Cyclacel is a clinical-stage biopharmaceutical company developing innovative cancer medicines based on cell cycle, transcriptional regulation, mitosis and DNA damage response (DDR) biology. Cyclacel’s strategy is to build a diversified biopharmaceutical business focused on hematology and oncology based on a pipeline of novel drug candidates. The transcriptional regulation program is evaluating fadraciclib (formerly CYC065) as a single agent in solid tumors and in combination with venetoclax in patients with relapsed or refractory (r/r) CLL and AML/MDS. The anti-mitotic program is evaluating CYC140 in AML/MDS patients. The DDR program is evaluating an oral combination regimen of sapacitabine and venetoclax in patients with r/r AML/MDS and an IST is evaluating an all-oral combination of sapacitabine-olaparib in BRCA mutated breast cancer patients. Cyclacel retains virtually all worldwide marketing rights to its compounds.

**A PIONEER IN CELL CYCLE BIOLOGY**

Applying its core strength in cell cycle biology, Cyclacel is advancing a pipeline of small molecule drugs designed to stop uncontrolled cell division. The Company’s founder, Prof. Sir David Lane, a leading authority in cell cycle biology (discovery of the p53 tumor suppressor gene) proposed CDK2/9 as an optimal target profile. Prof. David Glover, Cyclacel’s first Chief Scientist, is a leader in mitosis biology, who discovered the aurora (AURK) and polo (PLK) mitotic kinase families.

### FINANCIAL HIGHLIGHTS (as of March 31, 2021)

- **Cash and equivalents pro forma:** $51.3 million
- **Est. funding to early 2023**
- **Common stock outstanding:** 9.2 million

### KEY COMPANY HIGHLIGHTS

- **Reported data from a Phase 1 study of fadraciclib as a single agent at the Plenary Session of the 32nd EORTC-NCI-AACR (ENA) Symposium:**
  - Confirmed partial response (PR) after 1.5 months in a patient with MCL1-amplified endometrial cancer, who failed 7 lines of prior therapy; ongoing for >18 months with 96% reduction in target tumor lesions.
  - High bioequivalence vs. i.v. form observed in five patients treated with oral fadraciclib in part 3.

- Enrolled 14 patients in 065-03 study evaluating fadraciclib-venetoclax combo in r/r AML/MDS.
  - Reduction in peripheral blasts observed.

- Enrolled 5 patients in 065-02 study of fadraciclib-venetoclax combo in patients with r/r CLL reduction in lymph node size and MRD negative status achieved.

- Enrolled 7 patients with advanced leukemias in Phase 1 CYC140-01 (i.v.) study of CYC140.

- Enrolled 12 r/r AML/MDS patients in part 2 of the 682-11 Phase 1/2 study evaluating an oral combination regimen of sapacitabine-venetoclax.
  - Published fadraciclib discovery in PLOS ONE.

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FADRACICLIB CLINICAL PROGRESS
Cyclin-dependent kinase (CDK) 2 & 9 inhibitor

Fadraciclib aims to overcome resistance to available cancer treatments by suppressing pro-survival proteins.

**Solid Tumors:** Durable MCL1 suppression of at least 24 hours was observed in 11 out of 13 patients treated at the recommended Phase 2 dose once every 3 weeks (Phase 1 part 1). Stable disease with tumor shrinkage was observed in 6 patients with MCL1, cyclin E and/or MYC overexpression (reported at AACR 2018).

Part 2 tested a more frequent i.v. dosing schedule of 4 times every 3 weeks as a single agent. A heavily-treated endometrial cancer patient with MCL1 amplification achieved confirmed PR ongoing after 18 months with >96% tumor shrinkage (reported at ENA meeting 2020).

Part 3 is evaluating an oral form 4 times every 3 weeks. High bioequivalence observed in patients with comparable PK profile to part 2 i.v. schedule (reported at ENA meeting 2020).

**Hematological Malignancies:** Preclinical data showed synergistic benefit in CLL models by suppressing both MCL1 and BCL2. Resistance to venetoclax, a BCL2 inhibitor, is correlated with MCL1 amplification in CLL (1L/2L) as monoRx, and in AML patients unfit for chemo after progression on front-line combination with HMA.

A combination of i.v. fadraciclib and venetoclax is being evaluated in r/r CLL (065-02) and r/r AML/MDS patients (065-03). Reduction in peripheral blasts in AML and reduction in lymph node size and MRD –ve conversion were observed.

Streamlined Phase 1/2 clinical studies in solid tumors and also hematological malignancies are about to commence. They will evaluate single agent oral fadraciclib in multiple cohorts defined by cancer histology to identify clinical activity which may lead to registration-enabling outcomes.

CYC140 CLINICAL PROGRESS
Polo-like kinase1 (PLK1) Inhibitor

Promising preclinical activity in both solid tumors and hematological malignancies. A Phase 1 study is recruiting patients with advanced leukemias.

Streamlined, registration-enabling Phase 1/2 trials are being planned in multiple cohorts with different histologies with oral CYC140 in both solid tumors and hematological malignancies.

SAPACITABINE CLINICAL PROGRESS
Oral nucleoside analogue with unique DDR mechanism

Sapacitabine has shown single agent activity in r/r AML/MDS patients. Combining sapacitabine with venetoclax may offer an alternative to patients failing front line therapy. In part 2 of a Phase 1/2 study (682-11) 12 r/r AML/MDS patients have been enrolled.

**BRCA +ve solid tumors:** Based on data presented at AACR 2019 with a sapacitabine regimen, investigators are enrolling a Phase 1b/2 IST in combination with the PARP inhibitor olaparib (AstraZeneca/Merck) in BRCA mutant patients with advanced breast cancer. Five out of 9 patients treated thus far have achieved confirmed PR.

MD ANDERSON – CYCLACEL ALLIANCE

A three-year strategic alliance with The University of Texas MD Anderson Cancer Center encompasses four clinical studies of fadraciclib, CYC140 and sapacitabine either as single agents or in combination with approved drugs aiming to enroll up to 170 patients in total. All four studies are open and enrolling patients.

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 fadraciclib, sapacitabine and CYC140 are experimental drugs only for investigational use and are not approved for human use.