Translating cancer biology into medicines

NASDAQ CYCC

H.C. Wainwright 21st Annual Global Investment Conference

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Cyclacel Overview

- Apply deep understanding of cell cycle biology to disrupt cancer
    - **resistance**
    - **DNA repair** or evasion
- Targetable precision medicine strategy:
    - **MCL1** in leukemias (Phase 1)
    - **BRCA1/2** in breast cancer (Phase 1/2)
- Experienced management; estimated capital to end of 2020

Clinical Stage Value Drivers

CYC065

- CDK inhibitor with proof of mechanism (down-regulation of MCL1) in humans
- 2L venetoclax combination in leukemias (CLL, AML)

Sapacitabine

- Oral nucleoside analogue, unique DNA damage response mechanism for BRCA +ve patients
- 2L olaparib combination in BRCA +ve breast cancer

CYC140

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

Addressing Large Markets

CLL 2L

- 21k US incidence; majority on ibrutinib (BTKi)
- CYC065 venetoclax (1L with ibrutinib or 2L)

AML elderly unfit for chemotherapy

- ~16k US incidence; venetoclax+HMA (aza or dec)
- CYC065 venetoclax combination

BRCA +ve Breast Cancer

- ~11-15k US incidence; olaparib or other PARPi
- sapa olaparib combination

Suppressing Resistance Proteins

↑ *protein expression=survival/growth of cancer cells*

- **BCL2** > **venetoclax** approved in 2L CLL & 1L AML

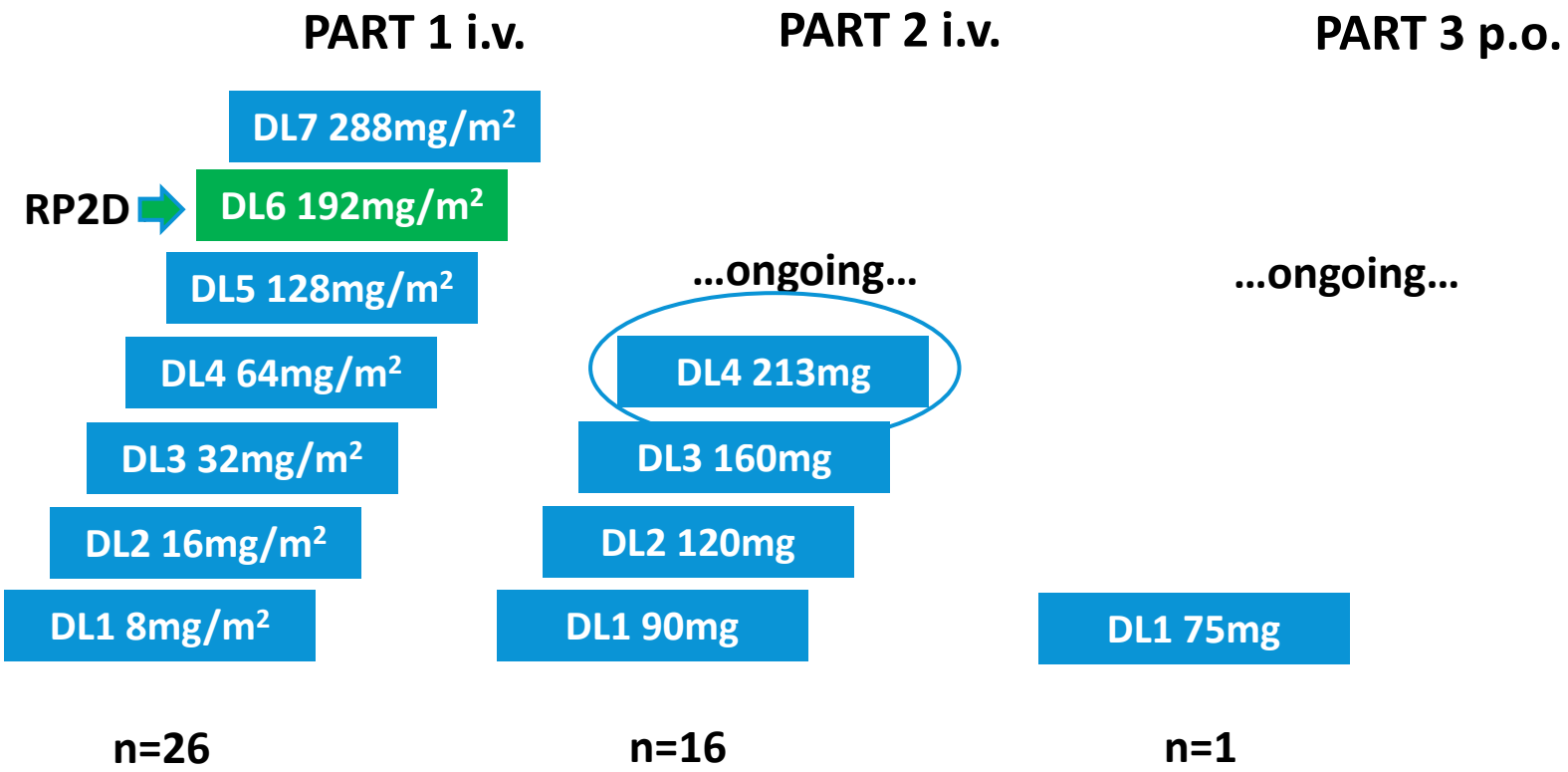
- **MCL1** > transcriptional CDKi, incl. **CYC065**

