Translating cancer biology into medicines

NASDAQ: CYCC

Dawson James Small Cap Growth Conference 2018

October 30, 2018

Disclaimer

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Cyclacel Pharmaceuticals Overview

- Apply deep understanding of cell cycle biology to disrupt
    a. cancer cell **resistance**
    b. **DNA repair** or evasion
- Pioneer in Cyclin Dependent Kinase inhibitors; rationally designed clinical programs in leukemias & breast cancer
- Focus on molecularly-defined patient populations (precision Rx)
- Experienced management; estimated capital through Q1 2020

Value Drivers

CYC065

- CDK inhibitor with Proof of Mechanism in Phase 1 data
- 2L CLL venetoclax combination addressing large market

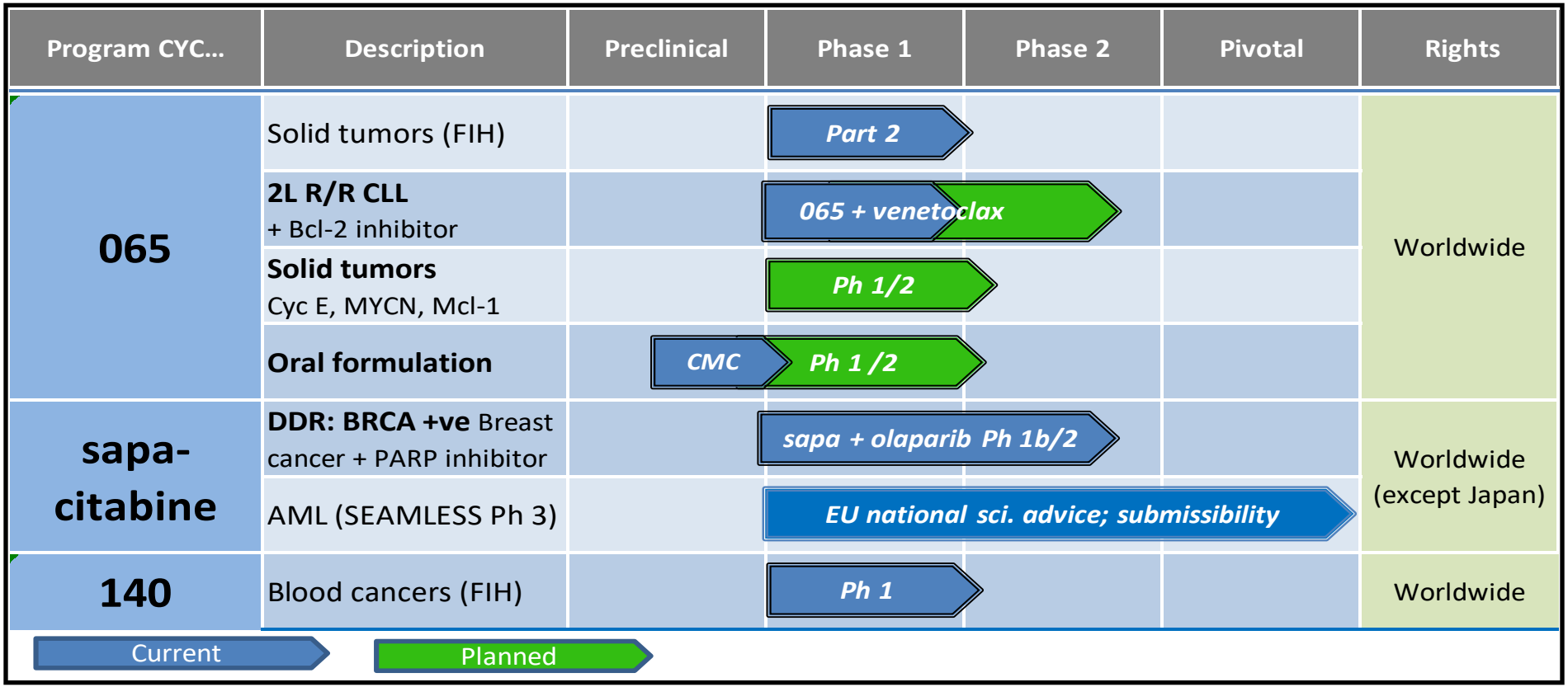
Sapacitabine

- Oral nucleoside analogue, unique MoA in DNA damage response in BRCA +ve breast cancer
- Phase 1b/2 olaparib combination study enrolling

