Cleveland Clinic Innovations

PRODUCT
Small molecule WDR5 inhibitor.

INDICATION
Glioblastoma.

VALUE PROPOSITION
- Blood-brain barrier penetrant compounds.
- Potential to improve patient survival.
- Stand-alone monotherapy or potential for use with SOC or other novel therapies.

DEVELOPMENT STAGE
In vivo studies demonstrated a reduction in tumor growth.

INTELLECTUAL PROPERTY
US Provisional 63/320,435 protecting composition of matter and method of use.

RELATED PUBLICATIONS
Mitchell K, et al. Genes Dev. 2023 Feb 1;37(3-4):86-102
PMID: 36732025.

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Brain Penetrant WDR5 Inhibitors for Glioblastoma Treatment

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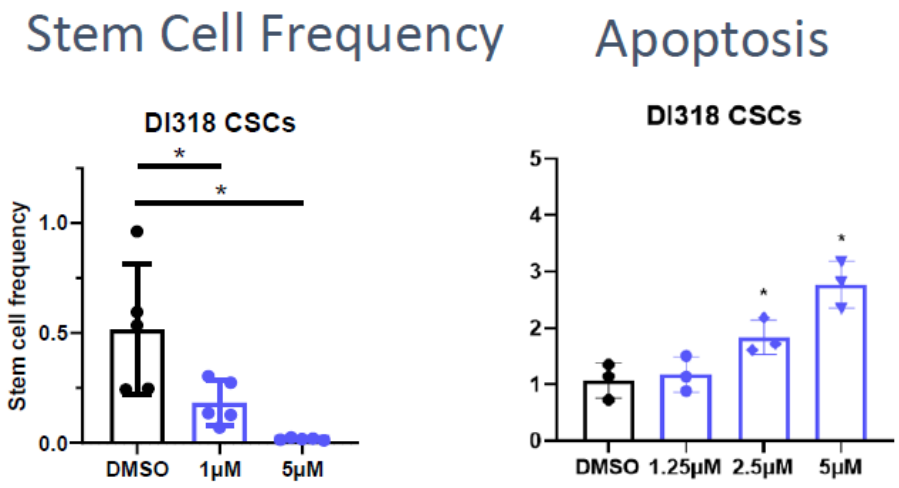
OPPORTUNITY

Glioblastoma is the most common and aggressive brain cancer, with more than 14,000 cases diagnosed annually in the U.S. and 240,000 worldwide. There are few approved treatments, and the standard of care combines surgery, radiation, and chemotherapy with recurrent cases often developing drug resistance. Relapse occurs in more than 90 percent of patients, and the five years survival rate is <10%. Developing new therapies that can penetrate the blood-brain barrier is a primary challenge.

SOLUTION

- The WD repeat domain 5 (WDR5) is often overexpressed in cancers and has been implicated in the proliferation and self-renewal of glioblastoma cells.
- Through a screen, the Lathia lab identified WDR5 as a protein associated with positive regulation of transcription in glioblastoma stem cells.
- The developed WDR5 inhibitors can penetrate the blood-brain barrier and are potent against WDR5 and glioma cells.
- Lead compounds exhibit favorable ADME properties while featuring exquisite potency for WDR5 and cell-based activity in patient-derived cell lines.
- Blocked expression of genes involved in relevant oncogenic pathways.



Lead WDR5 inhibitor demonstrated decreased stem cell frequency and increasing apoptosis (shown in figures) as well as PDX model viability and slowing of cell growth