Beta-amyloid cleaving enzyme-1 (BACE-1) is a transmembrane aspartyl protease that has been identified as the protease responsible for the critical first step in the processing of beta-amyloid precursor protein that ultimately leads to the production of Abeta peptides in the brain. Accumulation of these peptides has been implicated in the pathology of Alzheimer’s disease (AD). Thus, a BACE-1 inhibitor could potentially slow or halt the progression of AD. However, there are other many other approaches to drug discovery and development for AD, such as gamma-secretase inhibitors, anti-amyloid vaccines, neuroprotective agents, and agents to prevent neurofibrillary tangle formation. We will discuss evidence why BACE-1 is the leading drug target for AD.