  (one of ten most frequently overexpressed cancer genes)

Competitive race to develop drugs that suppress MCL1

CYC065 1st Rx to show durable MCL1 suppression in humans

CYC065-01 Phase 1 Escalation Schema



Source: Cyclacel data on file.

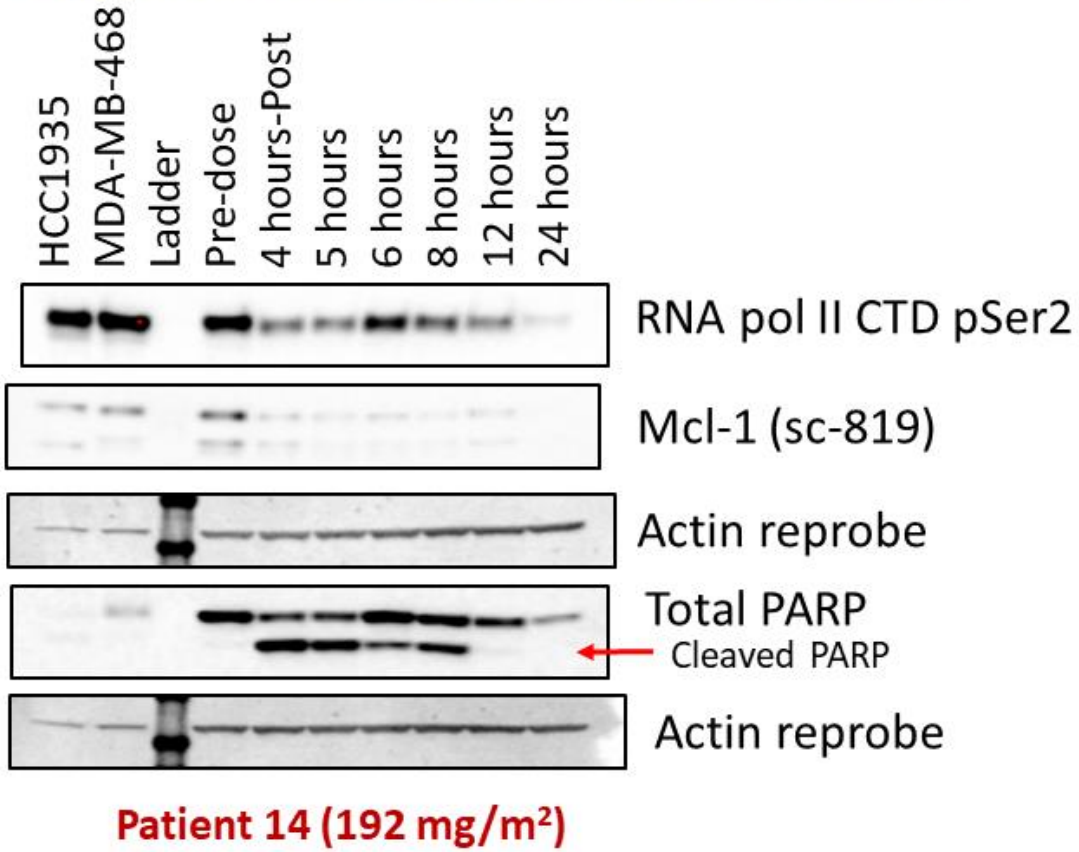
CYC065-01 First in Human Ph 1 part 1 (n=26)

