Cyclacel Pharmaceuticals, Inc.
Form FWP
July 10, 2017

Filed pursuant to Rule 433
Registration No. 333-218305
July 10, 2017

CYC 682 Translating cancer biology into medicines NASDAQ:CYCC | July 2017

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Overview § Mission: exploit cell cycle biology to disrupt cancer cell immortality § Pioneer in Cyclin Dependent Kinase inhibitors § Focus on genetically-defined patient populations § Rationally designed single agents/combinations in liquid & solid cancers § CDK inhibitor and DNA Damage Response clinical stage programs § Experienced management, estimated capital through YE 2018 Released JUL 2017 4

Cyclin Dependent Kinase inhibitors (CDKi) 2001 Nobel Prize for Physiology & Medicine culminating in approved Rx Paradigm-shift in breast cancer: CDK4/6i-based combinations with AI § IBRANCE® (palbociclib, PFE, approved 2015, ~$2.1bn 2016 sales) § KISQALI® (ribociclib, NVS, approved 2017) CYCC's CDK2/9i portfolio strategy: address key issue of resistance • Seliciclib 1st Gen, signals of anticancer activity (Ph 2) • CYC065 2nd Gen, more potent, better profile than seliciclib (Ph 1) 5

Pipeline Program Target/Indication Preclinical Phase 1/1b Phase 2 Pivotal Rights Solid tumors (FIH) Mcl-1 CLL Mcl-1 /Cyclin E solid tumors MYCN / Mcl-1 NB / MLL-r leukemias DDR*: HRD+ve Breast, ovarian,pancreatic DDR*: HRP+ve Breast, ovarian Sapacitabine AML CYC140 (PLK1 inhibitor) Solid & liquid cancers Seliciclib (CDKi) Cushings disease, cystic fibrosis, RA CYC065 (CDKi) Worldwide Worldwide RP2D Data Analysis Investigator Sponsored Trials (IST) CYC065 + venetoclax RR CLL CYC065 Ovarian CYC065 IST CDKi + sapacitabine + PARPi IND-ready Ph1 FIH *DDR=DNA Damage Response Current status Future studies Data Dependent 6

CDK inhibitor landscape CDK4/6 isoform - palbociclib (NYSE:PFE); ribociclib (SWX:NOVN) - Approved in combination with letrozole for ER +ve Her2 -ve advanced or met BC - abemaciclib (NYSE:LLY) Ph3 - trilaciclib (NASDAQ:GTHX) Ph1/2 CDK2/9 transcriptional isoform - CYC065 (CYCC 2Gen) Ph1 - seliciclib (CYCC 1Gen) Ph2 - dinaciclib (pan CDK, MRK) Ph3 - BAY1143572 (CDK9, BAY) Ph1 * Source: Cyclacel data on file. 7

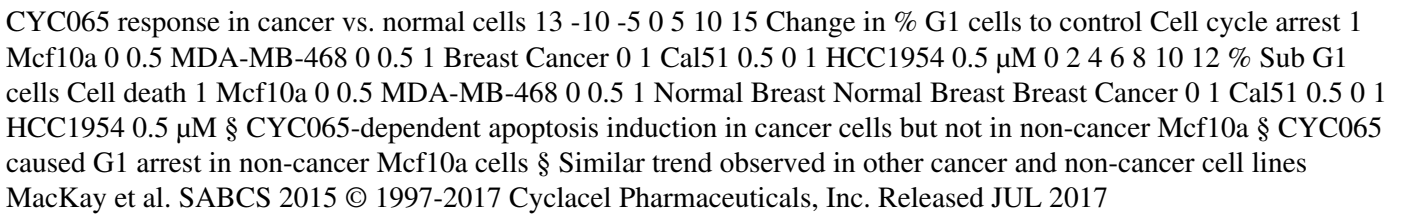
CYC065 CDK2/9 inhibitor summary Second generation, available by i.v. and oral route Unique kinase selectivity • CDK2 (cell cycle control) • CDK9 (regulation of transcription & survival) Differentiation vs. CDK4/6 or pan-CDK inhibitors • Selective pro-apoptotic, p53-independent MoA Completed Ph 1, FIH study, i.v. in advanced patients with solid tumors • Established safety, target engagement, RP2D Robust IP position; exclusivity beyond 2030 Addressing cancers: • dependent on Mcl-1 pro-survival protein • or addicted to Oncogenes Released JUL 2017 8

