The recognition of stem cells (SC) in the adult central nervous system and in association with gliomas has spawned an entire field of research and intense investigation. A large body of knowledge is being accumulated to gain insight into the pathobiology of gliomas with the intent of finally improving the grave prognosis that continues to beset patients with high grade gliomas (HGG). In this work, we provide a historical overview of the events leading to the discovery of SC and glioma stem cells (GSC). We then focus on the current understanding of GSC with respect to markers, clinical significance, and their targeting. We discuss current data and developments using SC as vehicles to delivery therapeutic agents to HGG, including our recent development of patient-specific human induced pluripotent stem cells (hiPSC). We conclude with a discussion of opportunities for future development and concepts aimed at reducing tumor recurrence and improving survival for patients with HGG.