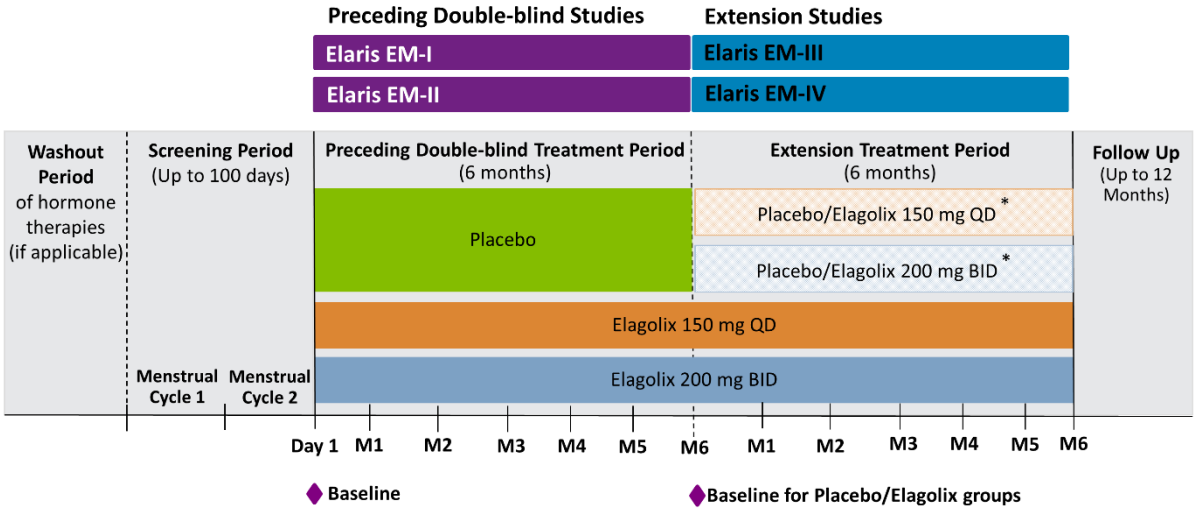
Appendix 1. Study design. *Eligible, consenting women on placebo during the preceding double-blind, placebo-controlled studies enrolled and were randomized to one of the two elagolix doses in the extension studies and received up to 6 months of elagolix treatment; data from these women will be reported in a separate publication.



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Appendix 2. **Other Efficacy Measures after 12 Months of Treatment: Patient Global Impression of Change Scores, Changes in Analgesic Use, and Numeric Rating Scale Scores**

	Elaris EM-III		Elaris EM-IV	
Secondary Efficacy Outcome	Elagolix 150mg QD	Elagolix 200mg BID	Elagolix 150mg QD	Elagolix 200mg BID
Change in pill count from baseline, LS mean ± SE	*N=117*	*N=110*	*N=122*	*N=116*
Any Analgesic Use	-0.40 ± 0.70	-0.56 ± 0.67	-0.45 ± 0.83	-0.59 ± 0.80
NSAID Only	-0.27 ± 0.52	-0.31 ± 0.43	-0.26 ± 0.57	-0.32 ± 0.38
Opioid Only	-0.13 ± 0.44	-0.25 ± 0.53	-0.20 ± 0.62	-0.27 ± 0.68
Change in overall endometriosis-associated pain from baseline*, LS mean score ± SE	-2.58 ± 2.27	-3.09 ± 2.03	-2.81 ± 2.06	-3.14 ± 1.93
n/N (%) with Much or Very Much Improved Responses on PGIC	77/111 (69.4)	93/102 (91.2)	86/114 (75.4)	89/106 (84.0)

Statistical comparisons between treatment groups were not predefined and not performed. Analgesic use and pain scores based on average over 35-day window. *Measured with the Numeric Rating Scale; women provided daily self-assessments of overall endometriosis-associated pain on a scale of 0 (no pain) to 10 (worst pain ever). QD = once daily, BID = twice daily, PGIC = Patient Global Impression of Change, LS = least-squares, SE = standard error of the mean, NSAID = nonsteroidal anti-inflammatory drugs

