SUPPLEMENTARY APPENDIX

Supplementary Appendix for: A Phase 1, Multicenter, Open-Label, First-in-Human Study of DS-6157a in Patients With Advanced Gastrointestinal Stromal Tumor

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Supplementary Methods

Dose-limiting toxicities (DLTs)
A DLT is defined as any of the following TEAEs that occur during the DLT evaluation period (21 days starting from Cycle 1 Day 1), excluding toxicities clearly related to disease progression or intercurrent illness, in patients participating in Dose Escalation (Part 1).

For hematologic toxicities, a DLT is defined as follows:

- Grade 4 neutrophil count decreased lasting >7 days
- Grade ≥3 febrile neutropenia
- Grade ≥3 anemia requiring transfusion
- Grade 4 anemia
- Grade 4 platelet count decreased, or
- Grade ≥3 platelet count decreased lasting >7 days
- Grade ≥3 platelet count decreased associated with clinically significant hemorrhage and/or requiring transfusion
- Grade 4 lymphocyte count decreased lasting ≥14 days

For hepatic organ toxicities, a DLT is defined as follows:

- Grade 4 aspartate aminotransferase (AST) or alanine aminotransferase (ALT) increased
- AST or ALT >3 × upper limit of normal (ULN) if accompanied by grade ≥2 blood total bilirubin increased with serum alkaline phosphatase <2 × ULN (based on Hy's law definition)
- In patients without liver metastases, AST or ALT >5 × ULN
- In patients with liver metastases, AST or ALT >5 × ULN, if the baseline level was ≤3 × ULN
- In patients with liver metastases, AST or ALT >8 × ULN, if the baseline level was >3 × ULN

For non-hematologic, non-hepatic major organ toxicities, a DLT is defined as follows:

- Symptomatic congestive heart failure
- Left ventricular ejection fraction (LVEF) decline to <40% or
- Subject has absolute >20% drop from their LVEF baseline
- Any LVEF decline from baseline leading to discontinuation of study treatment
- Grade ≥2 interstitial lung disease or pneumonitis
- Grade 3 skin toxicity lasting >7 days or grade 4 for any duration
- Grade ≥3 infusion-related reaction