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Merck KGaA, Darmstadt, Germany, Announces Initiation of Phase III Fertility Study with Pergoveris in Poor Ovarian Response Patients

- **The ESPART* Phase III clinical study focuses on patients that respond poorly to attempts at ovarian stimulation**
- **Study aims to recruit 946 patients across 17 European countries**

Darmstadt, Germany, March 27 – Merck KGaA, Darmstadt, Germany, the global pharmaceutical and chemical company, today announced the enrollment of the first patient into a new Phase III study in the area of fertility, marking another step in its efforts to explore innovative solutions in areas of unmet medical need.

The ESPART* study is designed to assess the efficacy and safety of Pergoveris® (follitropin alfa and lutropin alfa) versus GONAL-f® (follitropin alfa) for multifollicular development as part of an Assisted Reproductive Technology (ART) treatment cycle in women who are classified as poor ovarian responders (POR). Generally, in such patients, a low number of follicles develop during treatment, and, as a consequence, a small number of oocytes are retrieved through ART. The study aims to recruit 946 patients across 17 European countries. Pergoveris is a fixed combination of recombinant human follicle stimulating hormone (r-hFSH) and recombinant human luteinizing hormone (r-hLH) delivered via subcutaneous injection.

“The ESPART study is part of our ongoing commitment to working with fertility specialists to achieve the shared goal of increasing pregnancy rates and addressing the challenges that patients face in order to help them overcome the barriers to fertility,” said John Orloff, Head of Clinical Development of Merck KGaA, Darmstadt, Germany’s biopharmaceuticals

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division. “As a leader in reproductive health we hope that it will help us understand how to better address the challenges faced by women with poor ovarian response.”

Merck KGaA, Darmstadt, Germany has committed itself to finding innovative solutions to develop the next generation of fertility treatments. More than 72.4 million people are affected by infertility worldwide[1] and, according to the World Health Organization (WHO),[2] 15 percent of couples of childbearing age seek medical help for infertility. Infertility is one of the main focus areas and an important growth driver for the company’s largest division.

“A current trend in society is for women to delay pregnancy until later in their life and, as a consequence, women may face lower chances of pregnancy due to the reduced quantity and quality of oocytes in their ovaries, thus new treatment options are needed in fertility to maximize the chances of success,” said Professor Peter Humaidan, Aarhus University, Skive, Denmark, principal investigator of ESPART. “With the ESPART study we hope to gain clarity if poor ovarian responders would benefit from the addition of recombinant LH in the protocols of stimulation, to ultimately achieve higher pregnancy rates.”

The ESPART Phase III multicenter, randomized, controlled, single-blind trial compares Pergoveris versus GONAL-f in patients who are classified as POR, as aligned with the outcomes of the 2011 Consensus Meeting of the European Society of Human Reproduction and Embryology (ESHRE).[3] The primary endpoint of the ESPART study is total number of retrieved oocytes. Secondary endpoints include ongoing pregnancy rate, live birth rate, embryo implantation rate, clinical pregnancy rate and biochemical pregnancy rate. The design of this trial is supported by the outcomes of a meta-analysis published last month by Lehert and colleagues in the journal *Reproductive Biology and Endocrinology*.[4] This analysis suggests that the combination of r-hFSH plus r-hLH during ovarian stimulation might offer a benefit to a certain subgroup of patients who are classified as POR.

The Lehert meta-analysis reviewed data from 43 randomized controlled trials, investigating 6443 patients. The results of this meta-analysis showed no significant differences in the number of oocytes retrieved for the overall patient population, between the r-hFSH plus r-

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hLH and r-hFSH groups (weighted mean difference −0.03; 95% confidence interval [CI] −0.41 to 0.34). However, in POR patients treated with r-hFSH plus r-hLH, significantly more oocytes were retrieved than with r-hFSH alone (n = 1077; weighted mean difference +0.75 oocytes; 95% CI 0.14–1.36). Additionally, a significantly higher clinical pregnancy rate was observed with r-hFSH plus r-hLH versus r-hFSH alone, not only in the overall patient population analysed (risk ratio [RR] 1.09; 95% CI 1.01–1.18) but also in POR patients, where these differences were even more pronounced (n = 1179; RR 1.30; 95% CI 1.01–1.67; ITT population).[4]

*ESPART: Evaluating the **E**fficacy and **S**afety of **P**ergoveris® in **ART**

About Pergoveris
Pergoveris® is the first combined product of recombinant human follicle stimulating hormone (r-hFSH or follitropin alfa 150 IU) and recombinant human luteinizing hormone (r-hLH or lutropin alfa 75 IU). It is unique by combining the benefits of two consistent and pure recombinant products, r-hFSH and r-hLH for the treatment of infertility in specific indications. Pergoveris is indicated for the stimulation of follicular development in adult women with severe luteinizing hormone (LH) and follicle stimulating hormone (FSH) deficiency.

The ESPART study is a Phase III multicenter, randomized, controlled, single-blind, parallel arm trial, designed to assess the efficacy and safety of Pergoveris versus GONAL-f® (follitropin alfa) for multifollicular development as part of an ART treatment cycle in patients who are poor ovarian responders, aligned with the European Society of Human Reproduction and Embryology (ESHRE) criteria. The study's primary endpoint is total number of retrieved oocytes.

About GONAL-f
GONAL-f® a recombinant human follicle stimulating hormone, r-hFSH, follitropin alfa, is used to substitute or enhance low or lacking naturally occurring FSH causing female and male infertility. GONAL-f pens are filled by mass (FbM), which ensures consistency in the FSH dosage.

References
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About Merck KGaA, Darmstadt, Germany

Merck KGaA of Darmstadt, Germany, is a leading company for innovative and top-quality high-tech products in the pharmaceutical and chemical sectors. Its subsidiaries in Canada and the United States operate under the umbrella brand EMD. Around 38,000 employees work in 66 countries to improve the quality of life for patients, to further the success of customers and to help meet global challenges. The company generated total revenues of € 11.1 billion in 2013 with its four divisions: Biopharmaceuticals, Consumer Health, Performance Materials and Life Science Tools. Merck KGaA of Darmstadt, Germany is the world's oldest pharmaceutical and chemical company – since 1668, the name has stood for innovation, business success and responsible entrepreneurship. Holding an approximately 70 percent interest, the founding family remains the majority owner of the company to this day.