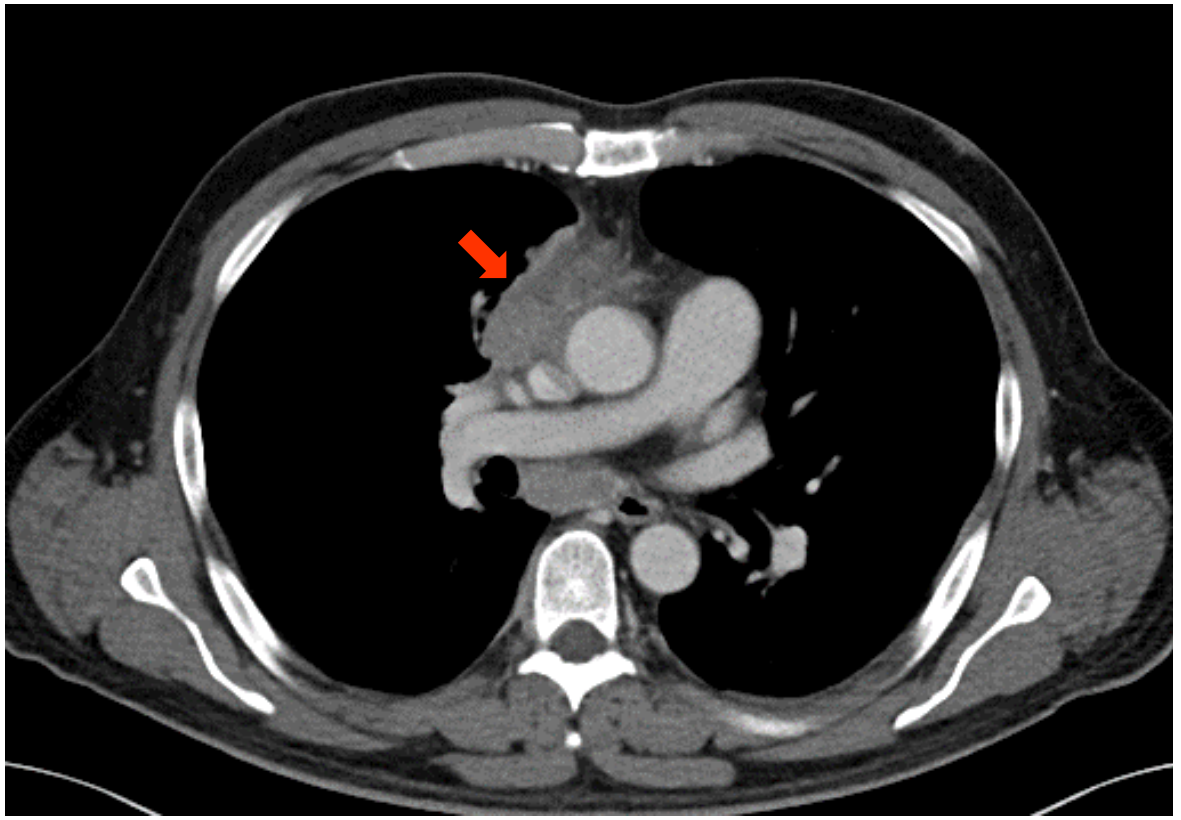
Data on file. PET scan images kindly provided by the principal investigator. ***CDKN2A deletions in 46% of PTCL-NOS patients,*** *Maura F et al Haematologica. 2021 Nov 1 106 11 2918.*

Squamous NSCLC patient *(oral 065-101, 1st cycle DL6A)*



Baseline scan 7-SEP-23

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



Cycle 1 scan 9-OCT-23

*SD shrinkage all target lesions **22**%. D1C1 14-SEP-23*

NGS: CDKN2B loss

CYCLACEL® *Data on file. CT scan images kindly provided by the principal investigator.*