CYC140

- PLK inhibitor with compelling preclinical data in liquid & solid cancers

Development Pipeline



Protecting our Investment in Cancer Meds

$107 bn in 2015 (+12% YoY). *Est. ~$150 bn in 2020*

Single Rx targeting mutations: validated approach

…↑ response but cures/long stable disease elusive…

EVOLUTION OF RESISTANCE TO CANCER Rx

OR ADDICTION TO CANCER GENES

- Strategy: combine approved Rx that is no longer working with resistance-modifying Rx or
- Rx that breaks addiction to oncogenes (MYC, cyclins)

Suppressing Resistance Proteins

Bcl-2, Bcl-XL, Mcl-1:

↑ *expression: survival & growth of cancer cells*

- **Bcl-2** > **venetoclax** approved in 2L CLL
- Bcl-XL > investigational drugs but safety issues
- **Mcl-1** > transcriptional CDKi, incl. **CYC065**

Competitive race to develop Rx that suppress Mcl-1 one of most frequently overexpressed cancer genes

Indication Rationale: 2L CLL (post BTKi)

1L US incidence 21,000; nearly all survivors receive 2L

Venetoclax does not ↓ Mcl-1; previous transcriptional CDKi active in CLL

Preclinical evidence of synergy for venetoclax + CYC065*

CYC065 1st CDKi to durably suppress ↓ Mcl-1 in patients

“Double-Hit” strategy to suppress Bcl-2 + Mcl-1

CYC065 + venetoclax study activated

** Source: Chen et al AACR 2018 Abs 5095; Cyclacel data on file.*

CYC065 First in Human Phase 1 (ongoing) part 1

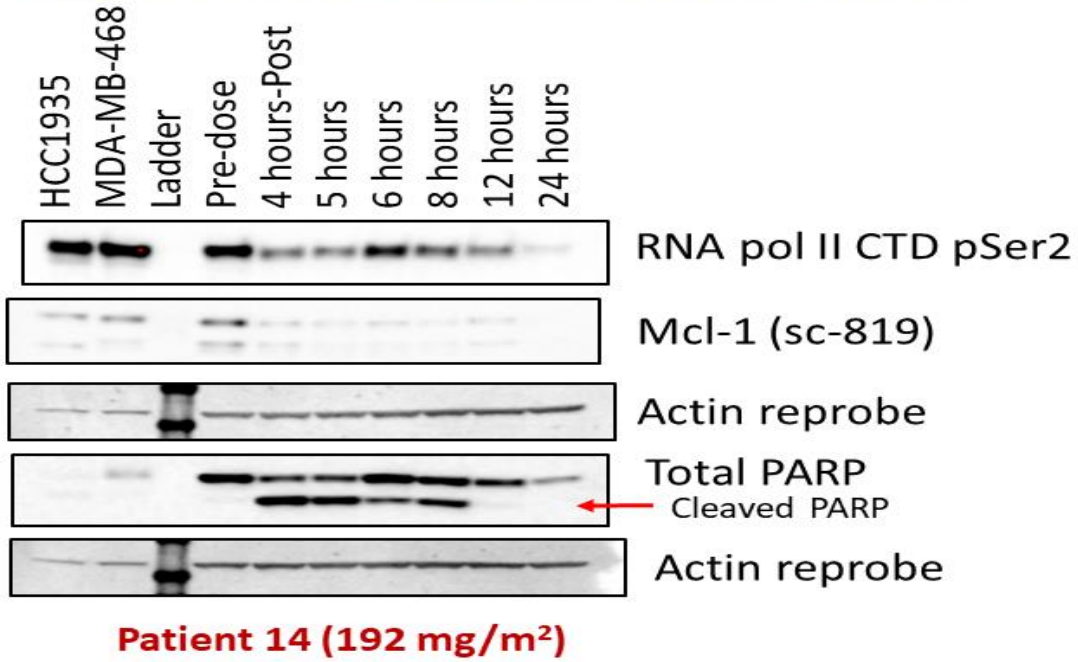
n=26 heavily pretreated patients with advanced solid tumors (13 in DL6 cohort RP2D)

- Durable **Mcl-1 suppression** >24h after single dose in 11/13 DL6 patients
- Anticancer activity in 6/13 patients (5 at RP2D)

