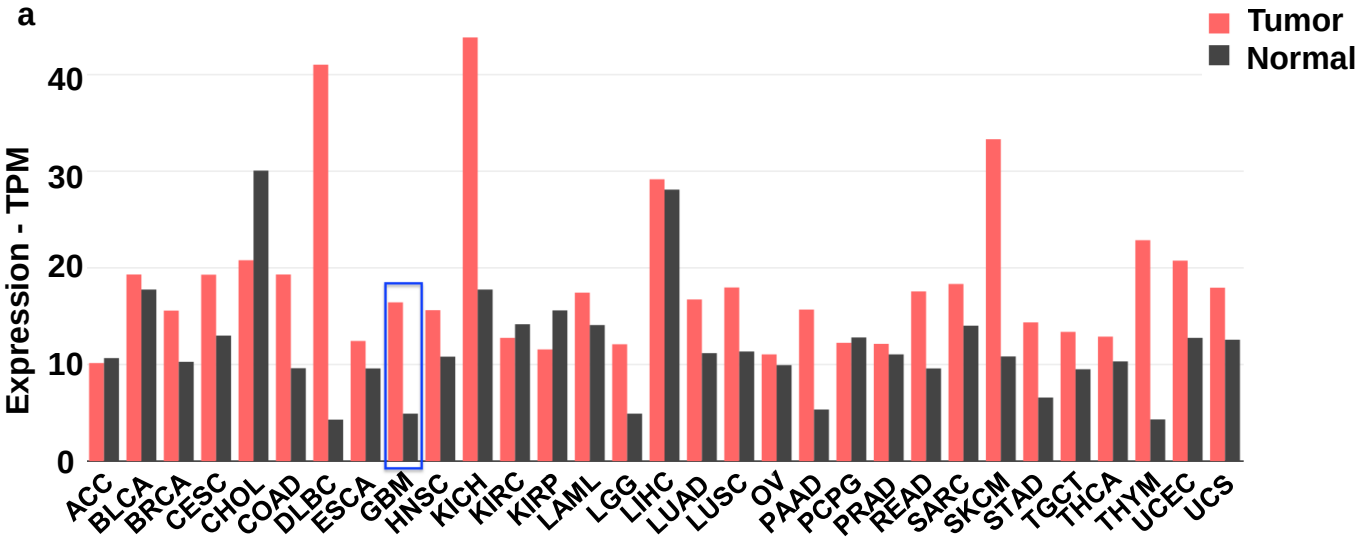
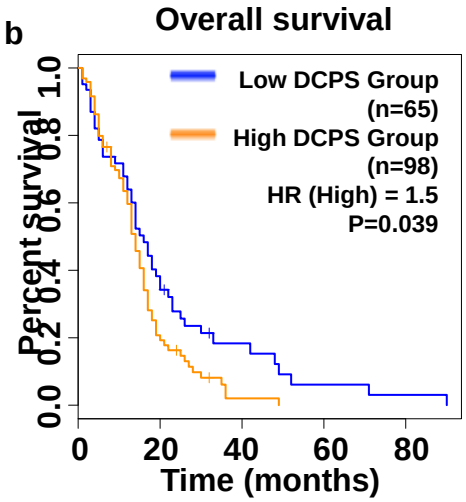
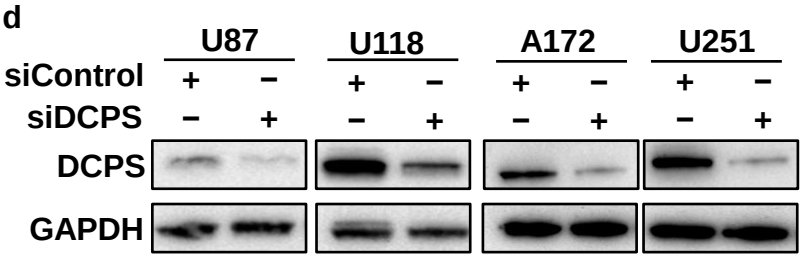
Figure S1


a
Tumor
Normal
Expression - TPM
0
10
20
30
40
ACC
BLCA
BRCA
CESC
CHOL
COAD
DLBC
ESCA
GBM
HNSC
KICH
KIRC
KIRP
LAML
LGG
LIHC
LUAD
LUSC
OV
PAAD
PCPG
PRAD
READ
SARC
SKCM
STAD
TGCT
THCA
THYM
UCEC
UCS


