Malaria remains a dominant global health problem, with more than 200 million cases causing around 445,000 deaths in 2016. Antimalarial chemotherapy is critical for treating symptomatic infections, but chemoprotection, using drugs that can prevent infection before malaria develops, plays a key role in protecting vulnerable populations. Developing chemopreventive drugs that target the malaria parasite during the asymptomatic liver stage has key benefits, and most leading clinical candidates in the drug development pipeline target the liver stage. Despite different proposed mechanisms of action, these compounds share a common characteristic: targeting the liver stage parasite during the very early phase of its development. Using single cell profiling of late liver stage development and infectivity, we demonstrate that early killing is not essential, and have implemented a novel multimodal screen to assess compound activity against the entirety of the P. berghei liver stage. Our results demonstrate overlooked liver stage activity of known antimalarials and provide a novel phenotypic approach towards understanding compound mechanism of action in primary screens, allowing rapid triage of novel or desirable compounds.