



***Translating cancer biology
into medicines***

**NASDAQ CYCC
Biotech Showcase - January 13, 2020**

Disclaimer



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Apply deep understanding of cell cycle biology to disrupt cancer

- **resistance**
- **DNA repair** or evasion

Targetable precision medicine strategy:

- **MCL1** in leukemias & solid tumors (Phase 1)
- **BRCA1/2** in breast, ovarian, pancreatic cancers (Phase 1/2)

Experienced management; estimated capital to end of Q1 2021

CYC065 CDK inhibitor (i.v. and oral)

Clinical proof of mechanism (MCL1 down-regulation & tumor shrinkage)

Combination with venetoclax in R/R leukemias (AML/MDS, CLL)

Sapacitabine nucleoside analogue (oral)

Unique DNA damage response mechanism for BRCA mutant patients with breast, ovarian and pancreatic cancers;

Combinations with venetoclax in R/R AML/MDS & olaparib in 2L BRCAm breast cancer

CYC140 PLK inhibitor (i.v. and oral)

Compelling preclinical data in liquid & solid cancers; first-in-human study in progress

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

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
- Use modifying Rx to break addiction to oncogenes (MYC, cyclin E)

Suppressing Resistance Proteins



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

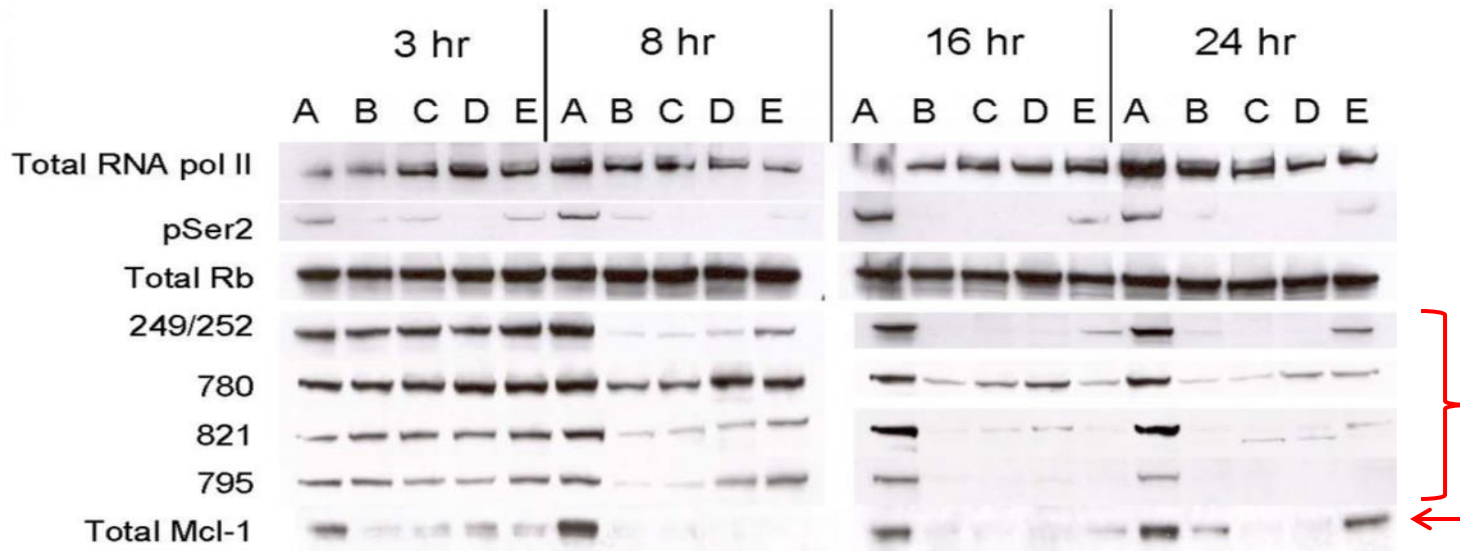
- **BCL2** > **venetoclax** approved in 1L & 2L CLL & 1L AML

- **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

Reduction of MCL1 by CDK Inhibition



A = DMSO
B = 2xIC₅₀ seliciclib (26 μM)
C = 2xIC₅₀ Cmpd2 (9 μM)
D = 2xIC₅₀ Cmpd5 (0.6 μM) **CYC065**
E = 2x IC₅₀ alvocidib (0.3 μM) (a.k.a. flavopiridol)

Colo205 cells treated for up to 24 hr. Source: Green, S.R. et al. AACR 2009 Abstract 3863.

