Translating cancer biology into medicines

BIO CEO Investor Conference

NASDAQ CYCC - February 12, 2018

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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.*

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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

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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)

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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 Rx that suppress Mcl-1

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

** Source: Cyclacel data on file.*

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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.*

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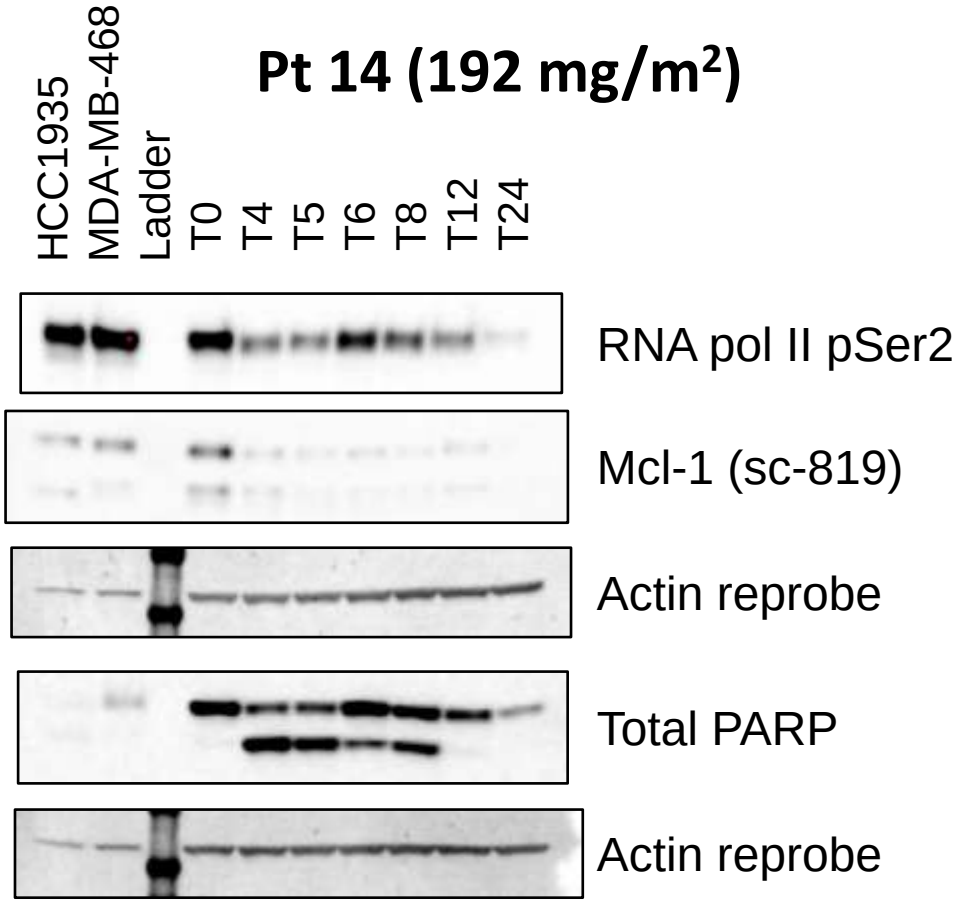
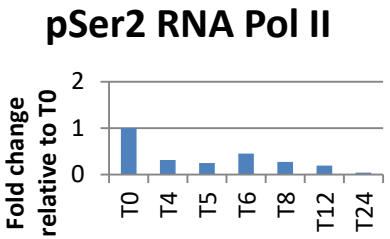
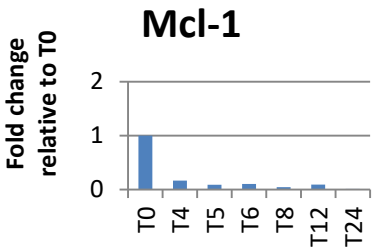
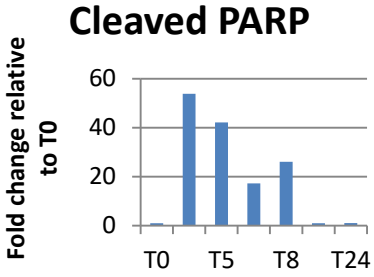
CYC065 First in Human Phase 1 Study (b)









Observations are representative for the cohort.