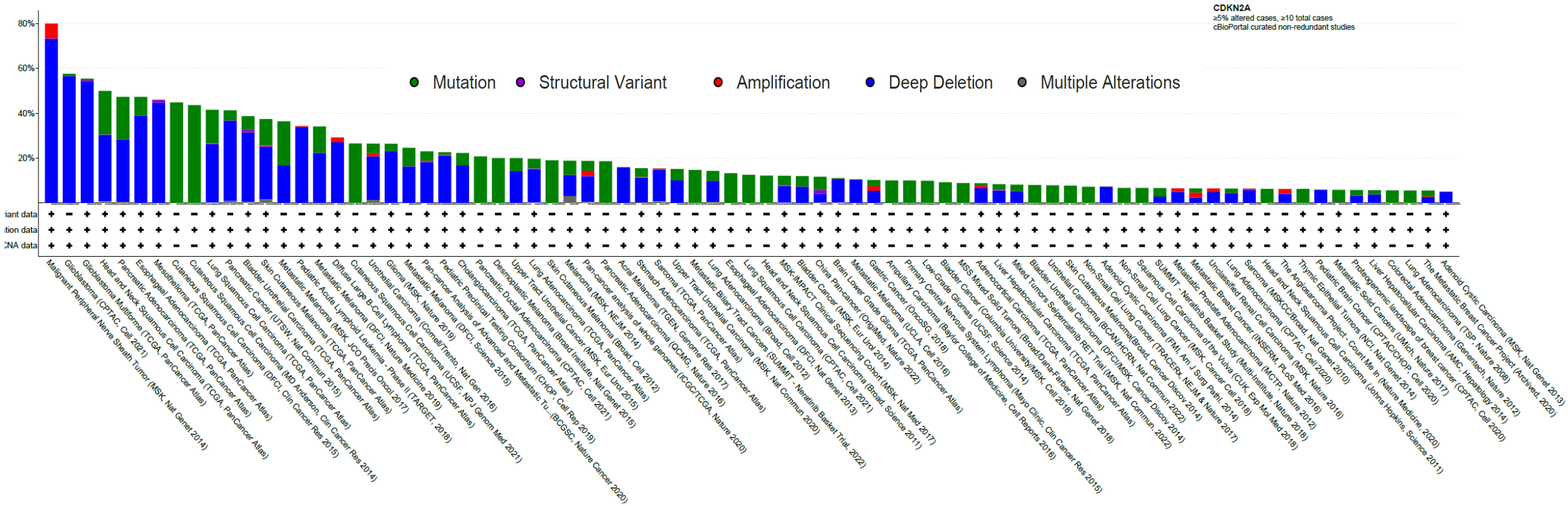
Responder Profiles

Patient *Study*	Histology	Best Response	Dose Level	Schedule	Mutation
51 *065-101*	NSCLC squamous	22% shrinkage C1	125mg BID	5d/wk 4/4 wks	CDKN2B loss
38 *065-01*	*Endometrial*	**CR**	213mg/m^2	2d/wk 2/3 wks	CDKN2A, CDKN2B, MTAP loss, MCL1 amp
14 *065-01*	*Ovarian*	**SD**	192mg/m^2	2d/wk 2/3 wks	CDKN2A loss, MYC amp
11 *065-01*	*Salivary gland*	**SD**	128mg/m^2	2d/wk 2/3 wks	CDKN2A, CDKN2B loss

