The giant enzyme proteasome is the essential protease of the ubiquitin-proteasome system. The system is responsible for maintaining proteostasis by highly regulated proteolysis of the majority of cytosolic proteins. In Parkinson’s disease (PD) proteostasis in neurons is seriously compromised and proteins that failed to be degraded aggregate in the form of Lewy bodies. One of natural substrates of the proteasome, α-synuclein, is a pathogenic hallmark of Parkinson’s disease and is the most abundant protein in Lewy bodies. Boosting the proteasome performance would be expected to have beneficial effects on proteostasis in PD and other neurodegenerative diseases, especially that proteasome's activity is compromised in the course of the diseases. To answer the call, we developed a set of small, nin-toxic peptide-based agonists of the proteasome that enhance degradation of α-synuclein in vitro and demonstrate promising anti-neurodegeneration effects in vivo.