What have we learned with CYC065?



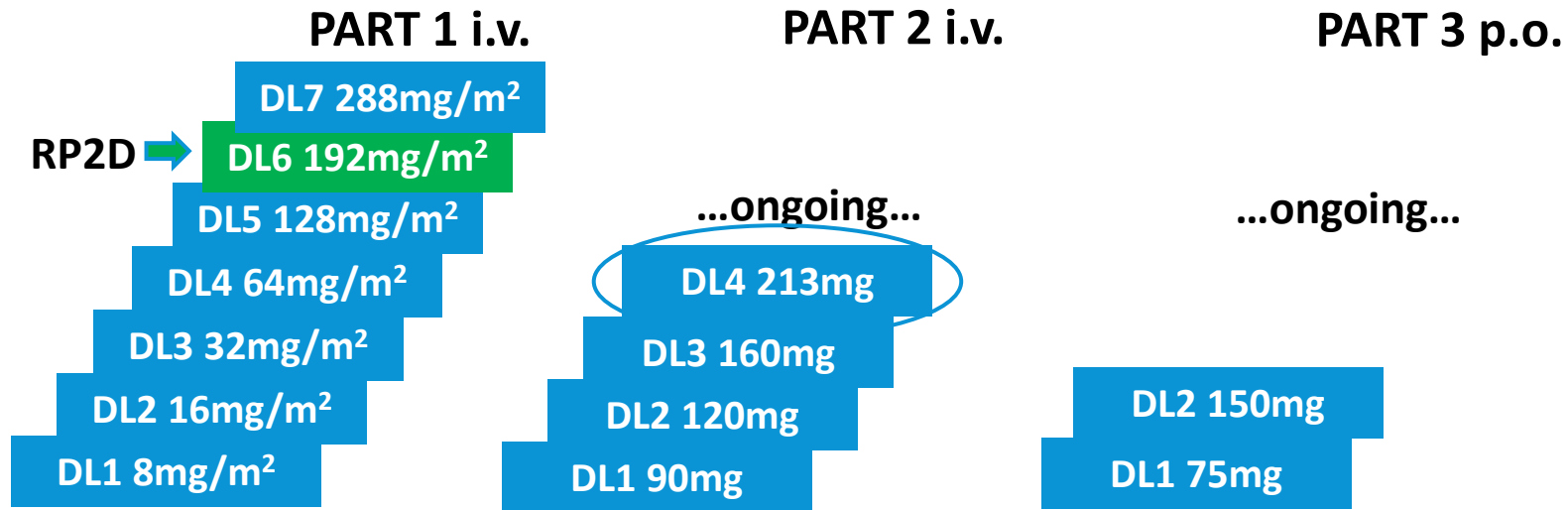
Single Agent:

- Durable MCL1 suppression at tolerable doses (i.v. once every 3 wks)
- MCL1 amplified endocrine cancer (i.v. 4x every 3 weeks): PR
- Cyclin E addicted ovarian cancer: SD with -29.7% tumor shrinkage

Combination with venetoclax:

- CLL: Reduced lymph node size and converted MRD +ve to MRD -ve
- AML/MDS: Reduced peripheral blast counts

