PROTOCOL SYNOPSIS

Protocol Title	Comparison of Oral anticoagulants for extended VEnous Thromboembolism (COVET)
Main Criteria for Inclusion	Age 18 years and older; confirmed acute, symptomatic first unprovoked lower extremity proximal DVT and/or PE, completed initial course of oral anticoagulation therapy for 3-12 months and recommended for continued anticoagulation, under the care of a healthcare provider for treatment of VTE during study participation
Study Objectives	1. Determine if apixaban is superior to warfarin in the reduction of clinically relevant bleeding. 2. Determine if rivaroxaban is superior to warfarin in the reduction of clinically relevant bleeding. 3. Determine if apixaban is non-inferior to warfarin in the prevention of recurrent venous thromboembolism. 4. Determine if rivaroxaban is non-inferior to warfarin in the prevention of recurrent venous thromboembolism. 5. An exploratory descriptive comparison of apixaban versus rivaroxaban for the prevention of clinically relevant bleeding and recurrent VTEs as a secondary objective.
Study Design	Randomized, open label, active comparator
Treatment Regimen	Warfarin, apixaban, or rivaroxaban
Duration of Study Participation	12 months
Number of Patients	Approximately 3000
Number of Sites	Approximately 60 sites in the US and Canada
Primary Efficacy Endpoint	Recurrent venous thromboembolism
Primary Safety Endpoint	Clinically relevant bleeding
Interim Analyses	There will be no formal interim analyses for the primary efficacy or safety endpoints. The Data and Safety Monitoring Board will meet regularly to review patient safety and overall study conduct.