

PROHOST  FILTERMORE GOOD NEWS FOR THE HEART

Tackling news about drugs that help heart failure patients yesterday, we highlighted [CV THERAPEUTICS \(CVTX\)](#) combination treatment and [AMGEN'S \(AMGN\) Aranesp \(See Prohost Filter 9/6/05\)](#). Today, after scrutinizing data from **Protein Design's Labs (PDL)** phase 2 clinical study of **ularitide** (a synthetic version of a natriuretic peptide produced in the kidney known as urodilatin) as a potential treatment for patients with acute decompensated heart failure (ADHF) we developed a lot of optimism towards the product. The data from the **SIRIUS II trial** were presented at the annual European Society of Cardiology (ESC) Congress, the largest cardiology meeting in Stockholm, Sweden.

Ularitide is well-tolerated and indicate **clear, dose-dependent favorable effects in treating the symptoms of ADHF without compromising kidney function.**

The drug seems to have significantly improved **dyspnea** and significantly decreased **pulmonary pressure**, in addition to increasing **cardiac index** (a measure of heart function) in the 15 and 30 ng/kg/min groups.

**With regard to kidney**, serum creatinine levels **were unchanged** in patients treated with ularitide (elevation would have been bad news) compared to placebo through 72 hours. This finding suggests that ularitide did not negatively affect kidney function in study patients.

**Length of hospital stay** was lower for the 15 and 30 ng/kg/min groups, compared to the placebo and 7.5 ng/kg/min groups. The length of hospital stay was lowest for the 15 ng/kg/min (122 hours) and 30 ng/kg/min (158 hours) groups, compared to the placebo (200.5 hours) and 7.5 ng/kg/min (192 hours) groups.

There was **no increase in mortality** in the ularitide treatment groups compared to placebo. The **mortality rate** through day 30 was **higher in the placebo group** compared to the three ularitide groups:

The most frequent adverse event was hypotension, which occurred in 1.9% of placebo patients and in 8.3%, 11.3%, and 16.4% of patients in the 7.5, 15, and 30 ng/kg/min groups, respectively. Other adverse events that occurred in greater than 2% of the ularitide-treated patients were blood pressure decrease (5.4% ularitide vs. 0% placebo), cardiac failure (4.8% ularitide vs. 1.9% placebo), sweating increase (4.2% ularitide vs. 0% placebo), dizziness (3.6% ularitide vs. 1.9% placebo), and asthenia (2.4% ularitide vs. 0% placebo). The frequency of serious adverse events through day 30 was comparable among the groups.

SIRIUS II results will also be presented as a poster at the 9th Annual Scientific Meeting of the Heart Failure Society of America on September 19 in Boca Raton, Florida.

Protein Design holds exclusive development and marketing rights for ularitide for all indications worldwide. The company intends to file a U.S. IND later this year and to proceed with the global development of ularitide as a treatment for ADHF.

**Ularitide** is a synthetic form of urodilatin, which is a naturally occurring human protein that belongs to the family of

**natriuretic peptides** and is produced in the kidney where it regulates levels of fluid and sodium. Urodilatin is excreted into the urine and exists in low levels in the systemic blood circulation. The peptide was first isolated by scientists affiliated with the group of Wolf-Georg Forssmann at Heidelberg University, and has been developed by a German company, CardioPep Pharma GmbH.



*When injected into the blood stream, ularitide causes relaxation of blood vessels, specifically in the arteries that feed the kidneys, lungs and heart, and stimulates natriuresis (excretion of abnormal amounts of sodium into the urine) and diuresis (increase in urination). These effects suggest a potential therapeutic role for ularitide in patients with ADHF.*

***Congestive heart failure** is a serious chronic medical condition in which the heart is unable to maintain adequate circulation of blood in the tissues of the body or to pump out the venous blood returned to it by the venous circulation. In the advanced stages of heart failure, the heart is unable to meet the body's demand for oxygen and congestion or fluid retention can occur in the lungs and other areas throughout the body. Patients who experience a gradual or sudden worsening of CHF may experience severe symptoms resulting in ADHF. Patients with ADHF require emergency treatment and can require hospitalization.*

*ADHF can result from an acute event (e.g. heart attack, acute myocardial infarction). During an acute episode, the inability of the heart to adequately circulate blood throughout the body worsens, kidney function may be diminished and the patient may experience difficulty in breathing.*

**Good News?** You bet it is.

#### NOVARTIS ALNYLAM (ALNY) DEAL

*Boosts RNA-Specialized Firms, like **Sirna (RNAI)** and **Hybridon (HBY)***

**Novartis** AG decided to acquire nearly 20 percent of **Alnylam** Pharmaceuticals Inc., as part of a deal to develop drugs based on RNA technologies. Novartis will make an upfront payment of \$56.8 million, or \$11.11 per share, for about 4.2 million shares of Alnylam stock, in order to help Alnylam develop and market its RNA interference technology. The agreement also grants Novartis a non-exclusive option to use the technology in its own drug development program. RNA interference is a technology for selectively silencing disease-causing genes. The partnership lasts for an initial three-year period and has two one-year options.

If the collaboration is successful, Alnylam could stand to make up to \$700 million plus royalties from multiple products, Novartis said. The two companies will form an advisory group to guide the effort and map out an overall strategy for scientific and clinical applications of the partnership.

**Prohost Comments:** What Novartis wanted is the IRN interference technology and related technologies. As we reiterated, these technologies are evolutions over other technologies like antisense and ribozyme technologies. New discoveries of natural RNA interference, Toll-like receptors and other discoveries made this technology amenable to developing advanced, far-reaching treatments. The news boosted stocks of firms specialized in the RNA technology like Sirna (RNAI), Hybridon (HBY) and others that we mentioned in our Newsletters and Faxletters.

This technology is what **OSI (OSIP)** looked for and decided by acquiring **Eyetech (EYET)**, a move that angered some analysts and investors and made them sell OSI stock.

#### FIGHTING CANCER

#### HANA BIOSCIENCES (HANB)

Hana Biosciences initiated a Phase I IPdR clinical trial in **colorectal, gastric, pancreatic and liver cancers**. The objectives of this clinical trial are to establish the safety, dose and preliminary efficacy of IPdR in combination with radiation therapy. IPdR is a novel, orally available, **thymidine analogue** and prodrug for IUdR, which demonstrated a **survival advantage in Phase 2 studies** in anaplastic **astrocytoma**, a type of brain tumor. Preclinical studies have also demonstrated that IPdR has dose responsive and synergistic effects when combined with radiation in human **glioblastoma** models. IPdR has also shown superior safety and efficacy compared to IUdR in pre-clinical studies, with a significantly lower toxicity profile that includes less gastrointestinal and hematological side effects.



Hana Biosciences licensed IPdR from **Yale University** and The Research Foundation of the State University of New York at Buffalo. IPdR is initially being developed for the treatment of colorectal, gastric, liver, and pancreatic cancers. In addition, a Phase I/II clinical trial in **glioblastoma multiforme**, a type of brain cancer, is planned.

**"IPdR is a promising oral compound** that builds on the well-defined mechanism of action and proven utility of intravenously administered IudR.

**This is HANA's third drug to enter into development.**

**This is Good News.**

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