CYCLACEL®

Translating cancer biology into medicines

NASDAQ CYCC – BIOCEO Conference
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Clinical Stage Value Drivers

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

Suppressing Cancer Resistance Proteins

↑ protein expression=survival/growth of cancer cells → Therapeutic strategy: inhibit transcription of labile cancer driver proteins

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

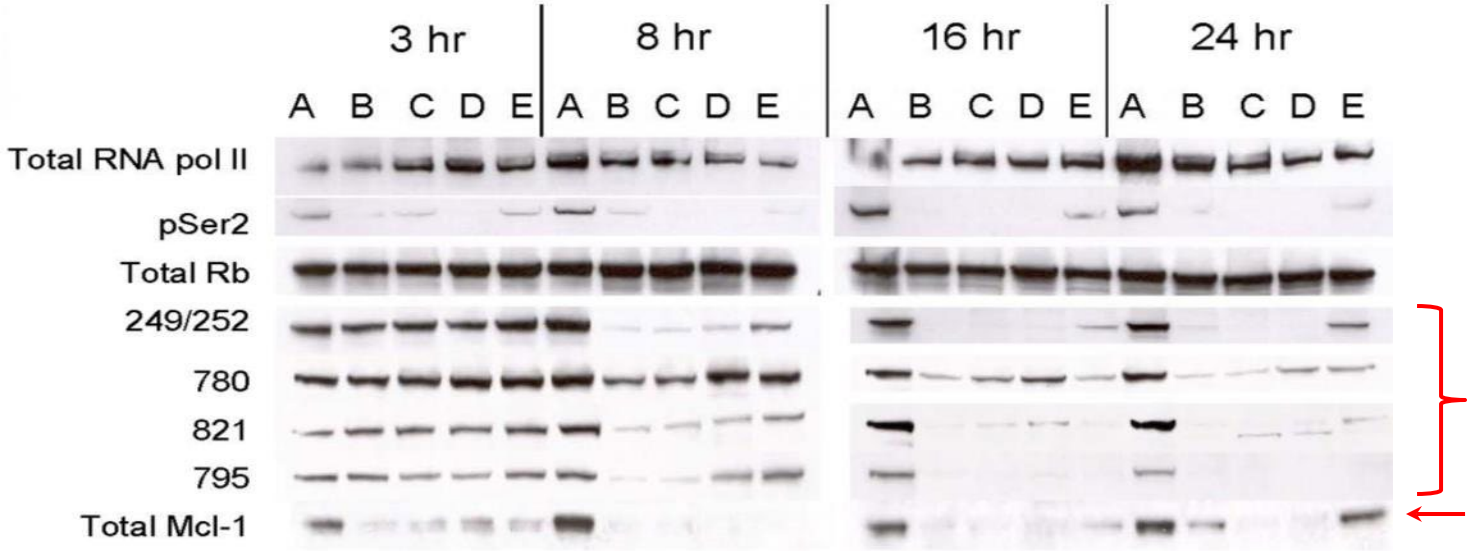
- **MCL1** > transcriptional CDKi, incl. **CYC065**, to ↓ MCL1, MYC

(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 = 2xIC_{50} seliciclib (26 μM)
C = 2xIC_{50} Cmpd2 (9 μM)
D = 2xIC_{50} Cmpd5 (0.6 μM)
E = 2x IC_{50} alvocidib (0.3 μM)

CYC065
(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?

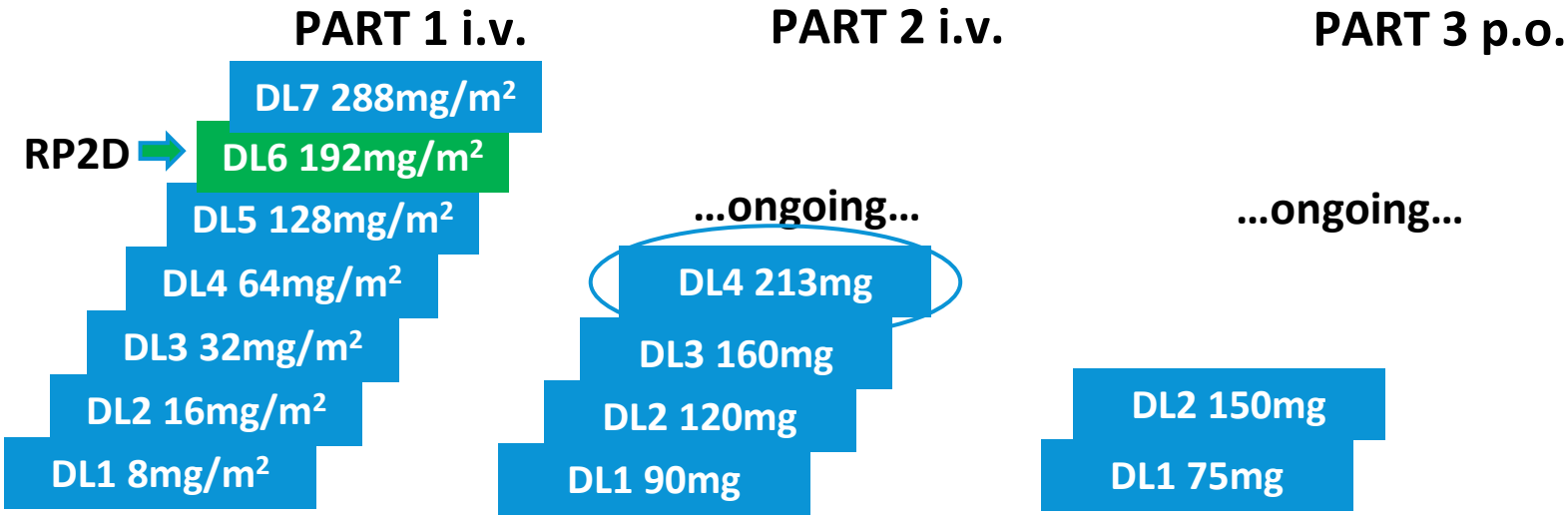
Single Agent:

