

FACT SHEET

ANDROGEN RESTORED CONTRACEPTIVE

Pantarhei Bioscience B.V. is an emerging specialty pharmaceutical company with a creative approach towards drug development. The Company is focused on developing innovative, proprietary therapeutic approaches for a variety of gender-related disorders. Within these disease areas, Pantarhei has generated product opportunities based on its unique ability to identify (novel) medical uses for endogenous human biologicals and/or (combinations of) existing drugs.

Pantarhei's approach:

- *Identify novel product concepts;*
- *Evaluate the product concept potential and prioritize;*
- *Seek patent protection;*
- *Conduct pre-clinical proof-of-concept studies;*
- *Select products with the greatest potential for commercial development;*
- *Establish proof-of-concept in man;*
- *Partner with a (bio)pharmaceutical company for the final stages of development and commercialization of its product candidates.*

Pantarhei believes that its differentiating approach towards drug development allows it to strongly benefit from the following key risk-reducing elements:

- *Pharmacology of the basic compound is already well-understood;*
- *Toxicity and safety risk is minimized;*
- *Clinical proof-of-concept can be established at an early stage;*
- *Clinical and regulatory pathways are simplified and relatively short;*
- *The active pharmaceutical ingredient is either available or can be manufactured quickly.*

Androgen restored contraceptive is a novel concept for oral contraception. By adding the natural human androgen dehydroepiandrosterone (DHEA) to an oral contraceptive (OC) subjective side effects frequently caused by OC's as mood changes, decrease of sexual desire and risk of venous thromboembolic events (and even the rare pulmonary embolism) are anticipated to be minimized.

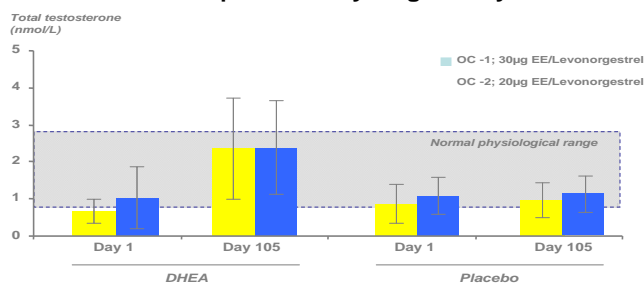
A-OC / Triple OC Development Rationale

- **Concept: a Combined Oral Contraceptive with an androgen**
- Pill use reduces ovarian Testosterone (T) synthesis and levels up to 50%, causing T deficiency in a significant number (30-50%) of pill users
- Pill use increases SHBG, which binds and inactivates about 40% of circulating T
- Clinical consequences may be a.o. sexual dysfunction, mood changes, loss of muscle and bone mass and strength and low T may be related to the increased risk of VTE during the pill
- Pills with an anti-androgenic progestogen (cyproterone-acetate, drospirenone) maybe even worse



A-OC / Triple OC Data

- **Increased testosterone levels after intake of DHEA plus an oral contraceptive in 138 young healthy women**



A-OC / Triple OC Concept support / dose finding DHEA studies

- Addition of a suitable formulation and dose of DHEA normalizes T-levels during OC use and is expected to counteract the clinical consequences of T-deficiency
- Preferred progestogen: drospirenone (Yasmin)
Anti-androgenic and market leader
- Studies in women with decreased T-levels during the pill are ongoing:
 - Sexual function: Dr. van Lunsen, Amsterdam, the Netherlands
 - Dinox, Groningen, the Netherlands
 - Mood changes: Prof. Foidart, Liege, Belgium
 - Biochemical parameters: Prof. Klufft, Leiden, the Netherlands (planned)

