Translating cancer biology into medicines

NASDAQ CYCC November 2017

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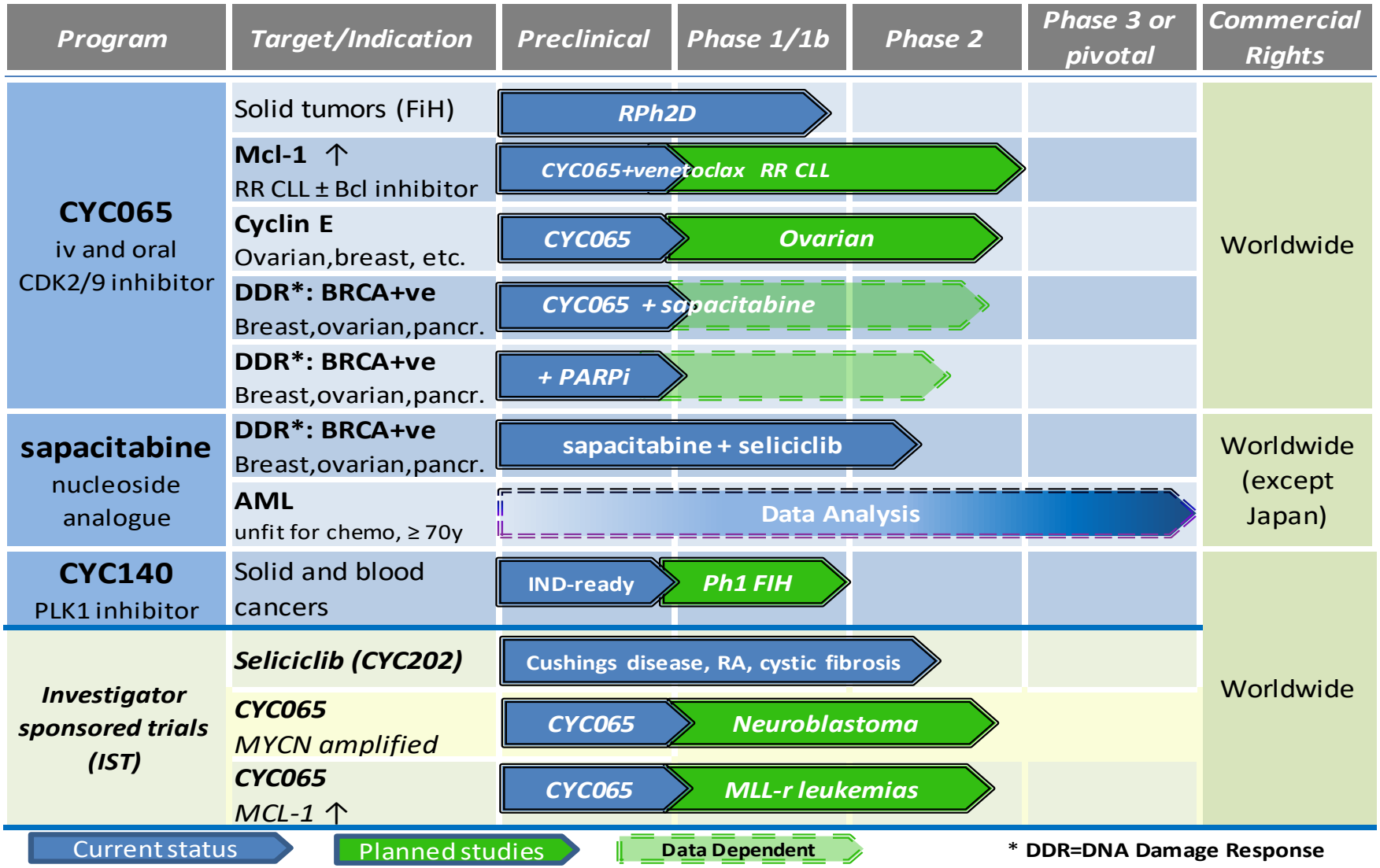
Cyclacel Pharmaceuticals Overview