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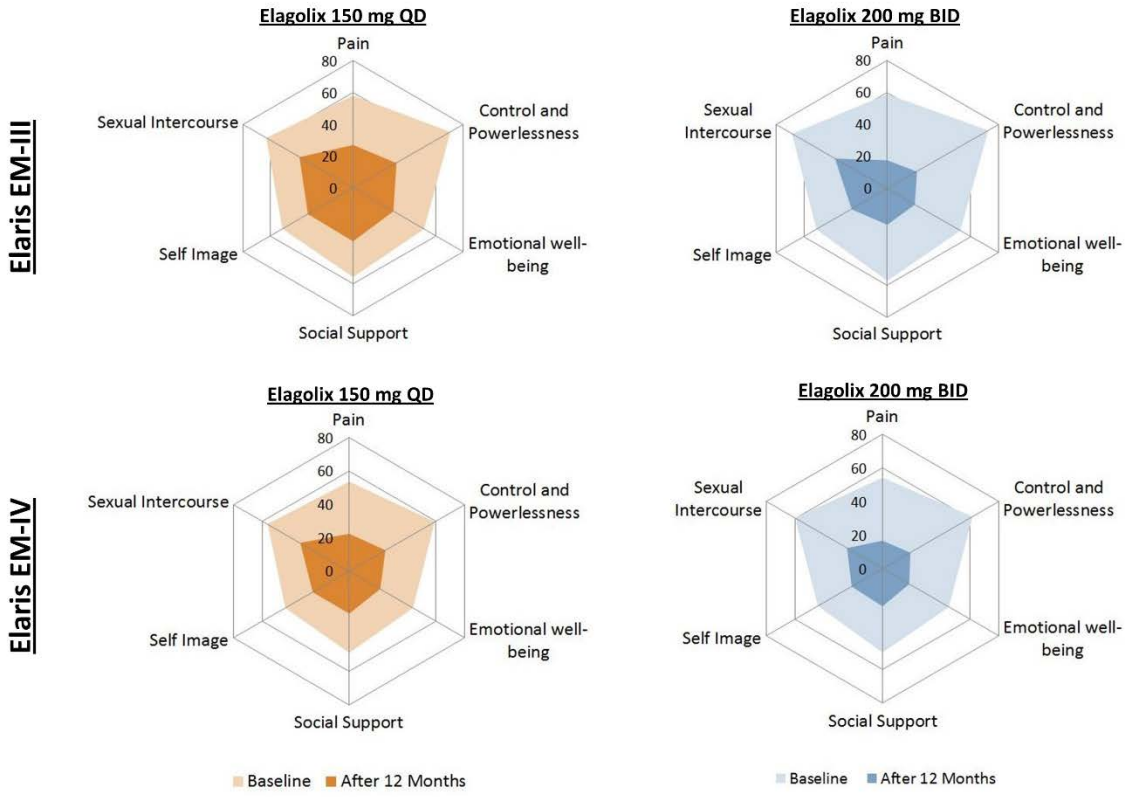
Appendix 3. Mean Endometriosis Health Profile-30 scores before and after 12 months of elagolix treatment. Baseline was prior to first treatment in the preceding double-blind, placebo-controlled trials. Statistical comparisons between treatment groups were not predefined and not performed. QD, once daily; BID, twice daily.



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Appendix 4. Adverse Events Occurring in ≥ 5% of Women in Each Study Over the Course of 12 Months of Elagolix*

