## SUPPLEMENTARY FIGURE LEGENDS

**Supplementary Figure S1:** Replication of human GBM in an animal model. The top panels show the intraoperative specimen smear for GSC126 and GSC11 patient GBM, the corresponding representative fresh frozen, formalin-fixed paraffin-embedded (FFPE) specimen, and subsequent patient- derived GSC line characterization using FACS analysis of Ki67, Nestin, Sox2, and GFAP in cell lines derived from the patient samples shown in the middle panel. Marker characterization demonstrates a stem- like pattern. The bottom panels show the respective highly oncogenic cell lines after orthotopic xenotransplantation into nude mice. The xenograft tumor visibly reproduces the human disease, including its significant nuclear atypia, mitoses, necrosis, pseudo-palisading cells, and vasculogenesis (Distances indicated in each slide is 50μm).

**Supplementary Figure S2:** Confirmation of expression of GFP in knockdown cells in vitro and ex vivo. **(a** and **c)** Differential interference contrast (DIC) and fluorescent images of GFP+veneurospheres cultured in control and doxycycline conditions in GSC11 and GSC126. **(b** and **d)**FACS of ex vivo GSC-derived cells of human origin from mouse brain. Left panel: GSC-derived human cells (APC+ve) from control mice. Right panel: GSC-derived human cells with *POSTN* knockdown (APC+veGFP+ve) from *POSTN-* knockdown, doxycycline-treated mice.

**Supplementary Figure S3**: Validation of *POSTN* knockdown in vitro and in vivo. Validation of knockdown of *POSTN* in GSC11 and GSC126 (a-c). Quantitative real time PCR analysis for determination of expression levels of *POSTN* gene in knockdown (KD) and control cells cultured in vitro (a). Relative expression levels of *POSTN* after normalization to that of GAPDH in respective samples is presented (N=3). (b) Western blot analysis of whole cell lysate from in vitro cultured control and KD cells (GSC11 and GSC126) using anti-*POSTN* antibody. GAPDH is loading control. (c) Immunohistochemistry staining of xenograft tumors from control and KD mice using anti-*POSTN* antibody. Scale bar is 100μm.

**Supplementary Figure S4:** Intensity normalization example of FLAIR and contrast-enhanced T1WI MR images across TCGA institutions. MD Anderson Cancer Center [MDACC], Henry Ford Hospital, University of California–San Francisco [UCSF], Emory, Case Western University, and Thomas Jefferson University.

**Supplementary Figure S5:** Intensity normalization example of FLAIR and contrast-enhanced T1WI MR images across MRI scanner brands/types (General Electric, no data available, and Philips).

**Supplementary Figure S6:** Intensity normalization of FLAIR and contrast-enhanced T1WI MR images across MRI scanner magnetic field strengths. Representative image intensity normalization for 2 patients (#1 and #2) with 1.5 Tesla and for 2 patients (#3 and #4) with 3.0 Tesla strength are shown.

**Supplementary Figure S7:** Immunofluorescence staining of xenograft tumor sections from control and KD mice using anti-CD31 and anit-Ki67 antibodies. Nuclei are stained with DAPI. Respective cell lines and conditions giving rise to orthotopic tumors are labelled on the side of micrographs. Scale bar is 50μm.

**Supplementary Figure S8:** Performance of radiomic feature based models to predict *POSTN* levels in patients Leave one out cross validation of *POSTN* levels in TCGA patient cohort. Accuracy in 93 patients was 99.17%; p-value <2e-16. 95% CI, sensitivity, specificity, PPV, NPV of models are shown in the plot.

## Supplementary Methods:

## *Patient-derived GSC culture*

Two independent MDACC patient–derived GSC lines (GSC126 and GSC11) were isolated from surgical specimens and cultured as described previously (50,51). Briefly, the cells were grown in GSC media consisting of Dulbecco’s modified Eagle’s medium/F12 (Corning, USA) including L-glutamine (Sigma, USA), 1x penicillin/streptomycin (Corning), 1x B27 without vitamin A (Life Technologies, USA), 20 ng/ml basic fibroblast growth factor (VWR, USA), and 20 ng/ml epidermal growth factor (EMD Millipore, USA) at 37oC in the presence of 5% CO2. Fresh media was added every other day, and adherent cells (GSC126) and neurospheres (GSC11) were passaged according to standard protocols with exposure to a cell detachment solution for 3 minutes (Accutase, EMD Millipore) at 37oC.

