CYCLACEL®

Translating cancer biology into medicines

NASDAQ: CYCC; CYCCP

Annual Meeting

June 25, 2020

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Restoring Apoptosis in Cancer & Runaway Inflammation

Normally, senescent/useless cells undergo programmed cell death (apoptosis)

Cancer and inflammatory cells block apoptosis and hence survive/grow by →

- ↑ expression of antiapoptotic driver proteins, incl. BCL2, Bcl-x_L*, Bfl-1#, **MCL1**, and
- addiction to dysregulated oncogenes, incl. **cyclin E (CCNE)**, MYC and MYB

Forcing aberrant cells into apoptosis is a validated therapeutic strategy in leukemia:

- venetoclax (BCL2 inhibitor ~$1 bn 2019 est. sales)

Patients stop responding to venetoclax: **MCL1** overexpression correlates with progression[1]

Patient resistance to palbociclib: **cyclin E** overexpression correlates with progression[2]

- breast cancer: palbociclib (CDK4/6 inhibitor ~$4 bn 2019 est. sales)

*[1] Bose P, et al, LeukLymph 2017;58(9):1. Tahir S, et al. BMC Cancer. 2017;17(1):399. [2] Turner NC, et al, JCO 2019 37 1169. * a.k.a. BCL2L1. # a.k.a. BCL2A1.*

Regulation of MCL1 to Enable Apoptosis

MCL1 is one of ten most frequently amplified cancer genes[1]

Competitive race to develop drugs that suppress MCL1

- Inhibiting protein directly is an option; but AMG397 MCL1 inhibitor on clinical hold
- Inhibiting transcriptional CDK enzymes suppresses MCL1 and can reinstate apoptosis

OUR SOLUTION:

- **Fadraciclib** (a.k.a. **CYC065**, potent and selective CDK2/9 inhibitor; i.v. and oral forms)
- We believe it is 1st Rx to show durable MCL1 suppression and anticancer activity in humans

[1] *Beroukhim R et al. Nature 2010.*

Fadraciclib (CYC065) Clinical Efficacy

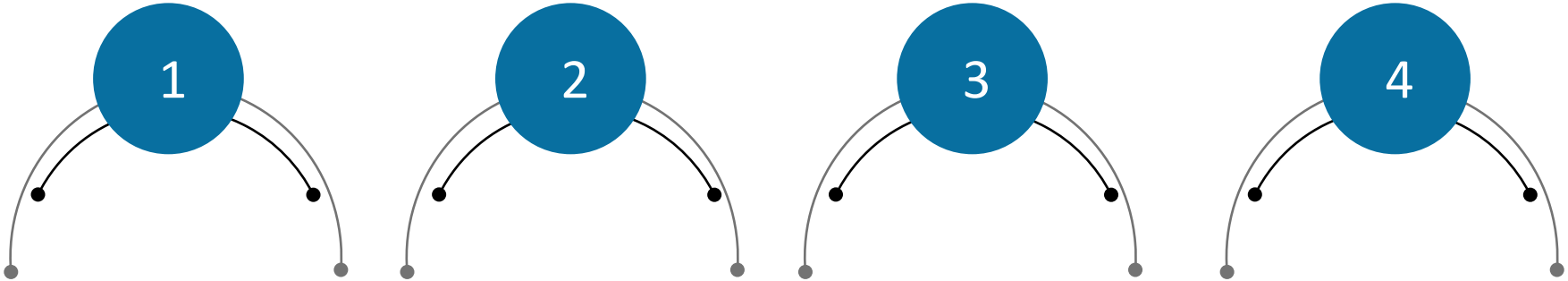
Single Agent:

- MCL1, cyclin E or MYC amplified solid tumors: durable MCL1 suppression at tolerable doses (i.v. once q3 weeks); durable SD
- MCL1 amplified endometrial cancer (i.v. 4x q3 weeks): durable PR
- Phase 1 data submitted for presentation at upcoming oncology meeting

Combination with venetoclax:

- CLL: ↓ lymph node size and converted MRD +ve to MRD –ve
- AML/MDS: ↓ peripheral blast counts, TLS (200mg/m^2 i.v. day 1, 15)

Ph 2 Design *(MCL1 &/or cyclin E amplified)*



Ovarian	**Endometrial/ Uterine**	**Breast**	*Rare cancers*
Single agent	Single agent	Single agent	MCL1 overexpressing NSCLC, HNSCC, sarcoma
Combo w/ chemo &/or PARP inhibitor	*Combo w/ IO or chemo &/or kinase inhibitor*	*CDK4/6 R/R Combo with Hormonal therapy*	Single agent *Combo w/ IO*

Combination with IO Possibility

CDK and immune checkpoint inhibition may be combined to improve therapeutic index

- Preclinical data suggest that dinaciclib causes immunogenic cell death[1]
- ↑ T cell infiltration and dendritic cell activation within tumor
- Efficacy in murine syngeneic models

Phase 1 dinaciclib (CDK1/2/5/9 inh) and pembrolizumab:[2]

- MYC overexpressing advanced TNBC; ≥ 2 lines of Tx
- ORR: 17%; CR: 3.4%; PR: 13.8% (n=29)

1. Hossain MSB et al; J Clin Invest; 2018 2. Source: ASCO 2020; https://meetinglibrary.asco.org/record/185238/abstract

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 poster AACR 2019: *CDK9i targeting MCL1: Antitumor responses with AZD4573 strongly correlate with selective MCL1 inhibitors, such as AZD5991. CDK9i targets other labile pro-survival proteins beyond MCL1 such as Bfl-1 (a.k.a. BCL2A1).*

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

Uni. of Edinburgh-Cyclacel Collaboration

- Aim to test **fadraciclib** vs. **seliciclib** in enabling apoptosis in inflammatory neutrophil cells in COVID-19 patient donor plasma
- Early peripheral blood neutrophil response associated with cytokine storm and poor outcome in COVID-19 disease
- Part of broader STOPCOVID project (funded by LifeArc $2.5m)
- If positive, include in adaptive clinical trial to test PoC

THE UNIVERSITY of EDINBURGH

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

Financial Position & Capitalization

Cash & cash equivalents (*pro forma*): $27.3m [1]

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

- ✔ 2016: ~ $10.1m [2]
- ✔ 2017: ~ $ 7.5m [2]
- ✔ 2018: ~ $ 6.7m [2]
- ✔ 2019: ~ $ 9.4m [2]

Fully diluted shares: 9.3 million[3]. No debt

Estimated capital to end of 2022

1. *March 31 2020 10Q: $8.9m cash & cash equivalents plus $18.4m equity financing net proceeds*
2. *10K*
3. *Common stock outstanding 4.9m, common stock warrants 4.3m, stock options 0.1m*

Clinical Stage Value Drivers

Fadraciclib (CYC065) CDK inhibitor (i.v. and oral)

- Clinical proof of mechanism (MCL1 / cyclin E 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 BRCA mutant breast cancer

CYC140 PLK inhibitor (i.v. and oral)

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

Key Milestones

- Updated **fadraciclib** Ph 1 safety, PK, efficacy data with frequent dosing schedule in patients with advanced solid cancers;
- Initial safety, PK data from Ph 1 study of **fadraciclib** oral formulation;
- FPI **fadraciclib** Ph 2 tissue agnostic precision medicine study;
- Initial safety, PoC data from **fadraciclib**-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.

Cyclacel Overview

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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