

PRESS RELEASE

Dutch BioTech Pantarhei Bioscience's success with new drug in Canada *Approval by Health Canada of a new oral contraceptive with the "forgotten" estrogen Estetrol*

Zeist, 22 March 2021 – Pantarhei Bioscience announces that Canada is the first country in the world to have approved the natural pregnancy estrogen Estetrol (E4) for use in the oral contraceptive Estelle®. The development of this new pill represents a joint effort between Pantarhei Bioscience and Mithra Pharmaceuticals in Belgium.

The Canadian Regulatory Agency "Health Canada" has approved the oral contraceptive Estelle®, containing the new estrogen Estetrol (E4), confirming that Estelle® complies with the strict demands of this Agency. In two phase III studies, performed by Mithra in more than 3,800 women, favorable effects of Estelle® were demonstrated on efficacy, safety, menstrual cycle regulation and tolerance. Estelle® is composed of 15 mg E4 and 3 mg of the progestin drospirenone. Estetrol is a natural estrogen, synthesized in considerable amounts by the human fetal liver during pregnancy, causing high concentrations in the blood of the fetus and the mother. The E4 in Estelle® is synthesized from plant precursors.

Estetrol was a "forgotten" hormone, discovered in 1965 by Egon Diczfalusy at the Karolinska Institute in Stockholm, Sweden and rediscovered by Herjan Coelingh Bennink, who founded Pantarhei Bioscience in 2000 to develop E4 for oral contraception (OC) and menopausal hormone therapy (MHT). Since 2001 Pantarhei has performed extensive preclinical and pharmacological studies with E4, followed by phase I and II clinical studies in female volunteers, focusing on safety, efficacy and dose-finding. As well as having a high oral bioavailability of 80%, E4 has less of an effect on liver function and blood coagulation factors compared to other natural and synthetic estrogens, suggesting better safety. In 2015 Pantarhei Bioscience sold the E4 portfolio to Mithra for further OC and MHT development and founded Pantarhei Oncology for the development of oncological applications of E4, especially for advanced breast and prostate cancer.

Herjan Coelingh Bennink, Founder and President of Pantarhei Bioscience stated: "We are very pleased with this decision by Health Canada. This is a first, major and important step for the introduction of the new estrogen E4 as a safe and effective new drug for human use. Experts in hormonal contraception, including Prof Carolyn L. Westhoff (Columbia University, NY, USA and Editor-in-Chief of Contraception) and Prof Kristina Gemzell-Danielsson (the WHO-Collaborating Centre for Research in Human Reproduction, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden), have expressed their scientific support for this new OC concept. At Pantarhei Oncology, we hope to be able to demonstrate the advantages of E4 for the treatment of advanced breast and prostate cancer in the near future. Studies with high dose E4 (HDE4) have already demonstrated "proof-of-concept" for both applications".

About Pantarhei

Founded in 2001 by the former Director R&D "Women's Health" (WH) of Organon, Herjan Coelingh Bennink, Pantarhei Bioscience and Pantarhei Oncology are Dutch Biopharmaceutical companies, developing unique and innovative, patent protected, new treatment concepts in the areas of WH and "Reproductive Endocrine Oncology" until "proof-of-concept" phase II in humans. All research and development activities are outsourced, creating virtual companies. At present Pantarhei Oncology is focusing on the further development of HDE4, conducting phase II (breast cancer) and phase III (prostate cancer) trials.

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