Source: Cyclacel data on file

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CYC065: Clinical Development Priorities

Molecularly-defined patient populations

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)

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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.*

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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: durable CR, PR, SD (n=76, ASCO 2016)

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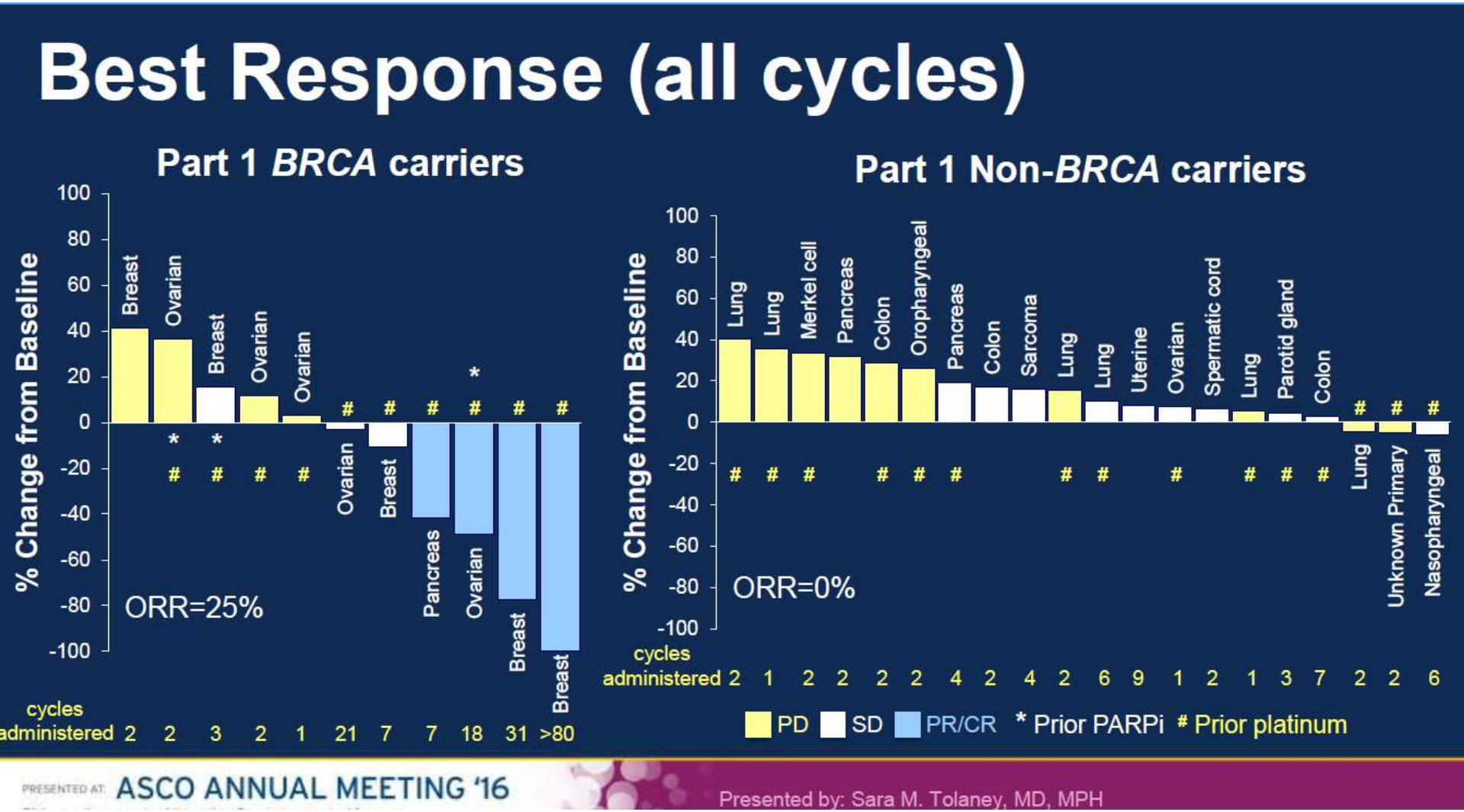
Sapacitabine & Seliciclib Phase 1 BRCA+ve Benefit*



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

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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.

