Translating cancer biology into medicines

Noble Capital Markets Conference

NASDAQ CYCC - January 30, 2018

Disclaimer

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Spending on Cancer Medicines

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

Price hikes, ↑ patient #, **longer duration of therapy**

Avg. annual patient out-of-pocket: **$7k iv, $3k oral Rx**

Major threat to this colossal investment:

RESISTANCE TO CANCER Rx

** Source: Aitken M, Kleinrock, M, IMS Institute for Healthcare Informatics, June 2, 2016.*

Precision Medicine in Oncology

Single Rx targeting mutations: validated approach

↑ response but few cures/long stable disease

EVOLUTION OF RESISTANCE OR

ADDICTION TO CANCER GENES

- Strategy: combine approved Rx that is no longer working with resistance-modifying Rx or
- Rx that breaks addiction

Our solution:

Cyclin Dependent Kinase CDK Inhibitors

Cyclin Dependent Kinase Inhibitors (CDKi)

2001 Nobel Prize for Physiology & Medicine (*CDKs & cyclins*)

3 approved CDKi:

- IBRANCE® (palbociclib, PFE, approved 2015, ~$3.3bn 2017E)
- 2017: KISQALI® (ribociclib, NVS), VERZENIO® (abemaciclib, LLY)
- CDK4/6 inhibitors → senescence → eventually resistance

*CDK2/9i strategy: overcome **resistance** by lowering killing threshold*

- CYC065 2nd Gen, highly potent, improved Rx profile (Ph 1)

Resistance Biomarkers

In many cancers resistance correlates with:

- ↑ ***pro-survival*** protein expression, such as Bcl-2, Bcl-XL, **Mcl-1**
- addiction to oncogenes, such as **MYC**, **cyclin E**

First Bcl-2 Rx: venetoclax (ABBV, CLL); does not ↓ Mcl-1

Competitive race to develop Mcl-1 inhibitors

- *CYC065 1st CDK inhibitor Rx: durable ↓ Mcl-1 in patients*

** Source: Cyclacel data on file.*

CYC065 First in Human Phase 1 Study (ongoing)

n=26 heavily pretreated patients with advanced solid tumors (13 in DL6 cohort RP2D)

- Durable **Mcl-1 suppression** >24h after single dose in 11/13 evaluable DL6 patients
- Anticancer activity in 6/13 patients (5 at RP2D)

** Source: Cyclacel data on file.*

CYC065: Clinical Development Priorities

Molecularly-defined patient populations

CYCLACEL

Hematological malignancies:

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

Solid tumors:

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

Neuroblastoma (NB): lethal children's cancer

Rare ped. Dx; 90% children <5y; few survive >10y

- *MYCN amplification ~40-50% of high risk NB*

CYC065 rare investigational Rx to show activity in adult patients with MYCN amplification

Discussions with KOLs ongoing

** Source: Cyclacel data on file.*

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 evade Rx; block DNA repair; ultimately become immortal

SoC HR deficient cancers (incl. BRCA): PARP inhibitors in ~ 50% of patients

CYCC DDR strategy: combine CDKi + sapacitabine

- CDKi modulate DNA repair via HR, NHEJ; ↓ expression of HR DNA repair genes incl. BRCA; disrupts cyclin E amplification
- Sapacitabine active in patients with BRCA +ve (HR def) cancers
- Encouraging clinical data (n=76) reported at ASCO

Sapacitabine & Seliciclib Phase 1 Best Responses*

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RECIST Evaluable BRCA Carriers