- 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 amplified ovarian cancer: SD with -29.7% tumor shrinkage

Combination with venetoclax:

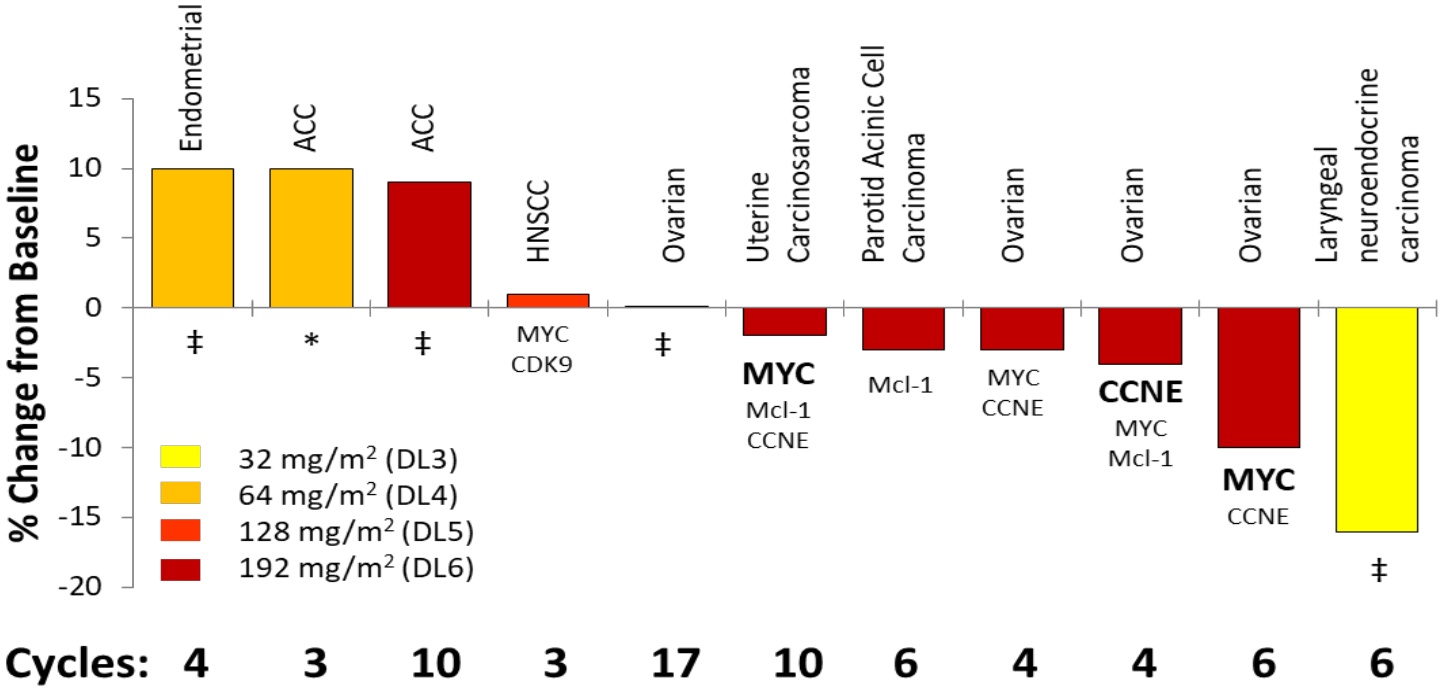
- CLL: Reduced lymph node size and converted MRD +ve to MRD –ve
- AML/MDS: Reduced peripheral blast counts

CYC065-01 Phase 1 Escalation Schema



Source: Cyclacel data on file.

CYC065-01 Phase 1 part 1 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**

American Association for Cancer Research

CYC065-01 Phase 1 part 2 (ongoing)

PART 2 i.v.

…ongoing…

- 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.

CYC065-01 Phase 1 part 2 (ongoing)

PART 2 i.v.

…ongoing…

- 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.

CDK & MCL1 Inhibitor Landscape

CDK2/9 transcriptional isoforms enabling apoptosis:

CYC065 (CDK2/9, CYCC) Ph1 data

BAY1251152; *atuveciclib BAY'572* **(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:

AMG176 i.v./**AMG397** oral - Clin. hold

S64315 (Servier, Ph1b ven combo AML)

AZD5991 (FiH Ph 1).

AZ paper AACR 2019: *CDK9i targeting MCL1 Antitumor responses with AZD4573 strongly correlate with selective MCL1 inhibitors, such as AZD5591. CDK9i targets other labile proteins beyond MCL1 such as BFL1.*

Source: data on file; Boiko S et al AACR 2019..

Financial Position & Capitalization

Cash & cash equivalents (*pro forma* September 30, 2019): $14.2m[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, no debt [1,4]

Estimated capital to end of Q1 2021

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, PoC data from CYC065-venetoclax Ph 1 in R/R AML/MDS & 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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