Full Results of PEARL IV Study presented at the European Society of Gynaecological Endoscopy (ESGE) congress confirms the efficacy of ulipristal acetate 5 mg for the long term management of uterine fibroids

Budapest, 12 October 2015 – Gedeon Richter Plc. (“Richter”) announces results of the PEARL IV study at ESGE. PEARL IV was a Phase III, randomized, double-blind, parallel group study investigating the efficacy and safety of repeated 3 months treatment courses of daily 5mg or 10mg\textsuperscript{a} ulipristal acetate (UPA) for the long-term management of symptomatic uterine fibroids, characterized by heavy bleeding.\textsuperscript{1} The study, which investigated 4 treatment courses in patients across 46 European centres in 11 countries, showed:

- Approximately 93\%\textsuperscript{b} of women or greater achieved controlled bleeding at the end of each treatment course and at least 76\%\textsuperscript{c} of women were in amenorrhoea\textsuperscript{d} at the end of each treatment courses
- There was a 67\% median reduction in fibroid volume at the end of treatment course\textsuperscript{4}\textsuperscript{e}
- 65.5\%, 73.5\%, 74.7\% and 78.1\% of patients had clinically significant reduction of the three largest fibroids (i.e. ≥ 25\% reduction) after each consecutive treatment course\textsuperscript{1} with UPA 5mg (4 courses in total)
- 73.5\% of women experienced both amenorrhea and clinically significant fibroid reduction (≥ 25\%) with 4 repeated courses
- The use of ulipristal acetate showed an improvement in quality of life (QoL) and pain which was maintained during the off treatment intervals
- The safety profile for UPA in this trial confirmed the previously reported safety profile. The vast majority of AEs (97.6\%) were of mild or moderate severity in both groups\textsuperscript{9}
- Hot flushes and headaches were the most frequently reported adverse reactions. (pooled 5 and 10 mg: Headache, ≤ 4.4\% for any treatment course; hot flush, ≤ 5.8 \% any treatment course)\textsuperscript{9}

"The PEARL IV data show that ulipristal acetate 5mg is an effective and well-tolerated treatment for the long-term management of uterine fibroids."

said Erik Bogsch, Managing

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\textsuperscript{a} Please note that the 10mg dose is not licensed
\textsuperscript{b} Data from per protocol 4 (PP4) population, where subjects had started and received at least 56 days of medication in the 4th treatment course
\textsuperscript{c} Data from PP4 population
\textsuperscript{d} Defined as no more than 1 day of spotting within a 35-day interval
\textsuperscript{e} Data from PP4 population
\textsuperscript{f} Data from PP4 population, based on data recorded after each treatment course plus 1 bleed
\textsuperscript{g} Data from PEARL IV safety population
Director of Gedeon Richter Plc. “At Gedeon Richter we are committed to women’s health and developing products that will enhance their quality of life and safeguard their fertility.”

“Unfortunately, uterine fibroids can have a serious impact on the physical and emotional wellbeing of women, and this has been made worse by the limited options that have been available to them in the past. I welcome the findings of all the PEARL studies, and particularly the PEARL IV study, demonstrating that ulipristal acetate 5mg is a well-tolerated and effective long term option for the management of uterine fibroids,” said Prof. Jacques Donnez, lead investigator in PEARL I and II and lead author of the NEJM articles.

“Women that have been diagnosed with uterine fibroids in the past often felt bewildered due to the lack of options available to them, especially when faced with extreme options such as a hysterectomy”, said Deborah Lancastle, Health Psychologist at the University of Wales, United Kingdom. “Providing women with a variety of treatment options, including a long-term management option that doesn’t involve surgery, will be a relief.”

The initial Marketing Authorization for UPA 5mg was granted in 2012 for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The new indication allowing intermittent medical treatment of the moderate to severe symptoms of uterine fibroids with UPA 5mg, was granted in May 2015 and provides an important opportunity for many women suffering from this condition to potentially avoid surgical interventions.

The PEARL IV study confirmed the efficacy and safety of repeated intermittent use of UPA, and the final results also confirmed already published data from previous Phase III studies (PEARL III and its extension and PEARL IV Part 1).

The full UPA 5mg tablets product information containing the revised SmPC is publicly available both in the registers of the European Commission / European Medicines Agency and of the National Institute of Pharmacy and Nutrition Register in Hungary together with their respective online sites: www.ema.europa.eu and www.ogyei.gov.hu.

About uterine fibroids
Uterine fibroids are the most common benign, solid tumours of the female genital tract, affecting between 20% and 40% of women of reproductive age. The condition is characterized by excessive uterine bleeding, anaemia, pain, frequent urination or incontinence, and infertility. Uterine fibroids are commonly treated surgically. Symptomatic uterine fibroids are the leading reason for hysterectomy. It is estimated that about 300,000 surgical procedures are performed annually in the EU for uterine fibroids, including approximately 230,000 hysterectomies. Available treatments were limited to short-term pre-operative use and comprised of either ulipristal acetate (Esmya) or gonadotropin releasing hormone (GnRH) agonists. Surgery may not be a suitable option for all patients, e.g. for medical or personal reasons or if the woman would rather wait for the symptoms of uterine fibroids to decrease as result of menopause. Thus, there was a medical need for a long-term medical treatment of fibroids.

About Esmya® (ulipristal acetate)
Esmya® 5mg tablets containing ulipristal acetate is an orally active, selective progesterone receptor modulator characterised by a tissue specific mixed progesterone antagonist/agonist effect. It reversibly blocks the progesterone receptors in target tissues. As previously

Esmya 5 mg tablets are indicated for pre-operative and intermittent treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age
published in the New England Journal of Medicine\textsuperscript{5-7} the short term treatment with Esmya\textsuperscript{®} 5mg proved to be effective to stop uterine bleeding, correct anaemia and shrink fibroid volume. Recently published data\textsuperscript{3,4} confirmed the efficacy and safety of repeated intermittent use of Esmya\textsuperscript{®} 5mg in long term management of uterine fibroids allowing the European Commission approval of Esmya for intermittent treatment in May 2015.

About Richter
Gedeon Richter Plc. (www.richter.hu), headquartered in Budapest/Hungary, is a major pharmaceutical company in Central Eastern Europe, with an expanding direct presence in Western Europe. Richter’s consolidated sales were approximately EUR 1.1 billion (US$ 1.5 billion), while its market capitalization amounted to EUR 2.1 billion (US$ 2.5 billion) in 2014. The product portfolio of Richter covers almost all important therapeutic areas, including gynaecology, central nervous system, and cardiovascular areas. Having the largest R&D unit in Central Eastern Europe, Richter’s original research activity focuses on CNS disorders. With its widely acknowledged steroid chemistry expertise, Richter is a significant player in the female healthcare field worldwide. Richter is also active in biosimilar product development.

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\textsuperscript{1} Donnez J, et al. Fertil Steril “in-press”