CYC065-01 Phase 1 Escalation Schema

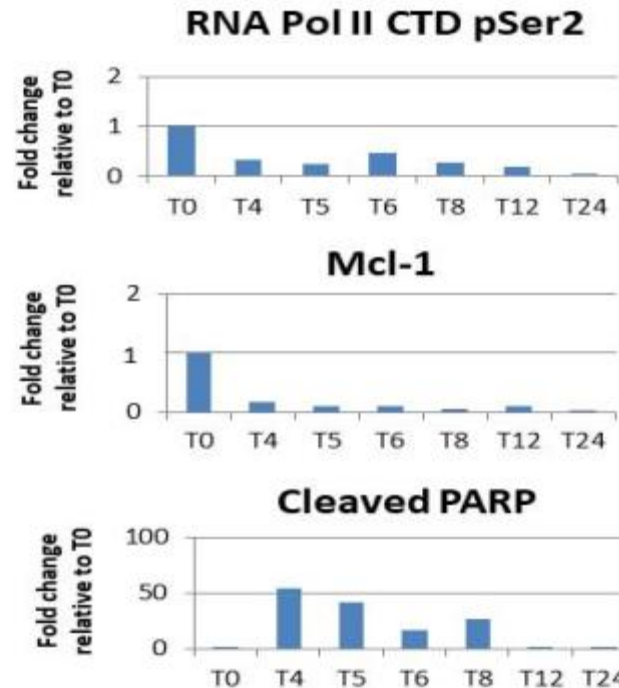
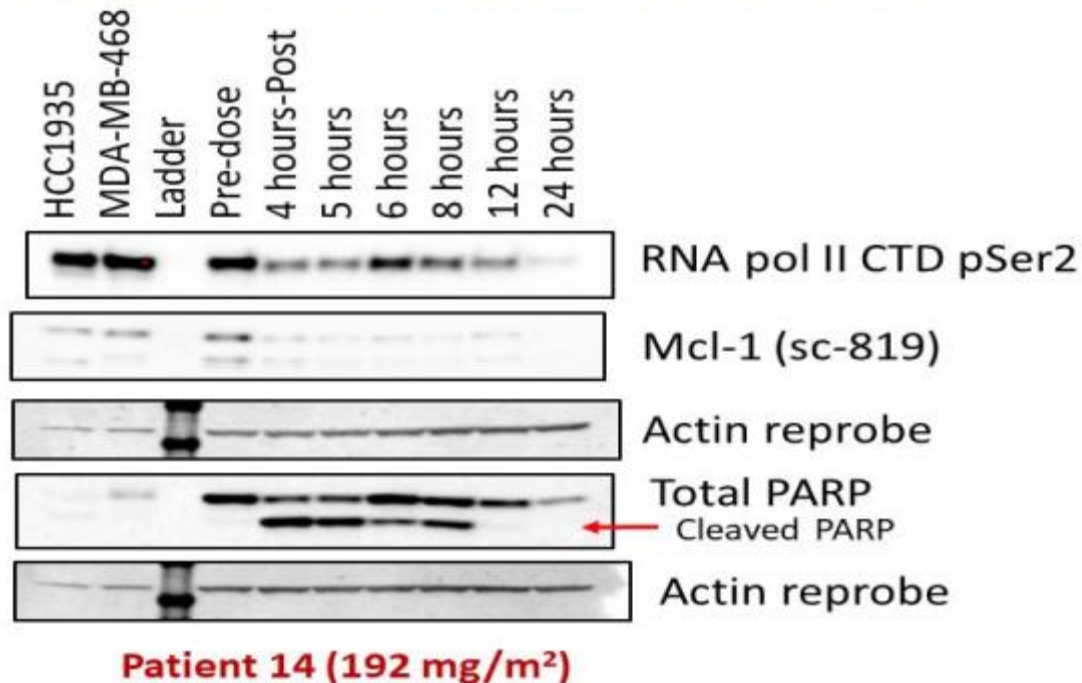


Source: Cyclacel data on file.