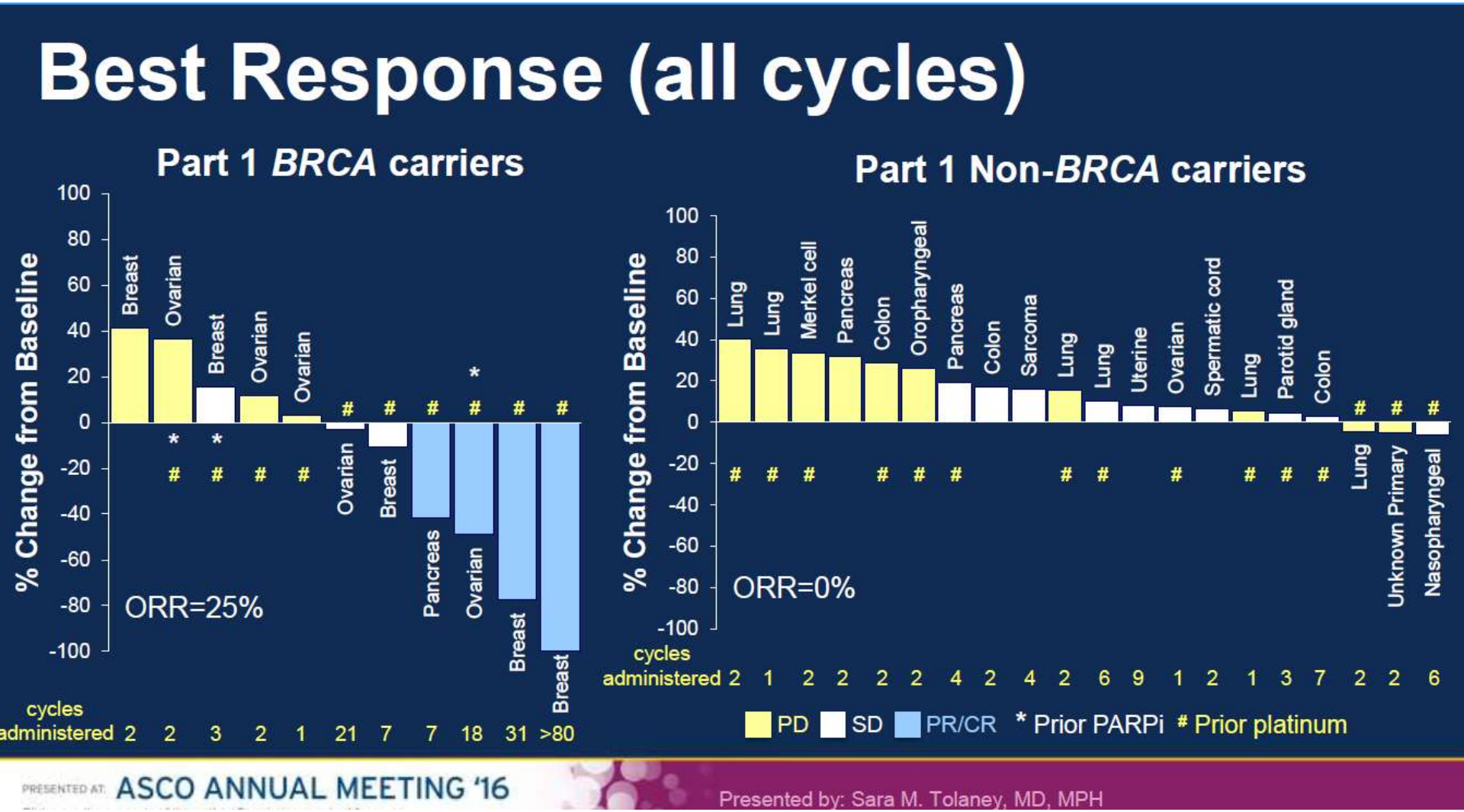
Cancer	Best Response	Prior Treatment	Total cycles
Part 1	*(n=16)*		
Breast	CR	adriamycin, cyclophosphamide, paclitaxel, cisplatin	>80
Breast	PR	adriamycin, cytoxan, paclitaxel, carboplatin	31
Ovary	SD	paclitaxel, carboplatin, gemcitabine	21
Ovary	PR	paclitaxel, carboplatin, gemcitabine, topotecan, iniparib	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*