CYC065 Genetically-Defined Patient Populations 1. Mcl-1 or MYC dependent ( ) liquid & solid cancers A. Venetoclax (Bcl-2i) treated CLL* with Mcl-1 B. Selected Mcl-1 amplified solid tumors, i.e. ovarian C. Cancers addicted to MYCN, i.e. neuroblastoma 2. Cyclin E amplified ( ) solid cancers A. HGSOC (BRCA mutually exclusive, PARPi not option) B. Selected Cyclin E solid tumors, i.e. breast HER2+ C. CDK4/6i resistant breast cancer * Also MLL-r leukemias, lymphoma, and multiple myeloma. Released JUL 2017 9

CYC065 First in Human Phase 1 Study n=23 heavily pretreated patients with various advanced solid tumors § Determined safety, DLT, PK in 7 DL, established RP2D § Treated n=10 in total at DL6 cohort; DL7 MTD neutropenia § Demonstrated target engagement and consistent Mcl-1 suppression over 24h after single dose in 7/9 DL6 patients § Anticancer activity observed in patients with: Ø Mcl-1 (ovarian), Ø Myc (larynx) and Ø cyclin E / Mcl-1 (ovarian) amplified tumors Similar CDK2/9 CYC065 CDK selectivity vs. seliciclib but 40x higher potency & improved pharmaceutical properties. 10

Phase 1 patient durable target inhibition Source: Cyclacel data on file. Observations are representative for the cohort.

CYC065 mechanism of action Inhibits CDK9-mediated oncogenic transcription • Rapidly induces apoptosis; preferentially kills cancer cells over non-cancerous cells • an -apoptotic proteins (Mcl-1, XIAP) & oncogenes (MYC, cyclins) Inhibits CDK2 (cell cycle control) • Targets cyclin E addicted, drug resistant tumors Potentiates effects of DNA damaging agents • expression of HR DNA repair genes (BRCA1 and BRCA2) Mcl-1 MYC Cyclins Cyclin E BRCA1 BRCA2 Cyclacel data on file. Released JUL 2017 12


CYC065 response in cancer vs. normal cells 13 -10 -5 0 5 10 15 Change in % G1 cells to control Cell cycle arrest 1 Mcf10a 0 0.5 MDA-MB-468 0 0.5 1 Breast Cancer 0 1 Cal51 0.5 0 1 HCC1954 0.5 μM 0 2 4 6 8 10 12 % Sub G1 cells Cell death 1 Mcf10a 0 0.5 MDA-MB-468 0 0.5 1 Normal Breast Normal Breast Breast Cancer 0 1 Cal51 0.5 0 1 HCC1954 0.5 μM § CYC065-dependent apoptosis induction in cancer cells but not in non-cancer Mcf10a § CYC065 caused G1 arrest in non-cancer Mcf10a cells § Similar trend observed in other cancer and non-cancer cell lines MacKay et al. SABCS 2015 © 1997-2017 Cyclacel Pharmaceuticals, Inc. Released JUL 2017

CYC065-venetoclax rational combination CLL § CLL unmet medical need • 30% all adult leukemias; 70% mortality rate; 70% aged > 65 years § Venetoclax ORR: 71-79%; CR: ~20% (R/R CLL with 17p del)1 § Tumor microenvironment Mcl-1 diminishing venetoclax effect2,3 § Mcl-1 overcomes venetoclax resistance (stimulated CLL)3 § CYC065 Mcl-1 effectively & durably (>24h) in Phase 1 patients at well tolerated doses § CYC065 and venetoclax synergistic in CLL (incl. 17p del), multiple leukemia & lymphoma cell line models4,5 ABT-263 ABT-737 CYC065 venetoclax Anti-apoptotic Pro-apoptotic Bak Bax APOPTOSIS Bcl-xL Bcl-w A1 Bcl-2 Mcl-1 Adapted from: Adams & Cory, Oncogene 2007 1 Roberts et al. 2016. 2 Smith et al. 2007; 3 Oppermann et al. Blood 2016, 4 Frame et al. AACR 2014, 5 Zheleva et al. SOHO 2015. Released JUL 2017 14

