



Cell cycle pioneers  
 Improving patients' healthcare  
 With orally available innovative medicines

# About Cyclacel www.cyclacel.com

Cyclacel is a biopharmaceutical company developing oral therapies that target the various phases of cell cycle control for the treatment of cancer and other serious diseases. Sapacitabine, Cyclacel's most advanced product candidate, is the subject of SEAMLESS, a fully enrolled Phase 3 trial being conducted under an SPA with the FDA as front-line treatment for acute myeloid leukemia (AML) in the elderly, and other studies including Phase 2 in myelodysplastic syndromes (MDS). Cyclacel's pipeline includes an oral regimen of CDK inhibitor seliciclib plus sapacitabine in a Phase 1 study of patients with Homologous Recombination (HR) repair-deficient breast, ovarian and pancreatic cancers, including BRCA positive tumors, and CYC065, a novel CDK2/9 inhibitor in a Phase 1 study of patients with solid tumors and with potential utility in both hematological malignancies and solid tumors. Cyclacel's strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a development pipeline of novel drug candidates.

**CYCLACEL PHARMACEUTICALS, INC.**  
 200 Connell Drive, # 1500  
 Berkeley Heights, NJ 07922, U.S.  
 Tel: +1 (908) 517-7330  
 Fax: +1 (866) 271-3466

Cyclacel Ltd  
 1 James Lindsay Place  
 Dundee, Scotland DD1 5JJ, U.K.  
 Tel: +44 (1382) 206 062  
 Fax: +44 (1382) 206 067

**FOUNDED:** 1996  
**STOCK LISTING:** NASDAQ: CYCC, CYCCP

**MANAGEMENT:**  
 Spiro Rombotis  
*President & Chief Executive Officer*

Paul McBarron  
*EVP, Finance & Chief Operating Officer*

Judy Chiao, M.D.  
*Vice President, Clinical Development & Regulatory Affairs*

Professor David Glover, Ph.D.  
*Chief Scientist*

Susan Davis, Ph.D.  
*Senior Director, Business Development and Project Management*

## DRUG PIPELINE

Product Candidate	Indication	Phase	1	2	3
Sapacitabine	Acute myeloid leukemia		▶	▶	▶
Sapacitabine	Myelodysplastic syndromes		▶	▶	
Seliciclib & sapacitabine	HR-deficient solid tumors		▶		
Seliciclib	Non-small cell lung cancer Nasopharyngeal cancer		▶	▶	
Seliciclib <small>*investigator-sponsored</small>	Cushing's Disease, Cystic Fibrosis, Rheumatoid Arthritis		▶	▶	
CYC065	Cancer (CDK inhibitor)		▶		
CYC140	Cancer (PLK1 inhibitor)	▶			

**CYCLACEL: PIONEERS IN CELL CYCLE BIOLOGY**

Applying its core strength in cell cycle biology, Cyclacel is advancing a pipeline of small molecules designed to stop uncontrolled cell division. Its founder, Prof. Sir David Lane, is an authority in cell cycle biology credited with the discovery of p53, a ubiquitously mutated tumor suppressor gene in cancer patients. Chief Scientist, Prof. David Glover, is an authority in mitosis. He discovered the aurora and polo kinases, essential cell cycle mechanisms that regulate cancer cell mitosis (division).



#### **FINANCIAL HIGHLIGHTS (as of December 31, 2015)**

- 12-month Stock Price Range: \$0.47 to \$2.13
- Common Shares Outstanding: 35.6 million
- Cash and Equivalents: \$20.4 million
- Market Capitalization: \$18.5 million

#### **EXPECTED 2016 CORPORATE MILESTONES**

##### ***Sapacitabine in SEAMLESS***

- Follow-up enrolled patients until required number of events (est. end 1H2016)
- Report top-line results
- Determine regulatory submissibility following analysis of mature data
- Progress a Paediatric Investigation Plan with EMA

##### ***Other Clinical Stage Programs***

- Initiate a Phase 1/2 trial of sapacitabine in MDS in combination with other agents
- Plan a Phase 2 randomized controlled trial of sapacitabine in combination following review of all relevant clinical data with mature follow-up
- Initiate expansion of Phase 1 seliciclib & sapacitabine study in BRCA positive breast cancer patients
- Report updated seliciclib & sapacitabine Phase 1 data

##### ***Early Pipeline***

- Report top-line results of the CYC065 Phase 1 trial
- Report data from seliciclib ISTs when available

#### **ANALYST COVERAGE**

Andrew S. Fein, H.C. Wainwright & Co., LLC

#### **INVESTOR/MEDIA CONTACT**

Paul McBarron, [pmcbarron@cyclacel.com](mailto:pmcbarron@cyclacel.com)

## **HIGHLIGHTS OF DRUG CANDIDATES IN CLINICAL TRIALS**

### **SAPACITABINE ORAL CAPSULES**

*An orally-available nucleoside analogue with a dual mechanism; interfering with DNA synthesis by causing single-strand DNA breaks and inducing arrest of cell cycle progression mainly at G2-Phase*

**Clinical status:** Currently evaluated in the fully-enrolled SEAMLESS registration-directed, Phase 3 study as front-line treatment in patients with AML, aged 70 years or older, who are not candidates for or have refused intensive induction chemotherapy. SEAMLESS compares a regimen of sapacitabine alternating with decitabine versus decitabine alone with a primary endpoint of overall survival and is conducted under a special protocol assessment (SPA) agreement with the US Food and Drug Administration. Interim results from an ongoing, multicenter, Phase 2 trial of sapacitabine in older patients with intermediate-2 or high-risk MDS after treatment failure of front-line hypomethylating agents, such as azacitidine and/or decitabine, reported median overall survival of 8-10 months across the 3 randomized arms of the trial. A combination of seliciclib & sapacitabine is under evaluation in a Phase 1 trial in patients with solid tumors and in particular those carrying BRCA mutations.

### **CDK INHIBITOR PROGRAMS:**

#### **SELICICLIB ORAL CAPSULES & CYC065**

*Highly-selective clinical stage inhibitors of cyclin-dependent kinases (CDK) 2 and 9 central to cancer cell growth, metastatic spread and DNA damage repair; targeted development potential in hematological malignancies and solid tumors*

Top line data from APPRAISE, a Phase 2b, randomized discontinuation, double-blinded, placebo-controlled, study of seliciclib in pretreated patients with NSCLC showed no difference in progression free survival, but increased median overall survival favoring seliciclib vs. placebo (388 vs. 218 days respectively).

CYC065 has improved properties vs. seliciclib in terms of specificity, mechanism of action, increased anti-proliferative potency, improved pharmaceutical properties and longer patent life. CYC065 has been shown to reverse resistance in trastuzumab-resistant breast cancer cells and is a rapid and potent mediator of cell death in leukemia cells with MLL rearrangements. CYC065 entered first in human Phase 1 studies in October 2015 (NCT02552953).

*This document contains forward-looking statements with respect to business conducted by Cyclacel Pharmaceuticals, Inc. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially. A discussion of those risks and uncertainties are more fully discussed under "Risk Factors" in the registration statements on Form 10-K and in the other reports of Cyclacel filed with the SEC. The compounds mentioned in this document including but not limited to sapacitabine, seliciclib, CYC065 and CYC140 are experimental drugs not approved for human use.*