Preventing biodiversity loss under global change will require proactive conservation over a long term and across large scales. This research attempted to develop an approach that can identify how threats from landscape- and climate change will impact wildlife populations and help guide conservation actions to address them. At the center of our research are predictive models that allowed us to project complex, species-specific responses to conservation and climate change scenarios for various wildlife populations over the next century in the Central Hardwoods region of the U.S. We embedded the models within a decision making framework that helped to overcome the uncertainties and complexities that are inherent in the process of long-term, large-scale planning, allowing us to identify conservation that could reduce risk from climate change across a range of species. Together this work demonstrated that planning for wildlife populations across large scales can be achieved under global change.