b
Overall survival
Low DCPS Group
(n=65)
High DCPS Group
(n=98)
HR (High) = 1.5
P=0.039
Percent survival
0.0
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80
Time (months)


d
U87
U118
A172
U251
siControl
siDCPS
DCPS
GAPDH

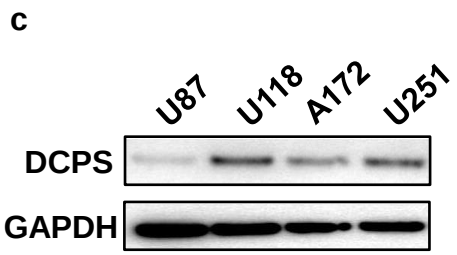

c
U87
U118
A172
U251
DCPS
GAPDH

**Figure S1. DCPS expression in GBM.**

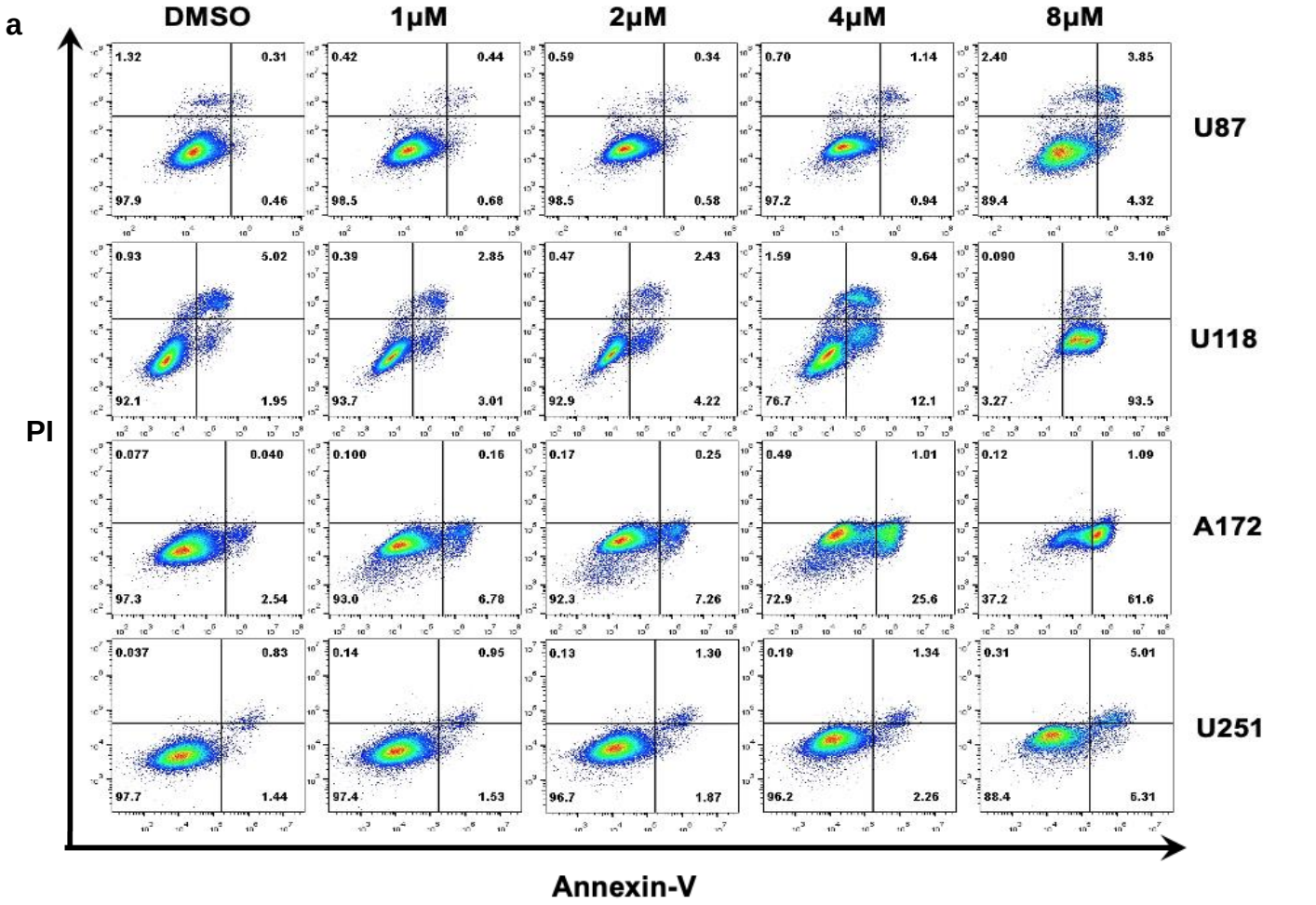
(a) The expression of DCPS in various malignancies and corresponding normal tissues in TCGA database. ACC, adrenocortical carcinoma; BLCA, bladder urothelial carcinoma; BRCA, breast invasive carcinoma; CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; CHOL, cholangiocarcinoma; COAD, colon adenocarcinoma; DLBC, lymphoid neoplasm diffuse large B-cell lymphoma; ESCA, esophageal carcinoma; GBM, glioblastoma multiforme; HNSC, head and neck squamous cell carcinoma; KICH, kidney chromophobe; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; LAML, acute myeloid leukemia; LGG, Brain lower grade glioma; LIHC, liver hepatocellular carcinoma; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; OV, ovarian serous cystadenocarcinoma; PAAD, pancreatic adenocarcinoma; PCPG, pheochromocytoma and paraganglioma; PRAD, prostate adenocarcinoma; READ, rectum adenocarcinoma; SARC, sarcoma; SKCM, skin cutaneous melanoma; STAD, stomach adenocarcinoma; TGCT, testicular germ cell tumors; THCA, thyroid carcinoma; THYM, thymoma; UCEC, uterine corpus endometrial carcinoma; UCS, uterine carcinosarcoma.

