PB2452

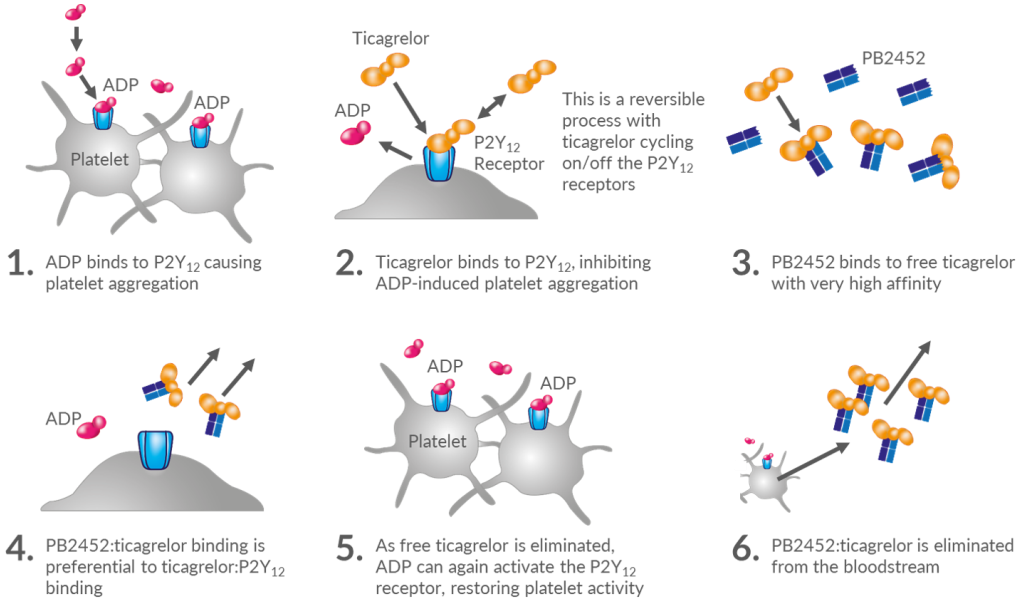
PB2452: A ticagrelor reversal agent **B2452** (formerly **MEDI2452**)

PB2452 is a novel recombinant human monoclonal antibody antigen-binding fragment, designed to reverse the antiplatelet activity of ticagrelor. Ticagrelor is an antiplatelet therapy widely prescribed to reduce the rates of death, heart attack and stroke in patients with acute coronary syndrome (ACS), or who have previously experienced a heart attack. The American College of Cardiology, American Heart Association and European Society of Cardiology guidelines recognize ticagrelor as the preferred antiplatelet therapy for ACS.

Ticagrelor binds to platelets to prevent them from forming blood clots, which could restrict blood flow. Due to ticagrelor's antiplatelet activity, patients on ticagrelor have an elevated risk of spontaneous bleeding. In addition, patients on ticagrelor who need urgent surgery cannot wait the recommended five days for ticagrelor's effect to dissipate and are at increased risk of major bleeding during and after surgery. There are currently no known reversal agents approved or in clinical development for ticagrelor or any of the other antiplatelet drugs.

In Phase 1 clinical trial, PB2452 achieved rapid and complete reversal of ticagrelor's antiplatelet activity, with potential customizable duration of reversal based on the dosing regimen, which has the potential to bring life-saving therapeutic benefit by increasing the safety of ticagrelor.The availability of a reversal agent could expand ticagrelor's use by mitigating concerns regarding bleeding risk and uniquely position ticagrelor as the only oral antiplatelet drug with a reversal agent.

PB2452 binds to ticagrelor with high affinity and specificity to reverse ticagrelor's antiplatelet activity, as illustrated below:



Recently completed a Phase 1 dose escalation clinical trial of PB2452 in healthy subjects who have been pre-dosed with ticagrelor. In this trial, we observed rapid and complete reversal of ticagrelor's antiplatelet activity within five minutes following initiation of infusion, and sustained reversal for over 20 hours in later dosing cohorts in which we administered PB2452 over an extended infusion period. There were no PB2452-related adverse events or serious adverse events in any of the dose cohorts. The exclusively licensed PB2452 from MedImmune Limited, a wholly owned subsidiary of AstraZeneca.