- Heavily pretreated patients with advanced solid tumors
- Durable **MCL1 suppression** after single dose observed at RP2D
- Anticancer activity in 6/13 patients

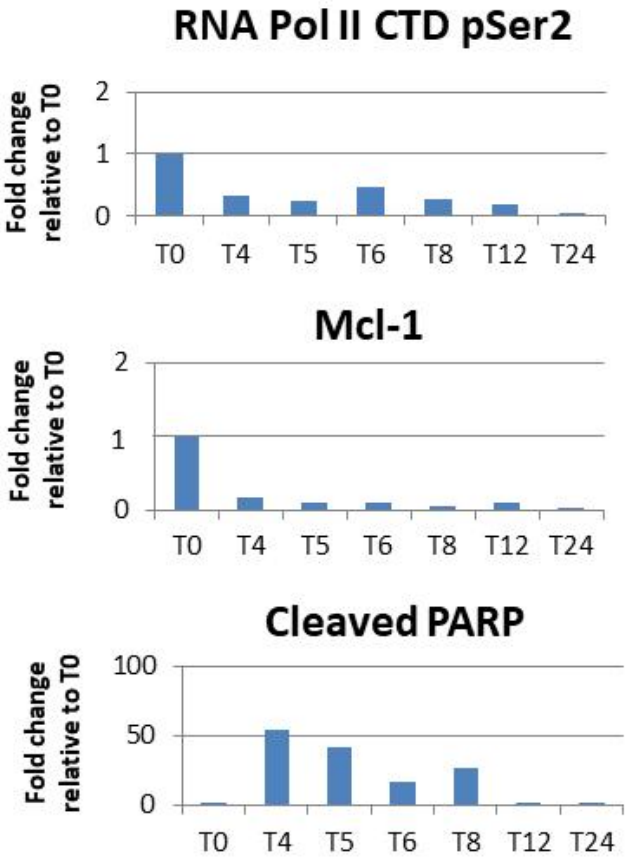
Source: Cyclacel data on file.

