Ripretinib is a novel switch control tyrosine kinase inhibitor specifically designed to broadly inhibit KIT and PDGFRA mutated kinases with a unique dual mechanism of action. Ripretinib was developed to block the function of mutated and WT versions of KIT and PDGFRA kinases using Deciphera’s proprietary switch-control kinase inhibition drug discovery platform and deep expertise in kinase biology. Ripretinib binds to both the switch pocket region and the activation switch securing the target kinase into an inactive conformation, resulting in the inhibition of downstream signaling and cell proliferation. Portions of ripretinib mimic the inhibitory loop and occupy the switch pocket, thereby preventing the activation switch’s entry. Other residues on ripretinib bind to the activation switch, stabilizing it out of the switch pocket and covering the ATP binding site, so phosphorylation cannot occur.

Ripretinib has emerged as a new standard of care for patients with ≥4th-line advanced GIST where there was an unmet medical need.

Patients progressing on the standard dose of ripretinib could derive further clinical benefit with dose-escalation to 150 mg BID, another area of significant unmet need as options are limited for patients progressing on ripretinib 150 mg QD. The dose-escalation strategy mirrors imatinib dose-escalation in 1st-line patients with GIST.

mPFS of 10.7 months in 2nd-line patients with GIST in the phase 1 study provides a rationale for the ongoing INTRIGUE (phase 3) study investigating ripretinib versus sunitinib in 2nd-line GIST.

Ripretinib, with its broad-spectrum activity, has the potential to maximize responses and induce more durable responses in a new generation of combination clinical trials in GIST.

Ripretinib is a ground-breaking therapy that has the potential to revolutionize the GIST treatment landscape.