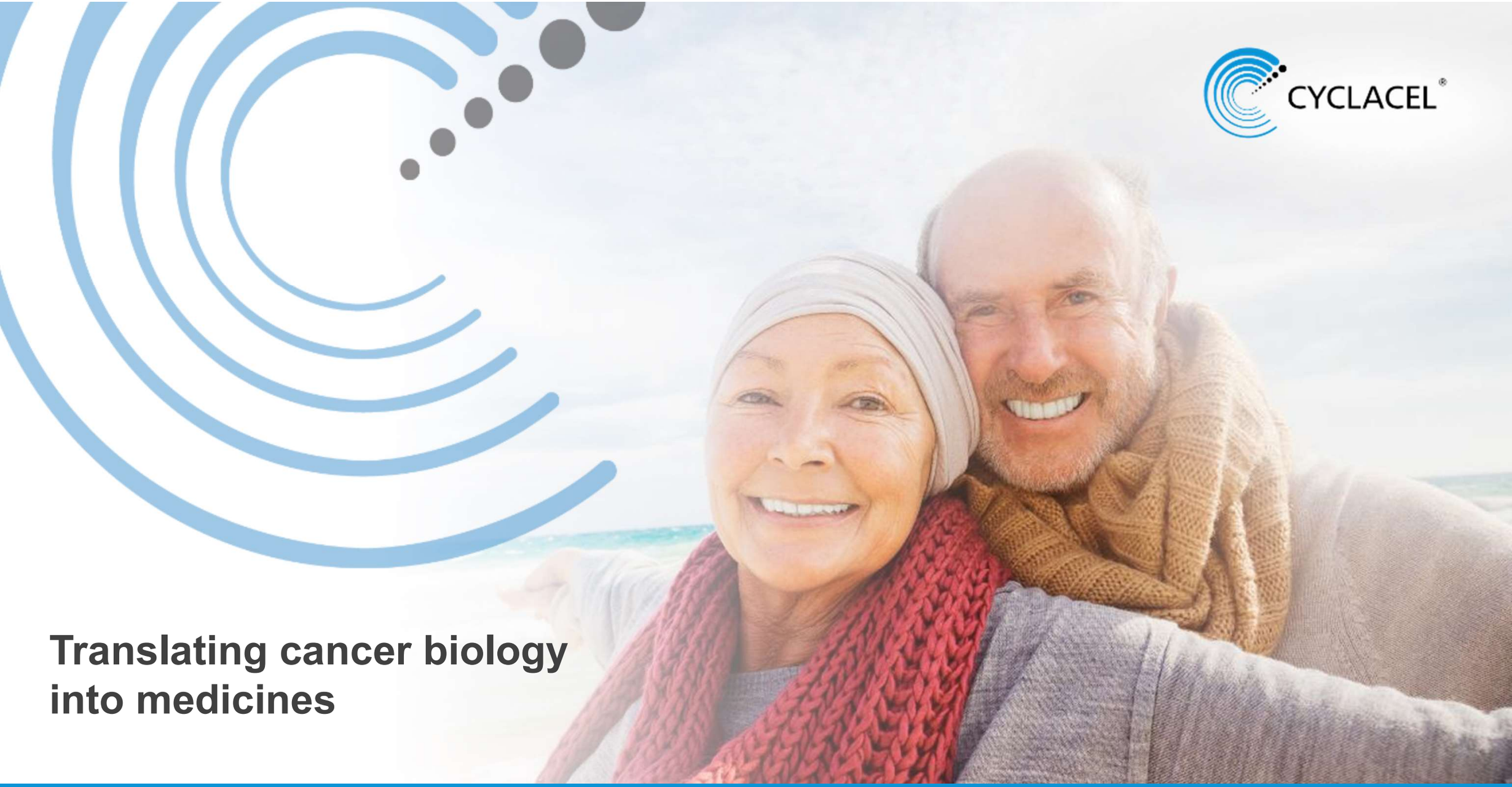


Translating cancer biology into medicines

Presentation JUNE 2023

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 Value Creation

- **STRATEGY:** Leverage understanding of cancer biology to develop differentiated targeted oncology medicines with 1st or 2nd mover advantage to address unmet needs in women's cancers & lymphoma
- **SCIENCE**: Leader in cell cycle checkpoint control and oncology drug innovator
- **ASSETS**: Two Phase 1/2 ongoing studies for solid tumors and lymphoma

  Fadraciclib - Oral CYC065, next generation CDK2/9 inhibitor

  - Single agent responses in unselected, late line solid tumors and lymphoma

  Plogosertib - Oral CYC140, PLK1 inhibitor with novel epigenetic MoA

  - Early indication of anticancer activity as a single agent
- **CATALYSTS:** Three key 2023 data readouts from registration-directed Phase 1/2 studies

CYCLACEL

Experienced Executive Leadership

Spiro Rombotis
President & CEO

Paul McBarron
COO & CFO

Mark Kirschbaum, MD
CMO

Therapeutic Strategy: Enabling Apoptosis

- **Durably suppress** proteins/genes associated with cancer resistance → enable **apoptosis**
- Suppress multiple, redundant, **anti apoptotic** cancer mechanisms with a **single drug**
- Optimize **mechanistically**-relevant, **dosing** strategy

CYCLACEL

Fadraciclib Potentially Addressing Large Markets (e.g. cyclin E)

High Grade Serous Ovarian Cancer 2L

- 27k US incidence; ~79k prevalence
- CCNE1 amplified >20% of patients; worse survival than BRCA mutant patients

Endometrial/Uterine 2L

- 5k US incidence; ~77k prevalence
- CCNE1 is 20% of high grade serous which is 50% of total

Breast HR+ 2L

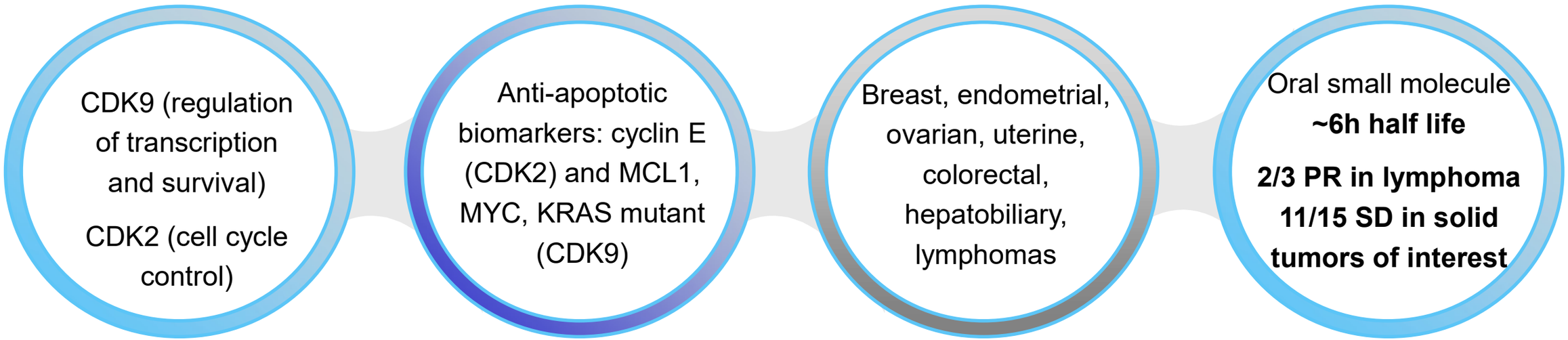
- 56k US incidence; ~735k prevalence
- CCNE1 is 30% of HR+ which is 73% of total

Breast Cancer BRCA1/2+

- 18k US incidence; ~238k prevalence
- CCNE1 is 40% of BRCA+ which is 17% of total

SEER Database. Company estimates. CCNE1 gene encodes cyclin E protein.

Fadraciclib (formerly CYC065, next gen CDK inhibitor) Snapshot



Ongoing Ph 1/2: biologically-optimal schedules require continuous dosing

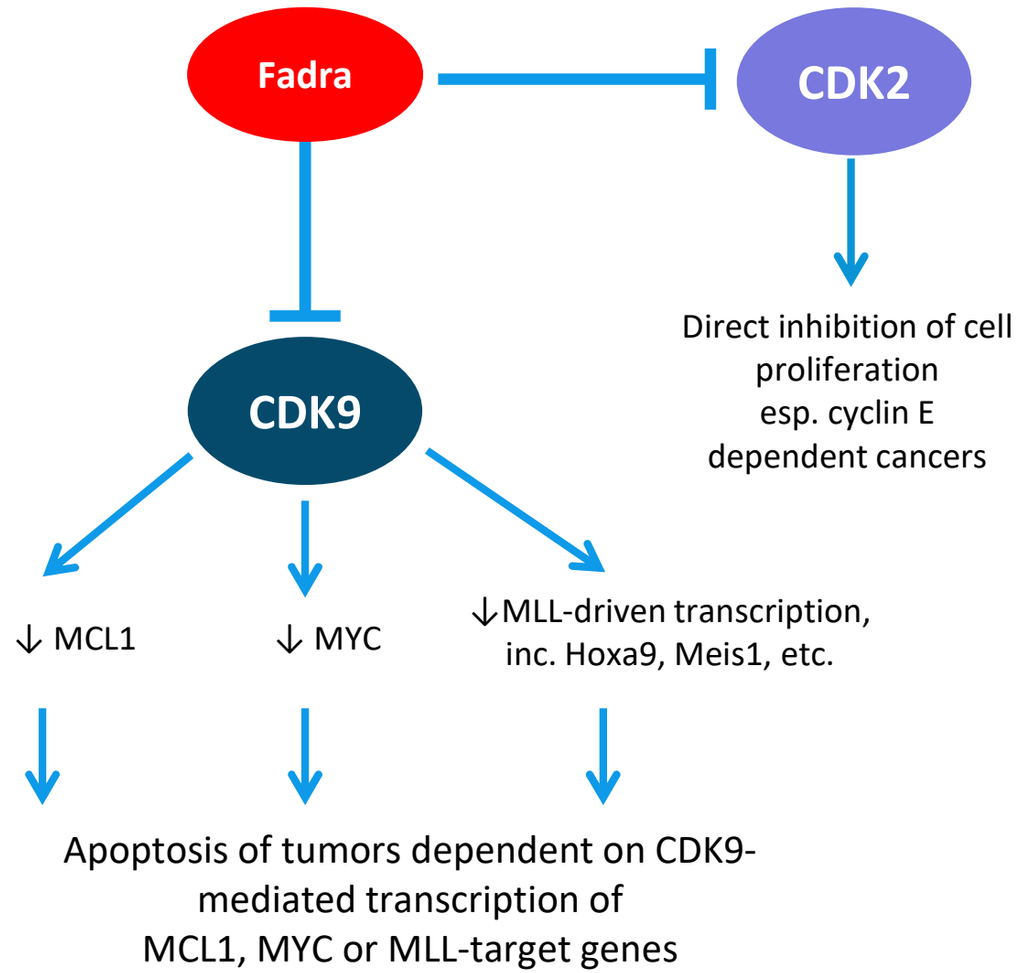
CDK2/9 Inhibition: Damaging Cancer's Anti Apoptotic Defenses

CDK2: Cyclin E (*CCNE*) overexpression > drug resistance in **women's cancers**, e.g.