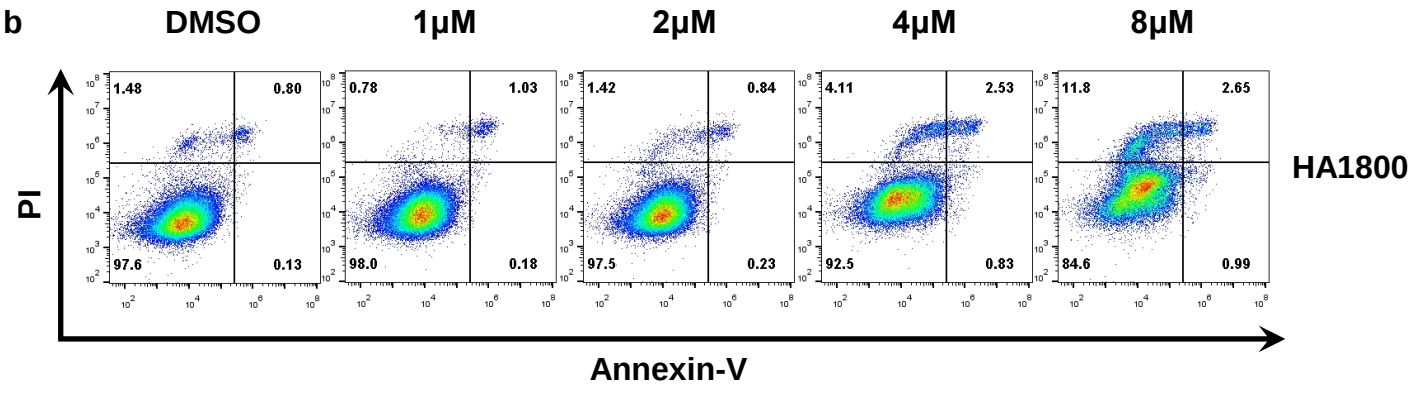
(b) Correlation of DCPS expression with overall survival was analyzed in TCGA database. Statistical analysis by two-sided log-rank test.

(c) Western blot analyses of DCPS expression in four GBM cell lines.

(d) Interference of DCPS expression in four GBM cell lines was confirmed by western blotting.

Figure S2


a
DMSO
1μM
2μM
4μM
8μM
U87
U118
A172
U251
PI
Annexin-V
1.32 0.31 97.9 0.46
0.42 0.44 98.5 0.68
0.59 0.34 98.5 0.58
0.70 1.14 97.2 0.94
2.40 3.85 89.4 4.32
0.93 5.02 92.1 1.95
0.39 2.85 93.7 3.01
0.47 2.43 92.9 4.22
1.59 9.64 76.7 12.1
0.090 3.10 3.27 93.5
0.077 0.040 97.3 2.54
0.100 0.16 93.0 6.78
0.17 0.25 92.3 7.26
0.49 1.01 72.9 25.6
0.12 1.09 37.2 61.6
0.037 0.83 97.7 1.44
0.14 0.95 97.4 1.53
0.13 1.30 96.7 1.87
0.19 1.34 96.2 2.26
0.31 5.01 88.4 5.31


b
DMSO
1μM
2μM
4μM
8μM
HA1800
PI
Annexin-V
1.48 0.80 97.6 0.13
0.78 1.03 98.0 0.18
1.42 0.84 97.5 0.23
4.11 2.53 92.5 0.83
11.8 2.65 84.6 0.99

