***Supplementary Table 1*: Summary of 33 Patients Treated with Abemaciclib in Dose Escalation**

Cohort	Dose and Frequency	Age and Sex	Tumor Type	Number of Cycles	Best Overall Response
1	50mg Q24H	46M	Colorectal cancer	-	Not Evaluable
		46F	Rectal cancer	2	Progressive Disease
		62M	Rectal cancer	2	Progressive Disease
		53M	Colorectal cancer	1	Progressive Disease
2	100mg Q24H	59F	NSCLC	6	Stable Disease
		73M	Colorectal cancer	2	Progressive Disease
		69F	Colorectal cancer	4	Stable Disease
3	150mg Q24H	68M	NSCLC	4	Stable Disease
		71F	Ovarian cancer	26	Stable Disease
		53F	Endometrial cancer	2	Progressive Disease
4	225mg Q24H	68M	Colorectal cancer	2	Stable Disease
		66F	Ovarian cancer	4	Stable Disease
		47M	Salivary ductal carcinoma	16	Stable Disease
5	75mg Q12H	56F	Melanoma	3	Stable Disease
		71F	Ovarian cancer	-	Not Evaluable
		60M	Liposarcoma	2	Progressive Disease
6	100mg Q12H	58F	Colorectal cancer	2	Progressive Disease
		45F	Chondrosarcoma	3	Stable Disease
		62M	Appendiceal mucinous cystadenocarcinoma	2	Progressive Disease
		50M	Colorectal cancer	2	Progressive Disease
7	150mg Q12H	61F	Colorectal cancer	2	Progressive Disease
		64F	Ovarian cancer	2	Progressive Disease
		67F	Colorectal cancer	4	Stable Disease
8	200mg Q12H	57M	Rectal Cancer	4	Stable Disease
		59F	Adenoid cystic carcinoma	-	Not Evaluable
		63F	Colorectal cancer	2	Stable Disease
		68F	Ovarian cancer	8	Stable Disease
		65F	Breast cancer	4	Stable Disease
		51F	Endometrial cancer	4	Stable Disease
		56F	Endometrial cancer	4	Stable Disease
9	275mg Q12H	52F	Colorectal cancer	2	Progressive Disease
		66F	Breast cancer	-	Not Evaluable
		44F	Adenoid cystic carcinoma	2	Progressive Disease

A best overall response of Stable Disease required at least 6 weeks (≥39 days) between first dose of abemaciclib and radiographic disease assessment. Patients without a disease assessment at least 6 weeks after enrollment and who had not already progressed were designated as Not Evaluable.

Abbreviations: Q12H = every 12 hours, Q24H = every 24 hours, NSCLC = non-small cell lung cancer

***Supplementary Table 2*: Baseline patient and disease characteristics**

Characteristic	Dose escalation (n=33)	Single-agent cohorts* (n=173)	Breast cancer (n=47)	NSCLC (n=68)	Glioblastoma (n=17)	Melanoma (n=26)	Colorectal cancer (n=15)	Breast cancer combination cohort (n=19)
Age (range), years	60 (44−73)	61 (24–85)	55 (28−80)	65 (24−85)	53 (28–73)	66 (39–82)	60 (38–80)	57 (39–80)
Male	11 (33%)	64 (37%)	1 (2%)	32 (47%)	7 (41%)	18 (69%)	6 (40%)	0 (0%)
ECOG performance status								
0	14 (42%)	60 (35%)	19 (40%)	13 (19%)	6 (35%)	15 (58%)	7 (47%)	10 (53%)
1	19 (58%)	101 (58%)	27 (57%)	48 (71%)	7 (41%)	11 (42%)	8 (53%)	9 (47%)
2	-	12 (7%)	1 (2%)	7 (10%)	4 (24%)	0 (0%)	0 (0%)	0 (0%)
Number metastatic sites								
1	9 (27%)	43 (25%)	8 (17%)	10 (15%)	NA†	5 (19%)	3 (20%)	5 (26%)
2	15 (45%)	45 (26%)	16 (34%)	17 (25%)	NA†	5(19%)	7 (47%)	10 (53%)
3 or more	9 (27%)	85 (49%)	23 (49%)	41 (60%)	NA†	16 (61%)	5 (33%)	4 (21%)
Prior surgery	32 (97%)	122 (71%)	42 (89%)	25 (37%)	17 (100%)	24 (92%)	14 (93%)	18 (95%)
Prior radiotherapy	12 (36%)	119 (69%)	42 (89%)	40 (59%)	17 (100%)	13 (50%)	7 (47%)	16 (84%)
Prior systemic therapies	32 (97%)	167 (97%)	47 (100%)	66 (97%)	17 (100%)	22 (85%)	15 (100%)	19 (100%)
≤3 regimens	14 (42%)	77 (45%)	11 (23%)	29 (43%)	14 (82%)	16 (62%)	7 (47%)	7 (37%)
≥4 regimens	18 (55%)	90 (52%)	36 (77%)	37 (54%)	3 (18%)	6 (23%)	8 (53%)	12 (63%)

