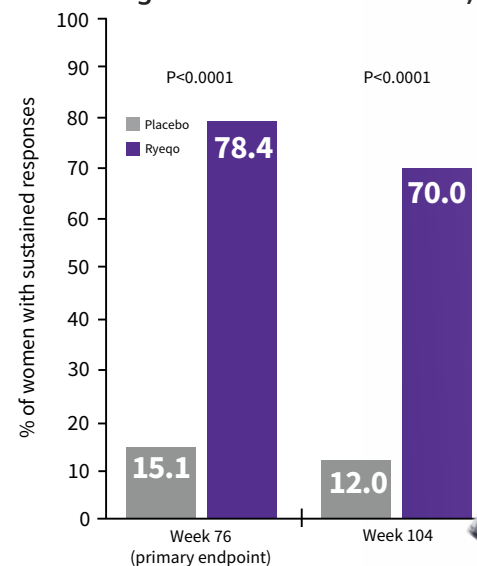


SHE NEEDS LONG-TERM EFFICACY

Ryeqo maintains long-term reduction in MBL¹

% sustained response rate (MBL <80ml through Week 76 and Week 104)



- With Ryeqo, all patient groups showed significantly greater maintenance of response vs placebo¹
- Significant sustained response rate maintained at Week 104¹

Control the distressing symptoms for the long-term, and improve her quality of life¹

PROVEN LONG-TERM EFFICACY AND SAFETY THAT IS DESIGNED TO FIT INTO HER BUSY LIFESTYLE

Robust LIBERTY trial programme over 104 weeks that proves Ryeqo^{1,5}:

- ✔ Maintains long-term reduction in MBL
- ✔ Reduces long-term risk of relapse in HMB
- ✔ Preserves bone health with an established safety profile comparable to placebo

Medicinal Product
Ryeqo belongs to the class of pituitary and hypothalamic hormones and analogues, anti-gonadotrophin-releasing hormones, ATC code: H01DC54. Each film-coated tablet contains 40 mg relugolix, 1 mg estradiol (as hemihydrate), and 0.5 mg norethisterone acetate. The main excipients are: Lactose monohydrate (approximately 80 mg, Mannitol (E421), Sodium starch glycolate, Hydroxypropylcellulose (E463), Magnesium stearate (E572), Hypromellose type 2910 (E464), Titanium dioxide (E171), Triacetin (E1518), Iron oxide yellow (E172). **Therapeutic Indication** Ryeqo is indicated for treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. **Posology and Method of Administration** One tablet of Ryeqo must be taken once daily, and the first tablet must be taken within 5 days of the onset of menstrual bleeding. Pregnancy must be ruled out prior to initiating treatment with Ryeqo. Ryeqo can be taken without interruption but a dual X-ray absorptiometry (DXA) scan is recommended after 1 year of treatment. **Contraceptive properties of Ryeqo** A nonhormonal contraceptive method is recommended for use for 1 month after initiation of treatment and for 7 days following 2 or more missed consecutive doses; hormonal contraceptives are contraindicated. Ryeqo inhibits ovulation if taken correctly and provides adequate contraception. **Special Populations** No dose adjustment for Ryeqo is required in patients with mild, moderate, or severe renal impairment or in patients with mild or moderate hepatic impairment, however Ryeqo is contraindicated in women with severe liver disease if liver function values have not returned to normal. **Contraindications** Ryeqo is contraindicated in women with any hypersensitivity to the active substance(s) or to any of the excipients, past history or present venous thromboembolic (VTE) disorder or arterial thromboembolic cardiovascular disease, liver tumours or severe hepatic disease, known osteoporosis or thrombophilic disorders, known or suspected sex steroid influenced malignancy, genital bleeding of unknown etiology, headaches with focal neurological symptoms/migraine headaches with aura or suspected/confirmed pregnancy and during breast-feeding. **Special warnings and precautions for use** Ryeqo must only be prescribed after careful diagnosis, and prior to the initiation or reinstitution of Ryeqo, a complete medical history (including family history) must be taken and physical examination carried out. **Risk of thromboembolic disorders** The risk of ATE/VTE with Ryeqo has not been established. If an ATE/VTE occurs, treatment must be discontinued immediately. **Risk of bone loss** The benefits and risks of Ryeqo in patients with a history of a low trauma fracture or other risk factors for osteoporosis or bone loss, should be considered prior to initiating treatment. It is recommended to perform a DXA scan before commencing treatment in these patients, and treatment should not be started if risk outweighs potential benefit. **Change in menstrual bleeding pattern** Patients must be informed that treatment with Ryeqo usually leads to a reduction in menstrual blood loss or amenorrhoea within the first 2 months of treatment. In case of persistent excessive bleeding, patients must