- Apply deep understanding of cell cycle biology to disrupt
    a. cancer cell **resistance**
    b. **DNA repair** or evasion
- Pioneer in Cyclin Dependent Kinase inhibitors
- Focus on molecularly-defined patient populations
- Rationally designed clinical programs in solid and blood cancers
- Experienced management
- Estimated capital through YE 2019

Development Pipeline



Cyclin Dependent Kinase Inhibitor Transcriptional Regulation Program

Cyclin Dependent Kinase inhibitors (CDKi)

2001 Nobel Prize for Physiology & Medicine culminating in approved Rx

Paradigm-shift in breast cancer: CDK4/6i-based combinations with AI

- IBRANCE® (palbociclib, PFE, approved 2015, ~$2.1bn 2016 sales)
- KISQALI® (ribociclib, NVS), VERZENIO® (abemaciclib, LLY) - approved 2017

CYCC's CDK2/9i strategy: overcome **resistance** via regulating transcription

- Seliciclib 1st Gen, signals of anticancer activity (Ph 2)
- CYC065 2nd Gen, more potent, better profile than seliciclib (Ph 1)

Overcoming the Problem of Cancer Cell Resistance

- CDK4/6 inhibitors → senescence → eventually resistance
- In many cancers resistance correlated with:
  - ↑ expression of pro-survival proteins (Bcl-2, Bcl-XL, **Mcl-1**, etc.) and/or
  - addiction to oncogenes (incl. ***MYC,*** **cyclin E** amplification)
- First Bcl-2 inhibitor: venetoclax (ABBV, for CLL, does not ↓ Mcl-1)
- Competitive race to develop Mcl-1 inhibitors
- CYC065:
  - *1st CDKi to ↓ Mcl-1 in patients with signals of clinical benefit*

** Source: Cyclacel data on file.*

CYC065 First in Human Phase 1 Study (ongoing)

n=26 heavily pretreated patients with advanced solid tumors

- Determined safety, DLT, PK in 7 DL, est. RP2D; DL7 MTD reversible neutropenia
- Treated n=13 in DL6 cohort
- Demonstrated target engagement and consistent **Mcl-1 suppression** over 24h after single dose in 11/13 evaluable DL6 patients
- Anticancer activity observed in 7/13 DL6 patients, including: [#]
  - **5 with ovarian cancer, of which 1 with MYC amplification,**
  - **1 with parotid gland and 1 with submandibular gland cancer.**
  - Also 1 with cyclin E/Mcl-1 amplified ovarian cancer achieved 40% CA125 ↓

** Source: Cyclacel data on file. [#] Excludes another MYC amplified patient with laryngeal cancer at DL4.*

CYC065: Clinical Development Priorities

Molecularly-defined patient populations

Hematological malignancies:

1. Combination with **venetoclax**, i.e. relapsed/ refractory CLL (Mcl-1 ↑)

Solid tumors:

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

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) Clinical Program

DNA Damage Response (DDR):

Overcoming Cancer DNA Repair & Evasion

Cancer cells evolve, eventually becoming immortal by blocking DNA repair

SoC for HR deficient cancers (incl. BRCA1, -2): PARP inhibitors in ~ 50% of patients

CYCC DDR strategies:

- CYC065 CDKi: modulate DNA repair via HR, NHEJ, etc. pathways
- ↓ expression of HR DNA repair genes (BRCA1 and BRCA2)
- Sapacitabine best clinical data: in BRCA +ve patients with various cancers

Clinical translation possibilities:

- Single agent in sensitive cancers
- Combinations with SoC

DDR: Sapacitabine & Seliciclib Ph 1 Best Responses*

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RECIST Evaluable BRCA Carriers