- **HR +ve** CDK4/6 inhibitor refractory **breast cancer**: *cyclin E overexpression stat sig correlated with palbociclib + HR regimen failure (PALOMA-3)* [1]
- **HER2 +ve** refractory **breast cancer**: *cyclin E amplification/overexpression is a mechanism of trastuzumab (Herceptin®) resistance* [2]

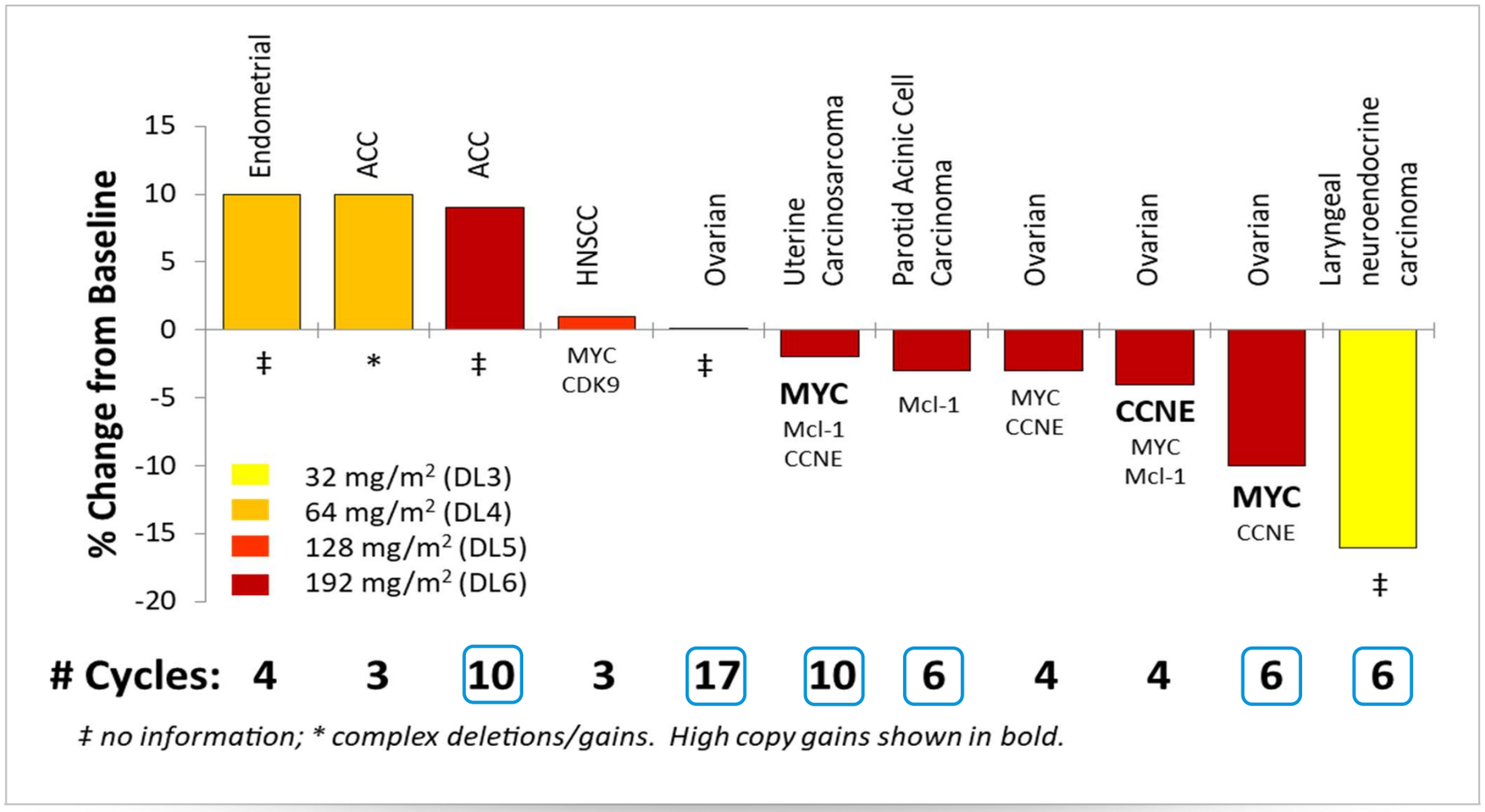
CDK9: Anti-**apoptotic** protein (**MCL1**, **MYC**, MYCN, MYB, MDM2, etc.[3,4]) overexpression in **solid and liquid tumors**

Addresses broad range of tumors vs. CDK2i or CDK9i



[1] Turner NC et al; JCO 2019. [2] Scaltriti M et al, PNAS, 2011. [3] Frame S et al, PLOS One, 2020. [4] Poon E et al, JCI 2020.

Fadraciclib IV 065-01 Ph 1 Part 1 Data *(completed, unselected, late line)*



AACR American Association for Cancer Research

Patients with high copy CCNE, MYC and/or MCL1 sensitive to single-agent fadraciclib

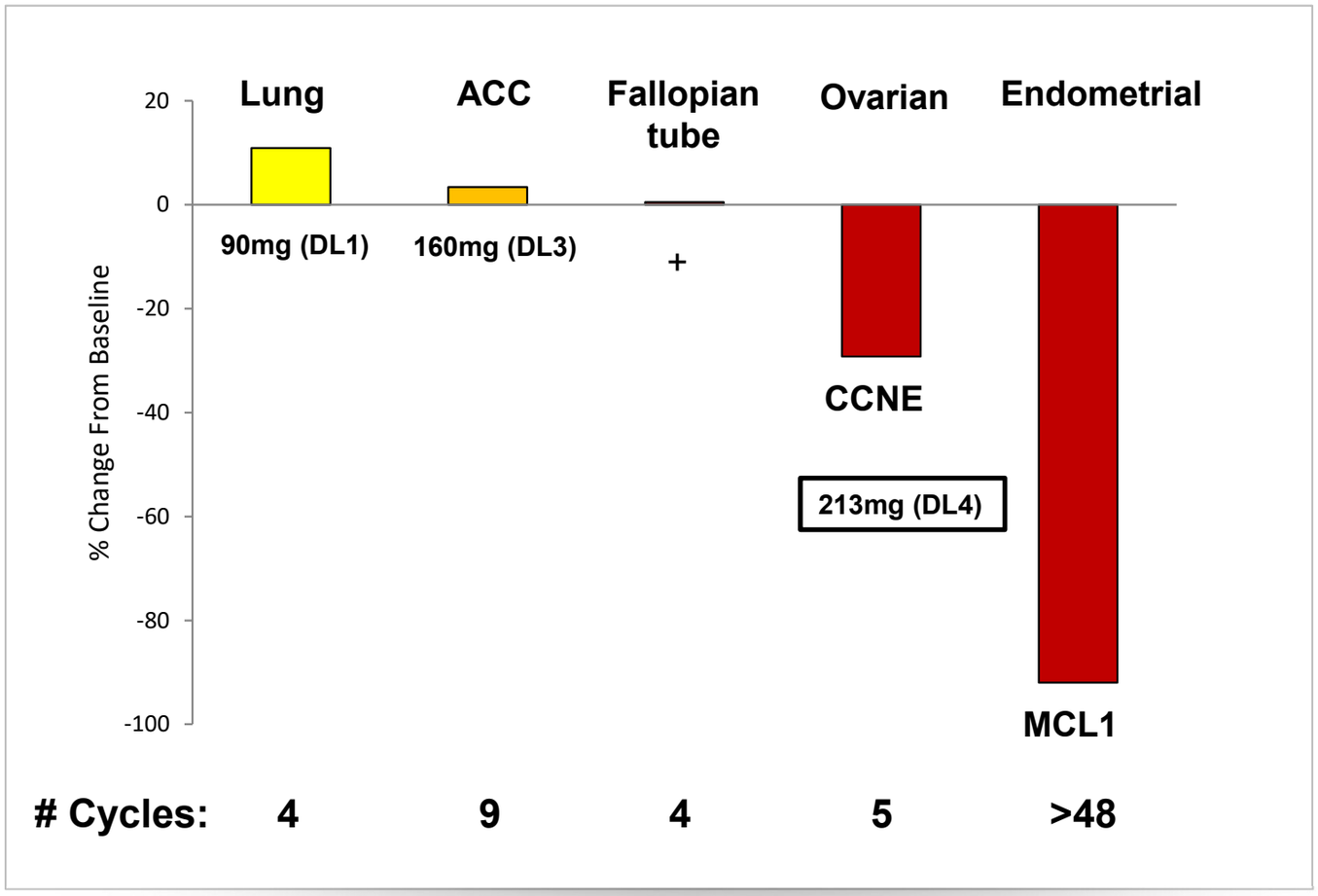
4h infusion every 3wk:

- 20/26 evaluable RECIST 1.1
- 6/11 SD ≥6 cycles (*boxed*)

CYCLACEL

Do, KT, et al., AACR Annual Meeting 2018.

