**Supplementary Materials**

**Supplementary Table S1: Patient demographics**

|                  |       |
|------------------|-------|
| Patients enrolled| 32    |
| Patients evaluable| 31   |
| Mean age (years) | 49    |
| Median age (years) | 53.5 |
| Age range (years) | 20-73 |
| **Gender**       |       |
| Female           | 14    |
| Male             | 18    |
| **Race**         |       |
| Caucasian        | 20    |
| Asian            | 5     |
| African American | 3     |
| Unknown          | 3     |
| American Indian or Alaska Native | 1 |
| **Accrual by Dose Level** |   |
| DL1              | 3     |
| DL2              | 3     |
| DL3              | 3     |
| DL4              | 6     |
| DL5              | 17    |
## Supplementary Table S2: Adverse events by dose level.

| Adverse Event                          | Grade | DL1 (n=3) | DL2 (n=3) | DL3 (n=3) | DL4 (n=6) | DL5 (n=16) |
|----------------------------------------|-------|-----------|-----------|-----------|-----------|------------|
| Alanine aminotransferase increased     | 2     |           |           |           |           | 1          |
|                                       | 3     |           |           |           |           |            |
| Alkaline phosphatase increased         | 2     |           | 1         |           |           | 1          |
| Allergic reaction                      | 2     |           |           |           |           |            |
| Alopecia                               | 2     |           |           |           |           |            |
| Anemia                                 | 2     |           |           |           |           | 1          |
|                                        | 3     |           |           |           |           |            |
| Anorexia                               | 2     |           |           |           |           | 1          |
| Aspartate aminotransferase increased   | 3     |           |           | 2         |           |            |
| Creatine increased                     | 2     |           |           |           |           |            |
| Dehydration                            | 2     |           |           |           |           |            |
| Dry skin                               | 2     |           |           |           |           | 1          |
| Dysgeusia                              | 2     |           |           |           |           |            |
| Fatigue                                | 2     |           |           |           |           |            |
| Febrile neutropenia                    | 4     | 2         |           |           |           |            |
| Flatulence                             | 2     | 1         |           |           |           |            |
| Hypertension                           | 2     | 3         | 2         | 2         | 3         | 5          |
|                                        | 3     |           |           |           | 1         | 2          |
| Hypoalbuminemia                        | 2     |           |           |           |           | 1          |
| Hyperbilirubinemia                     | 2     |           |           |           |           | 3          |
| Hypophosphatemia                       | 2     | 1         |           |           |           |            |
|                                        | 2     | 1         | 1         | 4         |           |            |
|                                        | 3     |           |           |           | 2         |            |
|                                        | 4     |           |           |           | 2         |            |
| Leucopenia                             | 2     |           |           |           |           | 1          |
|                                        | 2     | 1         |           |           | 2         |            |
|                                        | 3     | 1         |           | 1         | 2         |            |
|                                        | 4     |           |           |           | 1         |            |
| Lower gastrointestinal hemorrhage      | 2     |           |           |           |           | 1          |
|                                        | 2     | 1         |           |           | 2         |            |
| Lymphopenia                            | 3     | 1         |           |           | 1         | 2          |
|                                        | 4     |           |           |           |           | 1          |
| Nausea                                 | 2     | 1         |           |           |           | 1          |
| Neutropenia                            | 2     | 1         |           |           | 3         |            |
|                                        | 3     |           |           |           | 1         |            |
|                                        | 4     |           |           |           | 1         |            |
| Sepsis                                 | 4     |           |           |           |           | 2          |
| Skin Hypopigmentation                  | 2     |           |           |           |           | 1          |
| Stomach Pain                           | 2     | 1         |           |           |           |            |
| Thrombocytopenia                       | 2     |           |           |           |           | 2          |
| Weight loss                            | 2     | 1         |           |           |           |            |
## Supplementary Table S3: Histologies by patient