## *Flow cytometry*

GSC lines were proliferated in GSC media. After Accutase treatment, single cells were fixed with 4% paraformaldehyde for 10 minutes at room temperature and then washed twice with cold phosphate- buffered saline. The cells were permeabilized with permeabilization buffer containing 1% bovine serum albumin, 0.1% Triton X-100, and 0.09% sodium azide for 15 minutes at room temperature. Permeabilized cells were then incubated with the stem cell markers mouse anti-Sox2 antibody (#MAB2018, R&D Systems, USA) and rabbit anti-nestin antibody (Thermo Scientific Pierce, USA) and the proliferation marker rabbit anti-Ki67 antibody (Thermo Scientific Pierce) in permeabilization buffer for 30 minutes at room temperature. After three washes with permeabilization buffer, 1 µg of species-specific activated protein C (APC)-conjugated secondary anti-mouse (BD Cell Analysis, USA) and anti-rabbit (Thermo Scientific Novex, USA) antibodies were used for indirect labeling according to the manufacturers’ protocols. Florescence-activated cell sorting (FACS) analysis was performed with a Gallios flow cytometer (Beckman Coulter, USA) in MDACC’s Flow Cytometry and Cellular Imaging Facility. The gates for sorting were based on isotype control samples for each GSC line. The FACS data were analyzed using the FlowJo software program (version 10).

## *Western blot analysis*

Whole-cell protein extraction of the GSC lines were performed in the presence of protease and phosphatase inhibitors (Thermo Scientific Pierce) and analyzed with Western blotting for specific proteins. Briefly, 50-100 μg of whole-cell extract was resolved with 10-12.5% sodium dodecyl sulfate– polyacrylamide gel electrophoresis (Fisher BioReagents, USA) and transferred to a nitrocellulose membrane. Membranes were probed with mouse anti-*POSTN* (#TA804575, Origene, USA) and mouse anti-GAPDH (Abcam, USA) primary antibodies overnight at 4°C. Membranes were incubated with species-specific horseradish peroxidase–conjugated secondary antibodies for 1 hour at room temperature, exposed to Clarity Western ECL Substrate (BioRad, USA), and scanned with a c600 Western blot imaging system (Azure Biosystems). Scanned images were analyzed with cSeries Capture software.

***Inducible short hairpin RNA–mediated knockdown of POSTN***

Lentiviruses harboring tet-inducible shRNA against *POSTN* (SMARTchoice Inducible Human *POSTN* shRNA from GE Healthcare Dharmacon) were used for *POSTN* knockdown. Lentivirus particles with three independent constructs—VSH6376-224193850 (1-P), VSH6376-224207258 (2-P), and VSH6376-224207466 (3-P)—were added to GSCs at an approximately 0.3 multiplicity of infection. Resistant clones were selected with 1 µg/ml puromycin 24 hours after transduction. After 14 days of puromycin selection, the cells were exposed to 1 µg/ml doxycycline. After overnight exposure to doxycycline and IRES driven GFP expression was confirmed. After 6 days of doxycycline exposure, reverse transcriptase quantitative polymerase chain reaction (qRT-PCR) and Western blot analysis were performed to confirm *POSTN* knockdown at the RNA and protein levels, respectively. Three sets of human-specific qRT-PCR primers for *POSTN* were used: Set1-5'TTCTCATATAACCAGGGCAACA3' and 5'TTTGGGCACCAAAAAGAAAT3'; Set2-5'GCAGCCTTTCATTCCTTCC3' and 5'TTTGGGCACCAAAAAGAAAT3'; Set3-5'CAGCCTTTCATTCCTTCCAT3' and 5'TTCAACAGATTTTGGGCACC3'. Primers specific to human β-actin were used as a normalization control in the qRT-PCR reactions. The qRT-PCR results were analyzed using the ∆∆Ct method. Clones harboring the 2-P shRNA construct showed maximal knockdown and were used for the experiments.

