European Commission approves Esmya® for the pre-operative treatment of uterine fibroids (myomas)

Budapest, Hungary – 27 February 2012 – Gedeon Richter Plc. ("Richter") announces today that the European Commission (EC) has granted marketing authorization to Esmya® 5mg tablet as pre-operative treatment of moderate to severe symptoms of uterine fibroids.

This decision follows positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) on

16 December 2011 and is applicable for all Member States in the European Union.

- Ulipristal acetate controlled bleeding in over 90% of patients.

- Excessive bleeding was controlled significantly more rapidly with ulipristal acetate than with leuprolide acetate.

- Ulipristal acetate significantly reduced fibroid size and for patients who did not undergo surgery, the volume reduction was maintained for at least 6 months after treatment is discontinued.

The approval is based on the assessment of extensive pre-clinical data, quality data, and clinical data involving 498 subjects treated with Esmya®, which include data from the two Phase III pivotal clinical studies, PEARL I and PEARL II.

"This approval is a result of outstanding work done by our PregLem team. We are delighted to bring the benefits of Esmya® to patients and physicians in the EU in need of highly effective and convenient therapy for women suffering from uterine fibroids, ", said Erik Bogsch, Managing Director of Gedeon Richter Plc. "We remain committed to the development of female healthcare products which improve quality of life for the female population in all age groups."

"Today's approval of Esmya® means that thousands of patients suffering from fibroids across Europe will now have a new targeted approach for medical treatment of these benign tumours. Esmya® offers an effective and well-tolerated therapeutic option, while avoiding the drawbacks of currently available therapies", said Dr. Ernest Loumaye, Chief Executive Officer of PregLem.

"PEARL I and II clinical studies showed the benefits of Esmya® as a pre-surgical treatment for uterine fibroids in the rapid control of bleeding and reduction in fibroid size. These will help patients to be in a better condition for the surgery and possibly have a minimal invasive surgery" added Prof. Jacques Donnez, lead investigator in PEARL I and II.

About uterine fibroids

Uterine fibroids are the most common benign, solid tumours of the female genital tract, affecting between 20 and 25% of women of reproductive age. It is estimated that about 300,000 surgical procedures are performed annually in the EU for uterine fibroids, including approximately 230,000 hysterectomies. The condition is characterized by excessive uterine bleeding, anaemia, pain, frequent urination or incontinence, and infertility. So far, GnRH agonists were the only approved pre-operative treatment for uterine fibroids and their use has been relatively limited due to side effects resulting from the suppression of oestrogen to post-menopausal levels (hot flashes, depression, mood swings, loss of libido, vaginitis and loss of bone mineral density).

About Esmya®

Esmya® 5mg tablet containing ulipristal acetate is a first-in-class, orally active, selective progesterone receptor modulator. It reversibly blocks the progesterone receptors in target tissues. As recently published in the New England Journal of Medicine 1, 2, 3, the 12 weeks once-a-day oral therapy (vs. injectable GnRH agonist) is effective to stop uterine bleeding, correct anaemia and shrink fibroid volume. It improves quality of life and has no castration side effects unlike GnRH agonists. There are no data available on treatment with duration longer than 3 months.

About the pivotal studies

PEARL I, a randomized, parallel-group, double-blind, placebo-controlled, phase III trial showed:

- Uterine bleeding was controlled in 91% of the women receiving ulipristal acetate 5 mg and in 92% of those receiving ulipristal acetate 10 mg, and 19% of those receiving placebo ($P<0.001$).

- The rates of amenorrhea were 73%, 82%, and 6%, respectively, with amenorrhea occurring within 10 days in the majority of patients receiving ulipristal acetate.

- The median changes in total fibroid volume were −21%, −12%, and +3% ($P = 0.002$ ulipristal acetate 5 mg vs. placebo, and $P = 0.006$ ulipristal acetate 10 mg vs. placebo).

- As compared with placebo, both doses of ulipristal acetate led to reductions in pain (especially moderate or severe pain), as measured with the Short-Form McGill Pain Questionnaire.

- Ulipristal acetate induced benign histologic endometrial changes that had resolved by 6 months after the end of therapy.

- The rate of the occurrence of any adverse events did not differ significantly among the three groups. Headache and breast tenderness were the most common adverse events associated with ulipristal acetate but did not occur significantly more frequently than with placebo.

PEARL II, a double-blind, double-dummy, phase III trial comparing ulipristal acetate versus the injectable GnRH agonist (leuprolide acetate) showed:

- Uterine bleeding was controlled in 90% of patients receiving ulipristal acetate 5 mg and in 98% of those receiving ulipristal acetate 10 mg, and in 89% of those receiving leuprolide acetate.

- Excessive bleeding control was demonstrated with statistical significance to be more rapid in patients receiving either ulipristal acetate 5 mg or ulipristal acetate 10 mg, than in those receiving leuprolide acetate.

- Median times to amenorrhea were 7 days for patients receiving ulipristal acetate 5 mg, 5 days for those receiving ulipristal acetate 10 mg, and 21 days for those receiving leuprolide acetate.

- All treatments reduced the volume of the three largest fibroids, with median reductions at week 13 of 36% in the group receiving ulipristal acetate 5 mg, 42% in the group receiving ulipristal acetate 10 mg, and 53% in the group receiving leuprolide acetate.

- For patients who did not undergo hysterectomy or myomectomy, ulipristal acetate showed a more sustained effect on the reduction of fibroids volume during the 6 months follow up without treatment than did leuprolide acetate.

- Moderate-to-severe hot flashes were reported for 11% of patients receiving ulipristal acetate 5 mg, for 10% of those receiving ulipristal acetate 10 mg and for 40% of those receiving leuprolide acetate ($P<0.001$ for each dose of ulipristal acetate vs. leuprolide acetate).

- There were no significant differences between the ulipristal acetate groups and the leuprolide acetate group in the proportion of patients reporting other adverse events or discontinuing treatment because of adverse events.

About Richter

Gedeon Richter Plc. (www.richter.hu) headquartered in Budapest/Hungary, is a major pharmaceutical company in Hungary and one of the largest in Central Eastern Europe, with an expanding direct presence in Western Europe in the field of gynaecology. Richter's consolidated sales was approximately EUR 1.1 billion (USD 1.5 billion) while its market

capitalization amounted to EUR 2.1 billion (USD 2.7 billion) in 2011. The product portfolio of the Company covers almost all important therapeutic areas, including gynaecology, central nervous system and cardiovascular. The Company has the largest R&D unit in Central Eastern Europe. Original research activity focuses on CNS disorders with main clinical targets being schizophrenia, anxiety, chronic pain and depression. With its widely acknowledged steroid chemistry expertise Richter is also a significant player in the female healthcare field worldwide.

PregLem SA (www.preglem.com), the wholly owned subsidiary of Richter, is a Swiss speciality biopharmaceutical company, based in Geneva, dedicated to the development and commercialization of a new class of drugs for women's reproductive health conditions. PregLem has an experienced senior management team, with a proven track record in developing, registering and commercializing reproductive health products.

1. Donnez J. et al. N Engl J Med. 2012 Feb 2; 366(5): 409-420

2. Donnez J. et al. N Engl J Med. 2012 Feb 2; 366(5): 421-432

3. Stewart EA. N Engl J Med. 2012 Feb 2; 366(5): 471-473

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