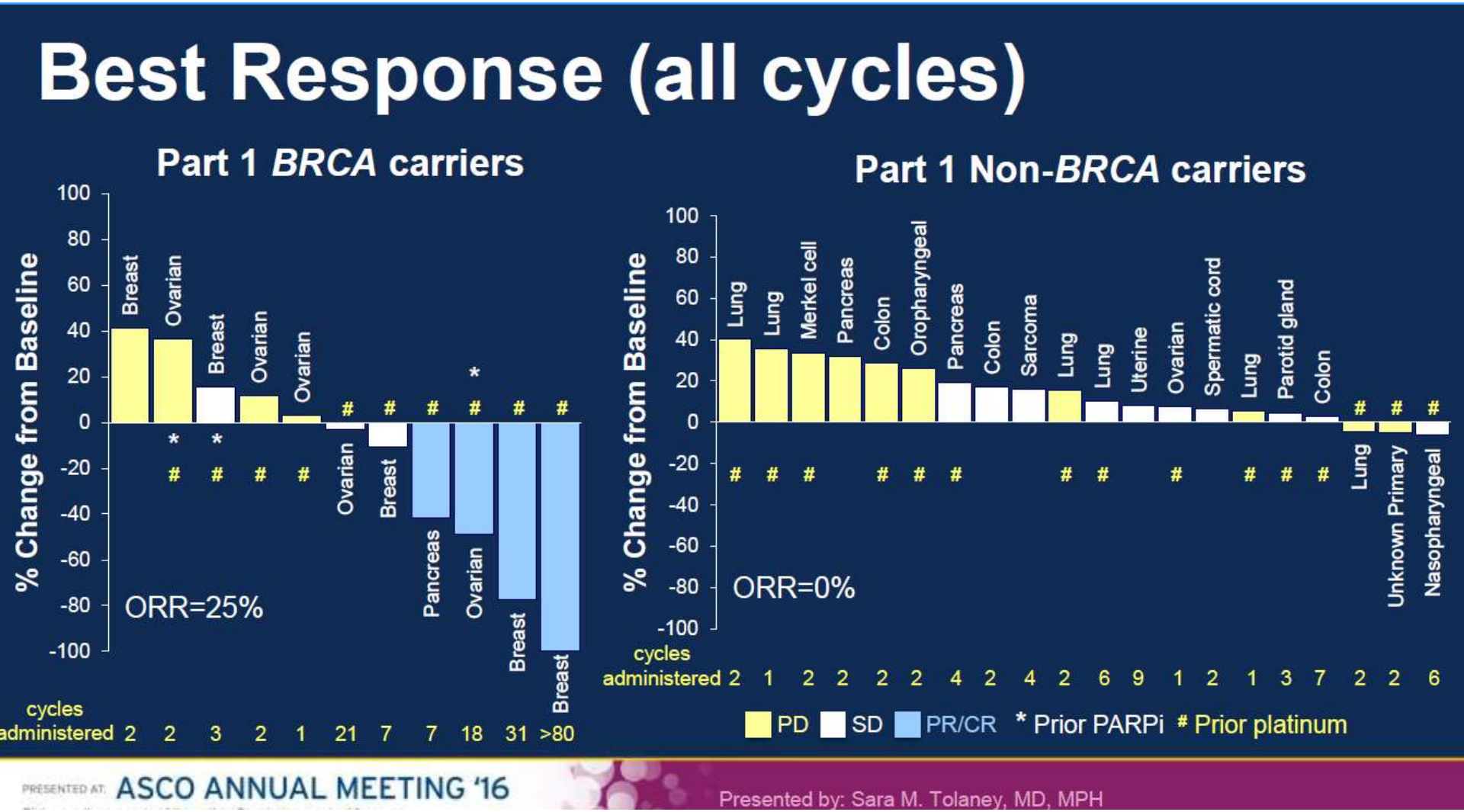
Cancer	Best Response	Prior Treatment	Total cycles
Part 1	*(n=16)*		
Breast	CR	adriamycin, cyclophosphamide, paclitaxel, cisplatin	>80
Breast	PR	adriamycin, cytoxan, paclitaxel, carboplatin	31
Ovary	SD	paclitaxel, carboplatin, gemcitabine	21
Ovary	PR	paclitaxel, carboplatin, gemcitabine, topotecan, iniparib	18
Breast	SD	tamoxifen, raloxifene, anastrozole, adriamycin, Cytoxan, paclitaxel, carboplatin, navelbine	7
Pancreas	PR	gemcitabine, 5-FU, oxaliplatin	7
Part 2	*(n=28)*		
Breast	PR	adriamycin, cytoxan, paclitaxel, capecitabine, irinotecan, ABT-888 (PARP inhibitor), MPDL3280A	>19
Ovary	SD	paclitaxel, carboplatin, doxil	22
Breast	SD	adriamycin, cytoxan, capecitabine, faslodex	12
Ovary	SD	paclitaxel, carboplatin, doxil, gemcitabine, topotecan, cytoxan, avastin	11
Ovary	SD	paclitaxel, carboplatin, doxil, olaparib (PARP inhibitor), cediranib	8
Ovary	SD	paclitaxel, carboplatin	4
Ovary	SD	paclitaxel, carboplatin, doxil, gemcitabine, alimta, cytoxan, avastin, olaparib (PARP inhibitor)	4
Pancreas	PR	gemcitabine, abraxane, docetaxel	4
Pancreas	SD	gemcitabine, cisplatin, abraxane, folfox, TH-302	4