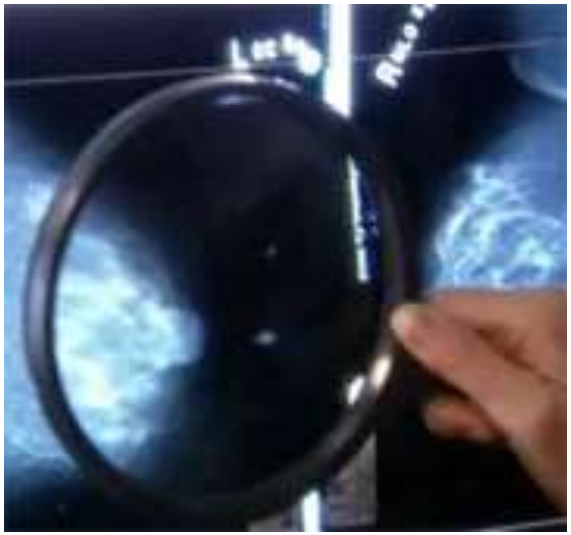


** Source: Tolaney S et al, JCO 34, 2016 (suppl; abs. 2503).*

DDR Strategy: sapacitabine + CDK inhibitor

All-oral, low toxicity regimen

- Parts 1 & 2 durable benefit (CR, PRs & SD) in BRCA+ve **breast, ovarian, pancreatic** cancers
- Part 3 ongoing: revised schedule including BRCA +ve ovarian, pancreatic cancer patients



Potentially substitute CYC065 in lieu of seliciclib

** 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

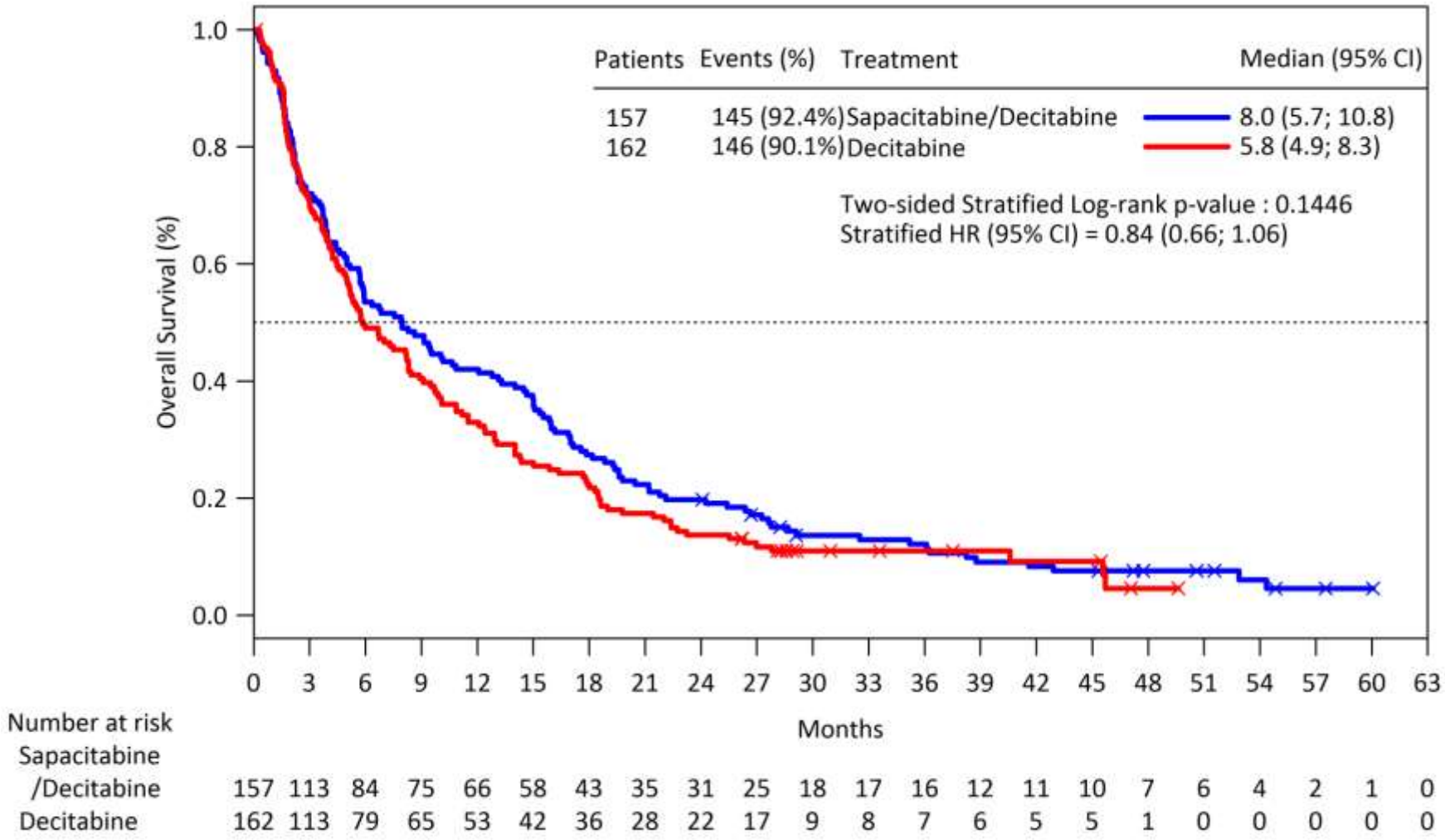
Sapacitabine in AML (SEAMLESS Ph 3 data)