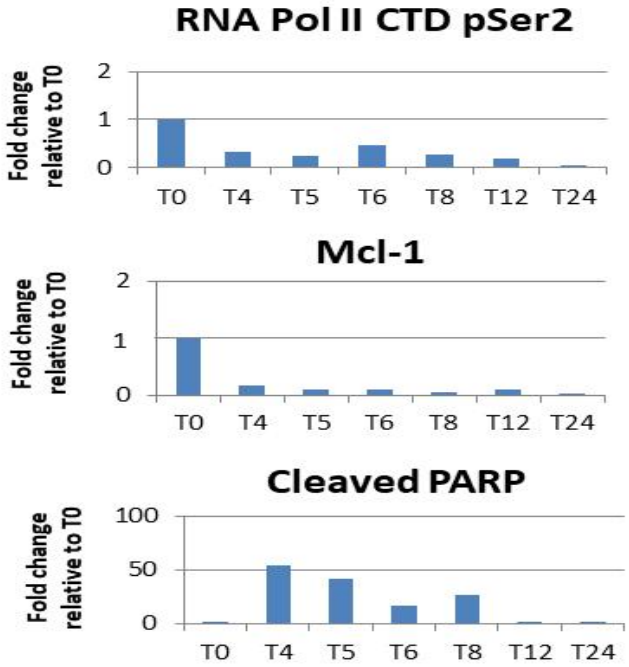
** Source: Cyclacel data on file.*

CYC065 First in Human Phase 1 part 1 (b)

Target inhibition detectable at 24 hours



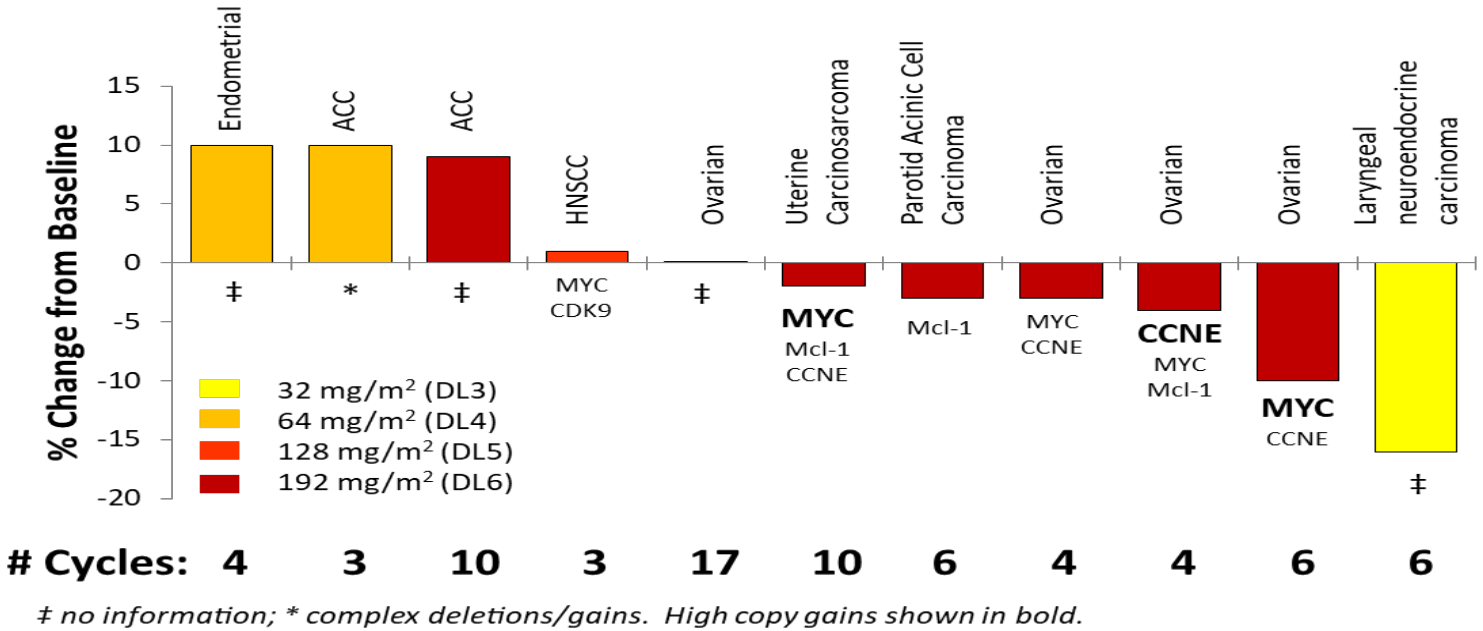
Patient 14 (192 mg/m²)



Khanh T. Do, AACR Annual Meeting 2018.