ED AT: ASCO ANNUAL MEETING '16 Presented by: Sara M. Tolaney, MD, MPH

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

ASCO American Society of Clinical Oncology

Sapacitabine & Seliciclib Phase 1 BRCA +ve Benefit*



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

DDR: Rational combo of sapacitabine + CDK2/9 inhibitor

*Activity in HR-repair deficient tumors **

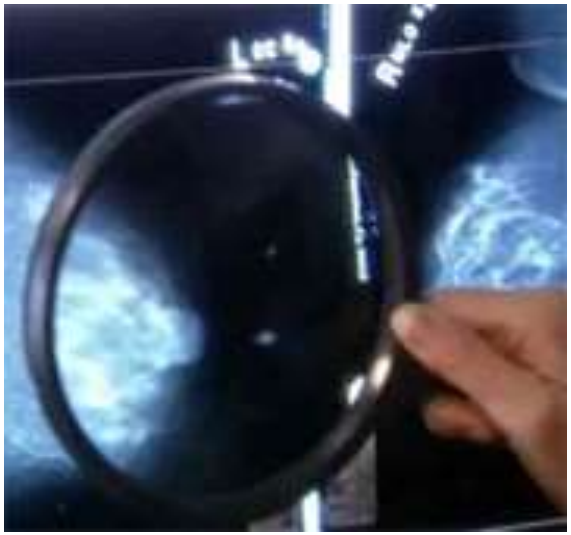
- All-oral regimen, complementary mechanisms:

  sapacitabine's dual MoA of DNA SSBs# and cell cycle arrest plus CDKi modulation

- Parts 1 & 2 durable clinical benefit (PRs & prolonged SD) in patients with BRCA +ve:

  breast, ovarian, pancreatic cancers

- Part 3 started: revised schedule including BRCA +ve ovarian, pancreatic cancer patients



Potential line extensions with CYC065 in lieu of seliciclib

ASCO American Society of Clinical Oncology

AACR American Association for Cancer Research

** Source: Tolaney S et al, J Clin Oncol 34, 2016 (suppl; abstr 2503); Shapiro et al, AACR Proceedings, 2013, LB-202. HR=homologous recombination. # single-strand breaks*

Sapacitabine in AML

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
- ▪ Karyotype analysis in progress followed by final analysis
- ▪ Oral presentation at ASH Annual Meeting 2017
- ▪ Determine submissibility to regulatory authorities
- ▪ Pre-submission End of Phase 3 meetings

Source: Cyclacel press releases and data on file.