CYCLACEL

Data on file. Pt20 (pancreaticobiliary; 192 mg/m2; 1 C only) ***CDKN2A.***

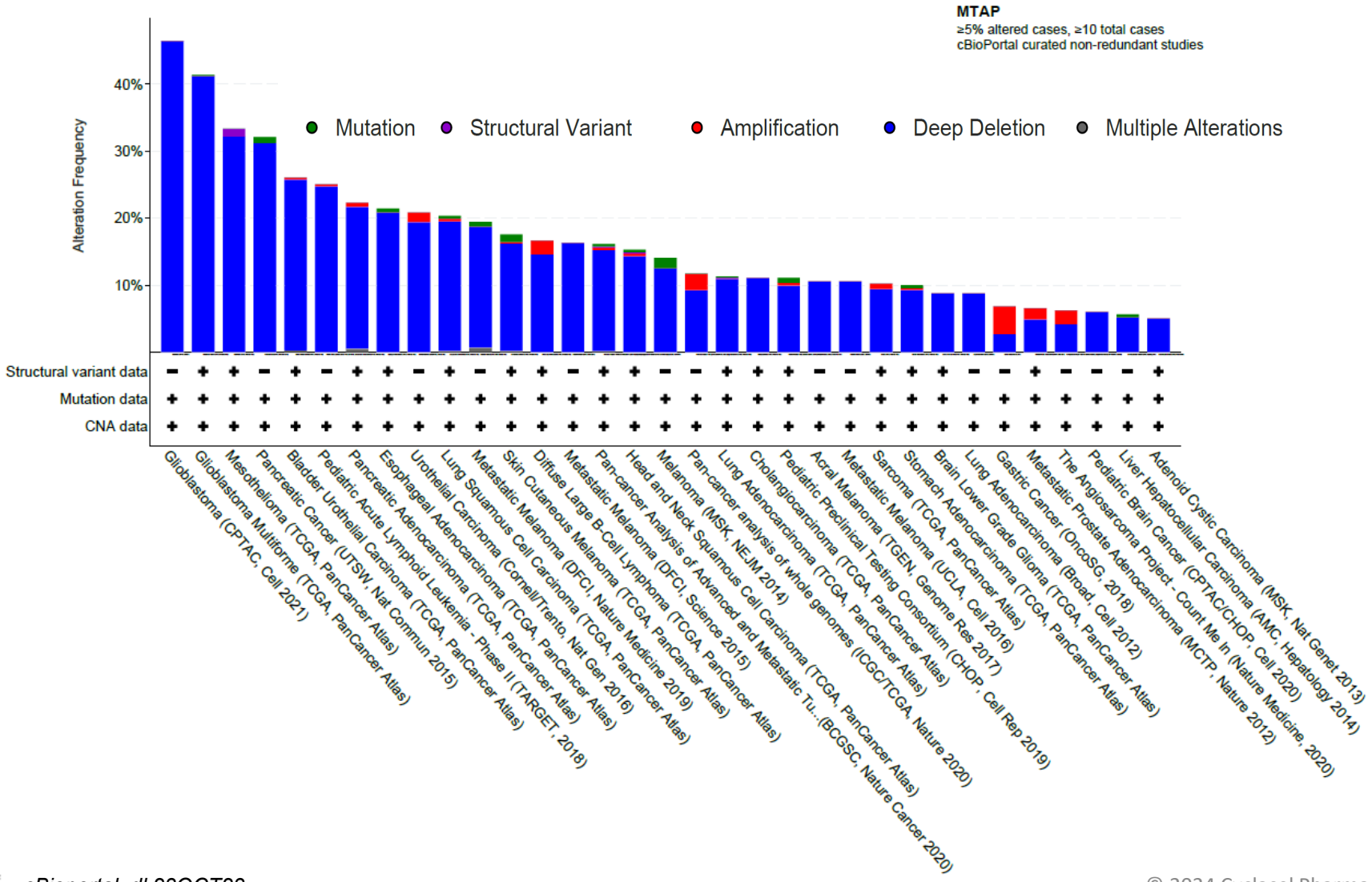
CDKN2A Alterations



Solid tumors >40%: glioma, H&N, pancreas, esophagus, lung (incl. squamous), bladder, melanoma, cutaneous sq.

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

MTAP Alterations (PRMT5 inhibition sensitive)

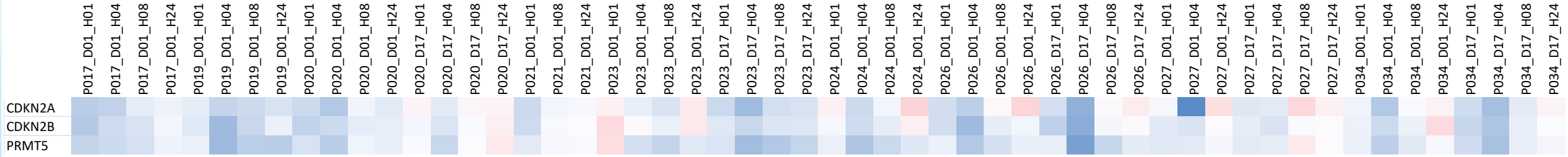


>25%: glioma, mesothelioma, pancreas, bladder, esophagus

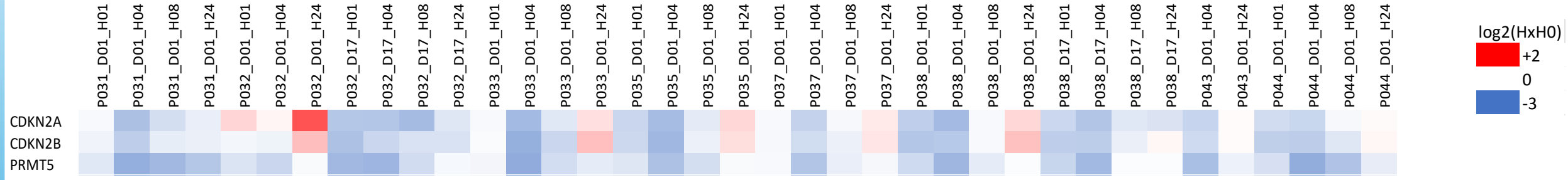
cBioportal, dl 23OCT23.

