Teaser Memorandum

HanAll BioPharma Co., Ltd.

Oral Protein Therapeutics for Treatment of Thrombocytopenia Using Resistein™ Technology

Executive Summary

□ HanAll BioPharma is a top-10 Korean-based R&D company established in 1973 with U.S. offices in Rockville, MD (subsidiary HanAll Pharmaceutical International, Inc.). The company was listed on the Korean stock market in 1989 with 2010 sales revenue of $100 MM and a market capitalization of $300 MM. In addition to its novel protein therapeutic pipeline, HanAll conducts R&D in the areas of cardiovascular (XC Hybrid Combinations), diabetes and dermatology. The company is currently in active discussions with multinational companies in support of its out licensing strategy for its pipelines and welcomes further inquiries from interested parties about licensing opportunities.

□ Included in HanAll's protein therapeutic pipeline are oral and injectable formulations of interferon-alpha, human growth hormone, interferon-beta, EPO, TPO, anti-TNF alpha proteins and human antibody for treatment of autoimmune disease. A Phase I clinical trial has been completed under a FDA sponsored IND for HanAll's lead molecule, Hanferon™ SC (Interferon-alpha), and there is an active IND for the second lead molecule, Vitatropin™, an orally bioavailable human growth hormone. There are a series of preclinical candidates at various stages of development, all demonstrating significant resistance to proteolysis.

Industry Sector :
Pharmaceutical, Personal Care

Therapeutic Target :
Thrombocytopenia, Platelets, megacaryocyte, thrombocyte

State of Development :
Preclinical stage

Key Technology Highlights

□ **Resistein™ Technology**

HanAll has developed a process and technique, Resistein™, involving the engineering of the native protein to significantly increase the half-life and bioavailability. This is achieved by increased protease resistance and enhanced absorption of the proteins across mucosal walls.

Proposal Abstract

□ Platelets are produced from megakaryocytes in bone marrow which is major organ for hematopoiesis. Diminished number of platelets lead to thrombocytopenia which refers to the state of being platelet count lower than 150,000/L in the peripheral blood.

□ Current therapy for thrombocytopenia includes steroids, spleenectomy, and transfusion. However, side-effects of steroids, potential infection accompanied by blood transfusion, and immune response by platelet transfusion prevent frequent use of these therapies. Many studies have found direct molecule towards human hematopoesis to find cure for thrombocytopenia without major side effects.

IP Owner Summary

Nov. 1973	Founded
Dec. 1989	IPO on KOSPI
Oct. 2008	Opened US Subsidiary, HanAll Pharmaceutical International Inc. for Clinical Development

□ **Business Field:**
- ▹ XC hybrid combination (FDC)
- ▹ Pro-apoptotic cancer drug
- ▹ Biotherapeutics

Personal Description of Researcher

□ Name : HyeaKyung Ahn
□ Present Position : Head Researcher
□ Major : Biology
□ Research interest :
Inflammation, Oncology, CNS
□ Office address :
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Market Feasibility

□ Domestic and global market size:
- Global market for thrombocytopenia drugs were $1 billion in 2010

□ Domestic and foreign market opportunity (competitors and competing product) :
- Competing product: Promacta® (GSK) and Nplate® (Amgen)

Trend & Partnership

□ Future outlook and trends related to technology :
Oral administration of biologics

□ Technology Transfer and commercialization conditions :
Consultation(exclusive license or non-exclusive license)

□ Type of business relationship sought (including licensing availability) :
Co-development, or exclusive licensing agreement (both worldwide and regional) can be considered.

Technology Overview

■ Technology Platform

HanAll has developed a process and technique, Resistein™, involving the engineering of the native protein to significantly increase the half-life and bioavailability. Through its high throughput Resistein™ technology, parent molecules are modified by amino acid substitution to produce resistance to proteases in tissue, serum and GI track while maintaining or significantly improving their PK/PD profile. With molecules that are resistant to proteolysis, the goal is to produce the next generation of injectable proteins with superior efficacy and PK profiles compared to current proteins but also to develop the first generation of oral protein therapeutics.

The pharmacokinetic profile of protein therapeutics is highly related to protein stability. The stability of a protein *in vivo* is highly affected by proteolysis in tissue/blood and the digestive tract especially in the case of oral delivery. Proteolysis is a highly defined and structured process in which digestion occurs at a proteolysis trigger site(s), defined 'entry site(s)', on the protein and follows a specific pathway down to protein fragments. Amino acid substitution at the 'entry sites' may result in a protein's resistance to proteolytic degradation, without altering its biological activity. Thus, HanAll's proprietary process of 'domain engineering' and 'single point mutations at the entry sites' inhibits proteolysis and render bioavailability and orders of magnitude greater potency and longer half-life compared to native proteins when administered orally.