Financials

Financial Position & Capitalization

Sept 30, 2017 cash & cash equivalents: $26.0m[1]

Current Operating cash burn (excludes non-cash items)

- ✓ 2014: ~ $18.7m annual [2]
- ✓ 2015: ~ $14.5m annual [2]
- ✓ 2016: ~ $10.1m annual [2]
- ▪ 2017: ~ $ 8.0m annual [3]

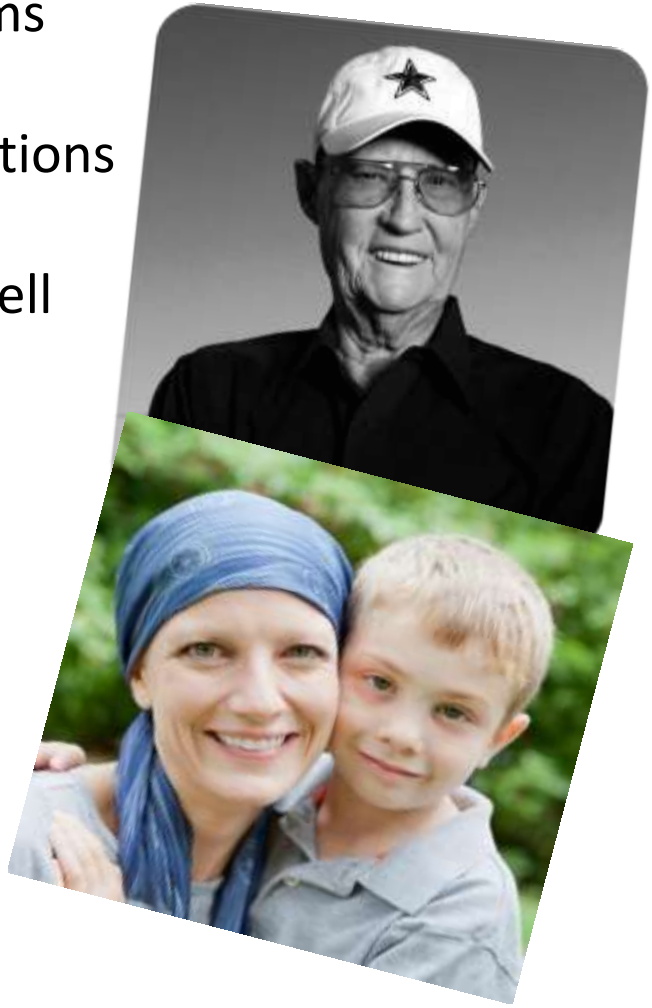
Fully diluted shares: ~ 20.0 million[1,4]

No debt

1. *10Q*
2. *10-K*
3. *Company estimate*
4. *Common stock outstanding: 11.9m*

Investment Thesis

- Clinical stage CDKi and DDR oncology programs
- Targeting molecularly-defined patient populations
- Treat difficult cancers and overcome cancer cell resistance & DNA repair
- CDK inhibitors: validated drug class
- Competitively positioned
- Significant market opportunities



Key Milestones

- Start CYC065 Ph 1b in RR CLL combo with venetoclax
- CYC065 Phase 1 data solid tumors
- ✓ Start Part 3 in BRCA +ve cancers beyond breast
- Sapacitabine/seliciclib update BRCA +ve breast cancer
- CYC140 (PLKi) IND submission
- Sapacitabine AML ASH data; determine submissibility

THANK YOU

Cyclacel Pharmaceuticals, Inc.

200 Connell Drive #1500
Berkeley Heights, NJ 07922
+1 (908) 517 7330

Contact: ir@cyclacel.com