Fadra Suppresses CDKN2A/B, PRMT5 Transcription in Patients

DL5



DL6A



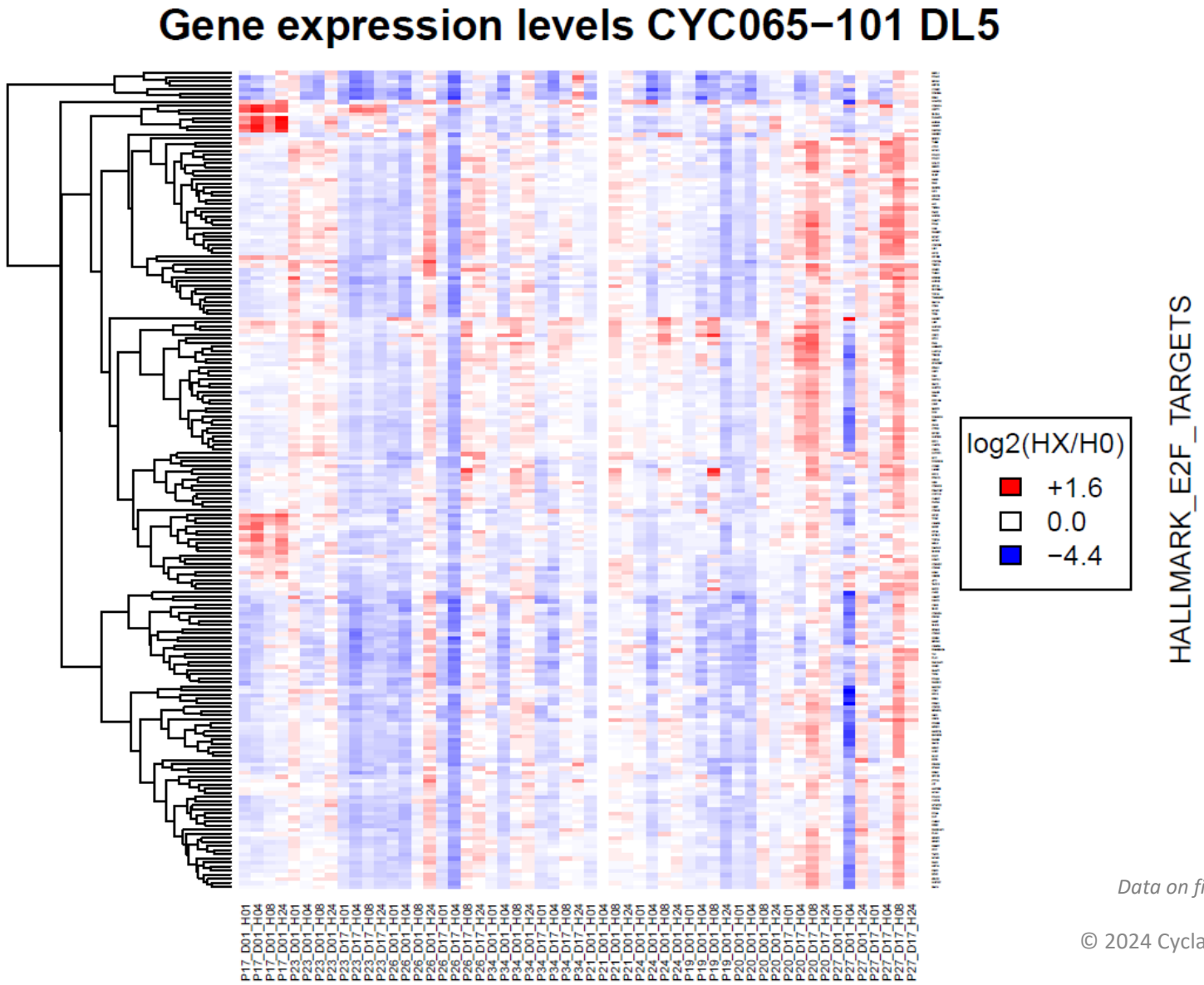
Expands applicable opportunity to patients with MTAP deletion.

MTAP co-located with CDKN2A/B in chromosome 9p21 and often co-deleted.

CYCLACEL

Data on file. RNAseq transcript data.

Fadra Suppresses E2F (CDK2 dependent) DL5 Phase 1 Patients



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

Oral Fadra Summary

Single agent responses; well tolerated in liquid and solid cancers

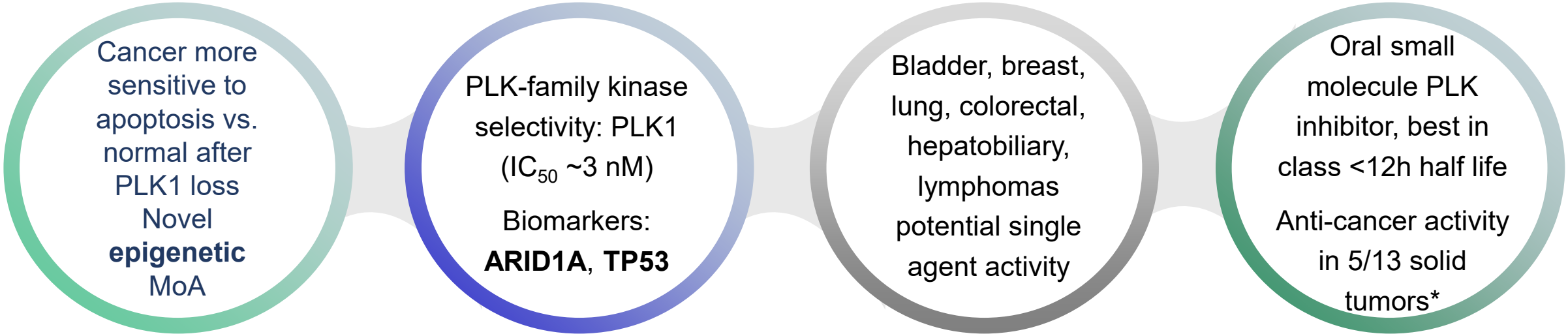
CDK2 + CDK9 inhibition may be superior to either CDK2 or CDK9

