Cyclacel is a clinical-stage biopharmaceutical company developing innovative cancer medicines based on cell cycle, transcriptional regulation and DNA damage response (DDR) biology. Cyclacel’s strategy is to build a diversified biopharmaceutical business focused in hematology and oncology based on a pipeline of novel drug candidates. The transcriptional regulation program is evaluating fadracilliclib (a.k.a. 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 DDR program is evaluating an oral combination regimen of sapacitabine and venetoclax in patients with r/r AML/MDS. The anti-mitotic program is evaluating CYC140 in AML/MDS patients. An all oral combination of sapacitabine-olaparib is being assessed (IST) in BRCA+ 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, Professor Sir David Lane, a leading authority in cell cycle biology, is credited with the discovery of p53, one of the most commonly mutated tumor suppressor genes. Professor David Glover, Cyclacel’s first Chief Scientist, is a recognized leader in mitosis biology, who discovered the aurora and polo mitotic kinase families.

<table>
<thead>
<tr>
<th>Rx Candidate</th>
<th>Phase 1</th>
<th>Phase 1b - Phase 2</th>
<th>Phase 3</th>
<th>MoA / Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>fadracilliclib i.v.</td>
<td>065-01 parts 1, 2 solid tumors</td>
<td>fadra + combinants basket (BC/Endo-USC/OC)</td>
<td>CDK2/9; w/w</td>
<td>w/w</td>
</tr>
<tr>
<td>fadracillicib oral</td>
<td>065-01 part 3 solid tumors</td>
<td></td>
<td>CDK2/9; w/w</td>
<td>w/w</td>
</tr>
<tr>
<td>fadracillicib i.v.</td>
<td>065-02 + venetoclax R/R CLL M</td>
<td></td>
<td>CDK2/9; w/w</td>
<td>w/w</td>
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<tr>
<td>fadracillicib i.v.</td>
<td>065-03 + venetoclax R/R AML/MDS M</td>
<td></td>
<td>CDK2/9; w/w</td>
<td>w/w</td>
</tr>
<tr>
<td>sapacitabine oral</td>
<td>682-11 sapacitabine + venetoclax R/R AML/MDS M</td>
<td></td>
<td>w/w excl. Japan</td>
<td>w/w</td>
</tr>
<tr>
<td>sapacitabine oral</td>
<td>IST sapacitabine + olaparib BRCA mutant breast CA</td>
<td></td>
<td>w/w excl. Japan</td>
<td>w/w</td>
</tr>
<tr>
<td>sapacitabine oral</td>
<td>682-12 SEAMLESS oral sapacitabine alternating with i.v. decitabine 1L AML &gt;70 y.o. (EU scientific advice – submissibility)</td>
<td></td>
<td>w/w excl. Japan</td>
<td>w/w</td>
</tr>
<tr>
<td>CYC140 i.x.</td>
<td>140-01 part 1 R/R AML/MDS M</td>
<td></td>
<td>PLK1; w/w</td>
<td>w/w</td>
</tr>
</tbody>
</table>

BC: breast cancer; Endo-USC: endometrial-uterine serous cancer; OC: ovarian cancer; M: MD Anderson alliance programs.

FINANCIAL HIGHLIGHTS (as of June 30, 2020)

- Cash and equivalents pro forma: $25.3 million
- Est. 2019 operating cash burn ~$9.4 million
- Est. funding to Q4 2022
- Common stock outstanding: 4.9 million

KEY COMPANY HIGHLIGHTS

- Investigators reported anticancer activity in fadracilliclib Ph1 part 2, single agent study (065-01); a patient with MCL1 amplified endometrial cancer achieved deep, confirmed PR (>80% tumor shrinkage); currently at cycle 19.
- Ongoing part 3 of 065-01 is evaluating 150mg oral fadracilliclib in patients with advanced cancers. Exhibits good bioavailability in early analyses.
- Enrolled 12 patients in 065-03 study evaluating fadracilliclib-venetoclax combo in r/r AML/MDS pts. Reduction in peripheral blasts observed.
- In 065-02 study of fadracilliclib-venetoclax combo in patients with r/r CLL reduction in lymph node size and MRD negative status achieved.
- CYC140-01 Ph1 study enrolled 6 patients with advanced leukemias.
- Enrolled 11 r/r AML/MDS patients in part 2 of the 682-11 Ph1/2 study evaluating an oral combination regimen of sapacitabine-venetoclax.

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FADRACICLIB CLINICAL PROGRESS
Small molecule targeting cyclin-dependent kinases CDK2 & CDK9

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 Phase 1 part 1; 11 out of 13 patients treated at the recommended Phase 2 dose (sparse dosing schedule). Stable disease with tumor shrinkage was observed in 6 patients with MCL1, cyclin E and/or MYC overexpression (reported at AACR 2018).

Part 2 is testing a more frequent i.v. dosing schedule of fadraciclib as a single agent. A previously treated endometrial cancer patient with MCL1 amplification achieved an ongoing, confirmed PR with >80% tumor shrinkage.

Part 3 is evaluating an oral form with initial data showing comparable PK profile with a similar part 2 i.v. schedule.

A Phase 1b/2a basket study in patients with advanced gynecological cancers, including breast, endometrial and ovarian, is being designed.

**Hematological Malignancies:** Preclinical data showed synergistic benefit in CLL models by suppressing both MCL1 and BCL2. Venetoclax, a BCL2 inhibitor, has been approved for 1st/2nd line CLL. It also received accelerated approval in 1st line in combination in chemo-unfit AML patients. Venetoclax resistance in these patients is often correlated with MCL1 amplification.

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

**CYC140 CLINICAL PROGRESS**

**Internally discovered, polo-like-kinase1 (PLK1) Inhibitor**

A Phase 1 study is recruiting patients with advanced leukemias. Preclinically, CYC140 showed promising activity in both solid tumors and hematological malignancies.

**SAPACITABINE CLINICAL PROGRESS**

**Oral nucleoside pro-drug with unique DDR mechanism**

Sapacitabine, a nucleoside analogue, has shown single agent activity in r/r AML/MDS patients. Combining sapacitabine, with venetoclax may offer innovative alternative for patients failing front line treatment. 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 in BRCA mutant patients with advanced breast cancer. Two out of 7 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.