

PMX-60056 Heptagonist Fact Sheet

www.polymedix.com

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Novel Anticoagulant Reversing Agent

PolyMedix's heptagonist, PMX-60056, is a synthetic, small-molecule that reverses the anticoagulant activity of both heparin and low molecular weight heparins (LMWH). PMX-60056 is designed to bind to pentasaccharide, a chemical sequence found on both heparin and LMWH that is essential for their activity. By binding to pentasaccharide, PMX-60056 prevents heparin and LMWH from interacting with antithrombin, thereby reversing the anti-clotting effect of these drugs. **PMX-60056 is currently in Phase 2 clinical trials.** PolyMedix's objective is to develop PMX-60056 to displace the current therapy used to reverse heparin, and to become the first reversing agent for LMWHs.

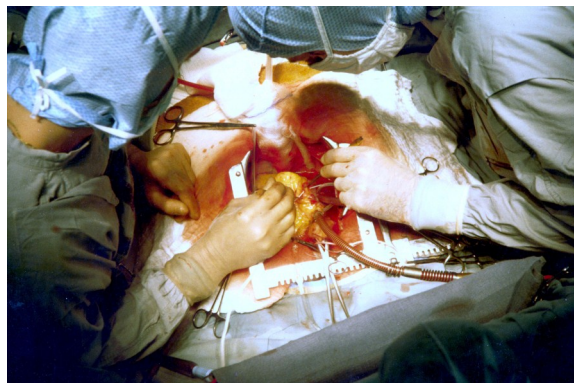
Proof of concept has been demonstrated in three pilot safety and efficacy studies which showed that PMX-60056 safely reversed the anticoagulant action of both heparin and LMWH, as well as allowed for re-anticoagulation and re-reversal. A Phase 2 clinical trial in interventional cardiology (Percutaneous Coronary Intervention) is currently underway.

Major Unmet Medical Need

Heparin is commonly used in cardiothoracic and orthopedic surgeries to prevent blood clots from forming during the surgery. After surgery, heparin must be reversed to allow normal blood clotting and healing. Protamine, approved in the early 1960's, is the only reversing agent available for heparin. Derived from fish sperm, there are many potentially dangerous side-effects possible with its use, including difficulty in titrating dose, anaphylaxis and allergic reactions, hemodynamic effects (reduced blood pressure), pulmonary hypertension, and post operative bleeding (since protamine affects both fibrin clot formation and platelet aggregation). Furthermore, protamine is not approved and not effective for reversal of LMWHs.

LMWHs are used for long term anticoagulation, such as in prevention of deep vein thrombosis, post heart attack, after orthopedic surgery, and in conjunction with cancer chemotherapy. There is no approved reversing agent for the LMWH's. With all LMWHs, there may be a potential 1-4% rate of major bleeding, and up to 20% incidence of clinically significant bleeding. The bleeding risk can be particularly high in certain patients, particularly those with hypertension, impaired renal function, and cancer. The current treatment regimens for bleeding complications with LMWH may include hospitalization, blood transfusions, and surgery, which have the potential to be expensive and unpredictable. PMX-60056 could be the first and only therapeutic agent to rapidly reverse the action of LMWH.

PMX-60056 could have major potential pharmacoeconomic advantages and cost-savings compared to current practices.

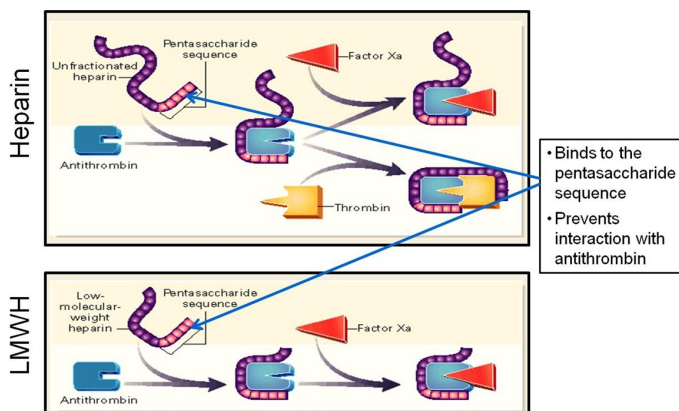
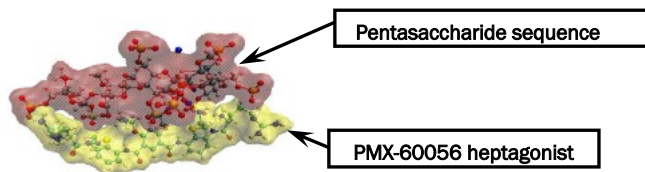


PMX-60056: Designed to Address Medical Needs

- No worsening of bleeding—even at significant excess doses, there is no intrinsic pro- or anti-coagulant activity, thus PMX-60056 should be easier to dose
- PMX-60056 is a synthetic small-molecule, there should be less risk of allergic or immune system reactions
- Superior fibrokinetics - PMX-60056 does not affect normal blood clotting (either fibrin clot formation or platelet aggregation), which may result in less risk of post-operative and other bleeding complications
- PMX-60056 is active in reversing LWMH
- PMX-60056 allows for rapid re-anticoagulation, which can be problematic with protamine

PMX-60056 Design and Unique Mechanism of Action

PolyMedix applied its proprietary computational drug design technologies that were developed at, and licensed from the University of Pennsylvania, and synthetic chemistry approaches to develop PMX-60056. PMX-60056 is a synthetic small-molecule specifically developed to interrupt a protein:protein interaction. By specifically binding to pentasaccharide, PMX-60056 disrupts its interaction with antithrombin, the essential step in the mechanism of action of both heparin and LMWHs.