- Cancer cells adapt to CDK2i; CDK2i work only when CDK9i silence MYC
- Exploiting cancer vulnerabilities:
  - CDKN2A/B, MTAP loss (suppressing PRMT5 transcription)
  - Cyclin E/CCNE1 overexpression/amplification
  - MYC or MCL1 overexpression/amplification

Fadra may be only next gen CDKi to have threaded the needle of transient suppression of anti-apoptosis proteins without hematological toxicity

Arora M et al, Cancer Res 2023 83 (7_Suppl): 5992. Knudsen E et al Cell Rep 2022 Mar 1 38 9.

Plogosertib (CYC140) Next Gen PLK1 inhibitor



Novel **epigenetic** mechanism with a unique **low dose** strategy

* 1/1 GYN (ovarian); 1/1 NSCLC; 1/1 BTC; 1/1 sinusoidal squamous; 1/1 ACC

CYCLACEL

Plogo 140-101 Oral Ph1/2 in Solid Tumors and Lymphoma *(ongoing)*

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

	Active
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=2) *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)*	✓

Schedule: 3 out of 4 wk per cycle.

ClinicalTrials.gov Identifier: NCT053583790

Proof of Concept (PoC)**

(Simon 2-stage; 2nd /3rd 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

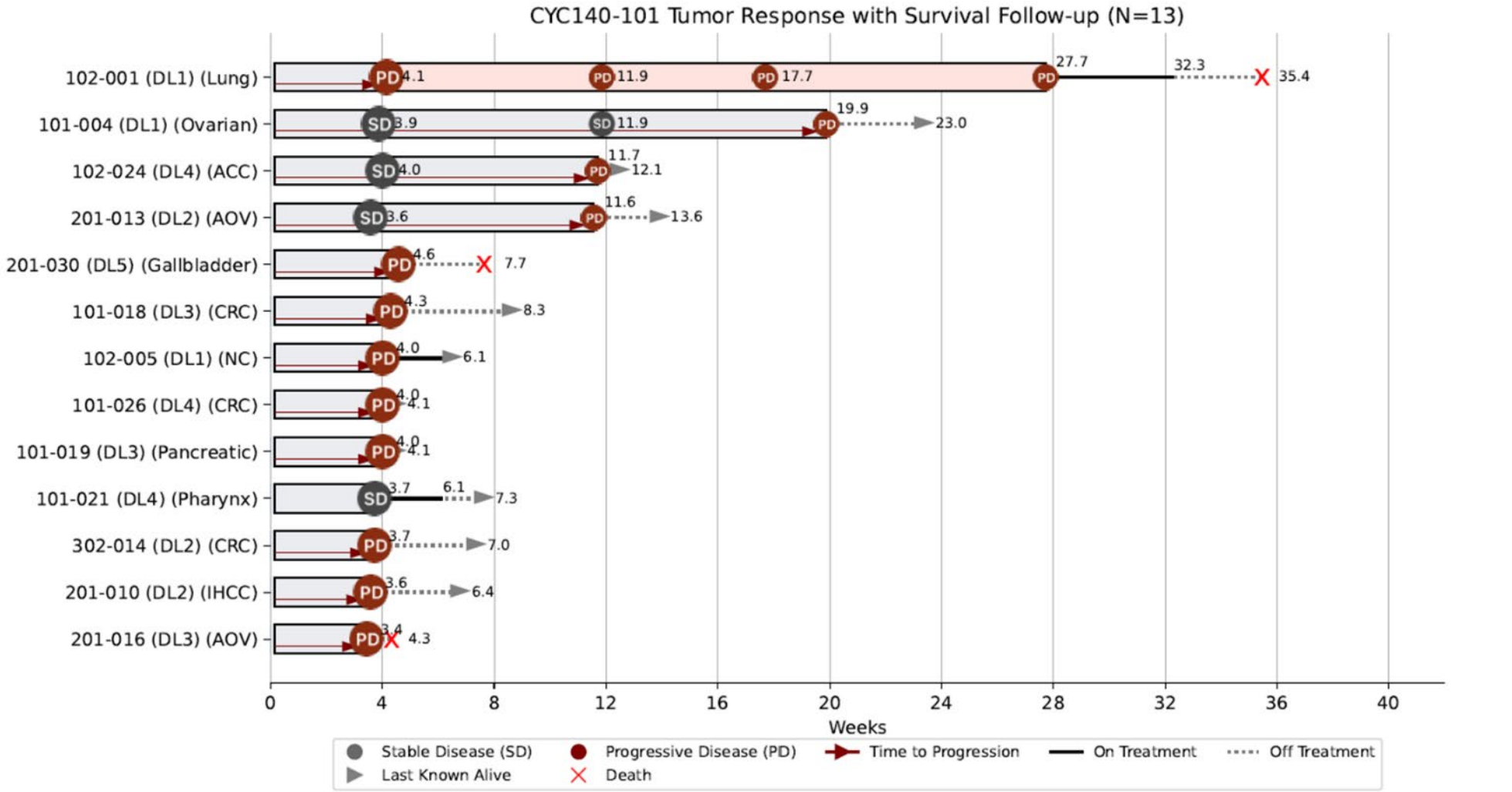
(if randomized study not needed)

