SUPPLEMENTAL FILE

Evaluation of the Bioequivalence and Food Effect on the Bioavailability of CC-486 (Oral Azacitidine) Tablets in Adult Patients with Cancer

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**Supplementary Table 1. Baseline demographic and disease characteristics**

|                          | Bioequivalence Cohort (Stage 1) (N = 30) | Food Effect Cohort (Stage 2) (N = 57) |
|--------------------------|----------------------------------------|--------------------------------------|
| **Age, median (range)**  | 68.5 (46, 86)                          | 62.0 (31, 88)                        |
| **Race, n (%)**          |                                        |                                      |
| White                    | 27 (90)                                | 53 (93)                              |
| Other\(^a\)              | 2 (6)                                  | 2 (4)                                |
| Not Collected or Reported | 1 (3)                                  | 2 (4)                                |
| **Sex, n (%)**           |                                        |                                      |
| Male                     | 20 (67)                                | 34 (60)                              |
| Female                   | 10 (33)                                | 23 (40)                              |
| **BMI, median (range)**  | 27.8 (16, 44)                          | 26.6 (19, 47)                        |
| **Malignancy type, n (%)**|                                       |                                      |
| Metastatic or inoperable solid tumors | 27 (90)                          | 57 (100)                              |
| Myelodysplastic syndromes | 1 (3)                                  | 0                                    |
| Acute myeloid leukemia    | 1 (3)                                  | 0                                    |
| Multiple myeloma          | 1 (3)                                  | 0                                    |
| **Time since diagnosis (years), median (range)** | 3.5 (0.1, 19.2) | 4.8 (0.2, 27.1) |
| **ECOG performance status score, n (%)** |                                  |                                      |
| 0                        | 7 (23)                                 | 20 (35)                              |
| 1                        | 23 (77)                                | 34 (60)                              |
| 2                        | 0                                      | 3 (5)                                |

\(^a\)Black or African-American, Asian, American Indian or Alaskan Native

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.
Supplementary Table 2. Plasma pharmacokinetic parameters for two formulations of CC-486 (2 x 150-mg tablets [Formulation A] and 1 x 300-mg tablet [Formulation B])

| Treatment                  | Statistics                | AUCt (ng*h/mL) | AUC∞ (ng*h/mL) | Cmax (ng/mL) | Tmax (h) | t1/2 (h) | CL/F (L/h) | Vz/F (L) |
|----------------------------|---------------------------|----------------|----------------|--------------|----------|----------|------------|----------|
| 2 x 150 mg tablets         | N                         | 30             | 30             | 30           | 30       | 30       | 30         | 30       |
|                            | Geometric Mean            | 225.0          | 228.5          | 143.0        | NA       | 0.544    | 1313       | 1031     |
|                            | Geometric %CV             | 63.7           | 62.6           | 53.1         | NA       | 32.0     | 62.6       | 67.4     |
|                            | Median                    | 226            | 232            | 149          | 1.0      | 0.52     | 1300       | 922      |
|                            | Min, Max                  | 71.8, 555      | 76.4, 557      | 34.5, 362    | 0.48, 3.0| 0.34, 1.1| 538, 3930  | 389, 3860|
| 1 x 300 mg tablet          | N                         | 30             | 30             | 30           | 30       | 30       | 30         | 30       |
|                            | Geometric Mean            | 239.1          | 241.6          | 145.1        | NA       | 0.492    | 1242       | 881.1    |
|                            | Geometric %CV             | 65.2           | 64.5           | 63.7         | NA       | 26.9     | 64.5       | 67.4     |
|                            | Median                    | 236            | 237            | 148          | 1.0      | 0.46     | 1270       | 900      |
|                            | Min, Max                  | 93.0, 640      | 94.5, 642      | 46.7, 362    | 0.50, 2.5| 0.33, 0.87| 468, 3170  | 317, 2790|

PK Parameter | Treatment | N  | Geometric Mean | Median Difference | 90% CI of Median Difference (Fed – Fasted) | P-value |
|-------------|-----------|----|----------------|-------------------|------------------------------------------|---------|
| AUCt (ng*h/mL) | 2 x 150 mg | 30 | 225.0          | -0.017            | (-0.25, 0.03)                            | <0.710  |
|             | 1 x 300 mg | 30 | 239.1          | 1.0               |                                          |         |
| AUC∞ (ng*h/mL) | 2 x 150 mg | 30 | 228.5          | -0.017            | (-0.25, 0.03)                            |         |
|             | 1 x 300 mg | 30 | 241.6          | 1.0               |                                          |         |
| Cmax (ng/mL)  | 2 x 150 mg | 30 | 143.0          | -0.017            | (-0.25, 0.03)                            |         |
|             | 1 x 300 mg | 30 | 145.1          | 1.0               |                                          |         |

N patients = the total number of patients for which the PK parameter could be calculated

*Median and median difference (Test vs. Reference), and 90% CI of the median difference, are from Hodges-Lehmann estimate. The P value is from Wilcoxon signed-rank test.

AUCt, area under the plasma concentration-time curve from time 0 extrapolated to infinity; Cmax, maximum plasma concentration; Tmax, time to Cmax; t1/2, terminal half-life; CL/F, apparent total clearance; Vz/F, volume of distribution; NA, not applicable.