American Association for Cancer Research

CYC065 First in Human Phase 1 part 1 (c)



‡ no information; * complex deletions/gains. High copy gains shown in bold.

Summary:

- 20/26 patients evaluable for response per RECIST 1.1
- 11/20 patients achieved stable disease (SD)
- 6/11 patients achieved SD for 4+ cycles

Do, Khanh T., et al, AACR Annual Meeting 2018.

American Association for Cancer Research

CYC065: Clinical Development Priorities

Molecularly-defined patient populations

Current (hematological malignancies):

1. Combination with **venetoclax** in patients with relapsed/ refractory CLL

Future (solid tumors):

2. Selected Mcl-1 ↑ or MYC ↑ solid tumors, i.e. neuroblastoma, ovarian, etc.
3. Selected Cyclin E ↑ solid tumors, i.e. breast, ovarian, uterine (USC)

CDK Inhibitor Landscape

CDK4/6 isoform

palbociclib (PFE), ribociclib (NVS), abemaciclib (LLY) Approved in combination with letrozole for ER +ve Her2 -ve advanced or met BC

trilaciclib (GTHX) Ph1/2

CDK2/9 transcriptional isoform

CYC065 (CYCC 2G) Ph1

seliciclib (CYCC 1G) Ph2

dinaciclib (pan CDK, MRK) Ph3

BAY1143572 (CDK9, BAY) Ph1

Other *(pan CDK or selective):*

SY1365 (CDK7, Syros);

voruciclib (CDK4/6/9, MEI Pharma)

** Source: Cyclacel data on file.*

DNA Damage Response (DDR)

Overcoming Cancer DNA Repair & Evasion

Cancer cells evade Rx; block DNA repair; ultimately immortalize

Homologous recombination (HR) deficient (incl. BRCA mutant) cancers (breast, ovarian, prostate, pancreatic, etc.) have an Achilles heel:

- Inhibition of PARP enzymes is synthetically lethal: accumulation of SSBs converted to DSBs; DNA cannot be repaired by HR
- SoC: 3 approved PARP inhibitors (olaparib, niraparib, rucaparib)
- Significant unmet medical need remains