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

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

CYCLACEL

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

• *Data on file;*

Plogo Oral 140-101 Related TEAEs *(interim DL1-4, ongoing)*

	Dose level	DL1 5mg, QD M-F Week 1 to 3 (25 mg/weekly)	DL 4 15mg, QD M-F Week 1 and 3 (75 mg/weekly)	DL5 15mg, QD M-F Week 1 to 3 (75 mg/weekly)
System Organ Class/Preferred Term	**Total (N=16) n/N**	**G1 (y=1) x/X**	**G1 (y=2) x/X**	**G2 (y=1) x/X**
Blood and lymphatic system disorders				
Anaemia	1 (6.2)	-	-	1 (33.3)
General disorders and administration site conditions				
Fatigue	1 (6.2)	1 (33.3)	-	-
Investigations				
Alanine aminotransferase increased	1 (6.2)	-	1 (33.3)	-
Aspartate aminotransferase increased	1 (6.2)	-	1 (33.3)	-

G1 - Mild, G2 - Moderate, G3 - Severe, G4 - Life threatening or disabling.

N = # unique subjects exposed to study drug as of 31-Aug-2023

n = # unique subjects who experienced ≥1 episode of a particular AE

x = # unique subjects randomized at a particular dose-level and experienced ≥1 episode of a particular AE

X = # unique subjects randomized at a particular dose level of study drug as of 31-Aug-2023

y = # unique subjects randomized at a particular dose-level and experienced ≥1 episode of a particular AE at a particular severity

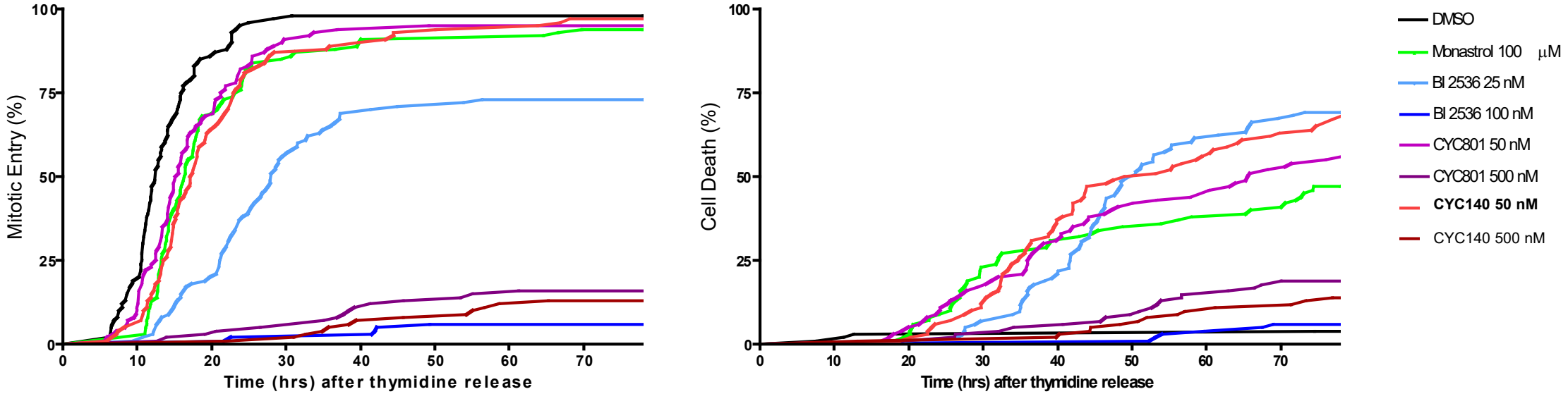
If a subject has multiple episodes of a particular AE, counted only once for that AE for this presentation.

