Expanded Access to ONC201 for Patients with H3 K27M-mutant and/or Midline High Grade Gliomas

The purpose of this study is to 1) provide expanded access to ONC201 for patients with previously-treated H3 K27M-mutant and/or midline high grade gliomas who cannot access ONC201 through clinical trials and 2) to evaluate the safety and tolerability of ONC201.

Gliomas in the midline of the brain are among the most aggressive types of primary malignant brain cancers. The disease arises from glial cells, which are cells that form the tissue that surrounds and protects other nerve cells found within the brain and spinal cord. H3 K27M refers to a specific mutation in proteins called histone H3 that frequently occurs in midline in midline gliomas and in young patients.

Due to location in the brain, aggressiveness, and low survival time, gliomas in the midline of the brain have a dismal prognosis. The discovery of H3 K27M as an oncogenic mutation occurred in the context of midline gliomas.

ONC201 is an anticancer small molecule that antagonizes dopamine receptor D2 (DRD2). It crosses the blood-brain barrier and has shown anti-tumor activity in non-clinical models of H3 K27M-mutant and other high grade gliomas. In preclinical trials, it has shown potential to address central nervous system tumors.

Key Inclusion Criteria:

- Must have one type of diagnosis below:
  - Glioma that is positive for the H3 K27 mutation
  - Grade III or IV glioma involving the thalamus, hypothalamus, brainstem, cerebellum, midbrain, or spinal cord
  - Diffuse intrinsic pontine glioma (DIPG)
- Unequivocal evidence of progressive disease
- Must have had previous therapy that includes radiotherapy
- Must be at least 3 years of age and weigh at least 10 kg

Key Exclusion Criteria:

- Qualifies for participation in an ongoing ONC201 clinical trial or is already participating in an ONC201 clinical trial
- Evidence of diffuse leptomeningeal disease or CSF dissemination