Protocol Title: A Phase 1/2 Study of the TRK Inhibitor LOXO-195 in Adult and Pediatric Subjects with Previously Treated NTRK Fusion Cancers

Target Population: Previously treated NTRK Fusion Solid Tumors

Summary: This is a Phase 1/2, multi-center, open-label study designed to evaluate the safety and efficacy of LOXO-195 when administered orally to patients age ≥ 1 month and older with NTRK fusion cancers treated with a prior TRK inhibitor.

Key Inclusion Criteria:
• Advanced solid tumor for which, in the opinion of the Investigator, no other standard therapy offers greater benefit.
• A solid tumor diagnosis in the setting of:
  o Documented NTRK fusion and clinical history of relapse following a response to a prior TRK inhibitor
  o Documented NTRK fusion unresponsive to a prior TRK inhibitor
  o Documented NTRK fusion and a clinical history of intolerance to a prior TRK inhibitor
• NTRK gene fusions will be identified via a CLIA certified (or equivalent) laboratory.
  o Exception: Patients with Infantile Fibrosarcoma (IFS) and congenital mesoblastic nephroma (CMN) may be enrolled based on ETV6+ FISH test without identifying NTRK3.
• Eastern Cooperative Oncology Group (ECOG) score ≤ 3 (age ≥16) or Lansky Performance Score (LPS) ≥40% (age<16).
  o If enrolled with primary CNS tumor to be assessed by RANO, Karnofsky Performance Status (KPS) (age ≥16) or LPS (age<16) ≥ 50%.
• Life expectancy > 4 weeks.
• Adequate hematologic, hepatic and renal function.
• Patients with stable CNS primary tumor, brain metastases, or treated spinal cord compression are eligible if neurological symptoms and steroid use (if applicable) have been stable for 7 days prior to the first dose of LOXO-195.
• Ability to receive study drug orally or by enteral administration.

Key Exclusion Criteria:
• Required treatment with certain strong CYP3A4 inhibitors or inducers.
• Clinically significant active cardiovascular disease or history of myocardial infarction within 3 months prior to planned start of LOXO-195 or prolongation of the QT interval corrected (QTcF) > 480 msec within the past 6 months.
• Major surgery within 7 days of enrollment.
• Uncontrolled systemic bacterial, fungal or viral infection.
• Pregnancy or lactation.
• Known hypersensitivity to any of the components of LOXO-195 or Ora-Sweet® SF and OraOlus, for patients receiving liquid suspension.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT03215511