Data on file.

CYCLACEL

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

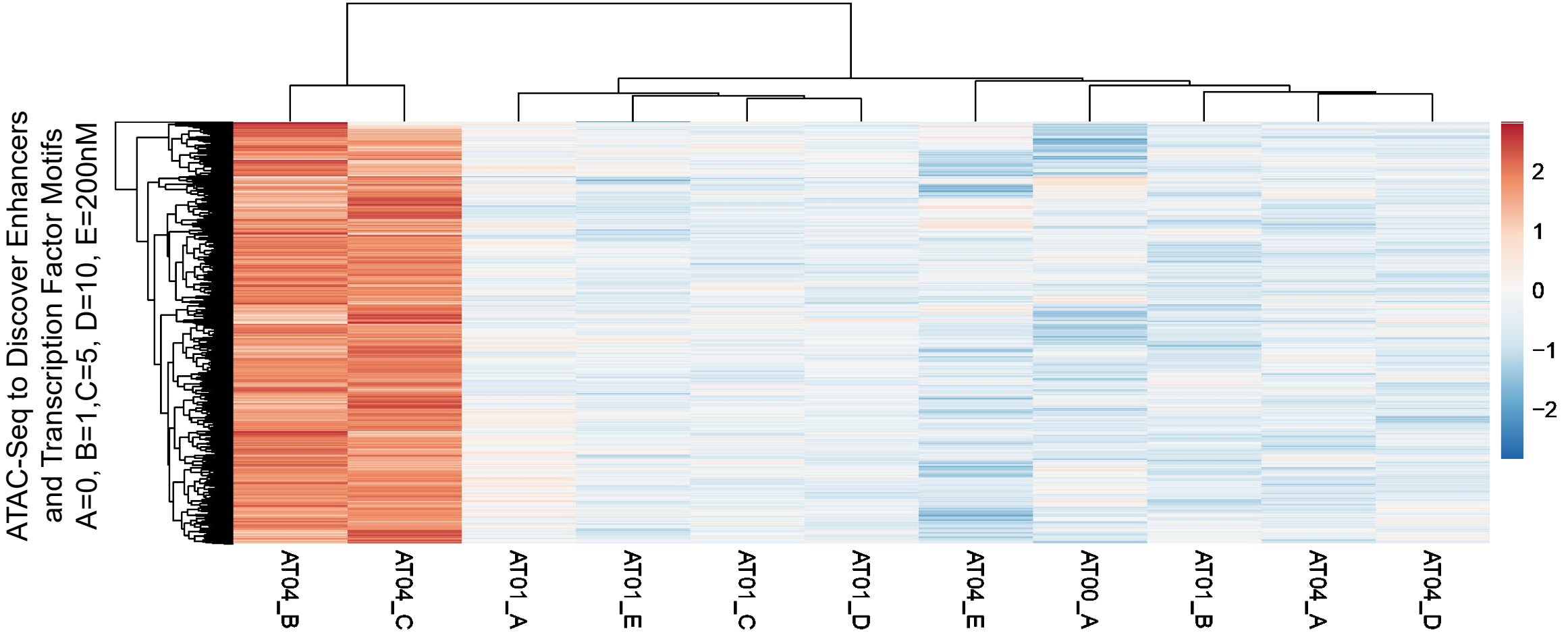


At high doses, PLK1i treatment stops growth; at lower doses PLK1i starts cell cycle and then more tumor cells die.

CYCLACEL®

Aspinal et al., Oncotarget, 2015, 6, 36472-88 and company data on file.

Low Dose Plogo has Dramatic Effect on Chromatin Access



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

Data on file. Top 1000 Highly Variable Peaks identified in ATAC seq analysis excluding 24 hrs timepoint.

