**Anti-Tumor Activity of Novel, Potent and Orally-Bioavailable Glutaminase Inhibitors**

Francesco Parlati1, T. Chernov-Rogan1, S. Demo1, M. Gross1, J. Janes1, R. Kawasi1, E. Lewis1, H. Rodriguez1, M. Rodriguez1, J. Yang1, F. Zhou1, A. Richardson2, M. Bennett1

1Calithera Biosciences Inc., South San Francisco, CA; 2Sanford-Burnham Medical Research Institute, La Jolla, CA.

---

**Abstract**

Glutaminase (GLS) is a key enzyme that plays a critical role in cellular metabolism, particularly in cancer cells, where it is overexpressed and plays a central role in glutamine-dependent tumor proliferation. In this study, we investigated the anti-tumor effects of two novel compounds, CB-839 and CB-498, which inhibit GLS both in vitro and in vivo. Our findings suggest that these compounds have potent anti-tumor activity and are orally bioavailable.

**In Vitro Anti-Proliferative Activity**

We conducted experiments to determine the anti-proliferative activity of CB-839 and CB-498 in various cancer cell lines. Our results indicate that these compounds significantly reduce cell proliferation in a dose-dependent manner.

**Oral Bioavailability, Pharmacodynamic Response and In Vivo Efficacy**

We also evaluated the oral bioavailability and pharmacodynamic response of CB-839 and CB-498 in mouse models. Our findings suggest that these compounds are efficacious and well-tolerated, with promising results in vivo.

**Biochemical Potency and Selectivity**

We performed biochemical analyses to determine the potency and selectivity of CB-839 and CB-498. Our results indicate that these compounds are highly selective and potent inhibitors of GLS.

**Impact on Cellular Metabolite Levels and Metabolic Flux**

We analyzed the effects of CB-839 and CB-498 on cellular metabolite levels and metabolic flux. Our results suggest that these compounds significantly alter the levels of key metabolites and disrupt metabolic pathways.

**Conclusions**

Our findings suggest that CB-839 and CB-498 are promising new anti-cancer agents with potential for clinical development.

---

**References**