CYC065-01 Ph 1 part 1 Proof of Mechanism

Target inhibition detectable at 24 hours



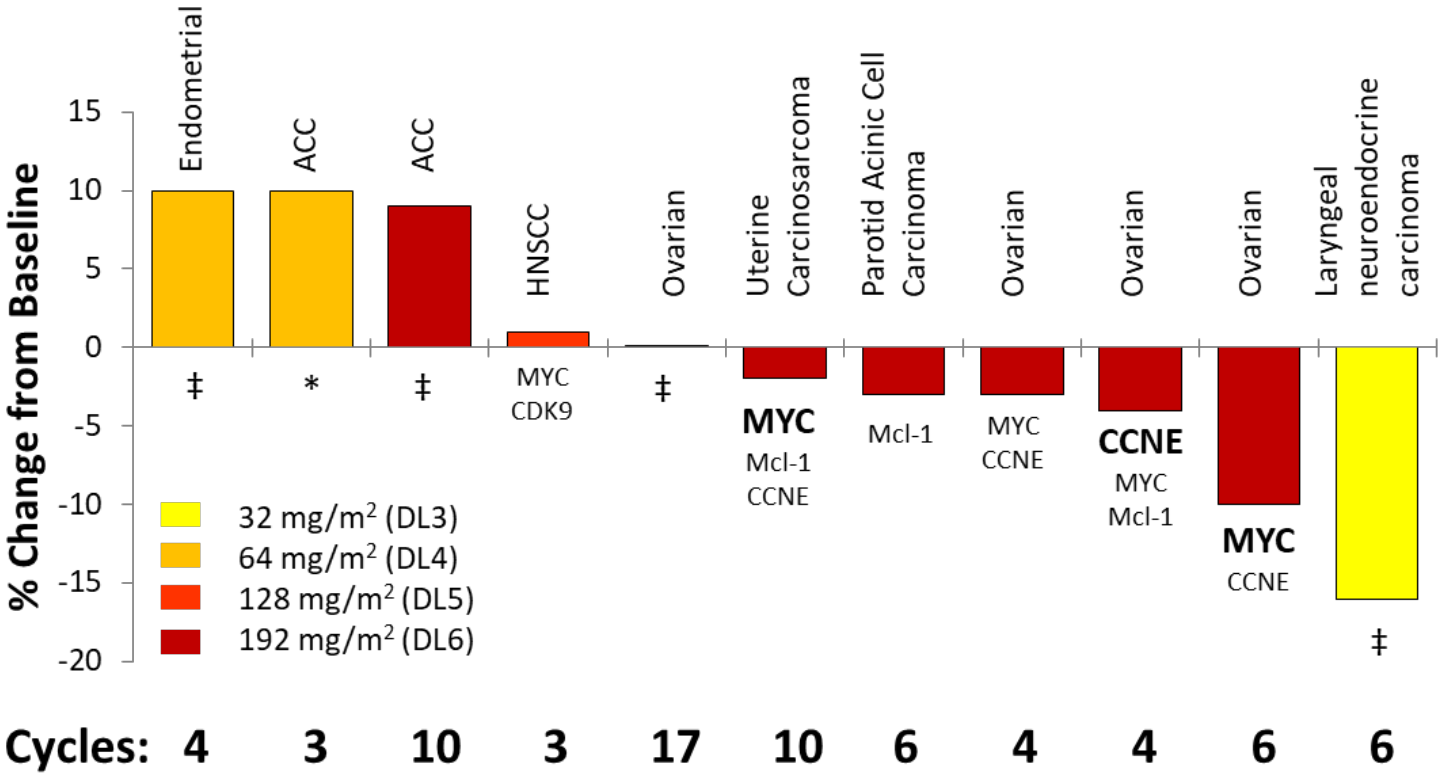
Patient 14 (192 mg/m²)



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

AACR American Association for Cancer Research

CYC065-01 Ph 1 part 1 Activity



‡ *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**

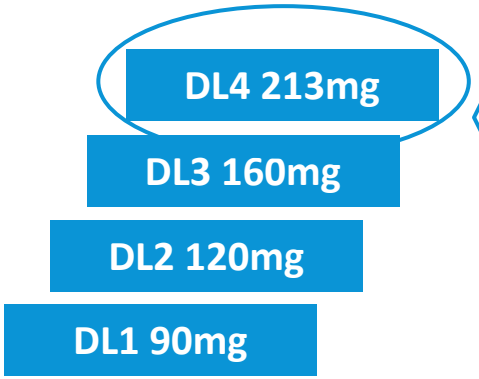
Do, Khanh T., et al, AACR Annual Meeting 2018.

AACR American Association for Cancer Research

CYC065-01 Phase 1 part 2 (n=16 ongoing)

PART 2 i.v.

…ongoing…



- Endometrial cancer patient with MCL1 amplification
- Tumor shrinkage of 15% after 2 cycles
- Treatment ongoing

Source: Cyclacel data on file.

CYC065-01 Ph 1 part 3 p.o. (n=1 ongoing)

- High solubility & permeability
- Oral route beneficial (esp. when combining with other oral agents)
- Aim to establish bioavailability
- Analyze PK/PD of oral form

Source: Cyclacel data on file.

