

Supplementary Figure 1 qRT-PCR analysis of effects of the indicated SHP099 treatment on levels of *CCND1*, *CCNE1*, *CCNE2* in mouse *Ink4a/Arf⁻⁻* astrocytes with or without ectopic expression of PDGFR α and PDGF-A. ***p < 0.001, by one-way ANOVA. Data represent three independent experiments with similar results.

A



Supplementary Figure 2 SHP099 promotes cell apoptosis in *Ink4a/Arf^{/-}* mAsts cells with or without overexpression of PDGFR α /PDGF-A

- A. Representative images of flow cytometry analysis of effects of SHP099 treatment on cell apoptosis.
- B. Percentage of early apoptosis cells in A.

Data are means \pm SD. **p < 0.05, by one-way ANOVA. Data or images represent two or three independent experiments with similar results.



- Supplementary Figure 3 SHP099 specifically inhibits cell cycle pathways in glioma stem-like cells with PDGFRlpha activation.
- A) Expression of JUN after SHP099 treatment using qRT-PCR analysis.
- B) Representative images from flow cytometric analysis of the influence of SHP099 treatment on cell cycle in GSC157.

Percentage of cells in G0/G1 phase in **B**. *p < 0.05, by one-way ANOVA.



Supplementary Figure 4 UPLC-MS analysis of SHP099 in plasma and brain post oral gavage in immunocompetent mice

Corresponding to Figure 5A, showing retention time and full-scan product ion spectrum of UPLC-MS analysis of SHP099 in standard solution, plasma, and brain post 4-h oral gavage in immunocompetent mice. 2-Amino-5-phenylpyrazine (Sigma 13535-13-2) was used as an internal standard of SHP099. Images represent two independent experiments with similar results.



Supplementary Figure 5 SHP099 does not impair GL261 tumor growth without PDGFR α activation.

A) WB analysis of expression levels of PDGF-A, PDGFR α , and p-PDGFR α in GL261 cells. *Ink4a/Arf⁻⁻* mAsts with ectopic expression of PDGF-A and PDGFR α were used as a control.

B) Treatment schemes for the evaluation of in vivo efficacy of SHP099 in GL261 xenografts. Animals were treated with 100 mg/kg SHP099 doses from Monday to Friday within two weeks.

C) Representative images of Haematoxylin & Eosin staining. Scale bars, 1 mm.

- D) Quantitation of tumor volumes in C.
- E) Kaplan-Meier survival analysis of animals with GL261 tumors (n=6 per group).

p value was calculated by two-tailed Student's *t*-test or log-rank analysis.