CYC065-01 Phase 1 part 1 Proof of Mechanism

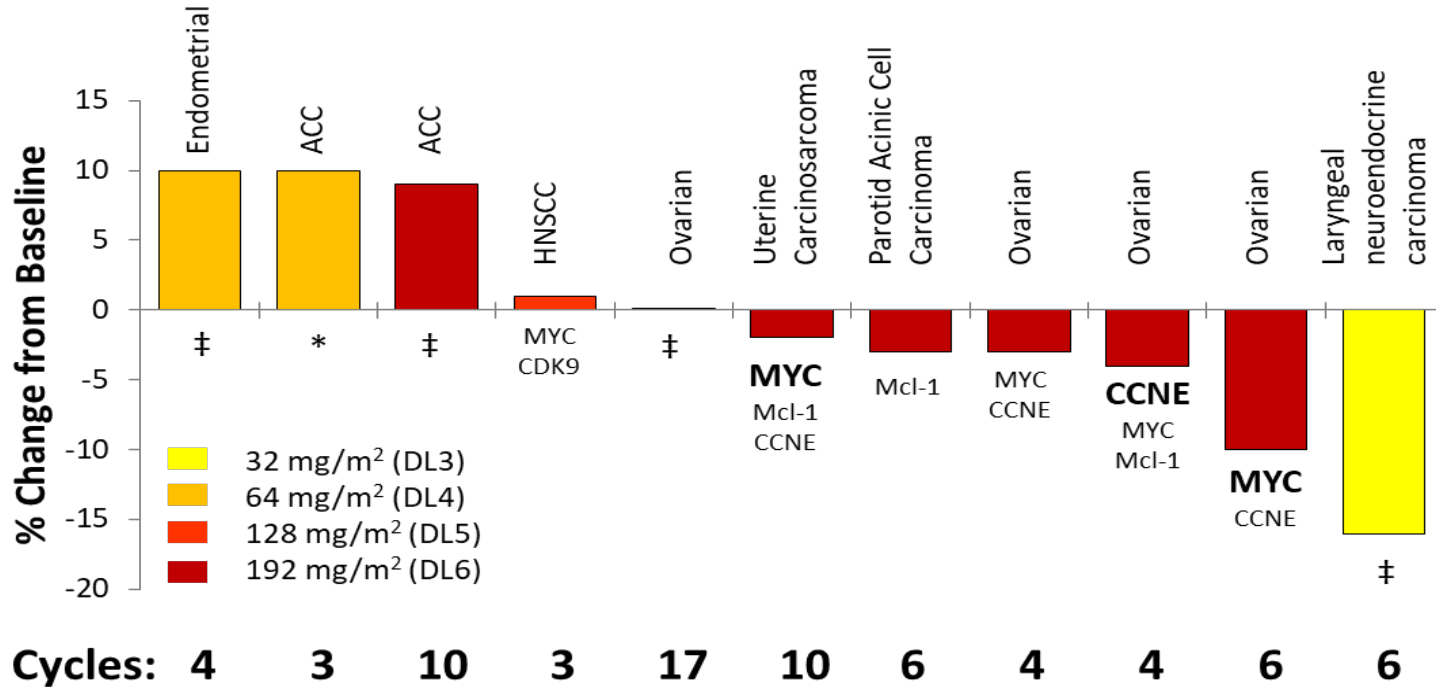


Target inhibition detectable at 24 hours



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

CYC065-01 Phase 1 part 1 Activity



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

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

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

PART 2 i.v.

...ongoing...

DL4 213mg

DL3 160mg

DL2 120mg

DL1 90mg

- Endometrial cancer patient with MCL1 amplification
- 16% tumor shrinkage after 2 cycles
- Confirmed PR
- 63% tumor shrinkage per investigator assessment

Source: Cyclacel data on file.

PART 2 i.v.

...ongoing...

DL4 213mg

DL3 160mg

DL2 120mg

DL1 90mg

- Ovarian cancer patient with cyclin E amplification
- SD with 19.0% tumor shrinkage after 2 cycles
- SD with 29.7% tumor shrinkage after 4 cycles

Source: Cyclacel data on file.