Fadraciclib IV 065-01 Ph 1 Part 2 Data *(completed, unselected, late line)*

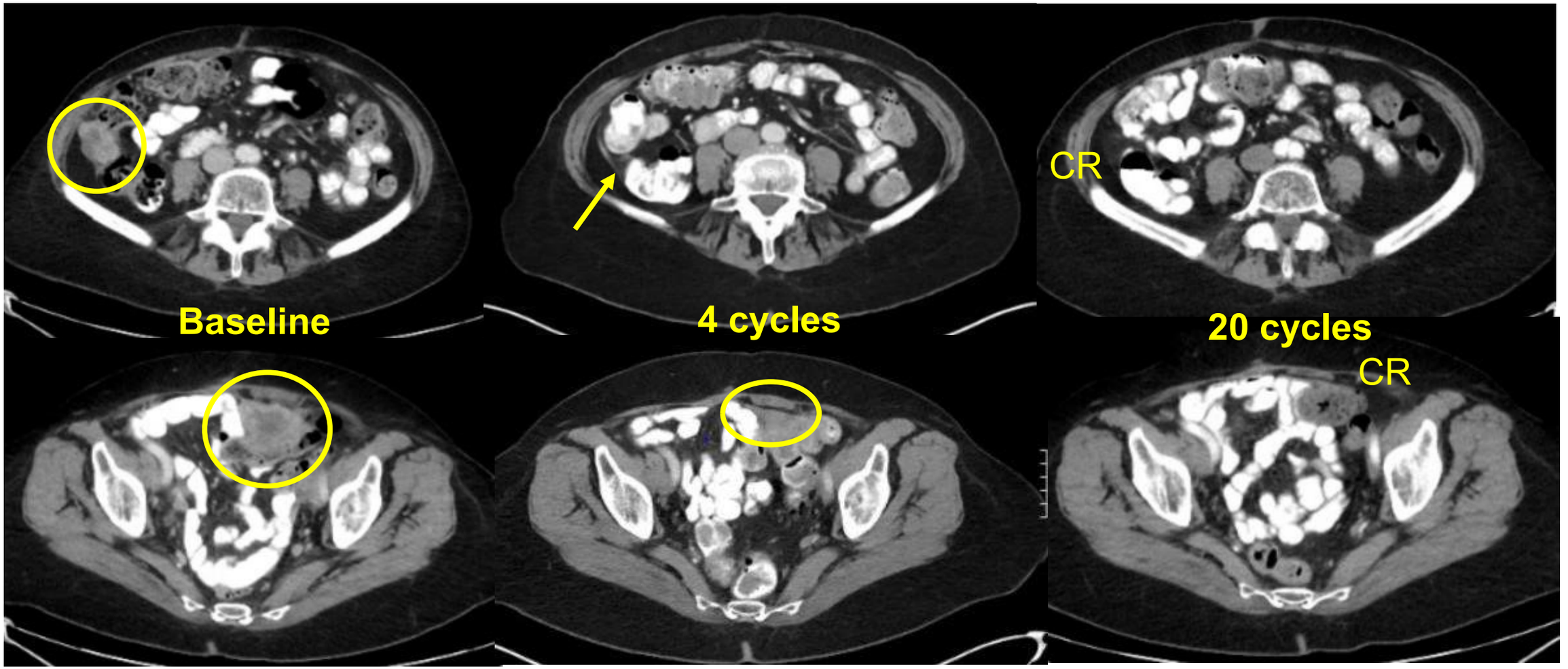


Tumors with MCL1 and CCNE overexpression respond to fadraciclib single agent

- Improved efficacy with more frequent 1h infusions on d1, 2, 8, 9 every 3wk
- SD >4 cycles in cyclin E amplified ovarian cancer; 29% shrinkage of all target lesions
- Confirmed PR at 4 cycles (MCL1 amplified endometrial cancer); 100% shrinkage of all baseline target lesions and CR at 1.5 years; deep ongoing response at 3 years

Data on file. + Non-measurable target tumor lesion.

PR then CR 065-01 Part 2 MCL1 Amplified Endometrial Patient

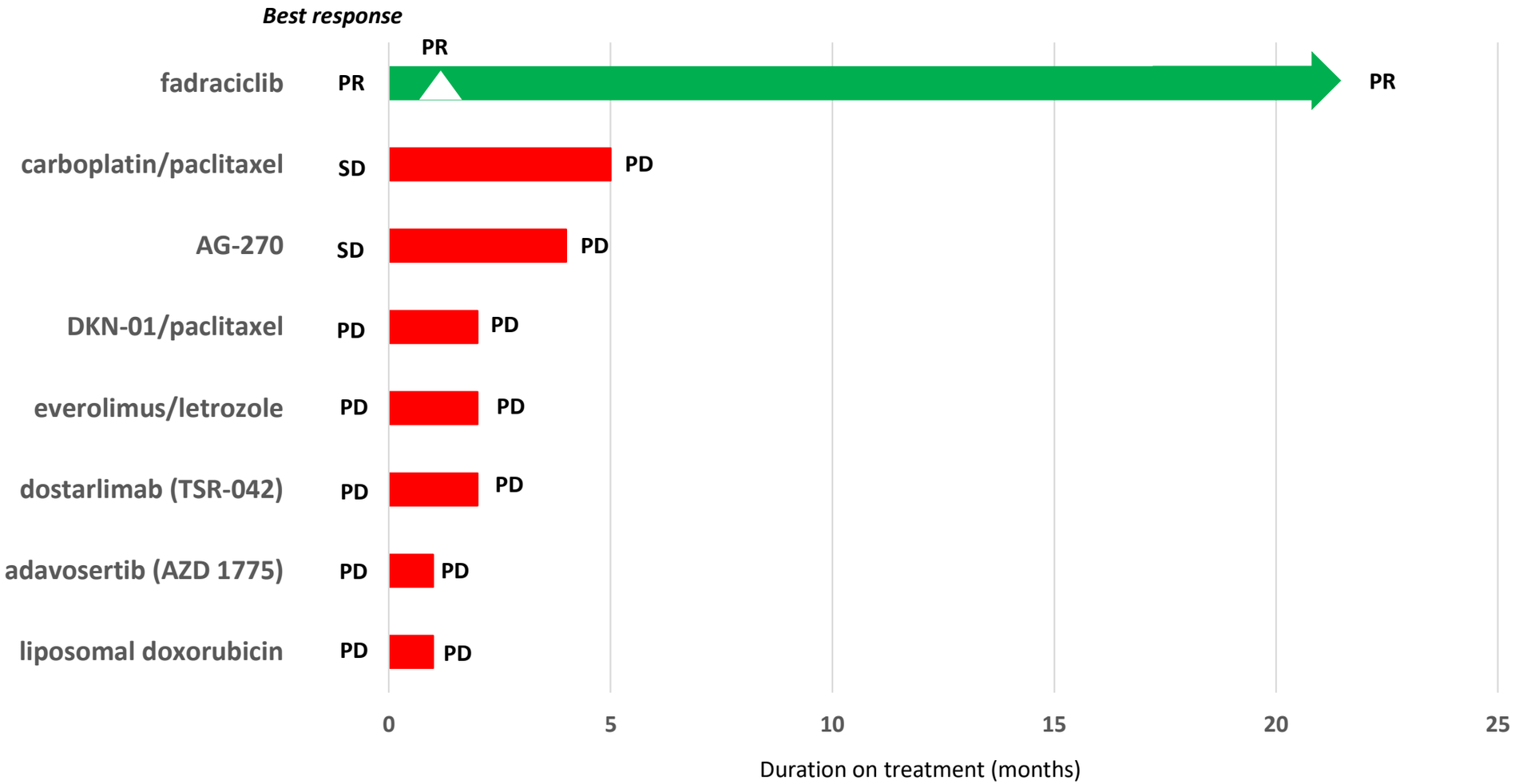


CYCLACEL

Do, KT, et al., 32nd EORTC/AACR/NCI Virtual Symposium 24-25 Oct. 2020. CR=complete response.

Fadraciclib Most Efficacious Treatment

(endometrial adenocarcinoma patient with MCL1 amplification in 065-01 part 2)



Do, KT, et al., 32nd EORTC/AACR/NCI Virtual Symposium 24-25 Oct. 2020. PD=progressive disease. SD=stable disease.