Indication Rationale: 2L CLL (post BTKi)

Venetoclax does not ↓ MCL1

"Double-Hit" strategy to suppress BCL2 + MCL1

Preclinical evidence of synergy for venetoclax + CYC065*

CYC065 1st CDKi to durably suppress ↓ MCL1 in patients

CYC065 + venetoclax Ph 1b study ongoing

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

CYC065-02 Phase 1 CLL (n=2, ongoing)

PART 1 i.v.

…ongoing…

DL1 64mg/m²

- 2nd pat.; ibrutinib failure; lymphoadenopathy
- PR on venetoclax ramp-up
- Lymph node shrinkage after 5 cycles of 065+venetoclax
- Treatment ongoing

CYC065-03 Phase 1 AML/MDS (n=2, ongoing)

PART 1 i.v.

…ongoing…

DL1 75mg

- MCL1 plays prominent role in AML
- Aim to suppress apoptotic pathways
- Combination with venetoclax post ramp-up

CYC065 Future Clinical Indications

1. ***Cancers addicted to cyclin E***
   - Breast
   - Ovarian
   - Uterine serous carcinoma (USC), etc.

2. ***Cancers addicted to MYC***
   - Lymphomas
   - Neuroblastoma
   - Ovarian, etc.

DNA Damage Response

Exploiting DDR to Overcome Cancer DNA Repair & Evasion

Homologous recombination deficient (HRD), incl. BRCA mutant, cancers have an Achilles heel:

- Synthetic lethality: accumulation of SSBs converted to DSBs; cannot repair DNA by HR (i.e. inhibition of PARP enzymes)
- Approved indications: breast, ovarian, pancreatic
- Future: prostate, hematological malignancies
- Significant unmet medical need remains

** SSB=single strand breaks; DSB=double strand breaks.*

Sapacitabine Oral Capsules

Metabolizes into CNDAC; induces SSBs via β-elimination reaction; converted into DSBs that cannot be repaired by HR

Multi-year treatment achieved in solid and blood cancers

Durable CR, PR, SD in patients with BRCA mutant breast, ovarian and pancreatic cancers