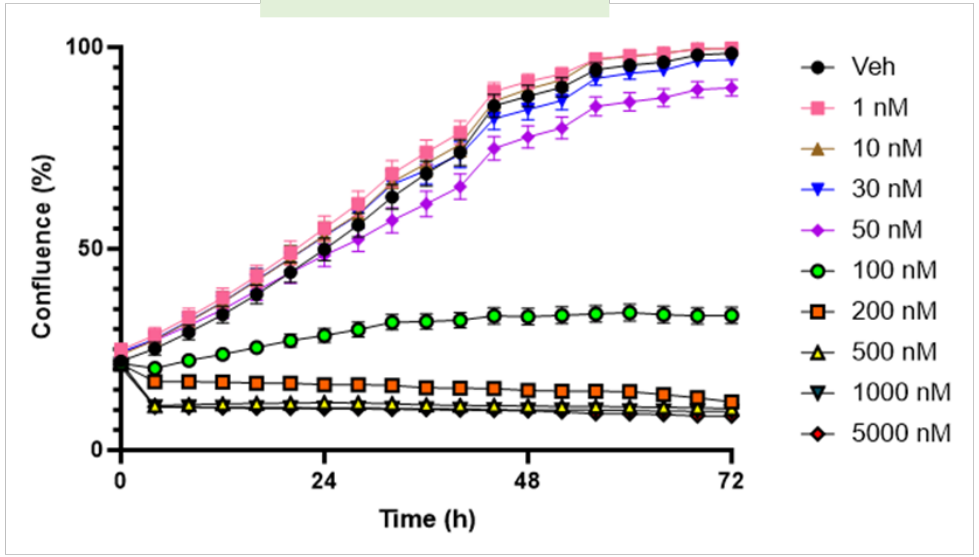
Plogo efficacy on ARID1A mut and WT CRC, ovary and lung cells

Cell lines	CYC IC50
A2780 (Ovarian)	8.9 nM
NCI-H1229 (Lung)	14 nM
NCI-H23 (Lung)	34 nM

These are ARID1A mutant (A2780) or SMARCA mutant (lung lines)

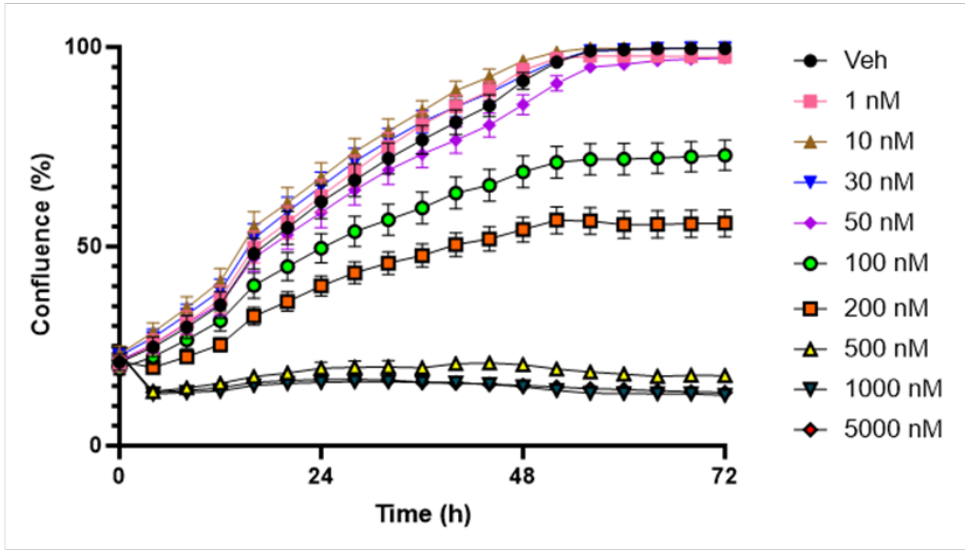
- PLKi in HCT116 ARID1A -/- and WT cells

HCT116 ARID1A KO



IC50: 26nM

HCT116 WT



IC50: 307 nM

CYCLACEL

Plogo Potentially “Only-in-Class” Epigenetic Innovation

Plogo enables **chromatin accessibility** at low concentrations

Potential activity across epigenetically sensitive tumors

- Sensitive in tumors bearing specific mutations
- Novel targets in molecular pathways with unmet medical needs
- Could lead to patient selected, biomarker driven Ph1 expansion group

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

CYCLACEL

Data on file.

Milestone Momentum

Fadra 065-101 - *Oral CYC065, CDK2/9 inhibitor in 065-101 Ph 1/2 trial*

- Phase 1 readout to include PK, PD, safety and activity data YE 2023
- Determine RP2D and begin Phase 2 solid tumor Proof of Concept 1H 2024
- Initial Phase 2 PoC data from disease specific cohorts* 2H 2024
- Complete tablet manufacture and validation 2H 2024

Plogo 140-101 - *Oral CYC140, PLK1 inhibitor with novel epigenetic MoA in 140-101 Ph 1/2 trial*

- Phase 1 dose escalation continues at DL5 to determine RP2D 1H 2024
- Phase 1 readout to include PK, PD, safety and activity data 1H 2024
- Disclose novel epigenetic mechanism 1H 2024
- Start biomarker driven PoC Ph 1 expansion cohort 1H 2024

CYCLACEL

Subject to available capital.

Thank You

Cyclacel Pharmaceuticals, Inc.

200 Connell Drive #1500
Berkeley Heights, NJ 07922

Contact: ir@cyclacel.com
+1 (908) 517 7330