Starting doses for abemaciclib in the tumor-specific cohorts: breast cancer cohort, 150 mg (n=25), 200 mg (n=22); NSCLC cohort, 150 mg (n=26), 200 mg (n=42); glioblastoma cohort, 150 mg (n=2), 200 mg (n=15); melanoma cohort, 150 mg (n=13), 200 mg (n=13); colorectal cancer cohort, 150 mg only (n=15), HR-positive breast cancer (abemaciclib + fulvestrant) combination cohort, 200 mg only (n=19).

Data are represented as n (%) or median (range).

*Includes all tumor-specific cohorts that received single-agent abemaciclib for breast cancer, NSCLC, glioblastoma, melanoma, or colorectal cancer.

†Glioblastoma is a primary brain tumor

Abbreviations: ECOG = Eastern Cooperative Oncology Group, HR = hormone receptor, n = number of patients, NA = not applicable; NSCLC = non-small cell lung cancer.

Supplementary Table 3: **Possibly related treatment-emergent adverse events (>10% all grades) for hormone receptor-positive breast cancer cohort (n=19) receiving combination therapy with abemaciclib plus fulvestrant**

TEAE	Grade 1	Grade 2	Grade 3	Grade 4	All grades[*]
Diarrhea	7 (37%)	7 (37%)	1 (5%)	0	15 (79%)
Fatigue	7 (37%)	5 (26%)	1 (5%)	0	13 (68%)
Nausea	6 (32%)	6 (32%)	0	0	12 (63%)
Neutropenia	0	2 (11%)	6 (32%)	0	8 (42%)
Vomiting	4 (21%)	3 (16%)	1 (5%)	0	8 (42%)
Anorexia	3 (16%)	3 (16%)	0	0	6 (32%)
Leukopenia	0	1 (5%)	5 (26%)	0	6 (32%)
Abdominal pain	1 (5%)	1 (5%)	2 (11%)	0	4 (21%)
Dehydration	1 (5%)	2 (11%)	0	0	3 (16%)
Hypokalemia	1 (5%)	2 (11%)	0	0	3 (16%)
Watering eyes	1 (5%)	2 (11%)	0	0	3 (16%)
Anemia	0	0	2 (11%)	0	2 (11%)
Constipation	2 (11%)	0	0	0	2 (11%)
Creatinine increased[†]	1 (5%)	1 (5%)	0	0	2 (11%)
Dyspepsia	0	2 (11%)	0	0	2 (11%)
Thrombocytopenia	2 (11%)	0	0	0	2 (11%)

Data are represented as n (%).
[*]No grade 5 events reported.
[†]Abemaciclib inhibits renal transporters that mediate tubular secretion of creatinine, so serum creatinine may not accurately reflect renal function in patients receiving abemaciclib.