	Elaris EM-III		Elaris EM-IV	
	Elagolix 150mg QD	Elagolix 200mg BID	Elagolix 150mg QD	Elagolix 200mg BID
n (%)	N=149	N=138	N=142	N=140
Hot flush	44 (29.5)	72 (52.2)	36 (25.4)	77 (55)
Headache	29 (19.5)	35 (25.4)	31 (21.8)	41 (29.3)
Nausea	18 (12.1)	34 (24.6)	25 (17.6)	21 (15)
Urinary tract infection	26 (17.4)	16 (11.6)	15 (10.6)	19 (13.6)
Sinusitis	18 (12.1)	18 (13)	11 (7.7)	16 (11.4)
Upper respiratory tract infection	25 (16.8)	10 (7.2)	11 (7.7)	14 (10)
Fatigue	19 (12.8)	13 (9.4)	6 (4.2)	8 (5.7)
Nasopharyngitis	15 (10.1)	16 (11.6)	16 (11.3)	22 (15.7)
Insomnia	12 (8.1)	18 (13)	14 (9.9)	15 (10.7)
Back Pain	11 (7.4)	17 (12.3)	11(7.7)	21(15.0)
Abdominal pain	11 (7.4)	13 (9.4)	9 (6.3)	8 (5.7)
Anxiety	11 (7.4)	13 (9.4)	8 (5.6)†	5 (3.6)†
Vomiting	13 (8.7)	10 (7.2)	7 (4.9)	9 (6.4)
Depression	13 (8.7)	9 (6.5)	3 (2.1)†	3 (2.1)†
Influenza	10 (6.7)	10 (7.2)	6(4.2)†	7(5.0)†
Bronchitis	11 (7.4)	9 (6.5)	7 (4.9)	8 (5.7)
Diarrhea	7 (4.7)	12 (8.7)	12 (8.5)	10 (7.1)
Mood swings	4 (2.7)	14 (10.1)	12 (8.5)	6 (4.3)
Gastroenteritis viral	6 (4)	12 (8.7)	5 (3.5)†	1 (0.7)†
Arthralgia	7 (4.7)	11 (8)	13 (9.2)	18 (12.9)
Vulvovaginal mycotic infection	10 (6.7)	8 (5.8)	4 (2.8)†	2 (1.4)†
Acne	9 (6)	8 (5.8)	6 (4.2)	9 (6.4)
Night sweats	6 (4)	10 (7.2)	1 (0.7)†	4 (2.9)†
Dizziness	8 (5.4)	8 (5.8)	10 (7.0)†	3 (2.1)†
Amenorrhea	4 (2.7)	11 (8)	8 (5.6)	17 (12.1)
C-reactive protein increased	6 (4)	9 (6.5)	5 (3.5)†	4 (2.9)†
Migraine	6 (4)	9 (6.5)	2 (1.4)†	2 (2.9)†
Weight Increased	8 (5.4) ‡	6(4.3) ‡	9 (6.3)	8 (5.7)
Constipation	8 (5.4)‡	6 (4.3)‡	7 (4.9)	7 (5.0)
Pelvic Pain	6 (4.0)‡	7 (5.1)‡	7 (4.9)	7 (5.0)

*In descending order of GnRH antagonist treatment overall in Elaris EM-III, then Elaris EM-IV; only women that received GnRH antagonist during the preceding double-blind, placebo-controlled trials, †Incidence not ≥ 5% overall in Elaris EM-IV, ‡ Incidence not ≥ 5% overall in Elaris EM-III. QD = once daily, BID = twice daily.

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Appendix 5. Summary of Adverse Events With New Onset in Each Extension Study

	Elaris EM-III		Elaris EM-IV	
	Elagolix 150mg QD	Elagolix 200mg BID	Elagolix 150mg QD	Elagolix 200mg BID
n (%)	N=149	N=138	N=142	N=140
Any adverse event (AE)	111 (74)	102 (74)	116 (81.7)	109 (77.9)
Any serious AE	5 (3.4)	4 (2.9)	7 (4.9)	8 (5.7)
Any severe AE	18 (12)	22 (16)	9 (6.3)	11 (7.9)
Any AE leading to discontinuation	6 (4.0)	12 (8.7)	8 (5.6)	10 (7.1)
Deaths	0	0	0	0
AEs occurring in ≥ 4% of women overall in each study* n (%)				
Urinary Tract Infection	17 (11.4)	11 (8.0)	10 (7.0)	11 (7.9)
Sinusitis	10 (6.7)	10 (7.2)	8 (5.6)	8 (5.7)
Upper Respiratory Tract Infection	16 (11)	4 (2.9)	6 (4.2)	6 (4.3)
Headache	10 (6.7)	8 (5.8)	9 (6.3)	9 (6.4)
Nasopharyngitis	9 (6.0)	9 (6.5)	6 (4.2)	9 (6.4)
Nausea	7 (4.7)	10 (7.2)	14 (9.9)	5 (3.6)
Back Pain	6 (4.0)	10 (7.2)	6 (4.2)	10 (7.1)
Vulvovaginal Mycotic Infection	8 (5.4)	6 (4.3)	1 (0.7) †	1 (0.7) †
Abdominal Pain	7 (4.7)	8 (5.8)	4 (2.8)†	6 (4.3)†
Bronchitis	8 (5.4)	7 (5.1)	4 (2.8)†	2 (1.4)†
Fatigue	9 (6.0)	5 (3.6)	0†	2 (1.4)†
Hot Flush	6 (4.0)	8 (5.8)	7 (4.9)	11 (7.9)
Depression	8 (5.4)	4 (2.9)	1 (0.7)†	0†
Influenza	6 (4.0)	6 (4.3)	3 (2.1)†	4 (2.9)†
Vomiting	6 (4.0)	6 (4.3)	4 (2.8)†	4 (2.9)†
Arthralgia	2 (1.3)‡	7 (5.1)‡	6 (4.2)	9 (6.4)
Diarrhea	2 (1.3)‡	5 (3.6)‡	6 (4.2)	6 (4.3)

*In descending order of elagolix overall in Elaris EM-III, then Elaris EM-IV; only women that received elagolix during the preceding double-blind, placebo-controlled trials, †Incidence not ≥ 4% overall in Elaris EM-IV, ‡ Incidence not ≥ 4% overall in Elaris EM-III. QD = once daily, BID = twice daily, AE = adverse event.