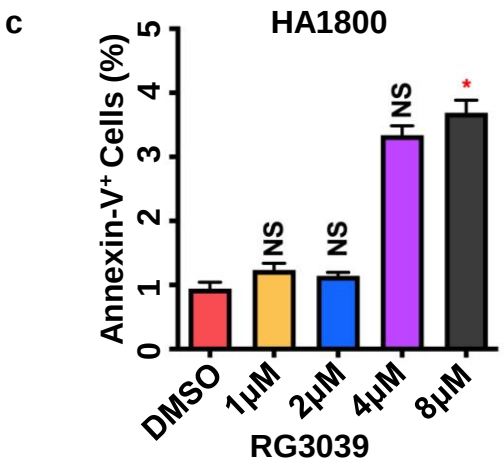

c
HA1800
Annexin-V⁺ Cells (%)
0
1
2
3
4
5
NS
NS
NS
*
DMSO
1μM
2μM
4μM
8μM
RG3039

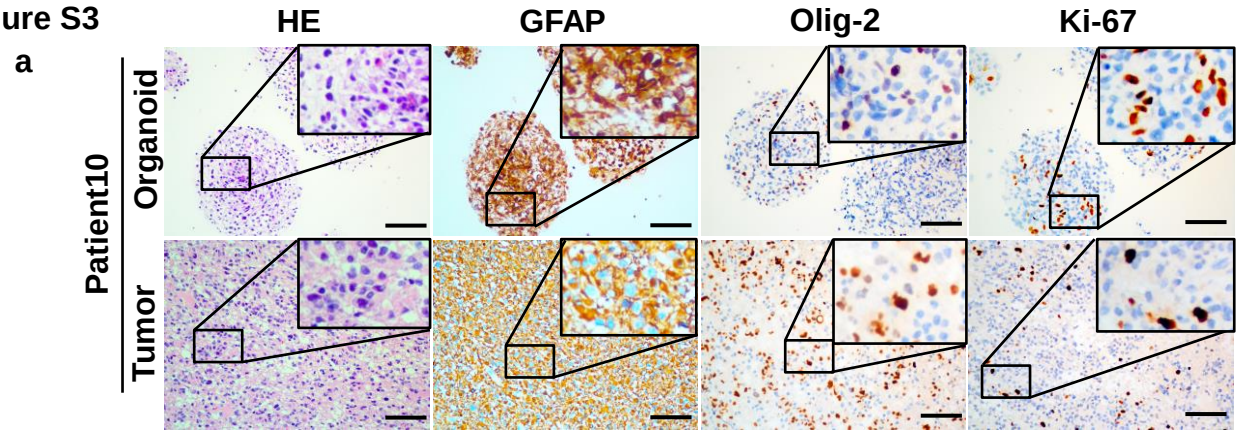
**Figure S2. Representative sorting of cell apoptosis assay treated with specific concentrations of RG3039.**