CR, CRp, PR and major HI in AML or MDS R/R to SoC

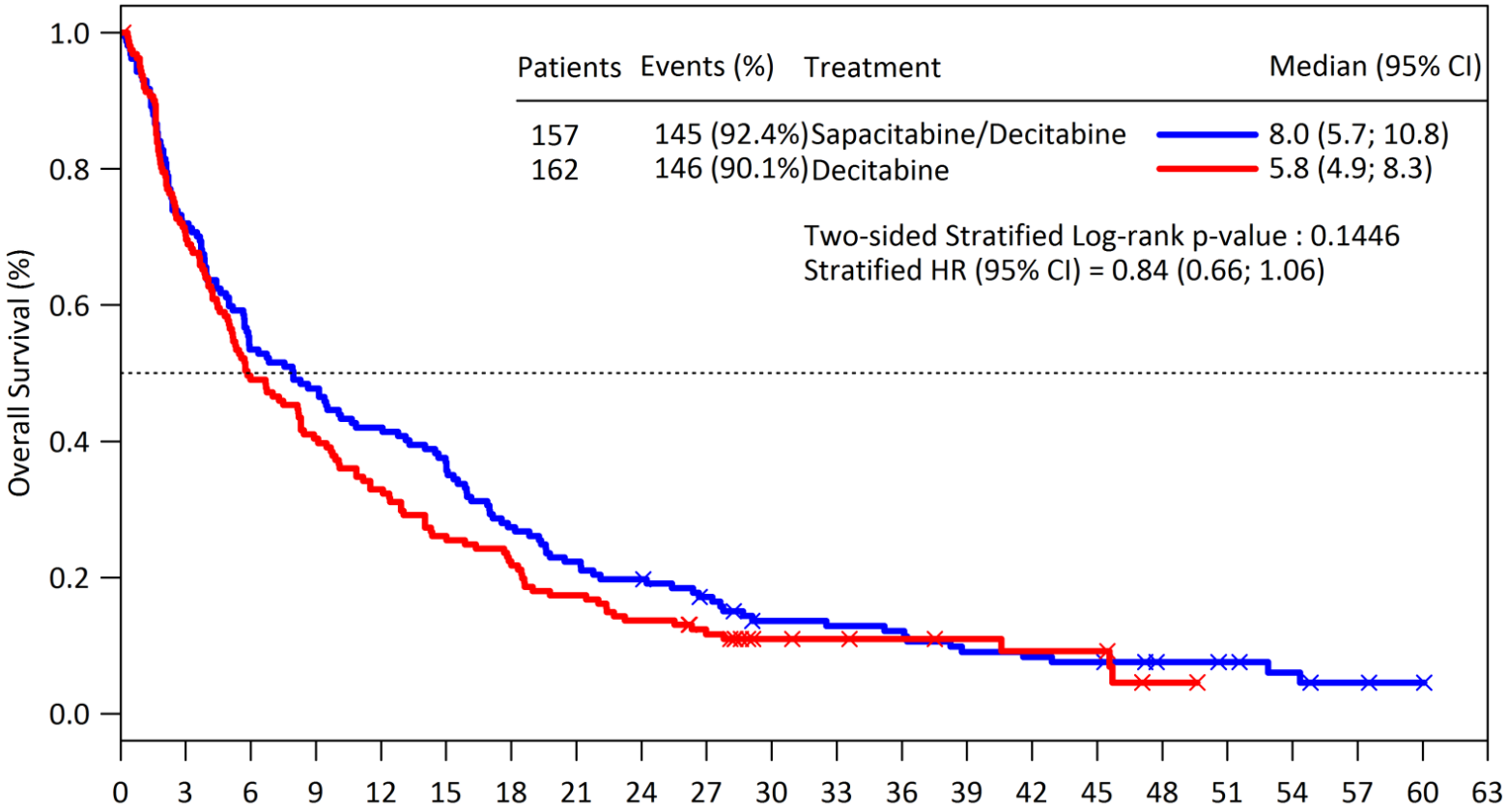
Sapacitabine in AML (SEAMLESS Ph 3 data)

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
- ✓ National regulatory consultations in various EU countries

Source: Cyclacel press releases and data on file.

SEAMLESS Overall Survival - WBC <10,000



Number at risk																					
Sapacitabine /Decitabine	157	113	84	75	66	58	43	35	31	25	18	17	16	12	11	10	7	6	4	2	1	0
Decitabine	162	113	79	65	53	42	36	28	22	17	9	8	7	6	5	5	1	0	0	0	0	0

** Source: Kantarjian H, et al, American Society of Hematology Annual Meeting Dec. 2017, Abstract #891.*

CYC682-11 sapa+venetoclax (n=3 ongoing)

- AML SoC: HMA (decitabine or aza)+ venetoclax
- HMA administered by i.v. or s.c. route
- Hypothesis generating SEAMLESS data
- Convenience of oral regimen to elderly patients
- Enrolling in AML or MDS to SoC

Source: Cyclacel data on file.

MD Anderson-Cyclacel Alliance

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

Cyclacel Development Pipeline

CYC- Drug Candidate	*Phase 1*	*Phase 2*	*Phase 3*	*MoA / Rights*
065 i.v.	065-01 parts 1/2 solid tumors			CDK2/9; W/W
065 oral	065-01 part 3 solid tumors			CDK2/9; W/W
065 i.v.	065-02 + venetoclax R/R CLL *M*			CDK2/9; W/W
065 i.v.	065-03 + venetoclax R/R AML/MDS *M*			CDK2/9; W/W
sapacitabine oral	682-11 sapacitabine + venetoclax all oral R/R AML/MDS *M*			W/W exc. Japan
sapacitabine oral	682-12 SEAMLESS sapacitabine alternating i.v. decitabine 1L AML >70 y.o. *(EU scientific advice – submissibility)*			W/W exc. Japan
sapacitabine oral	IST sapacitabine + olaparib all oral BRCA mutant breast cancer			W/W exc. Japan
140 i.v.	140-01 part 1 R/R AML/MDS *M*			PLK1; W/W

M = MD Anderson alliance programs.