Fadraciclib Oral 065-101 Ph 1/2 Solid Tumor *(ongoing, unselected, late line)*

- Enrolled n=23; currently evaluating dose level 6A (125mg bid daily 4 out of 4 weeks)
- 18 patients treated across 5 cohorts without DLT up to 100mg bid daily 4 out of 4 weeks
- PoC part of the study across multiple tumor types expected to begin 1H 2023

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

Active

- **DL6 (n=2)** *150mg bid daily M to F (4/4 wk)* ✓
- **DL6A (n=3 ongoing) 125mg bid daily M to F (4/4 wk)**
- **DL5 (n=6)** *100mg bid daily M to F (4/4 wk)* ✓
- **DL4 (n=3)** *100mg bid daily M to F (3/4 wk)* ✓
- **DL3 (n=3)** *75mg bid daily M to F (3/4 wk)* ✓
- **DL2 (n=3)** *50mg bid daily M to F (3/4 wk)* ✓
- **Starting DL (n=3)** *50mg bid daily 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

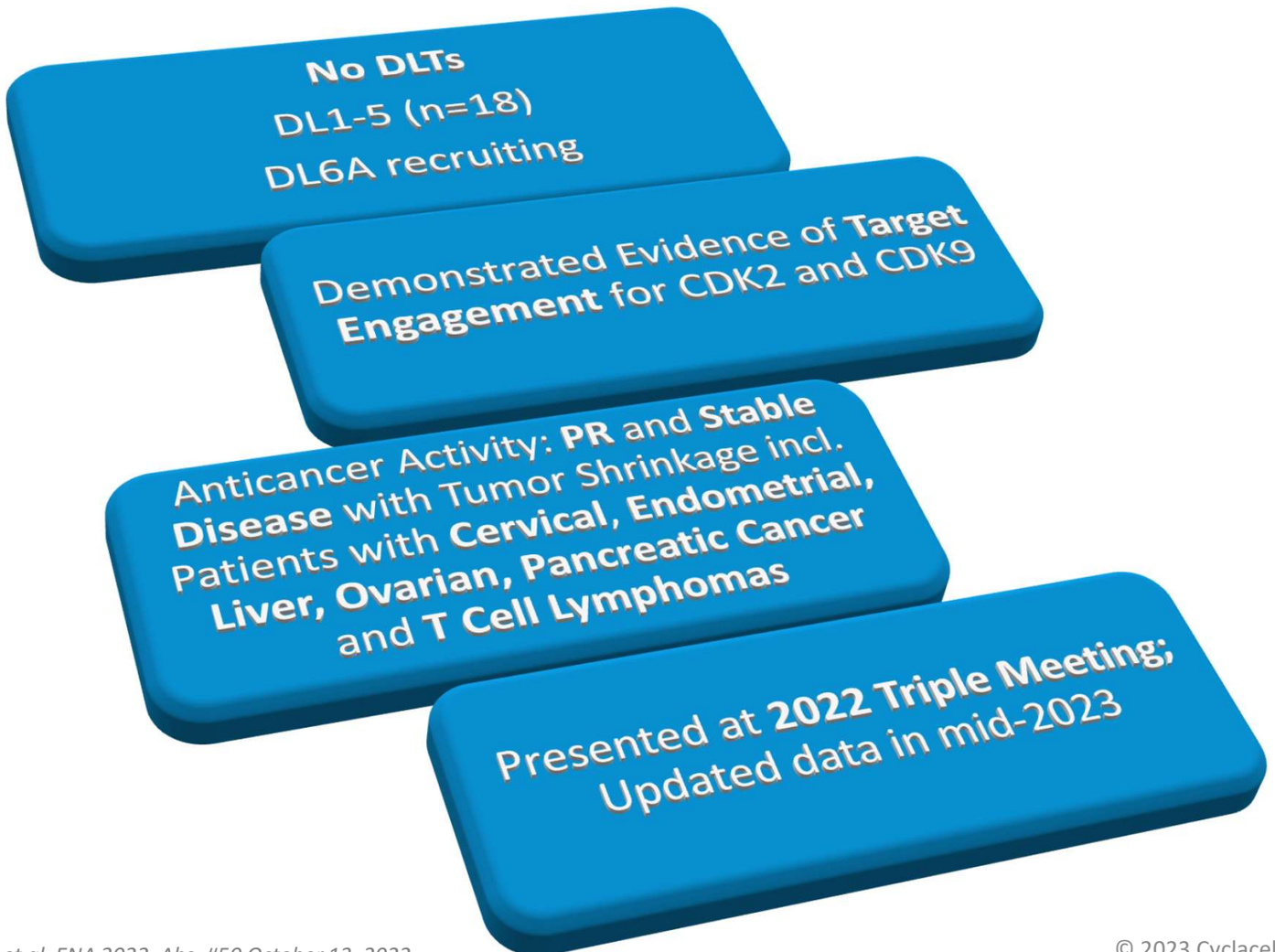
Pivotal indication to be determined based on clinical data from PoC

ClinicalTrials.gov Identifier: NCT04983810.

CYCLACEL

Single agent. Single agent; followed by combination. DLT: dose limiting toxicity. TBD: To be disclosed.*

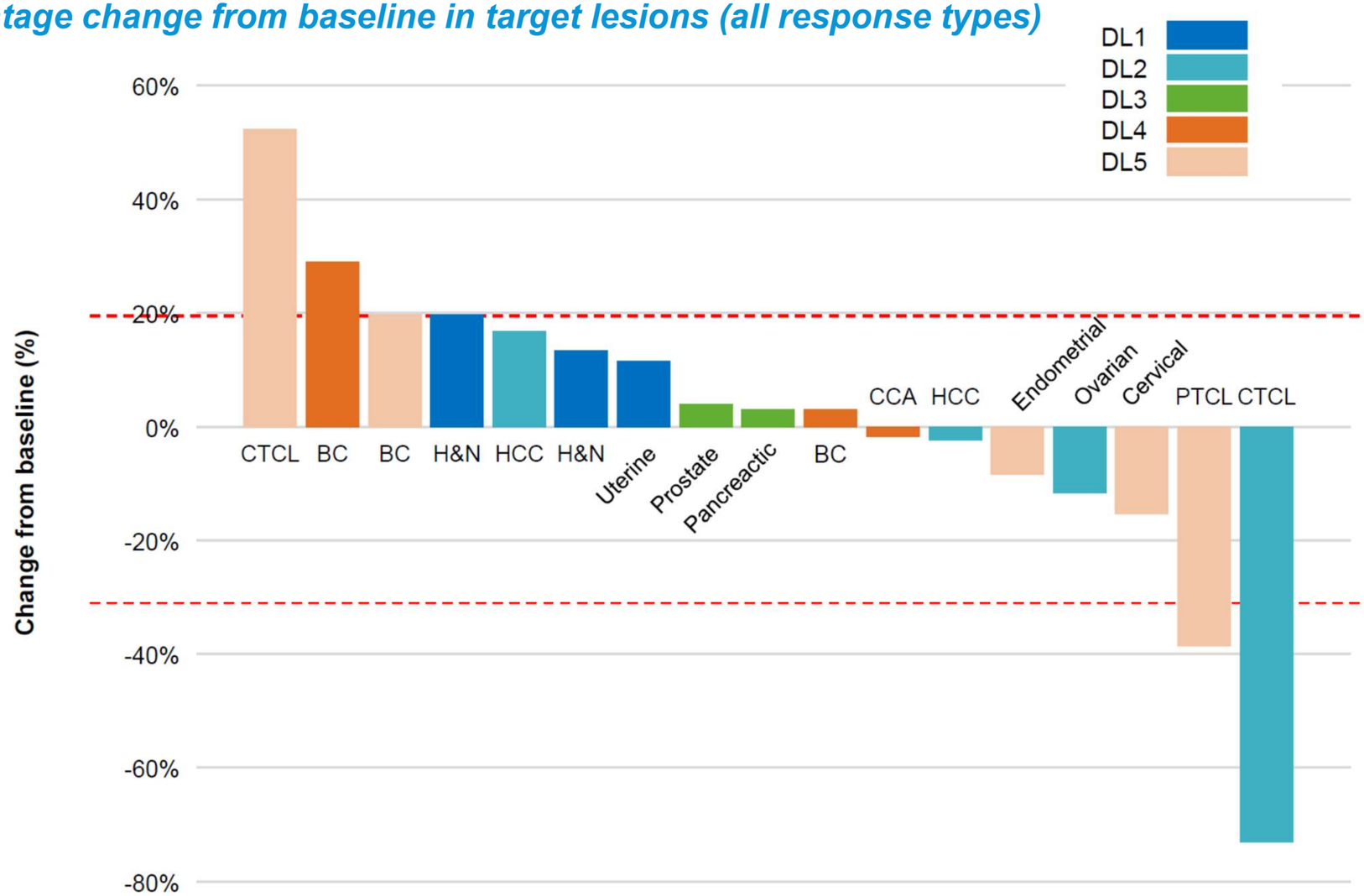
Fadraciclib Oral 065-101 Summary *(ongoing, unselected, late line)*



Piha Paul S, et al, ENA 2022, Abs. #50 October 13, 2022.

Fadraciclib Oral 065-101 DL1-5 Data *(ongoing, unselected, late line)*

Best percentage change from baseline in target lesions (all response types)



Response Criteria by:

- RECIST 1.1 (N=14)
- mSWAT (N=1)
- Lugano (N=2)