AML post venetoclax + HMA:

- MCL1 is major player; BCL2 less so: venetoclax modest single agent activity
- “Double-Hit” strategy to suppress MCL1 + BCL2

CLL post BTKi regimens; nearly all survivors receive 2L:

- Venetoclax does not ↓ MCL1 which is a major correlate of resistance
- “Double-Hit” strategy to suppress BCL2 + MCL1

Preclinical evidence of synergy for venetoclax + CYC065*

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

PART 1 i.v.

...ongoing...

DL4 150mg/m²

DL2 113mg/m²

DL2 85mg/m²

DL1 64mg/m²

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

Source: Cyclacel data on file.

PART 1 i.v.

...ongoing...

DL1 64mg/m²

- 2nd pat.; ibrutinib failure;
lymphadenopathy
- PR on venetoclax ramp-up
- Lymph node shrinkage after 5 cycles of
065+venetoclax
- Achieved MRD -ve

Source: Cyclacel data on file.

CDK & MCL1 Inhibitor Landscape



CDK4/6 senescence inducing isoforms

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

CDK2/9 transcriptional isoforms enabling apoptosis

CYC065 (CDK2/9, CYCC) Ph1 data

BAY1251152; atveciclib BAY1143572 (CDK9, BAY) Ph1 data

AZD4573 (CDK9, AZN) Ph1 ongoing

Other (pan CDK or selective):

flavopiridol/alvocidib (pan CDK, SUM) Ph2

dinaciclib (pan CDK, MRK) Ph3 terminated

voruciclib (CDK4/6/9, MEIP) Ph1 data

SY1365 (CDK7, SYRS) Ph1 data

MCL1 inhibitors: S64315 (Ph1b ven combo AML); AMG176 i.v./AMG397 oral (FiH); AZD5991 (FiH).

Source: Cyclacel data on file.

Development Pipeline



CYC- Rx 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 R/R AML/MDS ^M			W/W exc. Japan
sapacitabine oral	IST sapacitabine + olaparib BRCA mutant breast CA			W/W exc. Japan
sapacitabine oral	682-12 SEAMLESS oral sapacitabine alternating with i.v. decitabine 1L AML >70 y.o. (EU scientific advice – submissibility)			W/W exc. Japan
140 i.v.	140-01 part 1 R/R AML/MDS ^M			PLK1; W/W

^M MD Anderson alliance programs. W/W = worldwide.

CLL 2L

CYC065

- 21k US incidence; majority on BTKi regimens
- venetoclax (1L or 2L with ibrutinib +/- anti-CD20)

AML elderly unfit for chemotherapy

CYC065 / sapa

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

BRCA +ve Breast Cancer

sapa

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

Financial Position & Capitalization



September 30, 2019 cash & cash equivalents *pro forma*: \$14.2m¹

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

- ✓ 2016: ~ \$10.1m²
- ✓ 2017: ~ \$ 7.5m²
- ✓ 2018: ~ \$ 6.7m²
- 2019: ~ \$10.0m³

Fully diluted shares: ~27.1 million^{1,4}

No debt

1. 10 Q; includes \$1.2m of UK R&D tax credit in OCT19.
2. 10 K
3. Company estimate
4. Common stock outstanding 17.2 million

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

Key Milestones



- Updated Ph 1 safety, PK and efficacy data for CYC065 utilizing a frequent dosing schedule in patients with advanced solid cancers;
- Initial safety, PK data from Ph 1 study of oral formulation of CYC065;
- Initial safety and PoC data from CYC065-venetoclax Ph 1 in R/R AML/MDS;
- Initial safety and PoC data from CYC065-venetoclax Ph 1 in R/R CLL;
- Initial data from sapacitabine-venetoclax Ph 1/2 study in R/R AML/MDS;
- Initial data from CYC140 Ph 1 First-in-Human study in R/R leukemias; and
- Data from Phase 1b/2 sapacitabine-olaparib IST in BRCA mutant metastatic breast cancer when reported by the investigators.

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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