Ripretinib was evaluated in a phase 1 study for safety, pharmacokinetics, and early efficacy. The maximum tolerated dose (MTD) was not reached and recommended phase 2 dose (RP2D) of ripretinib was 150 mg QD. Ripretinib was effective at slowing the progression of unresectable GIST across lines of therapy in phase 1 clinical study. The median progression-free survival (mPFS) was 10.7 months for patients on 2nd-line therapy, 8.3 months (3rd-line), and 5.5 months (≥4th-line). The objective response rate (ORR) for 2nd-, 3rd-, and ≥4th-line therapies were 19.4%, 14.3%, and 7.2%, respectively.

Based on the proof-of-concept in GIST patients, INVICTUS, an international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial in 129 patients who had received ≥3 prior anticancer therapies for advanced GIST was initiated. Patients had a complex and heterogeneous mutational landscape and were heavily pre-treated. The population was representative of the real-world ≥4th-line patients with advanced GIST. Ripretinib provided clinically meaningful benefit in ≥4th-line advanced GIST in INVICTUS. The mPFS (BICR) was 6·3 months for ripretinib versus 1.0 month for placebo, reducing the risk of progression or death by 85%. Notably, the mPFS of 6.3 months in ≥4th-line GIST exceeds those of both sunitinib in 2nd-line (5.6 months) and regorafenib in 3rd-line (4.8 months). ORR was 9.4% for ripretinib versus 0% for placebo. Patients received a clinically meaningful survival benefit when treated with ripretinib versus placebo (median OS – 15.1 months in the ripretinib group versus 6.6 months in the placebo group). None of the prior phase 3 studies with sunitinib in 2nd-line (median OS: 17.0 months sunitinib versus 14.9 months placebo) or regorafenib in 3rd-line (median OS: 17.4 months for both regorafenib and placebo groups) demonstrated a clinically meaningful OS benefit compared to placebo. Ripretinib was generally well tolerated and patients were able to maintain quality of life in INVICTUS.

Abbreviations: BICR=Blinded Independent Central Review, OS=Overall Survival