Sapacitabine in HR deficient Cancers

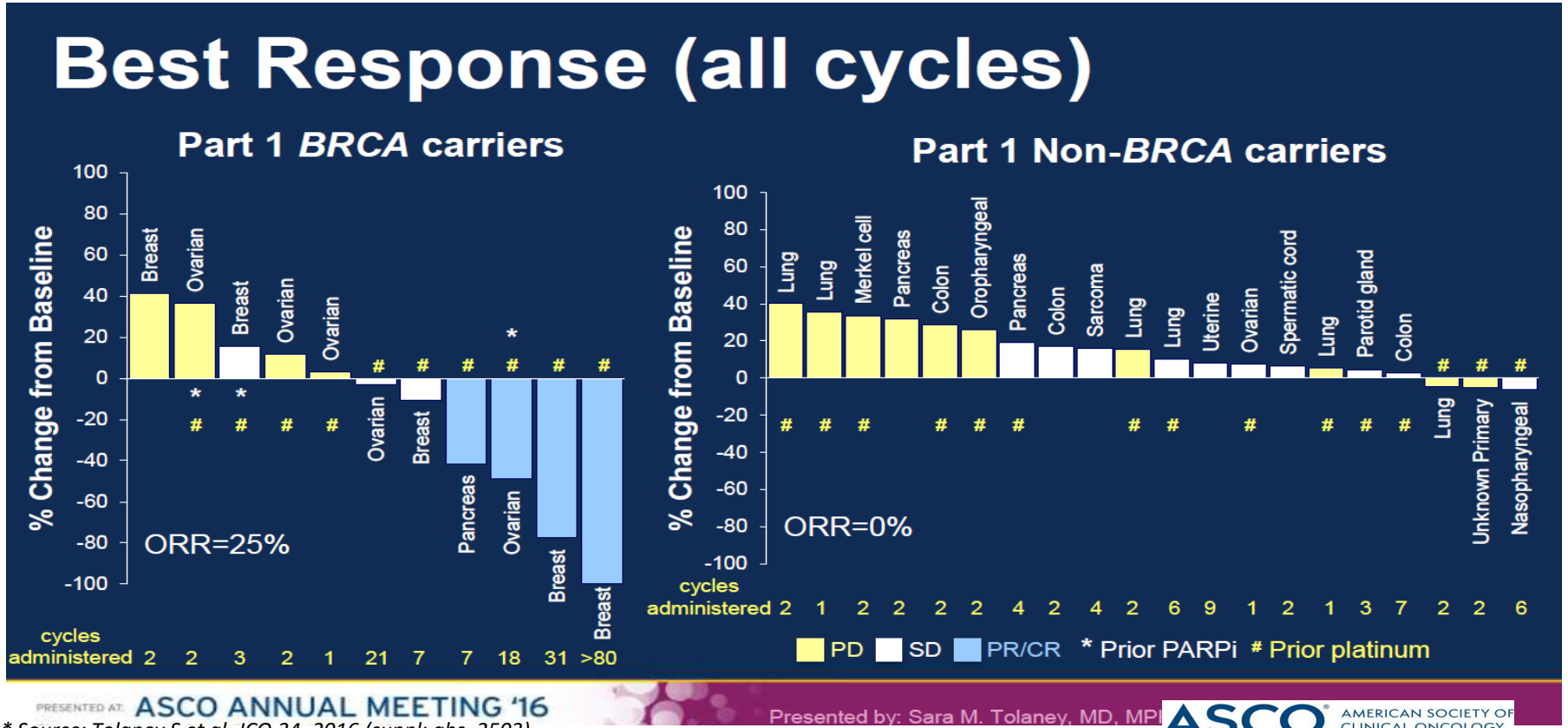
Sapacitabine is active in BRCA +ve patients with HR deficient cancers via a novel mechanism

- Oral Rx induces SSBs and metabolizes into CNDAC via β-elimination reaction converted into DSBs that cannot be repaired by HR

Efficacy: durable CR, PR, SD (n=76, ASCO 2016) in BRCA +ve patients with breast, ovarian and pancreatic cancers

Potential to combine with PARP inhibitors

Sapacitabine & Seliciclib Phase 1 BRCA+ve Benefit*



** Source: Tolaney S et al, JCO 34, 2016 (suppl; abs. 2503).*

Indication Rationale: HR def Breast Cancer

HR def = 8% of all breast cancers *

Increase durability of PARPi response

Preclinical evidence of synergy for PARPi + sapacitabine*

Different MoAs may increase therapeutic index

Oral combination of **olaparib (Lynparza®) + sapacitabine**

Dana Farber IST ongoing (AstraZeneca & Cyclacel clinical supply)

** Source: Heeke A, et al, ASCO 2017. Liu et al Mol Cancer Ther 2016 16 2302; Cyclacel data on file. Lynparza® is a registered trademark of AstraZeneca.*

Sapacitabine in AML (SEAMLESS Ph 3 data)

Optionality from potential regulatory submission

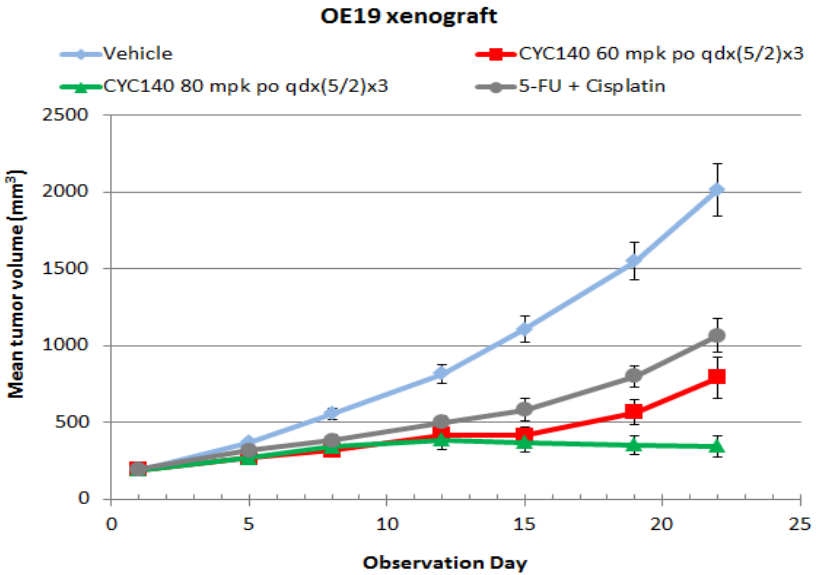
- ✓ Increase in median OS (primary endpoint) did not reach stat. sig.
- ✓ Doubling of CR rate (secondary endpoint)
- ✓ Improved median OS in large (2/3 of study) prospectively defined subgroup based on WBC level
- ✓ Oral presentation at ASH Annual Meeting 2017
- ✓ National regulatory consultations in various EU countries
- ▪ EMA regulatory consultation
- ▪ Determine submissibility

