Hansa Medical

- PRESS RELEASE -
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Positive IdeS phase I data published in scientific journal PLOS ONE

Hansa Medical AB (publ) today announced that the results from the phase I trial of its candidate drug have been published in PLOS ONE (http://dx.plos.org/10.1371/journal.pone.0132011).

The trial was a first-in-man, double blind, randomized study with single-ascending doses of IdeS in twenty-nine healthy male subjects who were given intravenous doses of placebo or IdeS at 0.01, 0.04, 0.12 and 0.24 mg/kg body weight. IdeS was considered safe with no serious adverse events. Furthermore, IdeS converted plasma IgG into single cleaved IgG (scIgG) with impressive efficacy within minutes after administration.

ScIgG has compromised effector functions with reduced binding to Fcγ receptors and reduced Fc mediated cytotoxicity (Brezski *et al.*, 2009), i.e. the function of the antibodies is significantly reduced. Full or close to full effect on IgG, i.e. conversion into $F(ab')_2$ and Fc fragments (complete IgG cleavage), was seen in all subjects dosed with 0.12 and 0.24 mg/kg BW. IgG reached the lowest concentrations 2-24 hours after dosing and remained low for more than a week, until newly synthesized IgG appeared in the plasma.

Data demonstrated that the entire extracellular IgG pool and not only the plasma pool, is cleaved by IdeS. This remarkable efficacy of IdeS outcompetes the effect of plasma exchange, which typically leaves approximately 35% remaining IgG. Furthermore, 24 hours after a plasma exchange the IgG levels are restored to 60% (Ismail et al., 2001).

“A single dose of IdeS rapidly and efficiently inactivates IgG in humans, and the effect remains for several weeks. IdeS alone or in combination with B-cell attenuating drugs is a very attractive therapeutic approach for many IgG driven conditions. The results uncover a new therapeutic concept to eliminate pathogenic IgG”, commented Hansa Medicals CSO Christian Kjellman.

Since *S. pyogenes* is a common human pathogen, all subjects had pre-formed anti-IdeS IgG antibodies and reacted as expected with an IgG response peaking two to three weeks after the IdeS infusion. Six to twelve months after dosing, all subjects were back to normal anti-IdeS antibody levels. The half-life of IdeS was 4.9 (±2.8) hours at 0.24 mg/kg with the main fraction eliminated from plasma during 24 hours.

The complete, rapid, but temporary removal of IgG provides a new potent therapeutic opportunity in IgG-mediated pathogenic conditions. IdeS treatment has the capacity to quickly and effectively remove IgG in HLA sensitized transplantation patients, thereby allowing transplantation and avoiding acute antibody-mediated rejection. The safety and efficacy of IdeS in removing anti-HLA antibodies in sensitized dialysis patients are investigated in ongoing phase II studies. IdeS is currently also considered for clinical studies within several acute antibody mediated conditions, e.g. antibody mediated graft rejection, Guillain-Barré syndrome and Goodpasture’s syndrome.

Brezski RJ, Vafa O, Petrone D, Tam SH, Powers G, Ryan MH, et al. (2009) Tumor-associated and microbial proteases compromise host IgG effector functions by a single cleavage proximal to the hinge. Proc Natl Acad Sci U S A 106: 17864-17869.

Ismail N, Neyra R, Hakim R (2001) Plasmapheresis. In: Daugirdas JT, Blake PG, Ing TS, editors. Handbook of dialysis, 3rd edn. 3 ed. Philadelphia: Lippincott Williams Wilkins. pp. 231-262.

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About IdeS
IdeS, a unique molecule with a novel mechanism, is a bacterial enzyme that cleaves human IgG antibodies. IdeS aims to degrade immunoglobulin G (IgG) and has been tested for safety and efficacy in numerous *in vitro* and *in vivo* models. During 2013, a Phase I clinical trial on 29 healthy subjects was conducted, demonstrating IdeS as efficacious and well tolerated with a favourable safety profile. During 2014, a Phase II study in 8 sensitized patients awaiting kidney transplantation was conducted. Preliminary data show that IdeS is effective in reducing anti-HLA antibody levels in highly sensitized patients on the kidney transplant waitlist. The study shows that IdeS has the capacity to make sensitized patients eligible for transplantation by decreasing HLA antibodies to levels acceptable for transplantation. In addition to transplantation, IdeS has potential applications in a variety of rare autoimmune diseases. IdeS is protected by several patents and results of studies with IdeS have been published in a number of peer reviewed medical and scientific journals.

About Hansa Medical AB
Hansa Medical is a biopharmaceutical company focused on novel immunomodulatory enzymes. Lead project IdeS is an antibody-degrading enzyme in clinical development, with potential use in transplantation and rare autoimmune diseases. Other projects include HBP (a market introduced diagnostic marker for severe sepsis) and EndoS (an antibody-modulating bacterial enzyme in pre-clinical development). The company is based in Lund, Sweden. Hansa Medical's share (HMED) is listed on Nasdaq First North in Stockholm with Remium Nordic AB as Certified Adviser.

The information in this press release is disclosed pursuant to the Securities Markets Act or the Financial Instruments Trading Act. The information was released for public disclosure on July 16, 2015, at 08:00 CET.