BC=breast cancer

CCA=cholangiocarcinoma

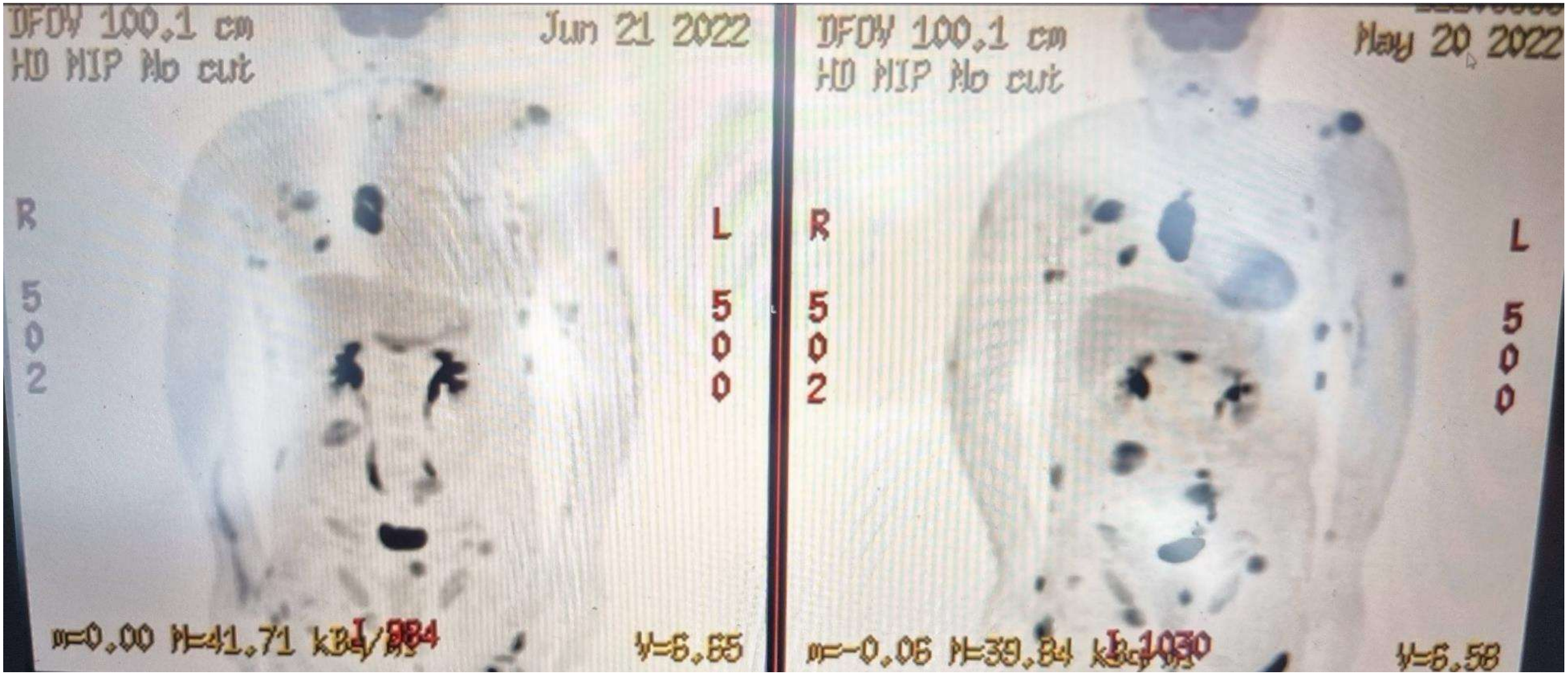
H&N=head & neck cancer

HCC=hepatocellular cancer

CYCLACEL

Piha Paul S, et al, ENA 2022, Abs. #50 October 13, 2022.

PR in angioimmunoblastic PTCL pt. *(oral 065-101 DL5 Lugano criteria)*



Data on file. PET scan images kindly provided by the principal investigator.

Fadraciclib Oral 065-101 SAE List *(interim DL1-5, ongoing)*

ID	Cohort	Event Preferred Term	CTCAE Grade	Causal Relationship
102-001	Dose Level 1	Abdominal pain	2	Not related
102-002	Dose Level 1	Accidental overdose	1	Not Applicable
		Wound secretion	2	Not related
		Obstructive airways disorder	2	Not related
		Productive cough	3	Not related
		Dysphagia	2	Not related
102-004	Dose Level 2	Acute respiratory failure	2	Not related
		Dyspnoea	2	Not related
		Urinary retention	2	Not related
		Disease Progression	5	Not related
		Spinal cord compression	3	Not related
102-009	Dose Level 2	Hyperglycaemia	3	Not related
		Accidental overdose	1	Not Applicable
101-010	Dose Level 3	Cerebral haemorrhage	3	Not related
		Brain edema	3	Not related
		Cerebral haematoma	3	Not related
101-013	Dose Level 3	Abdominal Pain	3	Not related
		Blood bilirubin increased	4	Not related
		Hyponatremia	3	Not related
302-016	Dose Level 4	Cholangitis	3	Not related
		Pain	2	Not related
102-024	Dose Level 5	Seizure	2	Not related

Fadraciclib Oral 065-101 Related TEAE List *(interim DL1-5, ongoing)*

Cohort	TEAE by Preferred Term	All Grades, n	Grade ≥ 3, n
Dose Level 3	Thrombocytopenia	1	0
	Diarrhoea	1	0
	Ageusia	1	0
	Decreased appetite	1	0
	Vomiting	1	0
	Nausea	1	0
	Taste disorder	1	0
Dose Level 4	Diarrhoea	1	0
	Nausea	3	0
	Dry mouth	1	0
Dose Level 5	Blood creatinine increased	2	0
	Diarrhoea	3	0
	Fatigue	2	0
	Nausea	3	0
	Vomiting	2	0
	Abdominal pain	1	0
	Neutrophil count decreased	1	0
	Lymphocyte count decreased	1	1
	Gastritis	1	0
	Thrombocytopenia	1	0
	Hyperglycaemia	1	0

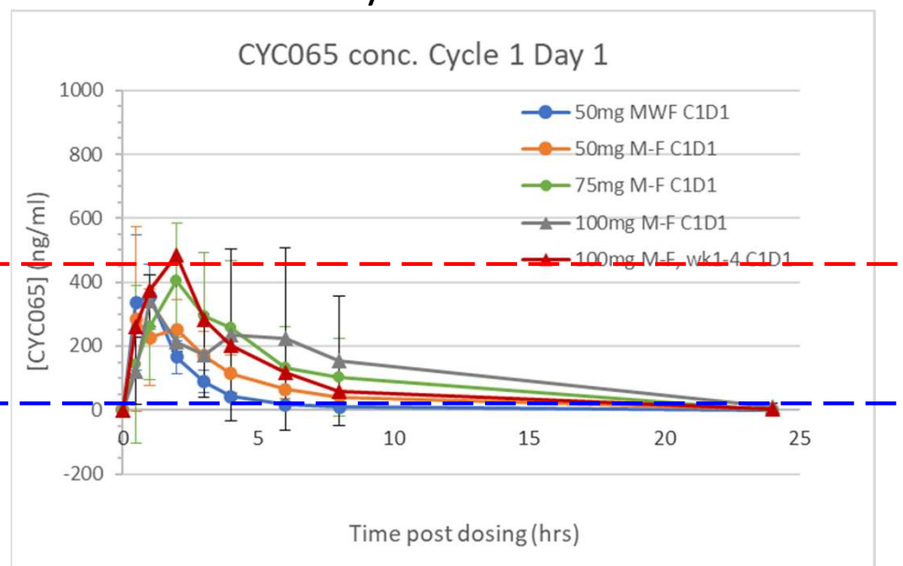
Data on file.

Target Engagement Levels Achieved for 5h on Continuous Dosing

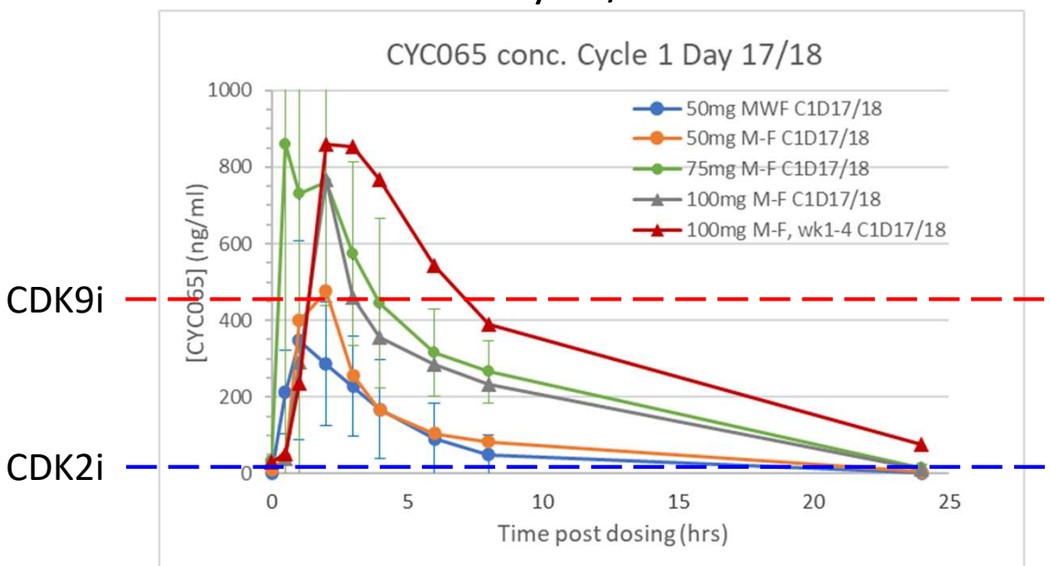
Plasma concentration post fadra treatment in DL 1-5 patients; samples collected on cycle 1 days 1 and 17/18

CDK9 target engagement
CDK2 target engagement

Day 1



Day 17/18



Fadra plasma concentration is dose proportional, crossing target engagement threshold levels with increasing duration at dose levels 4 and 5 after repeated oral administration.

Data on file and Piha Paul S, et al, ENA 2022, Abs. #50 October 13, 2022.

Best-in-Class Potential for Oral Fadraciclib

- Single agent responses demonstrated in liquid and solid cancers without hematological toxicity
- Activity depends on daily dosing and achieving C_{max}
- Dual inhibition of CDK2 **AND** CDK9 maybe superior to either 2 or 9
- Cancer cells adapt to CDK2 inhibition[1]; CDK9 inhibition should be transient[2]
- Oral fadraciclib potentially best-in-class properties (target profile and PK/PD)

CYCLACEL

[1] *Arora M et al, Cancer Res 2023 83 (7_Suppl): 5992. Tetsu O, McCormick F, Cancer Cell, 2003 Mar;3(3):233.*
[2] *Boiko, S et al, Blood, 2021 May 27 137(21) 2947.*

CDK2 Inhibitor Landscape

Rx	CDK	Company	Half life (h)	Schedule	Toxicity	Monotherapy Activity	Comments
fadraciclib *Oral & IV Ph 1/2*	2, 9	*Cyclacel*	**6**	twice daily 125mg 5d/wk	no DLT DL1-5; 1 DLT nausea DL6	**CR endometrial; PR CTCL, PR PTCL**	Target lesion reduction endometrial, cervical, liver, ovarian, SD pancreatic
PF-07104091 [&] *Oral Ph 1/2*	2	*Pfizer*	N/A	twice daily 300mg 7d/wk	≥G3 20/35 57% n&v, diarrhea, anemia, fatigue	3/16 PR 6/16 SD all breast cancer	Ph 2 + fulvestrant breast (n=144); ebvaciclib paused
BLU-222 [*] *Oral Ph 1/2*	2	*Blue-print*	N/A	twice daily 50-800mg	n&v, diarrhea, anemia, fatigue	1/27 PR breast cancer	Partial clinical hold for ocular tox lifted
INCB123667 *Oral Ph 1*	2	*Incyte*	N/A	once daily	not reported	not reported	

CYCLACEL®

Data on file, company reports. [&]ASCO 2023, JCO 41 2023 (suppl 16; abstr. 3010). [*]ASCO 2023. abstr.