notify their physician. **Hypertension** Although small increases in blood pressure have been reported in women taking Ryeqo, clinically relevant increases are rare. **Lactose** Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product. **Interaction with other medicinal products and other forms of interaction** Concomitant use of Ryeqo with oral P-gp inhibitors, strong CYP3A4 and/or P-gp inducers is not recommended. Ryeqo has no or negligible influence on the ability to drive and use machines. **Pregnancy and lactation** There is a limited amount of data from the use of relugolix in pregnant women or during lactation; Ryeqo is contraindicated during pregnancy and breastfeeding, and should be discontinued if pregnancy occurs. **Undesirable effect** Common adverse drug reactions ($\geq 1/100$ to $< 1/10$) include, hot flush, uterine bleeding (including menorrhagia and metrorrhagia), breast cysts, libido decreased, irritability, dyspepsia, alopecia, hyperhidrosis, night sweats. Reporting suspected adverse reactions after authorisation of the medicinal product is important. Healthcare professionals are asked to report any suspected adverse reactions via the relevant national reporting system. **Efficacy and safety over 24 weeks** During two replicate, 24 week, multinational, randomised, double blind, placebo-controlled studies, over 70% of patients treated with Ryeqo 'responded' (i.e. MBL volume of < 80 mL and $\geq 50\%$ reduction at 24 weeks. For those patients treated with Ryeqo and who completed 104 weeks of treatment the LS mean percent change from baseline in Bone Mineral Density (BMD) was 0.04%. **Shelf life & Storage** 2 years, and does not require any special storage condition. **MARKETING AUTHORISATION HOLDER** Gedeon Richter Plc, Gyömrői út 19-21, 1103 Budapest, Hungary **MARKETING AUTHORISATION NUMBER(S)** EU/1/21/1565 **DATE OF FIRST AUTHORISATION / DATE OF DOC PREPARATION** 20th July 2021 / 17th August 2021 **DATE OF REVISION OF THE TEXT** Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

References:

1. Al-Hendy et al. *Am J Obstet Gynecol* 2023; on-line ahead of print.
2. Available at ClinicalTrials.gov
3. Al-Hendy A et al. *N Engl J Med* 2021; 384:630-642.
4. Al-Hendy et al. *Obstet Gynecol* 2022; 140:920-930.
5. Ryeqo SmPC, October 2023

 GEDEON RICHTER

 **Ryeqo®**
relugolix, estradiol, and norethisterone acetate
Her life is our performance

THE LONG-TERM BALANCE SHE NEEDS.

THE LIFE SHE WANTS.

