the transition or senescent spans resulted in decreased mortality rate and extended longevity compared to the control, while supplementation during the entire adult life span or during the health span only led to decreased longevity in the normal-lived strain. The analysis of mortality curves indicated that there were no significant effects of the SAHA administration until the age of ~50 days. When the long-lived strain was administered with SAHA by the same scheme, mostly deleterious effects were detected. Remarkably, the SAHA-treated normal-lived *D. melanogaster* strain showed late-life extending effects similar to those seen in the same study for SB. The fact that these two different HDACIs, SB and SAHA, had similar effects on mortality rate during the senescent span indicates the similarity of mechanisms that underlie beneficial effects for this class of HDACIs. The authors suggested that HDACIs may significantly influence the mortality rate throughout the senescent phase by reducing the vulnerability of treated individuals, in a manner similar to that of dietary restriction. Indeed, as was mentioned above, genetic alterations in genes encoding HDACs and nutrition regiments partially interact in the course of longevity control.[31,32] HDACIs may affect several pathways involved in regulating gene expression patterns associated with healthy aging. The induction of these patterns of gene expression throughout senescence when they are not normally present may likely underlie the life-extending effects of HDACIs.

21.4 HDACIs in Preclinical and Clinical Trials

A lot of hope in geroscience is currently being pinned on pharmacological compounds targeted to epigenetic regulators of gene expression. Epigenetic modifications are known to be potentially reversible; this feature makes them attractive targets for pharmacological intervention. Over the past few years, a series of medications have been developed targeted to epigenetic regulators, including modulators of HDACs, HATs, DNA methyltransferases, and noncoding miRNAs, with potential effects against various types of disorders.[69,70] Several modulators of HDAC activity (primarily, HDACIs), among other drugs targeting epigenetic machinery, have been recently examined in human clinical trials, and some have been proposed as promising anti-ageing drug candidates.[13] However, as most HDACIs lack specificity,[71] their wide applicability is still questionable. Serious efforts are currently aimed at finding class-selective and isoform-selective HDACIs.[72]

HDACIs are expected to have clinical potential in preventing and/or treating many chronic pathological conditions, including cancer, cardiovascular disorders, metabolic and neurodegenerative disorders such as Parkinson's, Alzheimer's and Huntington's diseases, violated immune response, inflammation and arthritis. The research findings supporting the therapeutic properties of HDACIs in curing age-related pathologies are reviewed in the sub-sections below.