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
- ✓ Oral presentation at ASH Annual Meeting 2017
- ▪ Determine optimal cut-off for WBC
- ▪ Determine submissibility to regulatory authorities
- ▪ Pre-submission End of Phase 3 meetings

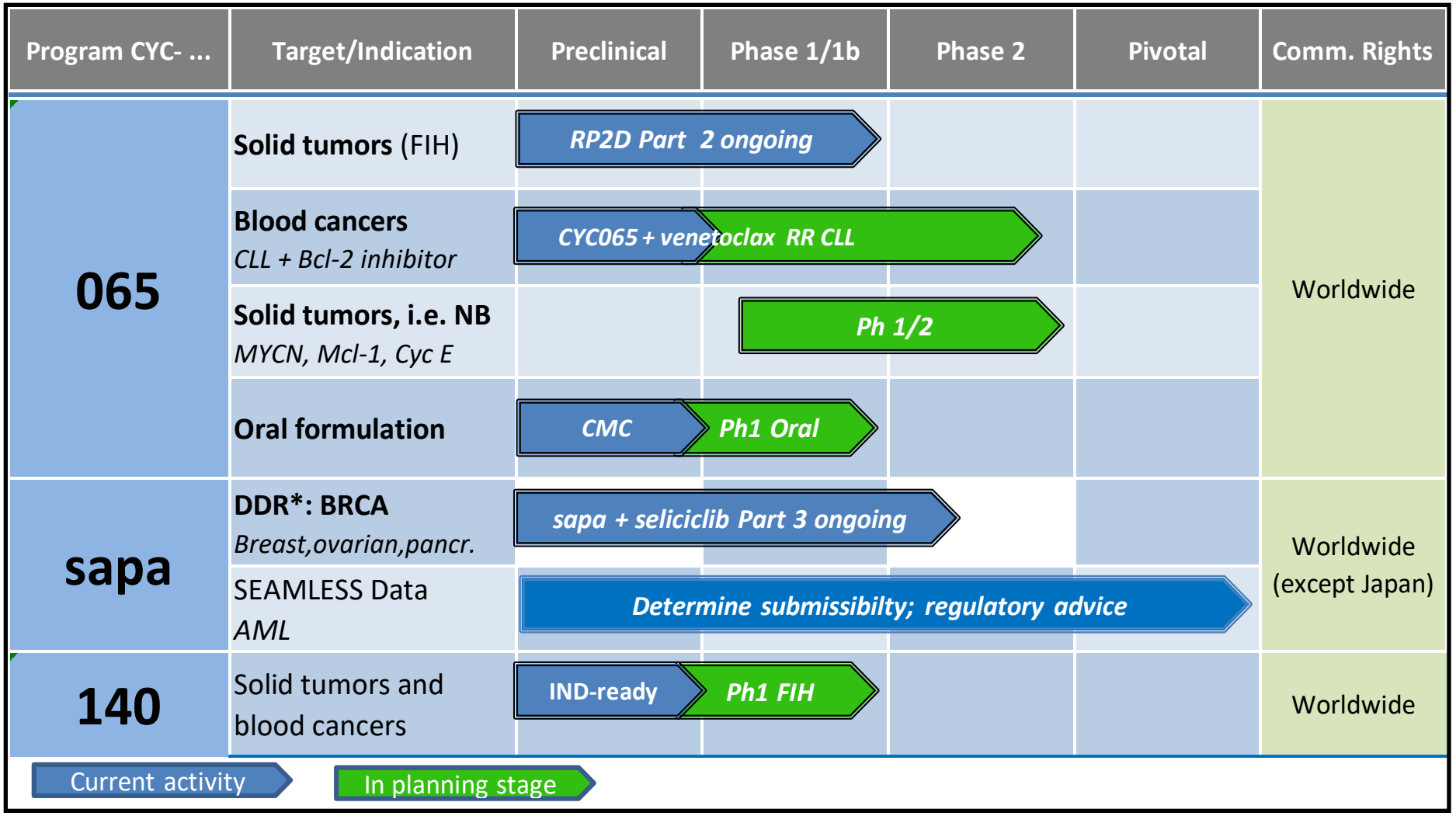
Source: Cyclacel press releases and data on file.