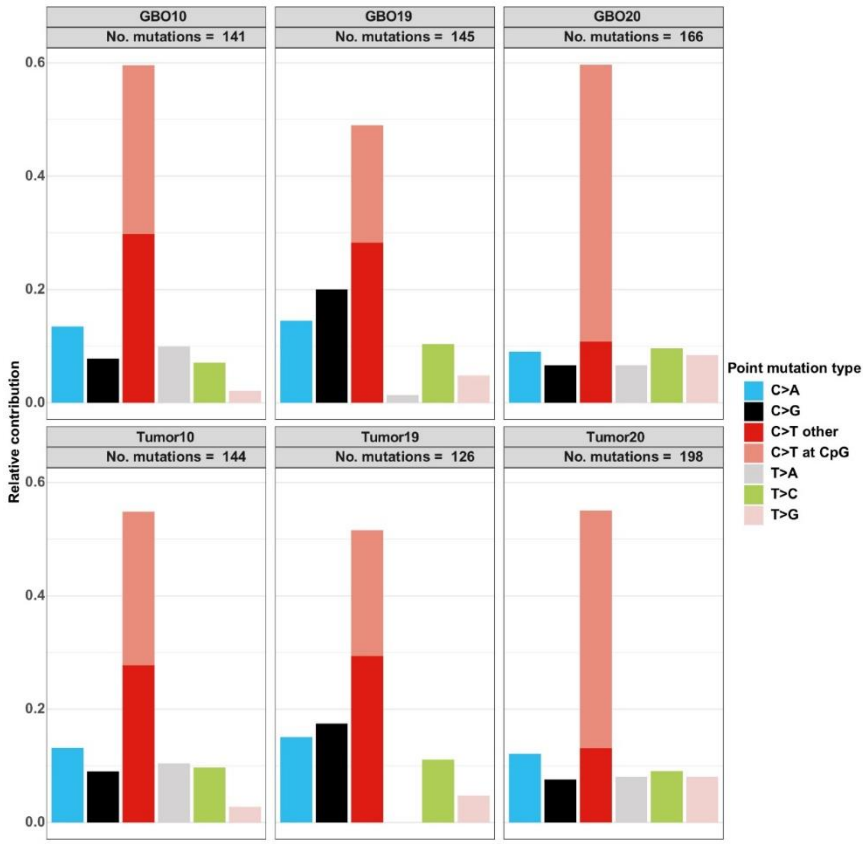
(a) GBM cell lines were treated with specific concentrations of RG3039 or DMSO for 48 h. Cell apoptosis was analyzed by using APC-Annexin V-based flow cytometry.

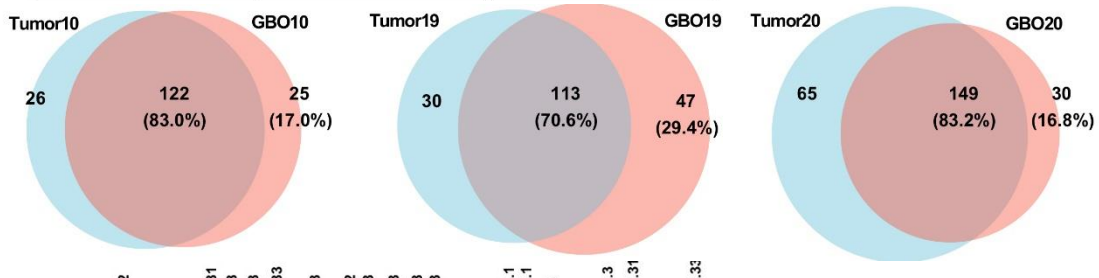
(b) HA1800 cells were treated with specific concentrations of RG3039 or DMSO for 48 h. Cell apoptosis was analyzed by APC-Annexin V-based flow cytometry.

(c) Quantified data of Annexin-V-positive cells in HA1800 cells treated with specific concentrations of RG3039 or DMSO (see Figure S2b for details, mean ± SEM, n = 3). Statistical analysis by unpaired t-test; NS, no significance; *, $p<0.05$.

Figure S3


a
HE
GFAP
Olig-2
Ki-67
Patient10
Organoid
Tumor


b
GBO10
No. mutations = 141
GBO19
No. mutations = 145
GBO20
No. mutations = 166
Tumor10
No. mutations = 144
Tumor19
No. mutations = 126
Tumor20
No. mutations = 198
Relative contribution
0.0
0.2
0.4
0.6
Point mutation type
C>A
C>G
C>T other
C>T at CpG
T>A
T>C
T>G


c
Tumor10
GBO10
26
122
(83.0%)
25
(17.0%)
Tumor19
GBO19
30
113
(70.6%)
47
(29.4%)
Tumor20
GBO20
65
149
(83.2%)
30
(16.8%)

