Contact Information

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Fact Sheet

rhTS13

A New Therapy for Treating Thrombotic Thrombocytopenic Purpura

Innovation in the DDP

ADAMTS13 Protein for the Treatment of Thrombotic Thrombocytopenic Purpura

Product Description

Recombinant human ADAMTS13 (rhTS13), a metalloproteinase which cleaves van-Willbrand factor (VWF) factor in blood has been engineered and cloned. rhTS13 was designed for solution dosing via intravenous injection for treatment of thrombotic thrombocytopenic purpura (TTP) and related diseases.

Indication and Market

Thrombotic thrombocytopenic purpura is a microvascular thrombosis - hemorrhage syndrome caused by the formation of platelet thrombi in the microcirculation with platelet reduction. Although the rate for TTP is low in the general population, patients with this disease have a high mortality rate. Patients with TTP are currently treated with plasma exchange therapy. It was reported that the survival at 6 months was 78% with plasma exchange and 63% with plasma infusion. As of now, there are no specific drugs approved for treatment of TTP and it is currently classified as a rare and neglected disease. Tentative market value for the treatment of this disease is estimated (based on special pricing afforded to drugs that treat rare and neglected diseases) between $75 to 300M per year.

Product Rationale

Proteases are naturally occurring protein-cleaving enzymes that regulate a wide variety of biological functions. At GIBH, we are using the potential of these enzymes as bio-therapeutics by directing them to cleave specific proteins in the blood to promote good health. Unlike standard drugs, a single proteinase molecule can inactivate or activate thousands of target molecules, resulting in higher efficacy and lower dosing regimens compared with small molecules or antibodies. It has been discovered that TTP is caused by loss of ADAMTS-13 activity in the blood, either due to an ADAMTS13 gene mutation or an autoimmune response against the protein. Currently, our team at GIBH is developing a recombinant version of ADAMTS-13 for the treatment TTP.

Preclinical Development

Cloning, expression and purification: Stealth versions of rhTS13 were engineered and cloned into pcDNA expression vectors and subsequently expressed in HEK293 cells. The stealth versions of rhTS13 were designed to be invisible to auto-antibodies found in the blood of patients with TTP. The protein was purified using His-tag isolation methodology and detected with an ADAMTS13 antibody.

Protease Activity: rhTS13 is catalytically active against a fluorescently-labeled peptide (FRETS-vWF73). More importantly, rhTS13 cleaves the scissile bond at Tyr1605/Met1606 of the native human VWF subunit, generating the predicted 140 kDa and 176 kDa fragments.

In vivo efficacy: ADAMTS13 KO mice provided by the National Institute of Biomedical Innovation in Japan were generated on a 129/Sv genetic background using a targeting vector that eliminates exons 3-6 of the Adamts13 gene. We are using these transgenic mice to develop a disease model of TTP for studying the efficacy of our rhTS13 proteins.

Intellectual Property

GIBH is in the process of filing intellectual property rights for composition of matter, production and medical use of our rhTS13 proteins for the treatment of TTP and other thrombotic diseases in China.

Product

Proteolytically active, soluble rhTS13 protein that is invisible to auto-antibodies and catalytically active against VWR.

Indication

Primary: TTP

Secondary: Thrombotic related diseases

Design

rhTS13 is prepared in solution for IV delivery into the blood of patients.

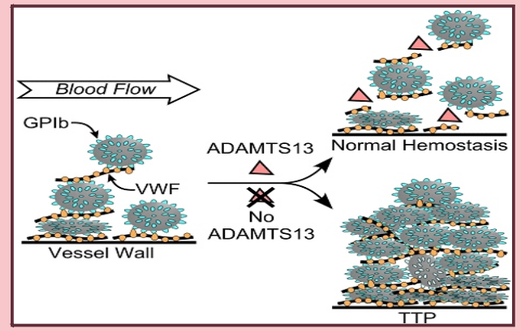
Development Status

Lead optimization: Preclinical proof-of-concept in several in vitro models of TTP. In vivo efficacy studies are ongoing in two rodent models of TTP. Candidate selection of the drug is scheduled for 2014 and IND filing is to be initiated in 2015.

Commercialization Strategy

Commercial partners are being sought for development and marketing in China.

Mechanisms of TTP disease



In the absence of ADAMTS13, VWR protein aggregates causing clotting of the blood.