CYC065 & venetoclax synergy in AML & ALL cells Example Fa:CI plots & median CI values for THP-1 (AML) cell line. Combination Index (CI) values calculated using Chou & Talalay method. CI of 0.9 to 1.1 indicate additivity, below 0.9 synergy. Median CI: 0.76 Median CI: 0.74 Median CI: 0.57 • CYC065 synergy with venetoclax (ABT-199) in AML & ALL cell lines • CYC065 synergy with Bcl-2/Bcl-xL/Bcl-w inhibitors ABT-263 or ABT-737 • CYC065 synergies demonstrated in several acute leukemia cell lines (AML: THP-1, HEL; ALL: Jurkat, SEM) Source: Frame et al, SOHO, 2014, Abs 209 Released JUL 2017 15

CYC065 transcriptional regulation of MYC Very common genomic alteration in aggressive tumors 0.1 1 10 100 GI50 (μM) CYC065 p = 0.016 No MYCN expression MYCN expression DMSO 1 μM CYC065 MYCN neuroblastoma highly sensitive § Amplification of MYC family oncogenes: poor clinical outcome in neuroblastoma (NB), SCLC, breast, prostate § No therapeutics against MYCN or MYC reported § CDK9 involved in MYCN transcriptional regulation § MYCN NB cells highly sensi ve to CYC065 § CYC065 inhibits NB cell proliferation, induces apoptosis and MYCN protein § CYC065 causes tumor regression & prolongs survival in MYCN-amplified NB models Potent in vitro and in vivo anti-tumor activity suggest that CYC065 may have therapeutic potential in NB with MYCN oncogene amplification. Poon et al. 4th Neuroblastoma Society Symposium 2015. 8 h treatment. SRB colony formation assay after 72 h. 16

CYC065 in MYCN NB: regression & survival Kelly xenograft (MYCN amplified) Poon et al. 4th Neuroblastoma Society Symposium 2015, 25-27 Nov, Newcastle. Treatment regimen: CYC065 – po, dq x 5/week x2 Th-MYCN GEMM of NB Cyclacel data on file. Released JUL 2017 17

Overcoming resistance in cyclin E amplified tumors 18 200 400 600 800 1000 1200 0 5 10 15 20 Tumor volume (mm3) Days of treatment Control Trastuzumab CYDCK026i.5 T+CCYDCK026i.5 CYC065 alone or in combination with trastuzumab causes very effective in vivo tumor growth inhibition of BT474R trastuzumab resistant HER2+ BC cell line, and increased apoptosis in vitro. Source: Scaltriti et al 2011 PNAS 108 3761 Trastuzumab resistant Her2+ breast cancer Drug-resistant Uterine Serous Carcinoma CYC065 active as a single agent and in combination ($p<0.03$) in ARK-1 (trastuzumab-resistant, PI3K mutant) xenograft model with without CCNE1 amplification CCNE1 amplified USC primary cell lines show increased CYC065 sensitivity Source: Cocco et al., AACR, 2015, Abs 3103; Cocco et al, BJC, 2016

Overcoming resistance to CDK4/6 inhibitors + AI CDK4/6i+AI inhibit proliferation; but senescence emergence of resistance, i.e. CDK2/cycE CDK2 activation or cyclin E amplifica on/overexpression acquired/intrinsic resistance to CDK4/6i in breast and ovarian cancer and AML models* Higher CCNE1 gene expression observed in BC resistant to neoadjuvant palbociclib + anastrozole* Cyclin E mediated resistance to letrozole in HR+ breast cancer is reversed by seliciclib* CDK4/6i + AI resistance CDK4/6 cyclin D CDK2 cyclin E Rb E2F E2F Rb P P Rb P E2F inactive active G1 S palbociclib ribociclib abemaciclib CYC065 estrogen signalling aromatase inhibitors fulvestrant proliferation cell cycle *Source: Herrera-Abreu et al. Cancer Res. 2016; Konecny & Slamon Clin. Cancer Res. 2011; Taylor-Harding et al. Oncotarget 2015; Caldon et al. Mol. Cancer Ther. 2012 ; Wang et al. Blood 2007; Ma et al. Clin Cancer Res. 2017; Akli et al, Clin Cancer Res. 2010. 19