CDK9 Inhibitor Landscape

Rx	CDK	Route	Half life (h)	Schedule	Toxicity	Monotherapy Activity	Comments
fadraciclib *Cyclacel Ph 1/2*	2, 9	**Oral**	**6**	twice daily 125mg 5d/wk	**no DLTs** (DL1-5)	**CR endometrial; PR CTCL, PR PTCL**	Target lesion reduction endometrial, cervical, liver, ovarian, SD pancreatic
AZD4573* *AstraZ P1, 2*	9	IV	**6**	once/week 12mg	G3-5 TLS 18/44; neutropenia 13/44	1/17 CR, 1/17 PR DLBCL; 3 CR PTCL	DLBCL responses w/acalabrutinib combo
enitociclib VIP152[&] *VinceRx Ph 1*	9	IV	3-9	once/week 25-30mg	G3-4 neutropenia/ thrombocytopenia (12-18%)	1/17 SD transformed FL	3 SD OVCA; continuing in CLL, lymphoma
KB-0742 *Kronos Ph 1*	9	Oral	24	intermittent 60mg [#]	N/A	N/A	Ph1 n=26, plans Ph2 solid/hem expansion
PRT2527 *Prelude Ph 1*	9	IV	4-5	once/week 15mg/m^2	G4 neutr.; n&v, TLS fatigue, diarrhea	3/11 SD	Hem: AML, DLBCL

CYCLACEL

*Data on file. N/A=not available. ^ AACR 2023. *EHA 2023; ASH 2022. [&]ASH 2022, DLT: TLS, acute kidney and liver injuries. [#]3d q wk s.t. NHL ^mLFS=morphologic leukemia free state.*

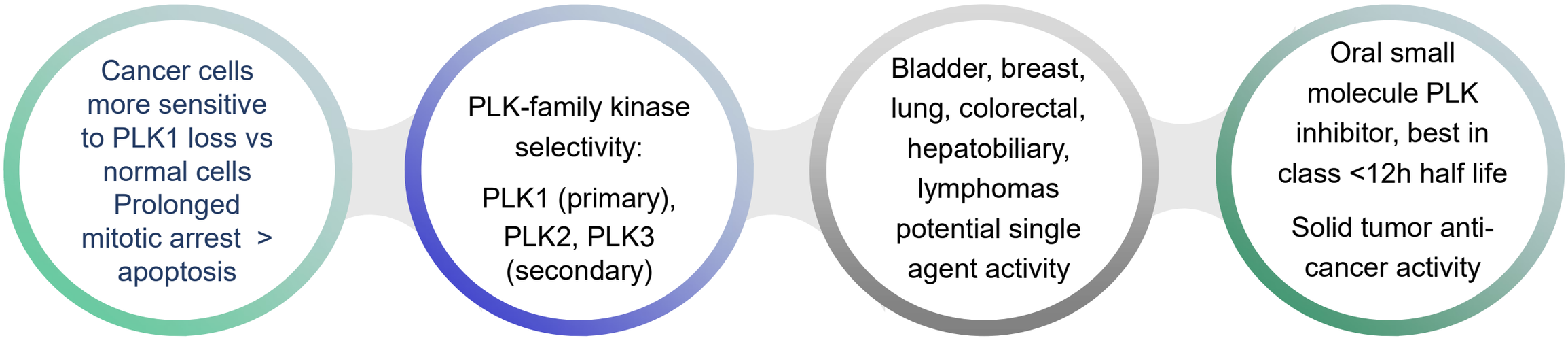
Fadraciclib Summary

- 23 patients treated thus far in 065-101 with oral fadraciclib
- n=18 median treatment duration 2.4 cycles; well tolerated thus far (DL1-5 range 1-5 cycles)
- Two PRs in T-cell lymphoma pts; 4 pts (cervical, endometrial, liver, ovarian cancer) target lesion reduction and a pancreatic cancer patient stable disease for 5 cycles
- Confirmed CR continues for 3 years in a subject with MCL1-amplified endometrial cancer dosed at 213mg IV 2d/wk every 2 wks q3w in earlier Phase 1 IV study of fadraciclib
- Capsule to tablet switch in Phase 1 to generate data with commercial drug product
- Expect to determine RP2D in mid 23 and begin Ph2 PoC part of 065-101 in 2H 23

CYCLACEL

Data on file and Piha Paul S, et al, ENA 2022, Abs. #50 October 13, 2022.

Plogosertib (formerly CYC140, next gen PLK inhibitor) Snapshot



Ongoing Ph 1/2: biologically-optimal schedules require continuous dosing

CYCLACEL

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

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 with chemo; prostate with abiraterone*; mPDAC with chemo
- Ph 2: Three arm RCT 2 doses triplet therapy vs control bevacizumab/chemo (n=90)

Plogosertib

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

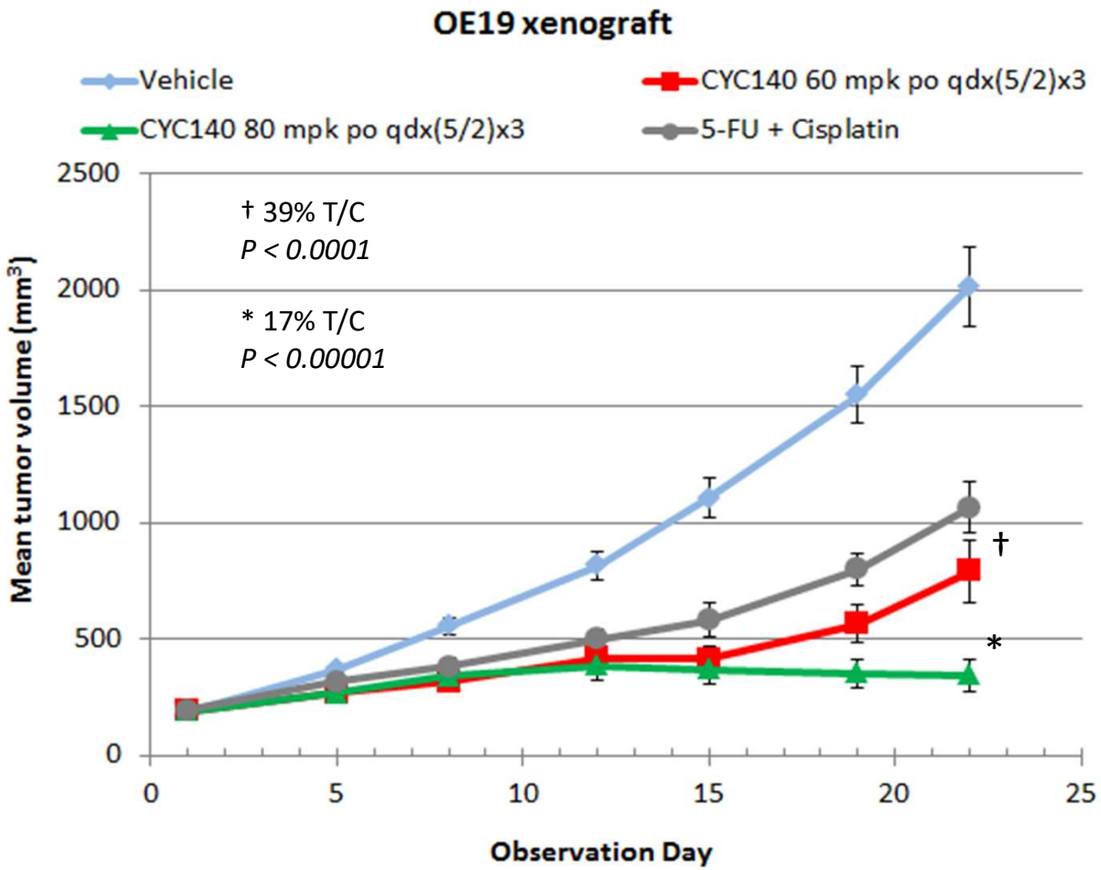
- Preclinical activity in multiple solid tumors and leukemias; terminal $t_{1/2}$ ~11h
- Single agent anticancer activity on first 3 dose levels in NSCLC, ovarian, biliary
- Registration-enabling, Ph 1/2 in multiple **solid tumors** and **lymphoma** in progress