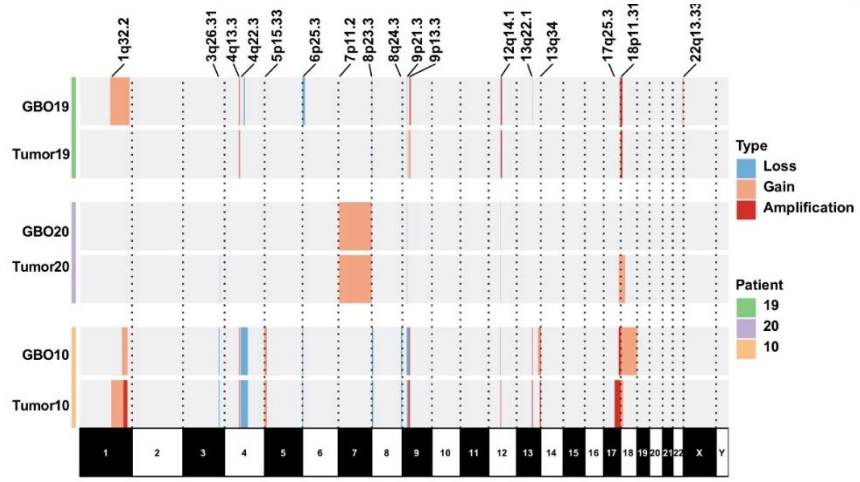

d
1q32.2
3q26.31
4q13.3
4q22.3
5p15.33
6p25.3
7p11.2
8p23.3
8q24.3
9p21.3
9p13.3
12q14.1
13q22.1
13q34
17q25.3
18p11.31
22q13.33
GBO19
Tumor19
GBO20
Tumor20
GBO10
Tumor10
Type
Loss
Gain
Amplification
Patient
19
20
10

**Figure S3. Patient-derived GBM organoids (GBOs) maintained histological features and genomic features of parental tumors.**

(a) Representative histological and immunohistochemical images of GBO and parental tumors. Scale bar, 100 μm.

(b-d) WES results of GBOs and parental tumors.

(b) The frequencies of point mutation types were well conserved in GBOs and parental tumors.

(c) Venn diagrams from point mutations showed that GBOs contained approximately 70.6%–83.2% of mutations in paired parental tumors.

(d) CNVs in GBOs and parental tumors were similar.

**Figure S4**

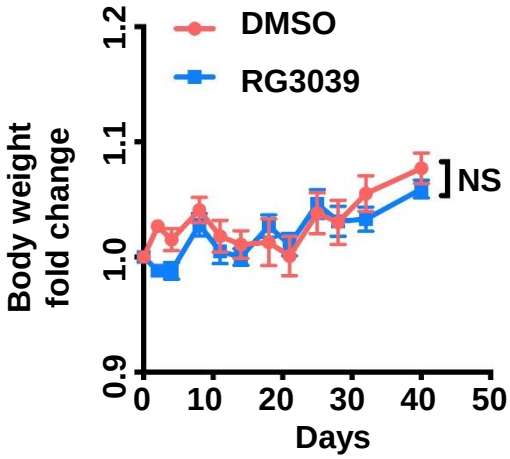



**Figure S4. Body weight of mice treated with RG3039.**

Body weight of healthy BALB/c nude mice was monitored for 40 days after treatment with RG3039 or DMSO (mean ± SEM). The fold changes of body weight at day 40 were statistically analyzed by unpaired t-test, NS, no significance.

