This thesis advances the methodology of Randomized Controlled Trials (RCTs) by developing approaches that enhance efficiency, robustness, and decision-making under uncertainty. Across several studies, we investigate strategies for optimally leveraging both internal and external information - such as early or surrogate outcomes, historical data, and multiple endpoints - to improve trial performance while maintaining strict statistical validity. Key contributions include: *i)* adaptive group sequential designs integrating surrogate endpoints and predictive metrics; *ii)* robust dynamic borrowing methods using mixture priors; and *iii)* frameworks for incorporating benefit-risk assessment into multi-arm, seamless phase II/III trials. The proposed methods are evaluated through theoretical analysis and extensive simulation studies, demonstrating their ability to increase trial efficiency, reduce the risk of premature or erroneous conclusions, and inform regulatory and clinical decision-making. Collectively, these developments provide practical tools to accelerate drug development while upholding scientific rigor and statistical integrity.