Joint Press Release

# NEXTSTELLIS® RECEIVES FDA MARKETING EXCLUSIVITY AND PHASE III DATA PUBLISHED

**27 May 2021, Adelaide, Australia and Liege, Belgium:** Mayne Pharma Group Limited (ASX: MYX) and Mithra Pharmaceuticals, SA (Euronext Brussels: MITRA) are very pleased to announce that the novel oral contraceptive NEXTSTELLIS® (3 mg drospirenone and 14.2 mg estetrol (E4) tablets) has been granted marketing exclusivity as a new chemical entity (NCE) from the US Food and Drug Administration (FDA). The exclusivity runs for five years from FDA approval of the New Drug Application for NEXTSTELLIS.

NEXTSTELLIS was approved by the FDA in April 2021 and is the first and only pill containing E4, a natural estrogen produced during pregnancy that is now made from a plant source. E4 is the first new estrogen introduced in the US in more than 50 years.

A new article has been published in *Contraception* – an international, peer-reviewed reproductive health journal - with the results of the NEXTSTELLIS North American Phase III clinical study involving nearly 2,000 women. The publication concluded that NEXTSTELLIS is an effective oral contraceptive with a predictable bleeding pattern for most women and a low rate of adverse events.

In addition to efficacy and safety, a predictable bleeding pattern is another key consideration for women and their healthcare providers. Bothersome breakthrough bleeding is a common side effect of hormonal contraception and can often lead to discontinuation of contraceptives. Unscheduled bleeding occurred in less than 2% of patients after cycle 2 (bleeding only) with less than 1 day of unscheduled bleeding or spotting on average per cycle after cycle 1.

"NEXTSTELLIS demonstrated contraceptive efficacy regardless of age or contraceptive history with low adverse events and favourable body-weight control. Most noticeable was the lack of venous thromboembolic (VTE) events among the 1,864 women who participated in this study[1]," **said Dr. Mitchell Creinin, M.D., Professor and Director of Family Planning at the University of California, Davis**. "For women taking birth control, unscheduled bleeding is one of the main reasons cited for stopping or switching to an alternate contraceptive. The bleeding pattern seen with NEXTSTELLIS was regular and predictable for most women - with low rates of unscheduled bleeding even at cycle 1 - providing clinicians with another important option when patients are concerned about breakthrough bleeding."

**Mayne Pharma's CEO, Mr. Scott Richards said**, "We are pleased to see the clinical trial results for NEXTSTELLIS being reported in the renowned journal *Contraception*. This data validates NEXTSTELLIS as being a new and innovative oral contraceptive which is safe and effective and that combines a natural estrogen (E4) with selective tissue actions together with the proven progestin drospirenone. Women now have the option of using a contraceptive pill that offers the anti-androgenic, anti-mineralocorticoid, and long half-life

[1] Large phase 4 studies will be needed to confirm the phase 3 findings that suggest NEXTSTELLIS use is associated with low clinical thrombosis risk.

benefits of drospirenone together with an estrogen that also has a long half-life and has a low impact on hemostasis and endocrine biomarkers, as well as on lipids, and glucose[2]"

**Mithra's CEO Mr. Leon Van Rompay said**, "The publication of these pivotal data is a testament to the extraordinary efforts of the Mithra team to develop a novel and effective contraceptive with a favourable safety profile. Sharing this data in a renowned peer-reviewed journal ensures clinicians have the most comprehensive information about NEXTSTELLIS and underlines our commitment to transparency and scientific rigor."

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**About NEXTSTELLIS®**
Developed by Mithra, NEXTSTELLIS is a novel, patent-protected combined oral contraceptive pill containing 3 mg drospirenone (DRSP) and 14.2 mg estetrol (E4). E4 is an estrogen naturally produced during pregnancy, which can now be made from a plant source. In two phase 3 clinical studies conducted in 3,725 women, NEXTSTELLIS was shown to be both safe and effective and met its primary efficacy endpoint of pregnancy prevention. It also met a variety of secondary endpoints that demonstrated favourable cycle control, bleeding pattern, safety, and tolerability.

Mayne Pharma has a 20-year exclusive license and supply agreement in the US and Australia for NEXTSTELLIS. The product has not yet been approved in Australia but is under review at the Australian Therapeutics Goods Administration (TGA). The full US prescribing information for NEXTSTELLIS can be found here.

**North American (US and Canada) phase III study**
The multicenter, open-label, phase III trial of NEXTSTELLIS enrolled 2,148 healthy participants, of whom 1,864 started the study drug, aged 16-50 years, with a body mass index (BMI) ≤35 kg/m$^2$. In a subset of 1,674 participants, aged 16 to 35 years, the contraceptive efficacy and bleeding pattern of NEXTSTELLIS were evaluated[3].

Women 16-35 years had a PI of 2.65 (95% CI 1.73-3.88), method-failure PI of 1.43 (95% CI 0.7-2.39) and 13-cycle life-table pregnancy rate of 2.1%. Scheduled bleeding occurred in 82.9% to 87.0% of women per cycle with a median duration of 4.5 days. Unscheduled bleeding and spotting decreased from 30.3% in Cycle 1 to 21.3-22.1% during Cycles 2-4 and remained stable (15.5-19.2%) thereafter through 12 cycles of use. The most frequently reported AEs that were unrelated to bleeding were mood disturbance (10.9%), breast symptoms (5.3%), and headache (4.8%). One-hundred thirty-two (7.1%) women discontinued the study early for an AE, most commonly for metrorrhagia (0.9%) and menorrhagia (0.8%). No thromboembolic events occurred.

The link to the *Contraception* article can be found here.

[2] Mawet M, et al. Eu J Contra Rep Hlth Care. 2015; 20, 463-475; Douxfils, J et al. Contraception. 2020; 102, 396-402; Klipping C et al. Contraception. 2021; 103, 213-221
[3] ClinicalTrials.gov Identifier: NCT02817841

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*Authorised for release to the ASX by the Chairman*

## About Mayne Pharma

*Mayne Pharma is an ASX-listed specialty pharmaceutical company focused on applying its drug delivery expertise to commercialise branded and generic pharmaceuticals, offering patients better, safe and more accessible medicines. Mayne Pharma also provides contract development and manufacturing services to more than 100 clients worldwide.*

*Mayne Pharma has a 40-year track record of innovation and success in developing new oral drug delivery systems and these technologies have been successfully commercialised in numerous products that continue to be marketed around the world.*

*Mayne Pharma has two facilities based in Salisbury, Australia and Greenville, USA with expertise in the formulation of complex oral and topical dose forms including potent compounds, modified-release products and poorly soluble compounds.*

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## About Mithra

*Mithra (Euronext: MITRA) is a Belgian biotech company dedicated to transforming Women's Health by offering new choices through innovation, with a particular focus on contraception and menopause. Mithra's goal is to develop products offering better efficacy, safety and convenience, meeting women's needs throughout their life span. Mithra explores the potential of the unique native estrogen Estetrol in a wide range of applications in women health and beyond (Covid-19, neuroprotection…). Mithra also develops and manufactures complex therapeutics in the areas of contraception, menopause and hormone-dependent cancers. It offers partners a complete spectrum of research, development and specialist manufacturing at its technological platform Mithra CDMO. Active in more than 100 countries around the world, Mithra has an approximate headcount of 300 staff members and is headquartered in Liège, Belgium. www.mithra.com*

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