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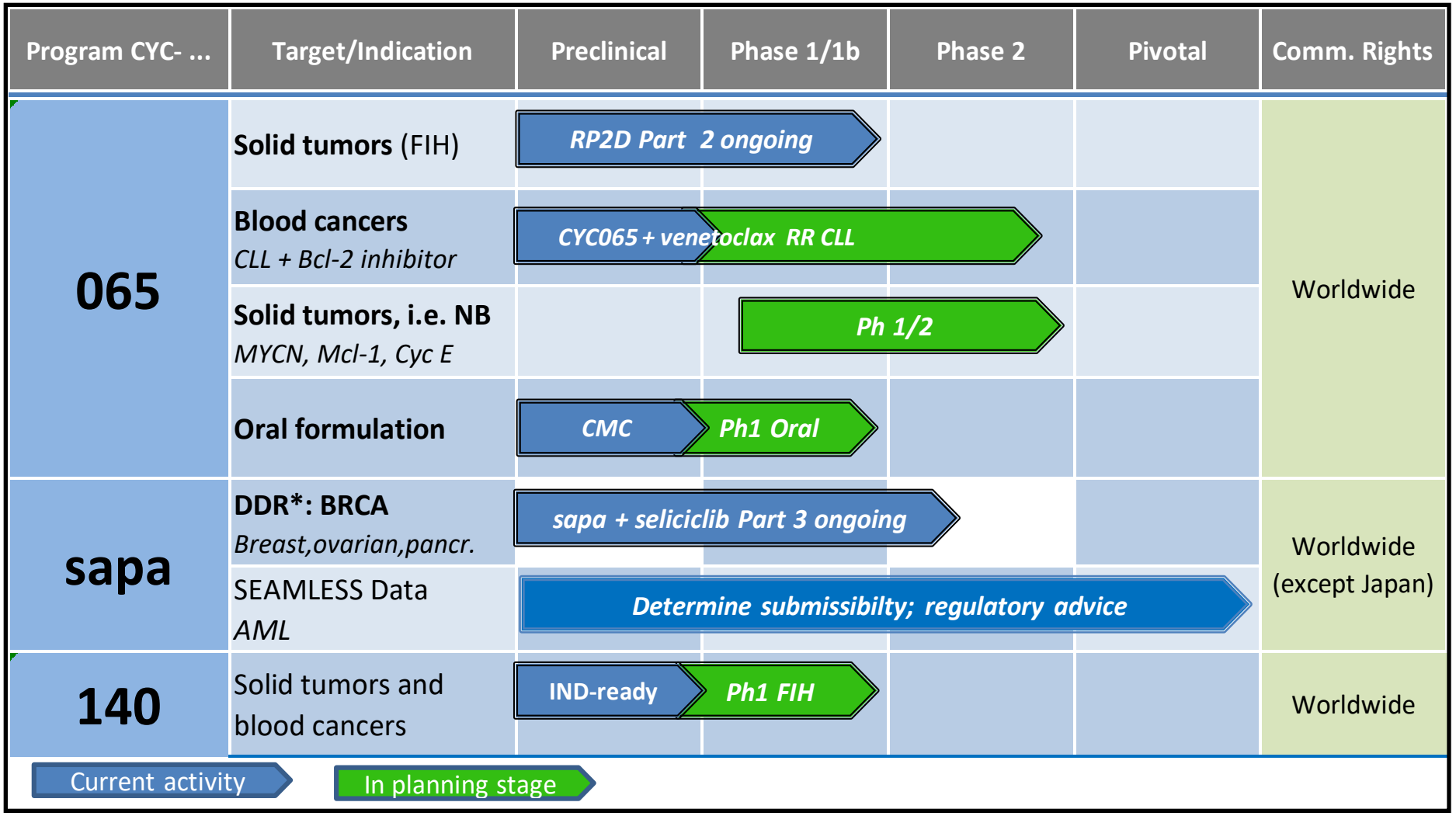
Development Pipeline



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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*

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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

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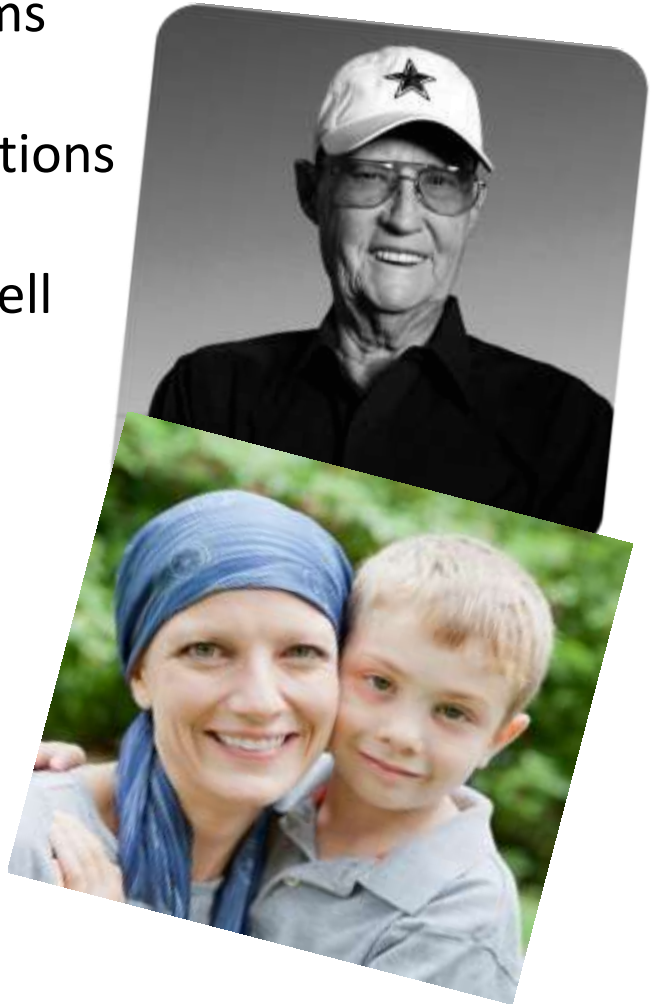
Investment Thesis

- 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



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THANK YOU

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