Financial Position & Capitalization

June 30, 2019 cash & cash equivalents: $15.2m[1]

Operating cash burn (annual; excludes non-cash items)

- ✓ 2016: ~ $10.1m [2]
- ✓ 2017: ~ $ 7.5m [2]
- ✓ 2018: ~ $ 6.7m [2]
- ▪ 2019: ~ $10.0m [3]

Fully diluted shares: ~27.1 million [1,4]

No debt

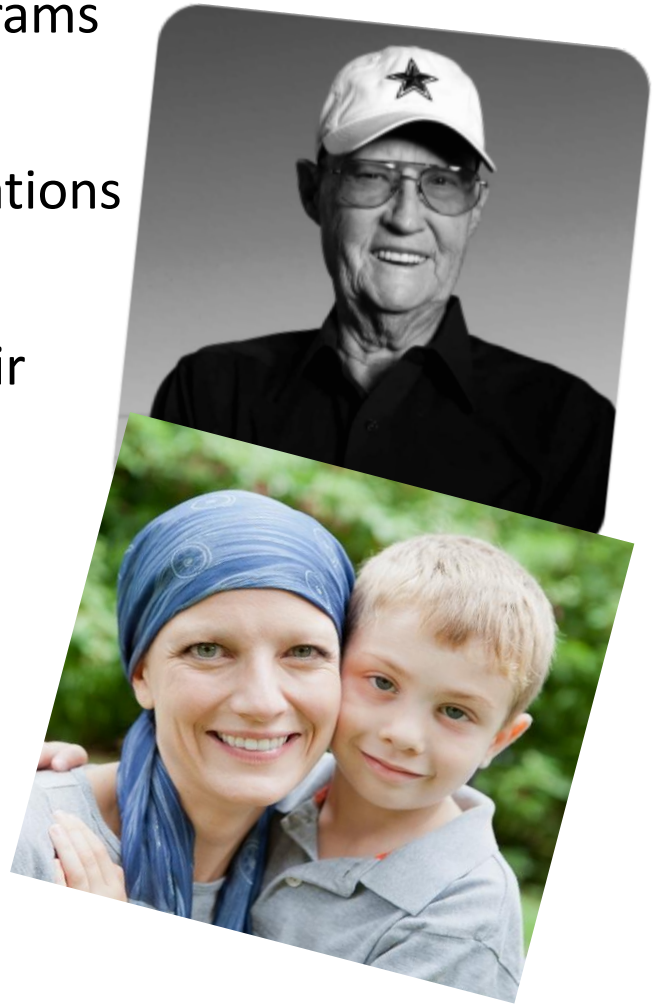
1. *10 Q*
2. *10 K*
3. *Company estimate*
4. *Common stock outstanding 17.2 million*

Key Milestones

- Report initial data from CYC065+venetoclax Phase 1 in R/R leukemias
- Report initial data from sapacitabine+venetoclax Phase 1 in R/R AML or MDS
- Report initial data from CYC140 Phase 1 First-in-Human study
- Report bioavailability from Phase 1 of oral CYC065
- Report updated CYC065 Phase 1 data in patients with advanced solid cancers
- Report data from sapacitabine-olaparib combination Phase 1b/2 IST in BRCA mutant metastatic breast cancer patients when reported by investigators
- Determine regulatory pathway/submissibility of sapacitabine in elderly AML

Investment Thesis

- Clinical stage, state-of the-art oncology programs
- Targeting molecularly-defined patient populations
- Overcome cancer cell resistance & DNA repair
- CDK inhibitors: validated drug class
- Competitively positioned
- Significant market opportunities



THANK YOU

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