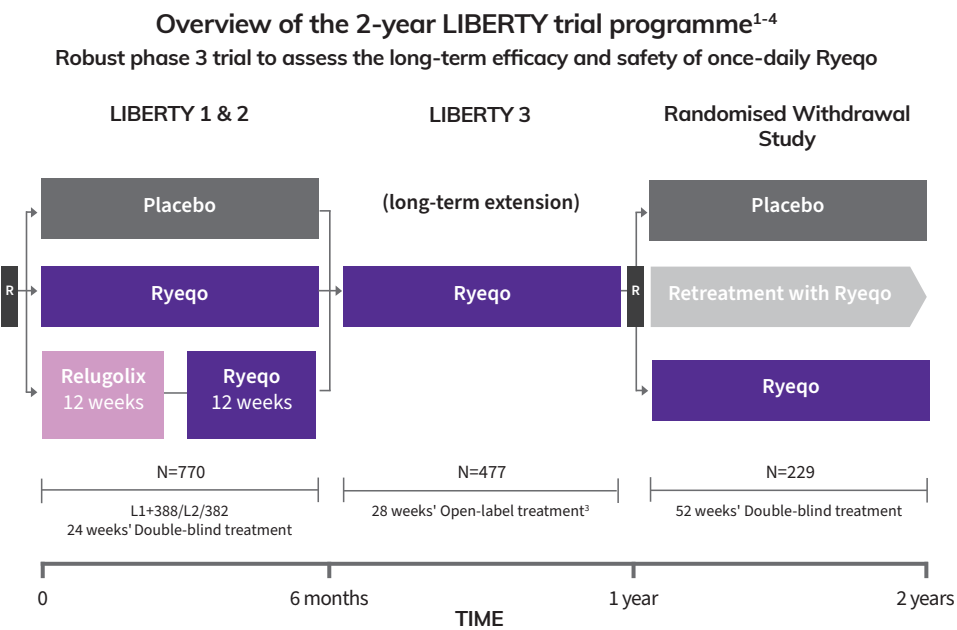
2-year efficacy and safety double-blind results for women with UF

“These data are clinically meaningful because they provide physicians with important efficacy and safety outcomes for up to two years of treatment with Ryeqo”

Prof Al-Hendy et al, *Am J Obstet Gynecol*, 2023


Ryeqo®
relugolix, estradiol, and norethisterone acetate
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LONG-TERM PERFORMANCE BUILT ON A ROBUST CLINICAL TRIAL PROGRAMME



³229 women were randomised and 228 received at least one dose of Ryeqo (placebo: 113 and Ryeqo: 115)

POPULATION
Premenopausal women aged 18 to 50 years with a diagnosis of UF and heavy menstrual bleeding (HMB) of ≥ 80 ml for 2 cycles or ≥ 160 ml in one cycle. Women needed to have completed the LIBERTY 28 weeks' LTE study and met the definition of responder (i.e. menstrual blood loss (MBL) volume of < 80 ml AND $> 50\%$ reduction from pivotal study baseline MBL volume, alkaline hematin method)

PRIMARY ENDPOINT
The proportion of women who maintained an MBL volume of < 80 ml through week 76. A single MBL volume measurement of ≥ 80 mL was considered relapse of HMB. Such women were offered rescue with open-label Ryeqo

- LIBERTY trial programme has a robust and consistent long-term follow-up¹⁻³
- Approximately half of all patients in the randomised withdrawal study were Black or African-American women:¹