Abbreviations: n = number of patients, TEAE = treatment-emergent adverse event

***Supplementary Table 4*: Summary of abemaciclib pharmacokinetic parameters following a single oral administration**

Geometric mean* (% CV)	Abemaciclib dose						
	50 mg (n=4)	**75 mg (n=3)**	**100 mg (n=7)**	**150 mg (n=85)**	**200 mg (n=117)**	**225 mg (n=3)**	**275 mg (n=3)**
C_{max} (ng/mL)	39.6 (54)	41.9 (21)	68.8 (117)	114 (83)	158 (92)	49.1 (60)	246 (75)
t_{max}† (h)	3.99 (2.12–4.35)	4 (2–4)	6 (4–10)	6 (2–70.53)	6.02 (1.98–72.45)	6 (6–6)	6 (6–7.92)
$AUC_{0\text{-}tlast}$ (ng*h/mL)	1060 (68)	878 (64)	1690 (95)	3420 (82)	4600 (96)	1820 (39)	6240 (39)
$AUC_{0\text{-}\infty}$ (ng*h/mL)	1270 (88)	943 (64)	1880 (96)	4010 (80)	5220 (105)	2700 (17)	7890 (5)
CL/F (L/h)	39.5 (88)	79.5 (64)	53.3 (96)	37.4 (80)	38.3 (105)	83.4 (17)	34.9 (5)
V_{ss}/F (L)	1460 (38)	2220 (62)	1660 (99)	1310 (73)	1300 (96)	4930 (84)	1360 (93)
$t_{1/2}$‡ (h)	25.8 (17.6–44.1)	17.4 (15.9–18.5)	20.8 (11.5–29.0)	22.8 (8.9–60.8)	21.3 (11.6–63.0)	38.1 (15.5–62.7)	25.0 (12.4–63.9)

*Individual values are reported when patient numbers <3.
†Median (range).
‡Geometric mean (range).

Abbreviations: $AUC_{0\text{-}tlast}$ = area under the plasma concentration-time curve from time 0 to the time of last quantifiable plasma concentration, $AUC_{0\text{-}\infty}$ = area under the plasma concentration-time curve from time 0 to infinity, CL/F = oral clearance, C_{max} = maximum observed plasma concentration, CV = coefficient of variation, n = number of patients, $t_{1/2}$ = terminal elimination half-life, t_{max} = time to maximum observed plasma concentration, V_{ss}/F = oral volume of distribution at steady state.

***Supplementary Table 5*: Summary of abemaciclib pharmacokinetic parameters following repeated once-daily (Q24H) or twice-daily (Q12H) oral administration**

Geometric mean* (% CV)	Abemaciclib dose							
	Q24H				Q12H			
	50 mg (n=2)	100 mg (n=3)	150 mg (n=3)	225 mg (n=3)	75 mg (n=3)	100 mg (n=8)	150 mg (n=72)	200 mg (n=52)
Tau (h)	24	24	24	24	12	12	12	12
$C_{min,ss}$ (ng/mL)	5.34,* 125	48.7 (168)	134 (47)	54.7 (27)	34.0 (57)	144 (61)	169 (95)	197 (82)
$C_{max,ss}$ (ng/mL)	28.6,* 254	102 (198)	189 (35)	121 (38)	58.7 (37)	226 (51)	249 (86)	298 (72)
$t_{max,ss}$† (h)	1.67,* 4.3	4.25 (4−4.33)	6 (6−6)	6 (4−8)	4.07 (0−8)	4 (2−6.03)	3.95(0−10.15)	4 (0−10)
$AUC_{0-\tau,ss}$ (ng*h/mL)	334,* 4557	1840 (172)	3448,* 5162	3164,* 1576	546 (43)	2250 (54)	2390‡ (90)	3000‡ (69)
$AUC_{0-24h,ss}$ (ng*h/mL)	334,* 4557	1840 (172)	3448,* 5162	3164,* 1576	1300 (49)	3910 (53)	4280‡ (94)	5520‡ (70)
R_{AUC}	0.76,* 7.80	2.46 (26)	1.86,* 5.82	5.16,* 0.981	1.85 (46)	3.01‡ (99)	2.63‡ (58)	2.53‡ (67)
R_{Cmax}	1.04,* 7.63	2.14 (43)	3.65 (68)	2.46 (107)	1.4 (26)	2.43‡ (94)	2.18‡ (58)	1.87‡ (58)
L	0.49,* 3.6	1.23 (20)	0.89,* 2.98	1.43,* 0.55	0.579 (34)	0.979‡ (90)	0.639‡ (54)	0.578‡ (46)

*Individual values are reported when patient numbers <3.
†Median (range).
‡Geometric mean and CV are based on patient numbers <N.