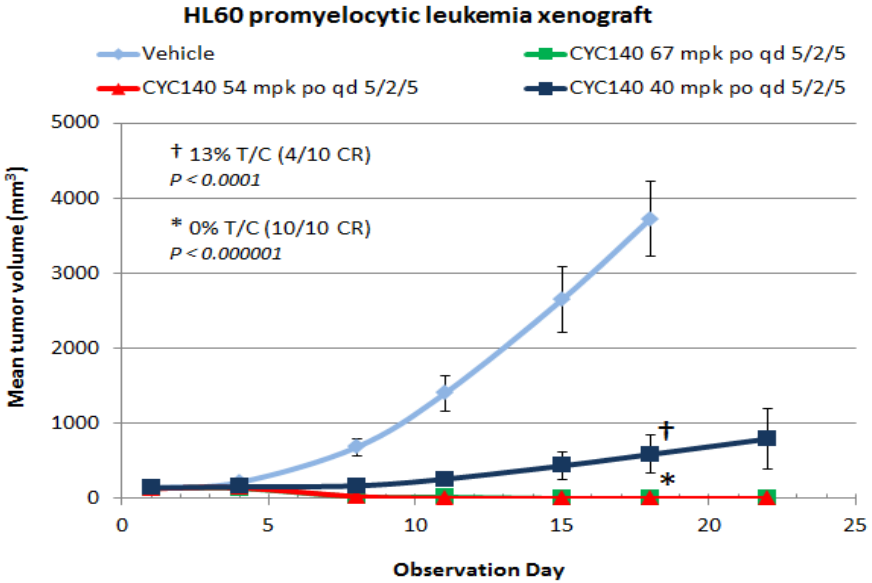
Source: Cyclacel press releases and data on file.

CYC140 PLK1 inhibitor

DNA damage checkpoint regulation

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





Source: Cyclacel data on file.

MD Anderson-Cyclacel Alliance

- Up to 170 patients with single agent or combinations of:
  - CYC065, CYC140, sapacitabine
- Risk Sharing: MDACC assumes patient costs; Cyclacel supplies drugs and limited support
- Payments to MDACC upon First Commercial Sale in indications studied

Financial Position & Capitalization

June 30, 2018 cash & cash equivalents: $19.8m[1]

Operating cash burn (excludes non-cash items)

- ✓ 2015: ~ $14.5m annual [1]
- ✓ 2016: ~ $10.1m annual [1]
- ✓ 2017: ~ $ 7.5m annual[1]
- ▪ 2018: ~ $10.9m annual[2]

Fully diluted shares: ~ 20.0 million[1,3]

No debt

1. *10 K, 10 Q*
2. *Company estimate*
3. *Common stock outstanding 12.0m*

Key Milestones

- ✓ CYC065 Phase 1 data solid tumors
- ✓ Sapacitabine plus olaparib Ph 1b/2 BRCA +ve breast cancer
- ✓ CYC065 Ph 1b combination with venetoclax in RR CLL activated
- ✓ CYC140 (PLKi) Ph 1 first-in-human study activated
- Start CYC065 studies in additional indications
- CYC065 oral formulation development
- Determine submissibility of sapacitabine in elderly AML

Investment Thesis

- Clinical stage, state-of the-art oncology programs
- Targeting molecularly-defined patient populations
- Treat difficult cancers to overcome cancer cell resistance & DNA repair
- CDK inhibitors: validated drug class
- Competitively positioned

THANK YOU

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