White:
50%



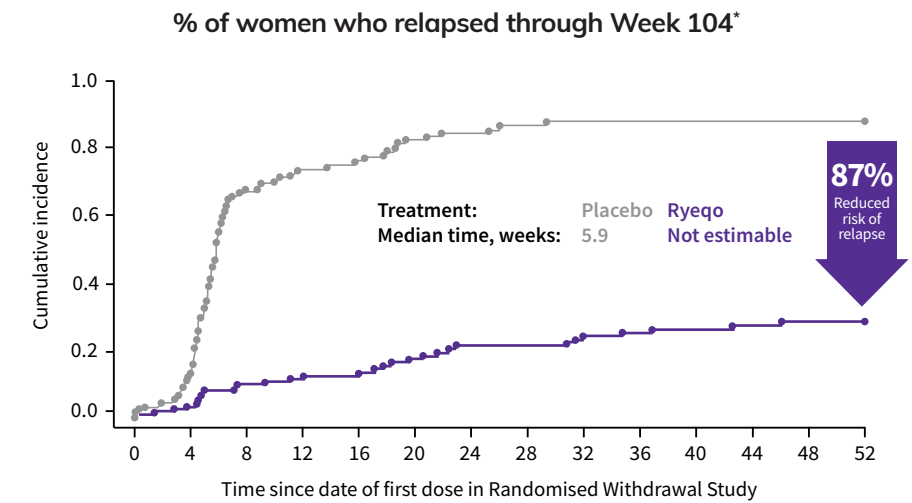
Black / African-American:
47%



Other:
3%

SHE DOESN'T WANT HER SYMPTOMS TO RETURN AND LOWER HER QUALITY OF LIFE

Ryeqo prevents long-term relapse of heavy menstrual bleeding¹



	Number of patients at risk														
Relugolix CT	115	106	96	92	91	85	81	80	76	72	70	69	64	46	
Placebo	113	93	34	28	24	16	14	11	9	8	8	8	8	6	

With Ryeqo

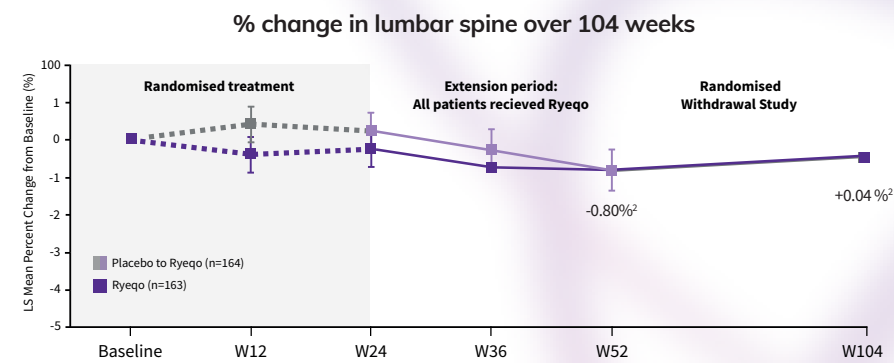
- There is an 87% lower risk of relapse¹
- Median time to relapse was not reached at Week 104 (compared with 5.9 weeks for placebo)¹

Significantly less risk of relapse means sustained improvement in her quality of life (specific UF- AND general HR-QoL)¹

* A single MBL volume measurement of ≥ 80 mL was considered relapse of HMB

THE BALANCE AND SAFETY SHE NEEDS

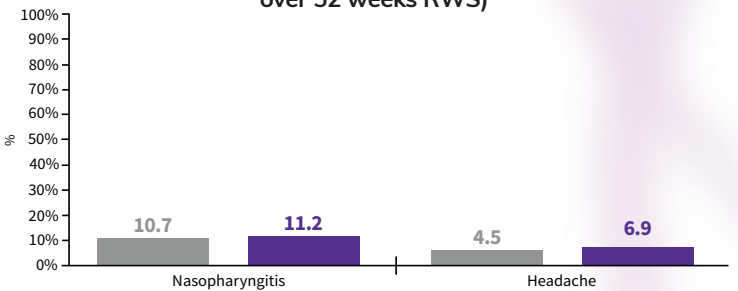
Ryeqo preserves long-term bone health with a proven safety profile over 104 weeks¹



- BMD was stable with minimal changes over 104 weeks

Ryeqo showed no new safety signals after 104 weeks¹

Most frequent adverse events ($> 5\%$ of patients in the Ryeqo group over 52 weeks RWS)¹



- Comparable safety profile to placebo^{1,5}
- Most adverse events ($> 98\%$) were mild to moderate¹

QR CODE

For further information see the full Ryeqo SmPC⁵

The precise control of hormones provides the balance of efficacy and safety needed for the long-term treatment of UF symptoms^{1,4}