Abbreviations: $AUC_{0-\tau,ss}$ = area under the steady state plasma concentration-time curve over a dosing interval, $AUC_{0-24hr,ss}$ = area under the steady state plasma concentration-time curve over 24 h, $C_{min,ss}$ = minimum observed plasma concentration at steady state, $C_{max,ss}$ = maximum observed plasma concentration at steady state, CV = coefficient of variation, L = linearity index, n = number of patients, Q24H = every 24 h (once daily), Q12H = every 12 h (twice daily), $t_{max,ss}$ = time to maximum observed plasma concentration at steady state, R_{AUC} = accumulation ratio for AUC, R_{Cmax} = accumulation ratio for C_{max}.

***Supplementary Table 6*: Efficacy for NSCLC cohort, overall and by *KRAS* status**

Endpoint	NSCLC overall* (n=68)	*KRAS*-mutated (n=29)	*KRAS*-wild-type (n=33)
Best overall response			
Complete response (CR)	0	0	0
Partial response (PR)	2 (3%)	1 (3%)	1 (3%)
Stable disease (SD)	31 (46%)	15 (52%)	12 (36%)
≥24 weeks	15 (22%)	9 (31%)	4 (12%)
<24 weeks	16 (24%)	6 (21%)	8 (24%)
Progressive disease	16 (24%)	7 (24%)	9 (27%)
Not evaluable	19 (28%)	6 (21%)	11 (33%)
Response rate (CR+PR) (95% CI)	3% (0.4−10.2)	3% (0.1−17.8)	3% (0.1−15.8)
Disease control rate (CR+PR+SD) (95% CI)	49% (36.2−61.0)	55% (35.7−73.6)	39% (22.9−57.9)
Median duration of overall response, months	7.5, 7.4 (2 patients)	7.4 (1 patient)	7.5 (1 patient)
Median progression-free survival (95% CI), months	2.0 (1.8−3.7)	2.8 (1.8−5.6)	1.9 (1.4−3.7)

Data are represented as n (%), unless otherwise specified.

*6 patients had unknown *KRAS* status.

Abbreviations: CI = confidence interval, CR = complete response, Kirsten rat sarcoma (*KRAS*); n = number of patients, NSCLC = non-small cell lung cancer, PR = partial response, SD = stable disease,.

Supplementary Table 7*: Efficacy for other tumor-specific cohorts

Endpoint	Glioblastoma (n=17)	Colorectal cancer (n=15)	Melanoma (n=26)
Best overall response			
Complete response (CR)	0	0	0
Partial response (PR)	0	0	1 (4%)
Stable disease (SD)	3 (18%)	2 (13%)	6 (23%)
Progressive disease	13 (76%)	10 (67%)	11 (42%)
Not evaluable	1 (6%)	3 (20%)	8 (31%)
Response rate (CR+PR) (95% CI)	0%	0%	4% (0.1–19.6)
Disease control rate (CR+PR+SD) (95% CI)	18% (3.8–43.4)	13% (1.7–40.5)	27% (11.6–47.8)
Median duration of overall response (95% CI), months	--	--	5.5 (NA–NA)
Median progression-free survival (95% CI), months	1.1 (1.0–1.9)	1.9 (1.7–1.9)	2.0 (1.8–3.7)

Data are represented as n (%), unless otherwise specified.
*Includes tumor-specific cohorts for glioblastoma, colorectal cancer, and melanoma receiving single-agent abemaciclib.

Abbreviations: CI = confidence interval, CR = complete response, n = number of patients, NA = not applicable, PR = partial response, SD = stable disease.