| Patient | Histology                                      |
|---------|-----------------------------------------------|
| 1       | Synovial sarcoma                              |
| 2       | Alveolar soft part sarcoma                    |
| 3       | Hurthle cell thyroid carcinoma                |
| 4       | Metastatic colon adenocarcinoma               |
| 5       | Hemangiopericytoma                            |
| 6       | Pleural mesothelioma                          |
| 7       | Chondrosarcoma                                |
| 8       | Malignant mesothelioma                        |
| 9       | Alveolar soft part sarcoma                    |
| 10      | Myxoid liposarcoma                            |
| 11      | Adenocarcinoma                                |
| 12      | Adenocarcinoma                                |
| 13      | Hepatocellular carcinoma                      |
| 14      | Granular cell tumor                           |
| 15      | Alveolar rhabdomyosarcoma                     |
| 16      | Adenocystic carcinoma                         |
| 17      | Metastatic renal cell carcinoma               |
| 18      | Papillary serous adenocarcinoma - ovary       |
| 19      | Non-small cell lung carcinoma                 |
| 20      | Prostatic adenocarcinoma                      |
| 21      | Neuroendocrine tumor                          |
| 22      | Metastatic granulosa cell tumor               |
| 23      | Malignant chondrosarcoma                      |
| 24      | Myoepithelial adenocarcinoma - parotid gland  |
| 25      | Renal cell carcinoma                          |
| 26      | Unspecified carcinoma                         |
| 27      | Leiomyosarcoma                                 |
| 28      | Ovarian carcinoma                             |
| 29      | Non-small cell lung carcinoma                 |
| 30      | Esophageal carcinoma                          |
| 31      | Colonic adenocarcinoma                        |
| 32      | Metastatic colonic adenocarcinoma             |
Supplementary Table S4: Pazopanib PK values by patient.

| Pazopanib Dose (mg) | Dose Level | Patient | Day 1 | Day 15 | D15/D1 AUC Ratio |
|---------------------|------------|---------|-------|--------|------------------|
|                     |            |         | C<sub>max</sub> (ng/mL) | AUC<sub>last</sub> (h*ng/mL) | T<sub>max</sub> (h) | C<sub>max</sub> (ng/mL) | AUC<sub>last</sub> (h*ng/mL) | T<sub>max</sub> (h) |             |
| 600 (n=2)           | 2          | 5       | 33    | 301    | 12               | 75    | 369    | 4          | 1.23        |
|                     |            | 6       | 10    | 83     | 1                | 20    | 109    | 2          | 1.31        |
|                     |            |         | Mean  | 22     | 192    | 6.5              | 48    | 239    | 3.0        | 1.27        |
|                     |            |         | SD    | 16     | 154    | 7.8              | 39    | 184    | 1.4        | 0.06        |
| 600 (D1 n=3, D15 n=2) | 3          | 7       | 33    | 300    | 4                | 40    | 223    | 4          | 0.74        |
|                     |            | 8       | 28    | 244    | 4                | 18    | 100    | 2          | 0.41        |
|                     |            | 9       | 36    | 310    | 4                |        |        |            |             |
|                     |            |         | Mean  | 32     | 285    | 4.0              | 29    | 162    | 3.0        | 0.58        |
|                     |            |         | SD    | 4      | 36     | 0.0              | 16    | 87     | 1.4        | 0.24        |
| 800 (D1 n=6, D15 n=5) | 4          | 10      | 19    | 150    | 2                | 57    | 297    | 4          | 1.98        |
|                     |            | 11      | 64    | 566    | 4                | 90    | 437    | 4          | 0.77        |
|                     |            | 12      | 39    | 312    | 4                | 46    | 220    | 4          | 0.71        |
|                     |            | 13      | 100   | 735    | 2                | 21    | 91     | 6          | 0.12        |
|                     |            | 14      | 39    | 347    | 4                | 100   | 463    | 4          | 1.33        |
|                     |            | 15      | 24    | 229    | 4                |        |        |            |             |
|                     |            |         | Mean  | 48     | 390    | 3.3              | 63    | 302    | 4.4        | 0.98        |
|                     |            |         | SD    | 30     | 220    | 1.0              | 32    | 154    | 0.9        | 0.70        |
| 800 (n=6)           | 5          | 16      | 23    | 197    | 2                | 58    | 29     | 1          | 0.15        |
|                     |            | 18      | 92    | 796    | 6                | 71    | 337    | 4          | 0.42        |
|                     |            | 19      | 64    | 559    | 4                | 59    | 266    | 6          | 0.48        |
|                     |            | 20      | 4     | 30     | 1                | 36    | 120    | 6          | 4.00        |
|                     |            | 21      | 16    | 125    | 2                | 20    | 97     | 1          | 0.78        |
|                     |            | 22      | 13    | 97     | 2                | 75    | 334    | 4          | 3.44        |
|                     |            |         | Mean  | 35     | 301    | 2.8              | 53    | 197    | 3.7        | 1.54        |
|                     |            |         | SD    | 35     | 306    | 1.8              | 21    | 132    | 2.3        | 1.71        |
Supplementary Table S5: Tivantinib PK values by patient.

