Small Molecule Antagonists of PF4 for the Treatment and Prevention of HITT

Opportunity Overview

The New York Blood Center (NYBC), one of the US' leading suppliers of blood products and services, boasts world class research that have paved the way for new blood-related products, techniques and therapies resulting in numerous landmark patents and licenses. Under the leadership of Vice President and Chief Medical Officer, Bruce Sachais, MD, PhD, the Platelet Research Laboratory's focus is on improved diagnosis and novel therapeutics for heparin induced thrombocytopenia/thrombosis (HITT). **Platelet factor 4 (PF4) antagonists (PF4As) represent a novel approach to the treatment and prevention of HITT, and show tremendous potential for this disorder.** NYBC is seeking partnership(s) in order to take our lead PF4 A (FC-7259) to IND.

HITT Consequences

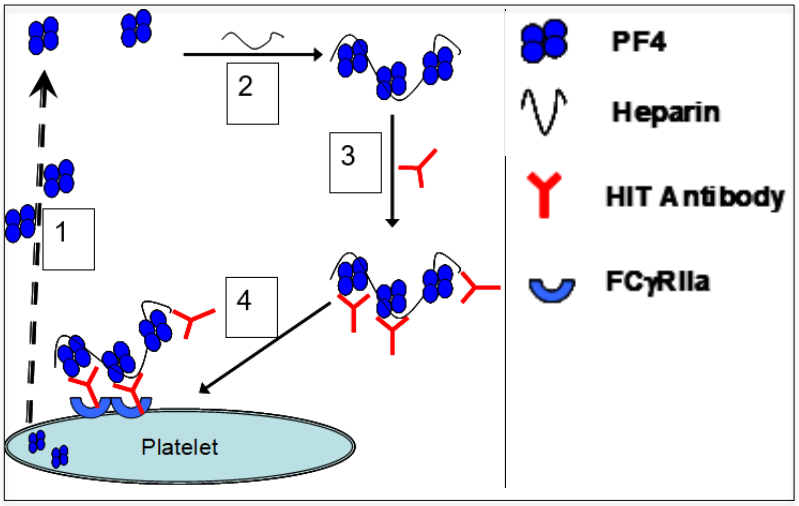
Heparin is an anticoagulant used in many hospitalized patients and in most cardiac surgical procedures. Heparin-Induced Thrombocytopenia (HIT), and subsequent thrombosis (HITT), is a serious complication of heparin therapy resulting in blockage to blood vessels. The consequences of HITT are dire and can lead blood clots to form within the blood vessels, resulting in limb amputations, strokes, heart attacks and death. HITT develops in approximately 1-5% of patients treated with heparin for 5-10 days and has a rate of occurrence of ~10-20 cases/yr/hospital. Affected individuals have a 20-50% risk of developing new thromboembolic events, a mortality rate ~20%, with an additional ~10% of patients requiring amputations or suffering other major morbidities.

Inadequate Treatment

Current drugs (general antithrombotics) used for treating HIT/HITT are generally not very effective and have safety issues regarding bleeding, the key adverse event monitored in clinical primary endpoints. The newer oral anticoagulants currently on the market, which may move into this indication, all have FDA boxed warnings regarding increased risk of thrombotic events, and in addition as oral medications, they have limited utility in a critical care setting. Furthermore, currently available HIT therapies treat only downstream thrombosis events.

HITT Pathology

It is now known that one of the key steps in the pathophysiology of HIT/HITT is that protein platelet factor 4 (PF4) is released from activated platelets largely as tetramers. Tetrameric PF4 then forms complexes with heparin called ultralarge complexes (ULCs). Pathogenic antibodies bind to ULCs and antibody-decorated ULCs bind to platelets and other cells (monocytes and endothelial cells) and activates these cells leading to further platelet activation and release of additional PF4.



Studies with transgenic and PF4 knock out mouse models have demonstrated that inhibition of PF4 tetramerization not only helps prevent the incident of HIT but is also not linked to an increased risk of bleeding, unlike current therapies.

Solution: Small Molecules Antagonists of PF4

NYBC, in collaboration with Thomas Jefferson University and Fox Chase Chemical Diversity Center, have developed novel inhibitors of HIT that targets PF4 tetramerization. These compounds have demonstrated potency in relevant in vitro assays including cellular activation to IC_{50} < 0.5 uM and blunting of thrombocytopenia and more rapid platelet recovery, and deceased thrombosis in a murine HIT model under preventive and intervention modes. These drugs do not cause bleeding in the mouse. **Lead candidate-FC-7259 directly addresses the pathophysiology of HITT with little or no increased risk of bleeding and has good drug properties for IV administration.** Provisional patent applications have been filed with the USPTO.

Partnering Opportunity and Structures

The asset is currently available for partnering with the possibility of resource sharing under an ongoing Phase IIB SBIR. NYBC is seeking development and commercialization partners with the strategic focus and financial wherewithal to bring the lead candidate through the global development, regulatory approval and commercialization processes. NYBC will consider a wide range of deal structures, including licensing arrangements, NewCo formation with equity participation, and others.

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