***Orthotopic tumor formation***

Five-week-old male nude mice (strain *nu/nu*, MDACC, Houston, TX) were anesthetized with ketamine intraperitoneally, (50,52) and a nylon bolt was implanted into each mouse 2 mm posterior and 1.5 mm lateral to the bregma in the right cerebral hemisphere. One week after bolting, mice were again anesthetized with ketamine intraperitoneally, and 5x105 GSC126 and GSC11 in 5 µl of Dulbecco’s modified Eagle’s medium (Corning, USA) were injected over 5 minutes through the bolts (50). Mice were randomly divided into control (sucrose) and *POSTN*-knockdown (doxycycline) groups. Weekly MRI was performed starting 14 days after implantation. Mice were humanely sacrificed at the earliest observed onset of neurological symptoms using CO2 chambers. Brains were collected, fixed in formalin, and embedded in paraffin. Paraffin-embedded tumor-bearing brains were cut into 5-μm slices, deparaffinized in xylene according to standard protocols, rehydrated in an alcohol series, and stained with hematoxylin and eosin according to standard protocols. Tumor-containing sections were stained for *POSTN* and CD31 using a mouse anti-*POSTN* and rabbit anti-CD31 antibodies, respectively. For double immunofluorescence staining, the sections were permeabilized and blocked with 5% normal donkey serum followed by overnight incubation at 40C with rat anti-Ki67 (Invitrogen catalog #: 14-5698-82) and rabbit anti-CD31 (Abcam catalog #: ab28364) primary antibodies. Donkey anti-rat, FITC conjugate (Millipore catalog #: AP189F) and Donkey anti-rabbit, Rhodamine conjugate (Millipore catalog #: AP182R) secondary antibodies were used for Ki67 and CD31, respectively. All animals were either used for MRI or histopathology, no animals were excluded from analysis. The *POSTN*- and hematoxylin and eosin–stained sections were imaged with a BX51 microscope (Olympus, USA) using a 10x objective and analyzed with the QCapture software program. Immunofluorescent images were captured with Leica DMi8 microscope using 40X objective and analyzed with Leica microsystems LAS X software.

## *Isolation of human cells from mouse brains*

Mouse brains with xenograft tumors were harvested and processed using the NeuroCult Enzymatic Dissociation Kit (Stemcell Technologies) according to manufacturer’s protocol. Briefly, xenograft tumor–bearing mouse brains were collected in NeuroCulttissue collection solution and processed in a sterile tissue culture hood. The right frontal lobe was dissected and minced into small pieces with a sterile surgical blade in the presence of NeuroCult dissociation solution. The minced tissues were incubated with 3 ml of NeuroCult dissociation solution for 7 minutes at 37°C. The enzymatic reaction was then stopped by the addition of 3 ml of NeuroCult inhibition solution and centrifuged at 700 rpm for 7 minutes at room temperature. Cell pellets were resuspended in 10 ml of NeuroCult resuspension solution and centrifuged for three additional rounds to remove debris. The final cell pellets were resuspended in 1 ml of stain buffer (bovine serum albumin; BD Pharmingen). All steps to prepare samples for FACS were performed in stain buffer. The human-specific rat anti-human human leukocyte antigen class I ABC xenograft marker antibody and the anti-rat secondary antibody conjugated with APC were used for FACS as described above. APC-positive cells from control mouse brains and APC- and GFP-positive cells from doxycycline-treated mouse brains were collected.

***RNA isolation, reverse transcription and real time polymerase chain reaction***

Total RNA from human cells within mouse brains was isolated with PureZOL reagent (Bio-Rad) according to the manufacturer’s protocol. RNAs were precipitated in the presence of 10 mg of linear acrylamide (Invitrogen) with isopropanol. RNA pellets were resuspended in RNase/DNase-free water and quantified using a NanoDrop (Thermo Scientific, USA). Approximately, 1µg of total RNA was subjected to reverse transcriptase reaction using iScript™ Reverse Transcription Supermix for RT–qPCR (Bio-Rad) to synthesize cDNA. These cDNAs were used as template in 2X iQ™ SYBR® Green supermix based real time PCR reactions along with gene specific primer sets (as described above).