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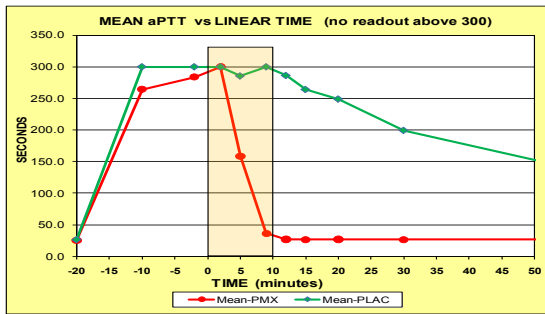
Phase 1 Clinical Data

In three successful Phase 1B/2 clinical trials, PolyMedix has shown the ability of PMX-60056 to safely reverse both heparin and LMWH. Two Phase 1B/2 clinical trials were similarly designed as double-blind, placebo-controlled, crossover studies conducted in six healthy subjects. With the crossover design, on the second treatment day, each subject received the alternate treatment, therefore, all subjects received both PMX-60056 and placebo. A third, dose-ranging trial showed that PMX-60056 could safely reverse surgical levels of heparin, and allowed for rapid re-anticoagulation. In all of these studies, safety is ascertained by blood pressure measurements, and efficacy is determined by measuring blood clotting time (aPTT, Activated Partial Thromboplastin Time, or ACT, Activated Coagulation Time).

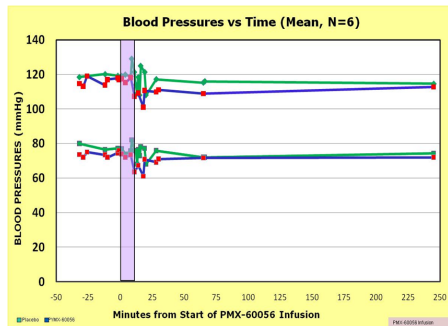
Heparin Reversal

Design: PMX-60056 (or placebo) was administered intravenously 20-minutes after an intravenous dose of heparin.

Efficacy: The graph below shows that PMX-60056 fully reversed heparin activity and normalized blood clotting time by 9 minutes (as measured by aPTT). Long term follow up revealed no rebound as may be seen with protamine, indicating that the binding of PMX-60056 to heparin is permanent.



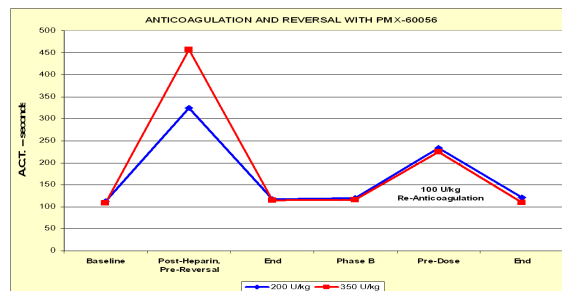
Safety: PMX-60056 administered in the presence of heparin had no clinically significant blood pressure changes compared to placebo.



Surgical Levels of Heparin Reversal

Design: In a dose-escalation Phase 1B study, 12 subjects received heparin (200 or 350 units/kg) 20-minutes before PMX-60056, followed by a second dose of heparin and PMX-60056.

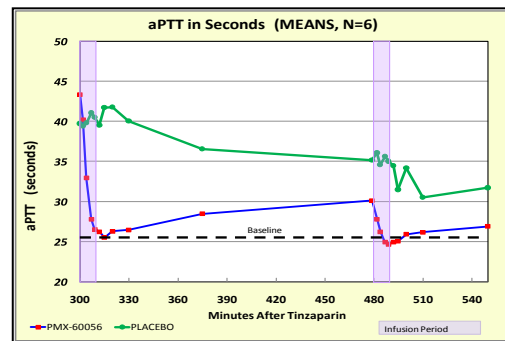
Efficacy: The graph on the right shows that PMX-60056 could reverse surgical levels of heparin, and allow for re-anticoagulation.



LMWH Reversal

Design: PMX-60056 (or placebo) was first administered intravenously 5-hours after the subcutaneous administration of tinzaparin (subcutaneous administration creates a reservoir of drug under the skin which is released slowly over a period of time). A second dose of PMX-60056 (or placebo) was administered 3-hours later to reverse the tinzaparin that continued to release into the blood stream.

Efficacy: Both administrations of PMX-60056 resulted in complete normalization of blood clotting time as measured by aPTT (chart below) which confirms the mechanism of action.



Safety: Changes in blood pressure were transient and not clinically relevant when LMWH was present.