| Tivantinib Dose (mg) | Dose Level | Patient | **Day 1** | | **Day 15** | | D15/D1 AUC Ratio |
|----------------------|------------|---------|-----------|----------------|-----------------|------------------|
|                      |            | C\text{max} (ng/mL) | AUC\text{last} (h*ng/mL) | T\text{max} (h) | C\text{max} (ng/mL) | AUC\text{last} (h*ng/mL) | T\text{max} (h) | |
| 120                  | 1          | 365     | 2540      | 6            | 227             | 830              | 2               | 0.33          |
| (n=3)                |            |         |           |              |                 |                  |                 |              |
|                      | 2          | 414     | 2649      | 4            | 305             | 1268             | 6               | 0.48          |
|                      | 3          | 1840    | 15560     | 4            | 2030            | 9685             | 4               | 0.62          |
|                      | Mean       | 873     | 6916      | 4.7          | 854             | 3928             | 4.0             | 0.48          |
|                      | SD         | 838     | 7486      | 1.2          | 1019            | 4991             | 2.0             | 0.15          |
| 120                  | 2          | 1760    | 12536     | 4            | 1120            | 4221             | 4               | 0.34          |
| (n=2)                |            |         |           |              |                 |                  |                 |              |
|                      | 5          | 1084    | 7787      | 3.0          | 971             | 3816             | 3.0             | 0.73          |
|                      | 6          | 957     | 6717      | 1.4          | 211             | 573              | 1.4             | 0.56          |
|                      | Mean       | 1084    | 7787      | 3.0          | 971             | 3816             | 3.0             | 0.73          |
|                      | SD         | 957     | 6717      | 1.4          | 211             | 573              | 1.4             | 0.56          |
| 240                  | 3          | 609     | 4557      | 6            | 495             | 1777             | 4               | 0.39          |
| (D1 n=3, D15 n=2)    | 7          | 1663    | 13496     | 6.0          | 2103            | 11284            | 4.0             | 0.61          |
|                      | 8          | 1132    | 10514     | 0.0          | 2273            | 13444            | 0.0             | 0.31          |
|                      | 9          | 1520    | 10850     | 6            |                 |                  |                 |              |
|                      | Mean       | 1663    | 13496     | 6.0          | 2103            | 11284            | 4.0             | 0.61          |
|                      | SD         | 1132    | 10514     | 0.0          | 2273            | 13444            | 0.0             | 0.31          |
| 240                  | 4          | 1990    | 10583     | 4            | 1200            | 4775             | 4               | 0.45          |
| (n=5)                | 10         | 1990    | 10583     | 4            | 1200            | 4775             | 4               | 0.45          |
|                      | 11         | 1910    | 10894     | 4            | 1230            | 3545             | 4               | 0.33          |
|                      | 12         | 969     | 6256      | 4            | 773             | 3082             | 2               | 0.49          |
|                      | 13         | 2940    | 26410     | 6            | 5470            | 28530            | 2               | 1.08          |
|                      | 14         | 804     | 6017      | 6            | 642             | 2717             | 4               | 0.45          |
|                      | Mean       | 1723    | 12032     | 4.8          | 1863            | 8530             | 3.2             | 0.56          |
|                      | SD         | 866     | 8362      | 1.1          | 2033            | 11207            | 1.1             | 0.30          |
| 360                  | 5          | 1570    | 12029     | 6            | 800             | 400              | 1               | 0.03          |
| (n=6)                | 16         | 1570    | 12029     | 6            | 800             | 400              | 1               | 0.03          |
|                      | 18         | 2730    | 18914     | 6            | 1390            | 4799             | 6               | 0.25          |
|                      | 19         | 2740    | 22680     | 6            | 1430            | 5019             | 6               | 0.22          |
|                      | 20         | 966     | 6235      | 4            | 753             | 3210             | 4               | 0.51          |
|                      | 21         | 316     | 1471      | 2            | 473             | 1971             | 2               | 1.34          |
|                      | 22         | 1210    | 7655      | 6            | 755             | 3096             | 4               | 0.40          |
|                      | Mean       | 1589    | 11497     | 5.0          | 934             | 3083             | 3.8             | 0.46          |
|                      | SD         | 978     | 8041      | 1.7          | 387             | 1740             | 2.0             | 0.46          |