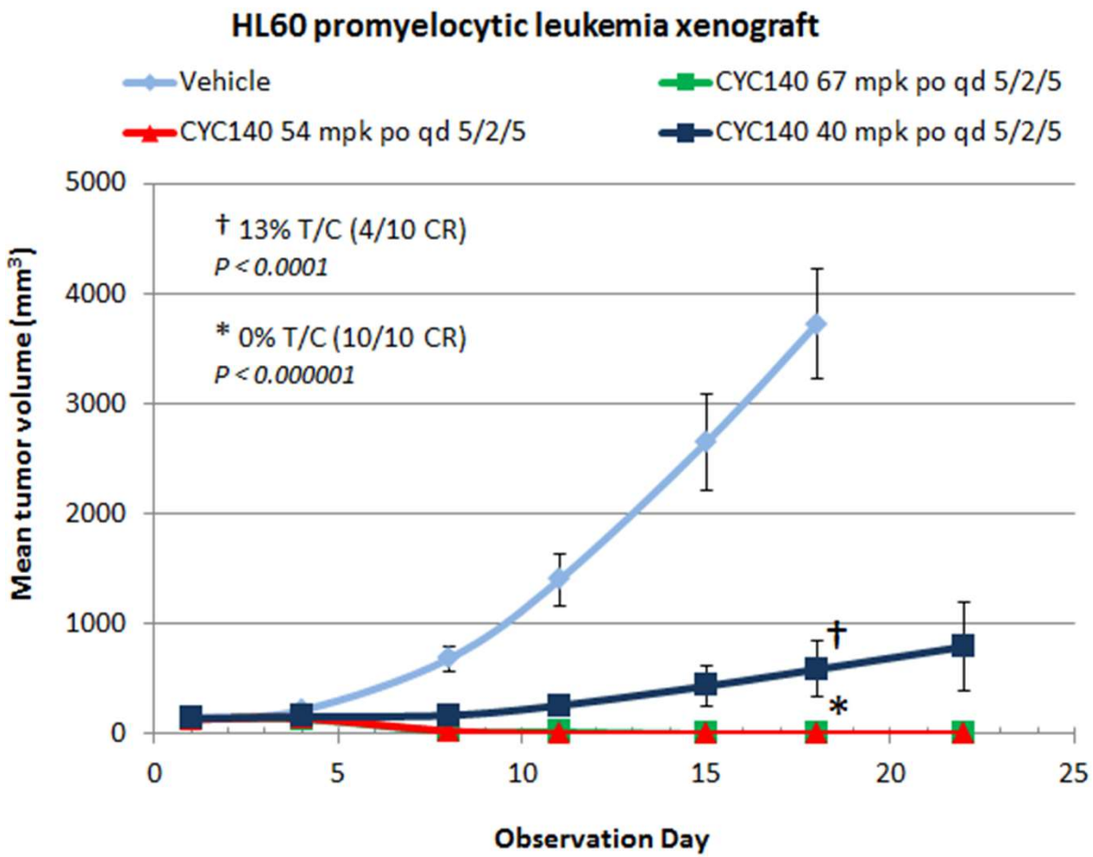
CYCLACEL

*Data on file. *Valsasina B et al Mol Can Ther 2012 11 1006; https://mct.aacrjournals.org/content/11/4/1006.figures-only.*

Plogosertib Preclinical Efficacy Esophageal & Leukemia Models

Potent and selective inhibitor (PLK1 IC_{50} ~3 nM)

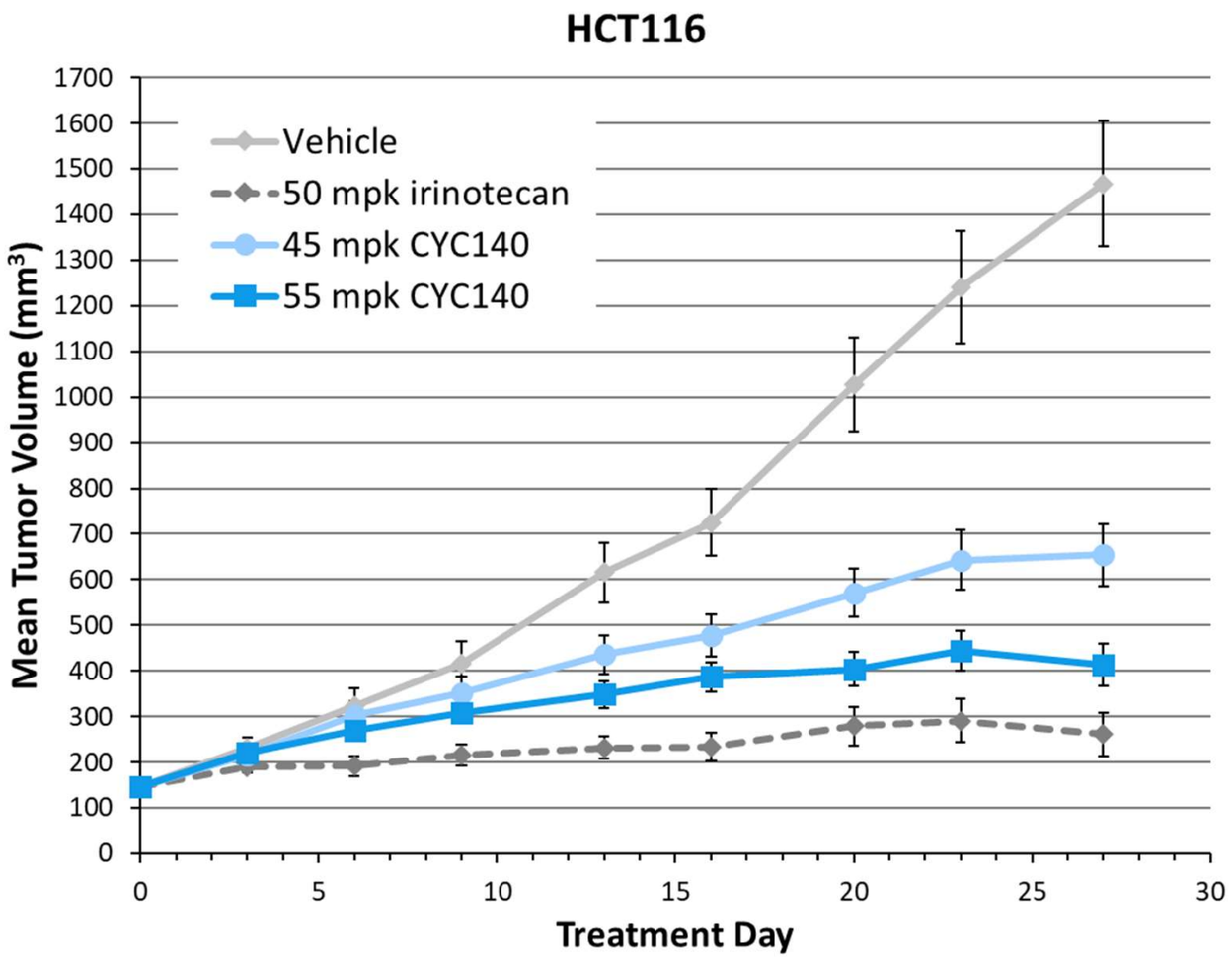




CYCLACEL

Data on file.

Plogosertib Preclinical Efficacy KRAS G13Dm Colorectal Cancer

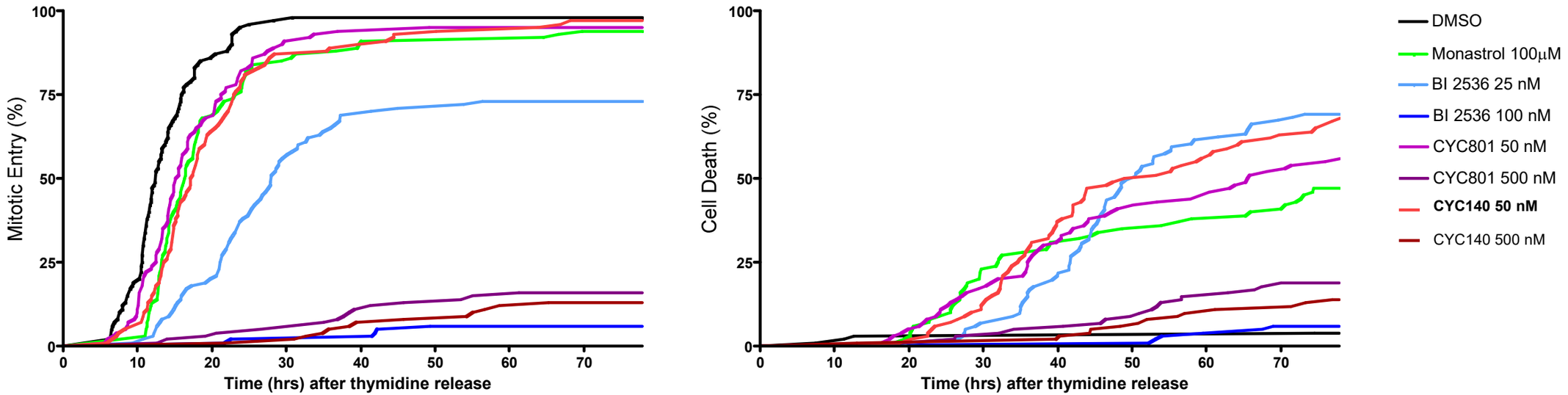


Treatment	Route/ Schedule	Efficacy
50 mpk irinotecan	ip Q4D x 4 wk	Not tolerated >10% Mean BW Loss 18% T/C (Day 27)
45 mpk CYC140	po (qdx5/wk) x 4 wk	45% T/C (Day 27)
55 mpk CYC140	po (qdx5/wk) x 4 wk	28% T/C (Day 27)

Data on file. HCT116 is a human colorectal carcinoma cell line. T/C=tumor over control.

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.

