Myosin modulators are a novel class of pharmaceutical agents designed to treat patients with cardiomyopathies by directly modulating cardiac myosin function in the sarcomere. Compounds including omecamtiv mecarbil (OM), danicamtiv (Dani), and deoxy-ATP (dATP) have previously been shown to increase myofibril ATPase activity while mavacamten (Mava) reduced ATPase activity. In the absence of actin, ATPase activity is a combination of the direct effects of nucleotide binding and the equilibrium between the high activity (DRX) and low activity (SRX) states of myosin. In this study, we investigate how these small molecules affect the single turnover kinetics of pig cardiac heavy meromyosin (pcHMM) in the absence of actin. pcHMM bound to fluorescent mant.ATP or mant.dATP is rapidly mixed with a high concentration of unlabeled ATP. The rate constant for replacement of mant.ADP by ATP defines the turnover of mant.ATP. Preliminary titration experiments demonstrate that OM, Dani, and Mava all inhibit ATP turnover with an IC50 of 0.59 µM, 3.5 µM, and 0.276 µM, respectively. 100% dATP increases the ATP turnover by 100%. These experiments indicate that each myosin modulator differentially alters cardiac HMM activity. We will discuss how each modulator affects ATP turnover by a direct effect on catalytic activity vs an effect on the amount of HMM in the super-relaxed population.