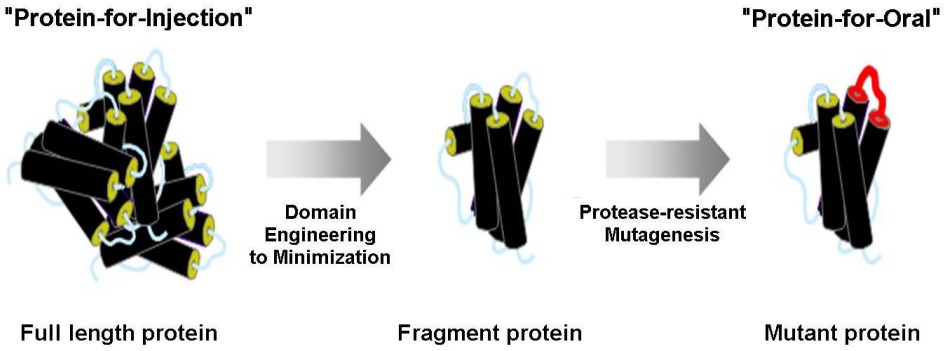

Fig. 1. HanAll BioPharma Resistein™ Technology

■ Background and unmet needs

Many companies have been trying to develop human thrombopoietin as an injectable form to find a cure for thrombocytopenia. However, since the needle-based delivery accompanies pain, infection, and other risk factors, alternative methods such as prolonged dosage interval or oral administration have been attempted. Increased stability of human thrombopoietin is prerequisite to meet these goals while the protease activity remains the major set back in solving the problems ahead. In this circumstance, one of the most important aim of developing oral therapeutic protein is to generate a protease resistant form of a protein with low molecular weight, and retaining its biological activity as well.

■ Discovery and Achievements

Modified TPO shows enhanced resistance to protease existing in serum and tissue and activates signal pathway for proliferation and differentiation of megakaryocytes through binding to c-mpl (TPO receptor).

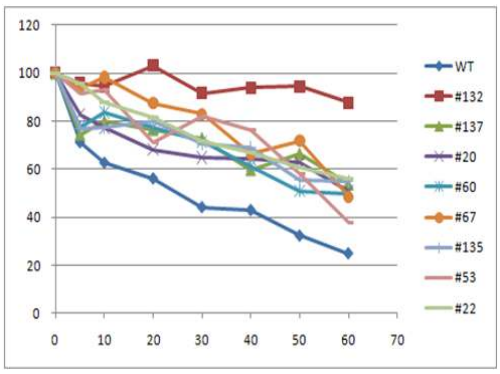

Fig. 2. Increased stability of modified TPO

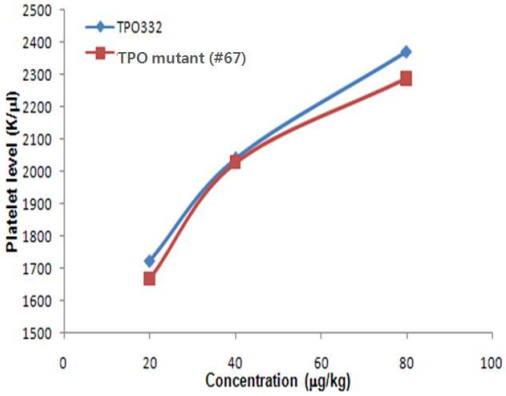

Fig. 3. Modified TPO activity for platelets proliferation

Table 1. Relative Protease Resistance of modified TPO

Mutant #	201	149	53	67	133	225	30	16	60	70
Relative Protease resistance	550%	522%	273%	185%	176%	165%	158%	155%	154%	152%

■ **Toxicological data**

N/A

Patents and Publications

Country	Appln. No.	Status	Description
Korea	10-01040396	Granted	The present invention provides a modified human thrombopoietin polypeptide fragment that has platelet proliferative activity *in vivo* and *in vitro* and enhanced resistance to protease existing *in vivo*.
US	13/145513	Pending	〃
Europe	10733639	Pending	〃

Contact Point

KHIDI (Korea Health Industry Development Institute) is currently receiving inquiries from interested parties in this transaction. If you are interested, please contact any of the KHIDI professionals below :

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