Survival - Baseline WBC <10,000



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

Development Pipeline



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

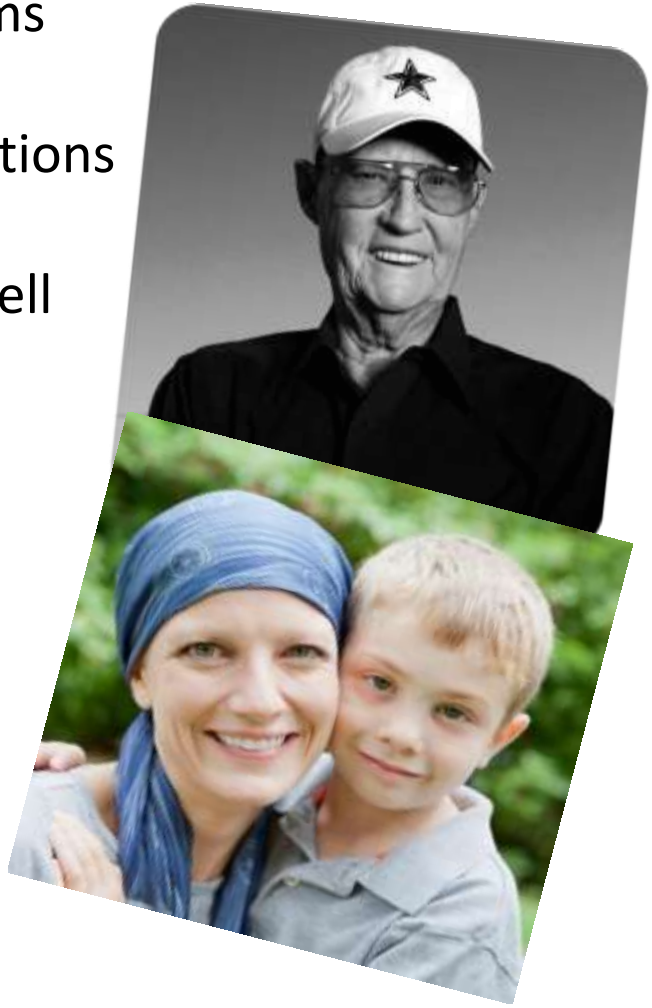
1. *10Q*
2. *10-K*
3. *Company estimate*
4. *Common stock outstanding: 11.9m*

Key Milestones

- Start CYC065 Ph 1b in RR CLL combo with venetoclax
- Start CYC065 Phase 1/2 in solid tumors, incl. NB
- CYC065 Phase 1 data solid tumors
- CYC065 oral formulation development
- Sapacitabine/seliciclib update BRCA +ve breast cancer
- CYC140 (PLKi) IND submission
- Determine submissibility of sapacitabine in eAML

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



THANK YOU

Cyclacel Pharmaceuticals, Inc.

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

Contact: ir@cyclacel.com