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

CYC140-101 Oral Ph1/2 Solid Tumor Study Design

Dose Escalation* (3+3; unselected, 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; 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)

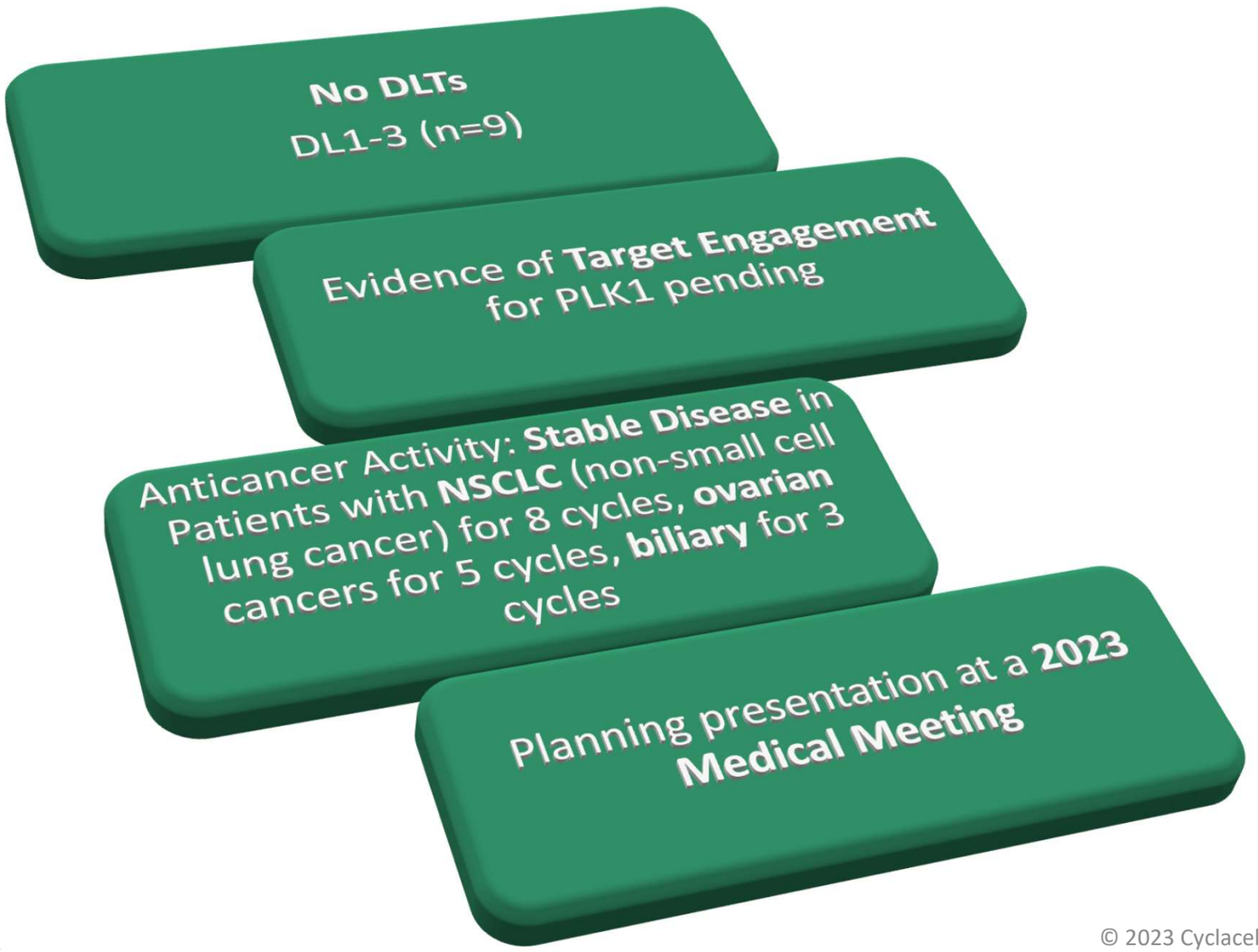
Pivotal
(if randomized study not needed)

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

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

CYCLACEL *Single agent **Single agent; followed by combination TBD: To be disclosed.

Plogosertib Oral 140-101 DL1-3 Data *(ongoing, unselected, late line)*



CYCLACEL® *Data on file.*

Plogosertib Summary

- Optimized short half life and oral dosing
- Improved kinase profile over other PLK1 inhibitors, incl. BRD4 inhibition at low nM range (suggesting novel epigenetic mechanism)
- Broad single agent preclinical activity supports monotherapy trial design
- Phase 1/2 solid tumor and lymphoma ongoing at DL4 (n=14)
  - Anticancer activity in patients with NSCLC, ovarian and biliary cancers
  - No DLT thus far
  - Report interim data in 2023 medical conference

CYCLACEL

Financial Position & Capitalization

Proforma Cash & cash equivalents: **$16.1 million** (as of March 31, 2023)

Incl. UK R&D Tax Credit of $4.7 million received in April 2023

Operating cash burn (excludes non-cash items):

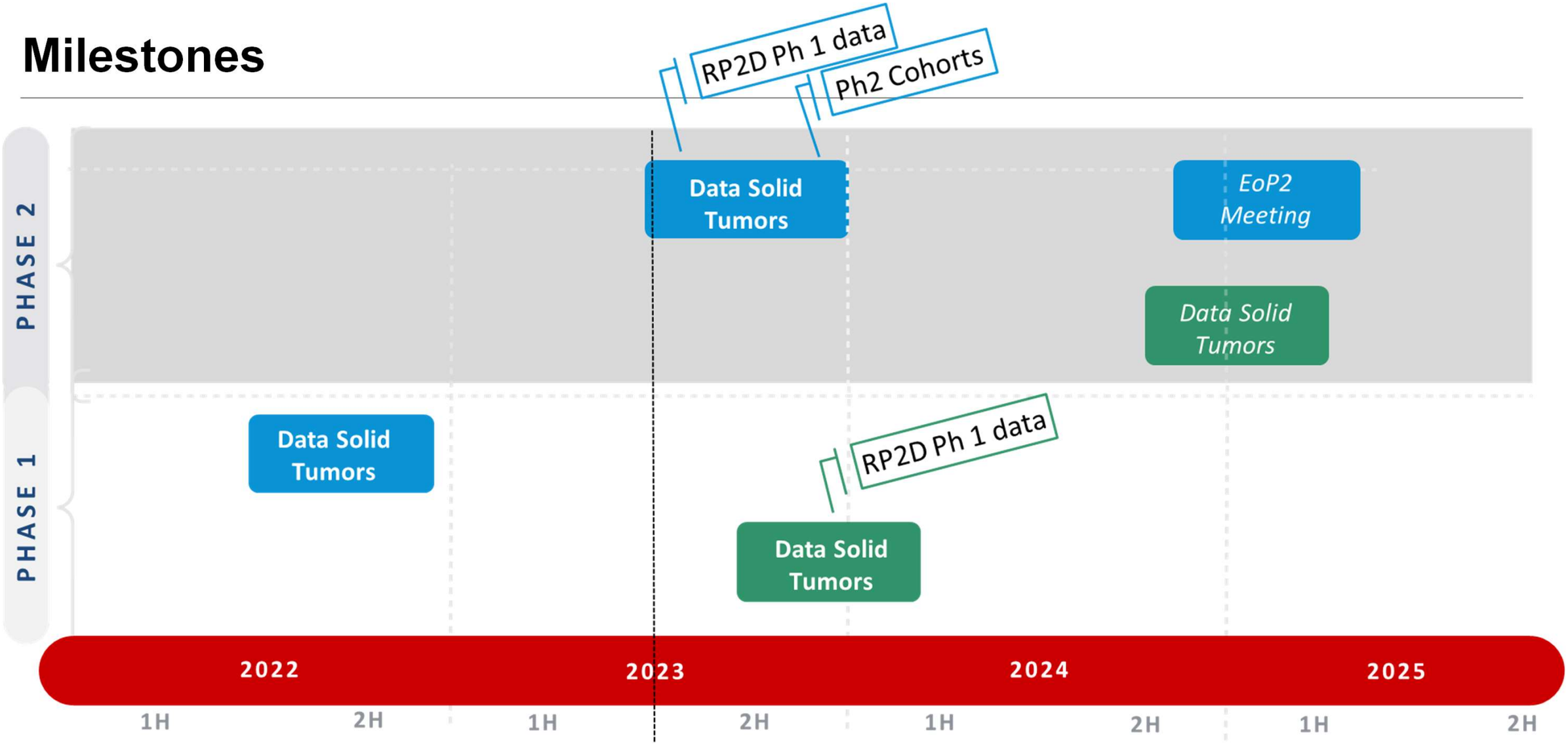
- 2021 Annual: $18.5 million[1]
- 2022 Annual: $20.8 million[1]

Fully diluted shares: 18.6 million[1]; no debt

Estimated capital into Q1 2024

[1] *10K; common stock outstanding 12.5m, preferred stock 1.2m, common stock warrants 3.1m, options 1.8m.*

Milestones



Fadra

Plogo

Cyclacel data on file. FPI = First Patient In.

Cyclacel 2023 Milestone Momentum

Fadraciclib 065-101 - Oral CYC065, CDK2/9 inhibitor

- Phase 1 readout & RP2D in early 2H 2023 to include PK, PD, safety and activity data
- Capsule to tablet switch in Phase 1 to generate data with commercial drug product
- Phase 2 solid tumor Proof of Concept to begin 2H 2023
- Clinical development plan with 8 cohorts including T-cell lymphoma (responses 2/3 pts)
- Initial clinical activity data from selected cohorts from the Phase 2 study 2H 2023

Plogosertib 140-101 - Oral CYC140, PLK1 inhibitor with novel epigenetic MoA

- Phase 1 dose escalation continues at DL4 (initial activity seen at DL1-3 in NSCLC, ovarian and biliary)
- Interim dose escalation readout 2H 2023 to include PK, PD, safety and activity data

CYCLACEL

DL= dose level.

Investment Thesis

- CYCC discovered, developed and now optimizing its clinical cell cycle drug portfolio
- Top-tier funds have invested in CYCC
- Single-agent activity has been observed with good tolerability
- Leadership position in both therapeutic classes
- Lean operational efficiency
- Multiple 2023 inflection points anticipated
- Public company with derisked pipeline at near-zero pre money

CYCLACEL

Thank You

Cyclacel Pharmaceuticals, Inc.

200 Connell Drive #1500
Berkeley Heights, NJ 07922

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