**Figure S5**

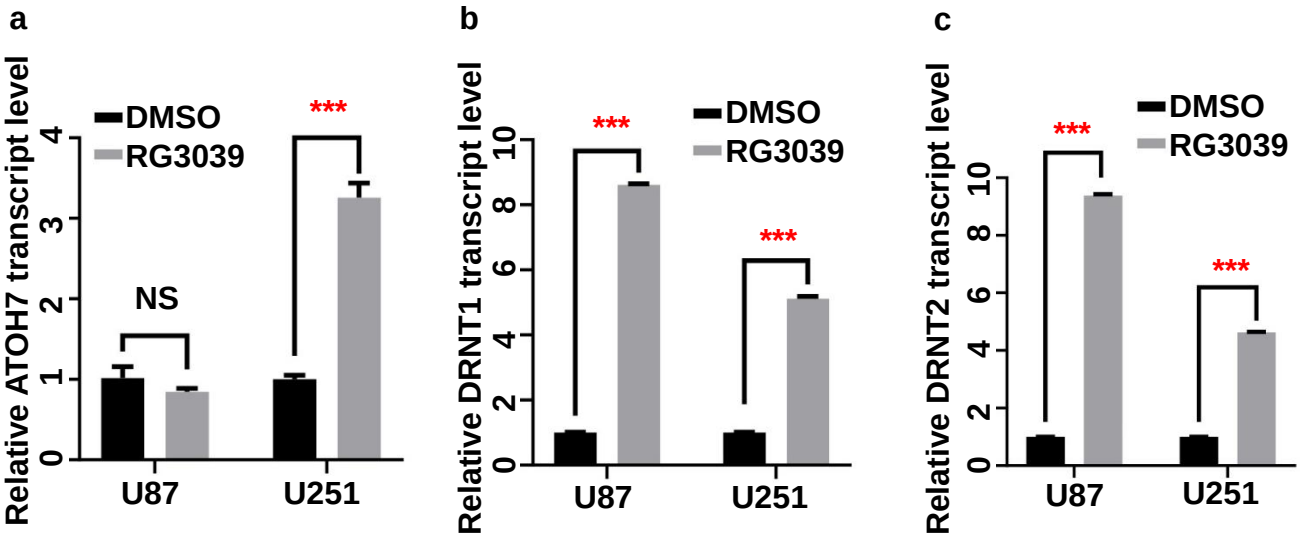



**Figure S5. The effects of RG3039 on the expression of previously identified target transcripts ATOH7, DRNT1, and DRNT2 in GBM.**

(a) GBM cell lines were treated with RG3039 (6 μM) or DMSO for 48 h. The transcript level of ATOH7 was analyzed by RT-qPCR and normalized to that of β-actin (mean ± SEM, n = 3). Statistical analysis by unpaired t-test; NS, no significance; ***, $p<0.001$.

(b) GBM cell lines were treated with RG3039 (6 μM) or DMSO for 48 h. The transcript level of DRNT1 was analyzed by RT-qPCR and normalized to that of β-actin (mean ± SEM, n = 3). Statistical analysis by unpaired t-test; ***, $p<0.001$.

(c) GBM cell lines were treated with RG3039 (6 μM) or DMSO for 48 h. The transcript level of DRNT2 was analyzed by RT-qPCR and normalized to that of β-actin (mean ± SEM, n = 3). Statistical analysis by unpaired t-test; ***, $p<0.001$.

