Qinlock™ (ripretinib) – New orphan drug approval

- On May 15, 2020, the FDA announced the approval of Deciphera Pharmaceuticals' Qinlock (ripretinib), for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib (eg, Gleevec®).

- Approximately 4,000 to 6,000 adults are diagnosed annually with a GIST in the U.S. GISTs arise when abnormal cells form in the tissues of the gastrointestinal (GI) tract. GISTs most commonly occur in the stomach, small intestine, and large intestine but can start anywhere along the GI tract.

- Qinlock is the first drug specifically approved as a fourth-line treatment for advanced GIST.

    — Qinlock is a tyrosine kinase inhibitor that inhibits KIT proto-oncogene receptor tyrosine kinase (KIT) and platelet derived growth factor receptor A (PDGFRA) kinase, including wild type, primary, and secondary mutations.

- The efficacy of Qinlock was established in INVICTUS, a randomized, double-blind, placebo-controlled study in 129 patients with unresectable, locally advanced or metastatic GIST. Patients had received prior treatment with imatinib, Sutent® (sunitinib), and Stivarga® (regorafenib). Patients received Qinlock or placebo until disease progression or unacceptable toxicity. The major efficacy outcome measure was progression-free survival (PFS). Additional efficacy outcome measures included objective response rate (ORR) and overall survival (OS).

    — Median PFS was 6.3 months and 1.0 months for Qinlock and placebo, respectively (hazard ratio [HR] 0.15; 95% CI: 0.09, 0.25; $p < 0.0001$).
    — ORR was 9% (95% CI: 4.2, 18) and 0% (95% CI: 0, 8) for Qinlock and placebo, respectively ($p = 0.0504$; not statistically significant).
    — Median OS was 15.1 months and 6.6 months for Qinlock and placebo, respectively (HR 0.36; 95% CI: 0.21, 0.62). OS was not evaluated for statistical significance as a result of the sequential testing procedure for the secondary endpoints of ORR and OS.

- Warnings and precautions for Qinlock include palmar-plantar erythrodysesthesia syndrome; new primary cutaneous malignancies; hypertension; cardiac dysfunction; risk of impaired wound healing; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Qinlock use were alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, palmar-plantar erythrodysesthesia, and vomiting. The most common Grade 3 or 4 laboratory abnormalities (≥ 4%) were increased lipase and decreased phosphate.

- The recommended dose of Qinlock is 150 mg orally once daily with or without food until disease progression or unacceptable toxicity.

- Deciphera Pharmaceuticals plans to launch Qinlock next week. Qinlock will be available as a 50 mg tablet.