GISTs are rare, heterogeneous sarcomas but are also the most common sarcomas of the gastrointestinal tract. An estimated 4000 to 6000 new cases of GIST present clinically in the US each year. The annual worldwide incidence and prevalence of GISTs are estimated to be approximately 10 to 15 per million people and 129 per million people, respectively.

KIT and PDGFRA kinase mutations commonly drive GIST disease pathophysiology. About 80% of GIST have primary mutations in KIT, and 5-10% of GIST have a mutation in the homologous PDGFRA. Approximately 10-15% of GIST patients have wild type (WT) mutations (i.e., the disease is not driven by KIT or PDGFRA but by other genetic mutations). Advanced GIST is marked by the development of secondary drug resistance mutations, which play a key role in disease progression. Broad inter-and intra-tumor heterogeneity exists among secondary resistance mutations, whereby a single patient may have multiple mutations within or between tumors. The extensive mutational heterogeneity drives resistance to established therapies. Thus, advanced GIST, a heterogeneous disease with a complex mutational landscape, presents with significant treatment challenges.

The standard of care for patients with GIST are tyrosine kinase inhibitors: imatinib (1st-line), sunitinib (2nd-line), and regorafenib (3rd-line). Avapritinib is approved for GIST harboring PDGFRA exon 18 mutations, including the PDGFRA D842V mutation (in about 6% of patients). There was a need for broad-spectrum inhibition of KIT/PDGFRA primary and secondary kinase mutations that fuel resistance and progression in advanced GIST. Ripretinib was specifically designed to broadly inhibit the function of mutated and WT versions of KIT and PDGFRA kinases, primary drivers of treatment resistance and disease progression in advanced GIST.

There was a significant unmet medical need for ≥4th-line patients with advanced GIST who progressed on or were intolerant to 3rd-line regorafenib prior to the approval of ripretinib (≥4th-line) in advanced GIST.