Figure S6

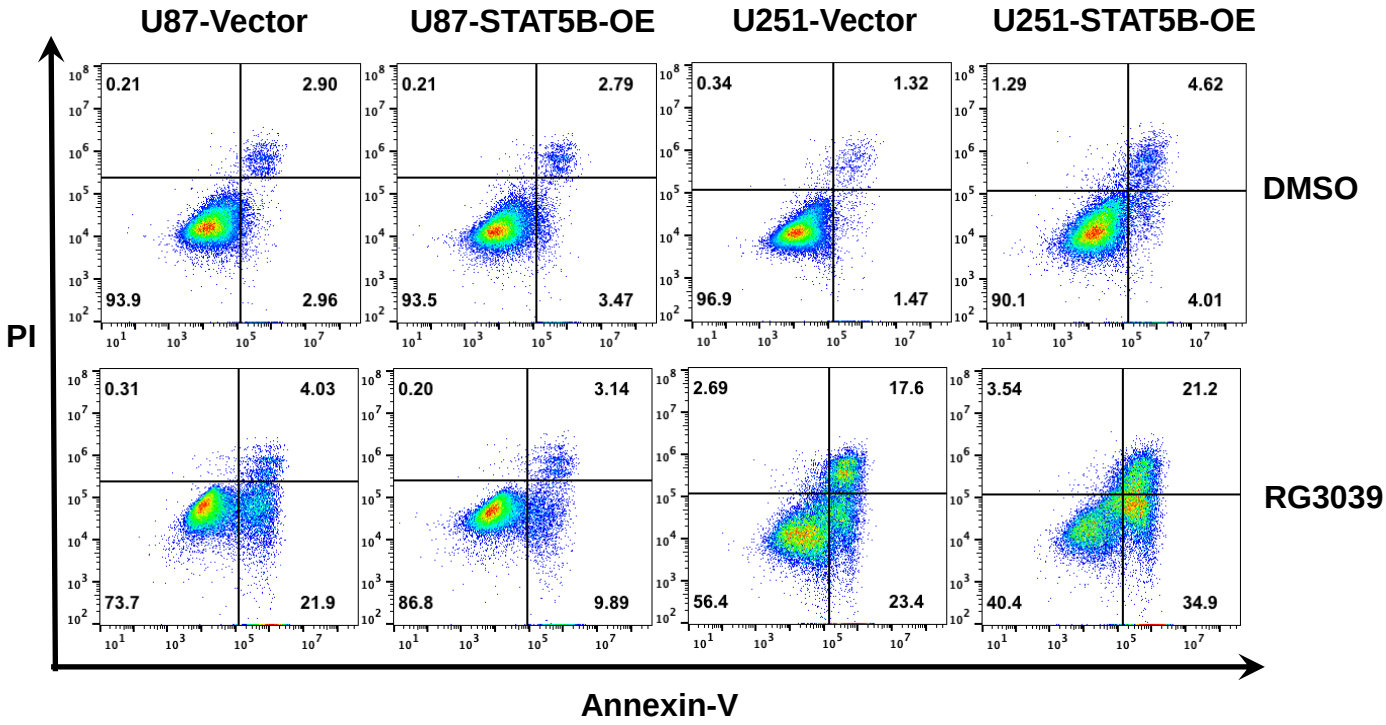



**Figure S6. Representative sorting of cell apoptosis assay treated with RG3039 in GBM cell lines with or without overexpressed STAT5B.**

GBM cell lines with STAT5B overexpression or vector expression were treated with RG3039 (6 μM) or DMSO for 48 h. Cell apoptosis was analyzed by APC-Annexin V-based flow cytometry.

**Table S1 Survival analysis of DCPS expression and clinicopathologic features in GBM patients**

| **Variable** | Median OS | Univariate | Multivariate | | |
|---|---|---|---|---|---|
| | Months | ***P*** | **HR** | **95%CI** | ***P*** |
| **Age at diagnosis** | | **0.004** | | | |
| Median (range), years | | | | | |
| ≤55 years | 27.0 | | Reference | Reference | |
| > 55 years | 15.0 | | 1.4 | 0.6-3.4 | 0.412 |
| **Sex** | | 0.490 | | | |
| Male | 20.0 | | Reference | Reference | |
| Female | 24.0 | | 0.5 | 0.2-1.2 | 0.140 |
| **Location of lesions** | | 0.195 | | | |
| Midline structure | 16.0 | | Reference | Reference | |
| Left hemisphere | 24.0 | | 12.1 | 0.7-203.7 | 0.084 |
| Right hemisphere | 19.0 | | 29.1 | 0.9-911.7 | 0.055 |
| Bilateral hemisphere | 48.0 | | 20.1 | 0.7-614.3 | 0.085 |
| **Number of lesions** | | 0.684 | | | |
| Single | 22.0 | | Reference | Reference | |
| Multiple | 24.0 | | 1.2 | 0.1-11.3 | 0.890 |
| **Maximum diameter of lesions** | | 0.790 | | | |
| Median (Range), cm | | | | | |
| ＜5 cm | 22.0 | | Reference | Reference | |
| ≥5 cm | 20.0 | | 0.7 | 0.3-1.6 | 0.359 |
| **Preoperative KPS** | | 0.679 | | | |
| <80 | 20.0 | | Reference | Reference | |
| ≥80 | 23.0 | | 2.5 | 0.9-7.4 | 0.086 |
| **SVZ involvement** | | **0.023** | | | |
| Noninvolved | 24.0 | | Reference | Reference | |
| Involved | 13.0 | | **5.5** | **1.9-16.0** | **0.002** |
| **EOR** | | **0.033** | | | |
| STR | 13.0 | | Reference | Reference | |
| GTR | 24.0 | | **0.2** | **0.1-0.6** | **0.002** |

| | | | | | |
|---|---|---|---|---|---|
| **Adjuvant therapy** | | **< 0.001** | | | |
| Non-Stupp | 16.0 | | Reference | Reference | |
| Stupp regimen | 58.0 | | **0.2** | **0.1-0.4** | **< 0.001** |
| **IDH-1 mutation status** | | 0.249 | | | |
| Wildtype | 19.0 | | Reference | Reference | |
| Mutant | 26.0 | | 1.0 | 0.4-2.5 | 0.952 |
| **MGMT promoter status** | | **0.026** | | | |
| Unmethylated | 22.0 | | Reference | Reference | |
| Methylated | 26.0 | | 0.7 | 0.3-1.5 | 0.331 |
| **DCPS expression** | | **0.029** | | | |
| Low | 26.0 | | Reference | Reference | |
| High | 19.0 | | **2.4** | **1.0-5.4** | **0.042** |

EOR, extent of resection; GTR, Gross total resection; IDH, isocitrate dehydrogenase 1; KPS, Karnofsky performance status; MGMT, O6-DNA-methylguanine methyltransferase; STR, subtotal resection; SVZ, subventricular zone