IO strategy: modulate antitumor immune response CDK2/9i synergy with IO agents § Dinaciclib synergistic with anti-PD-1 in mouse syngeneic tumor models § Dinaciclib induces immunogenic cell death (ICD) with evidence of T cell infiltra on and dendritic cell activation in tumors1 § MC38 mouse colorectal carcinoma in C57BL/6 mice, 12 per group, dinaciclib 40 mg/kg, anti-PD-1 5 mg/kg each dosed once daily for 25 days2 § Phase 1 open-label study evaluating safety and efficacy of pembrolizumab + dinaciclib in relapsed or refractory CLL, MM, DLBCL3 (1) Hossain et al., Cancer Res, 2015 (2) US20160193334A (3) NCT02684617 20

CYC065 CDK2/9i investment highlights § CDKis: validated drug class § Targeting genetically-defined patient populations § Significant market potential § Potential to treat difficult cancers and overcome cancer cell resistance § Single agent and combination opportunity 21

DNA Damage Response (DDR) Clinical Program © 1997-2017 Cyclacel Pharmaceuticals, Inc. Released JUL 2017
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Modulation of DNA Damage Response (DDR) Cyclacel's CDK inhibitor-based DDR strategies: • Modulate DNA repair via HR, NHEJ, etc. pathways • expression of HR DNA repair genes, i.e. BRCA1 / BRCA2 • an -apoptotic survival signalling , i.e. Mcl-1 Cyclacel's oral sapacitabine may work best in HR-deficient tumors: Clinical utility observed in combination with CDK inhibitor; future options • Combinations with SoC, i.e. PARP inhibitors • Single agent treatment in sensitive cancers Released JUL 2017 23

DDR sapacitabine/seliciclib in HR-repair deficient tumors* § Oral combo of complementary mechanisms: sapacitabine's unique, MoA (DNA SSBs# & cell cycle arrest) combined with CDKi modulation § Parts 1 & 2: durable clinical benefit (PRs & prolonged SD) in patients with BRCA +ve: breast, ovarian, pancreatic cancers § Part 3 to start: revised schedule including BRCA +ve ovarian, pancreatic cancer patients … Plan to substitute seliciclib with CYC065 ... * 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 Released JUL 2017 24

DDR: sapacitabine/seliciclib Ph 1 best responses* * Source: Tolaney S et al, J Clin Oncol 34, 2016 (suppl; abstr 2503). Released JUL 2017 25

Sapacitabine/seliciclib Phase 1 BRCA +ve benefit* A * Source: Tolaney S et al, J Clin Oncol 34, 2016 (suppl; abstr 2503). 26

Sapacitabine/seliciclib Phase 1 BRCA +ve benefit* B * Source: Tolaney S et al, J Clin Oncol 34, 2016 (suppl; abstr 2503). 27

Financial position & capitalization Mar. 31 2017 Pro Forma Cash & cash equivalents: $15.7m1 Current Operating cash burn (excludes non-cash items) ü 2014: ~ $18.7m annual 2 ü 2015: ~ $14.5m annual 2 ü 2016: ~ $10.1m annual 2 ü 2017: ~ $ 8.0m annual 3 Fully diluted shares: ~ 4.6 million4,5 No debt 1. Cyclacel press release 2. 10-K. 3. Company estimate 4. 10Q - 31 March 2017 5. Common stock outstanding: 4.3m. Released JUL 2017 29

Key milestones § CYC065 First-in-Human, Phase 1 data solid tumors § Start CYC065 Phase 1, Part 2 in solid tumors § Start CYC065 Ph 1b in R/R CLL combo with venetoclax § Sapacitabine/seliciclib update BRCA+ve breast cancer § CYC140 (PLKi) IND submission Released JUL 2017 30

Cyclacel Highlights § Transcriptional CDKi and DNA Damage Response clinical stage oncology programs § Treat difficult cancers and overcome resistance § Competitive positioning § Large markets Contact: ir@cyclacel.com. Thank you. 31