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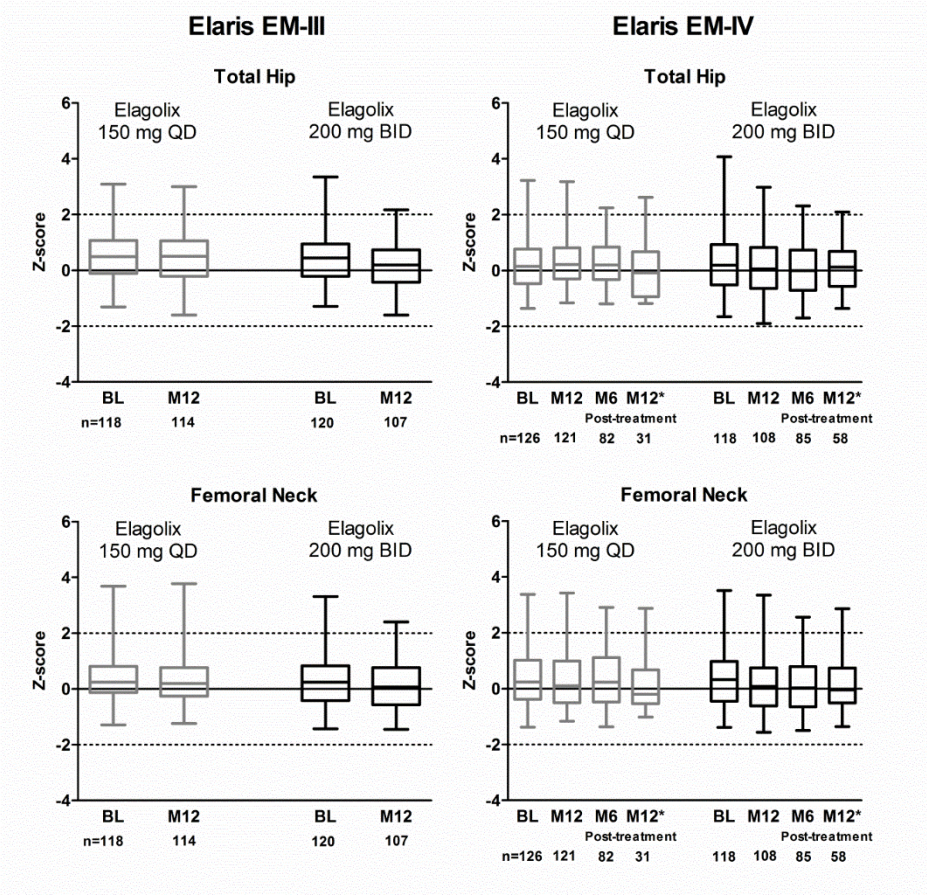
Appendix 6. Median, quartile 1, quartile 3, minimum and maximum of bone mineral density Z-scores over the course of 12 months of elagolix treatment (Elaris EM-III and IV) and at post-treatment months 6 and 12* (Elaris EM-IV only). Baseline was prior to dosing in the preceding double-blind, placebo-controlled trials (Elaris EM-I and Elaris EM-II). Dotted lines indicate the normal age- and race-matched range. Month 12 during the extension treatment period includes women who prematurely discontinued and women that had ≥12 months of elagolix treatment (as discussed in the methods). Error bars represent 95% confidence interval for mean percentage change from baseline. Statistical comparisons between treatment groups were not predefined and not performed. *Elaris EM-III was not designed to evaluate post-treatment bone mineral density recovery for all women. For Elaris EM-IV, all women were required to have a follow-up DXA at 6 months post-treatment. However only women who had a decrease > 1.5% from baseline in lumbar spine or a decrease > 2.5% in total hip BMD at 6 months post-treatment were required to have a follow-up DXA at 12 months post-treatment. QD, once daily; BID; twice daily; BL, baseline; Ext, extension; M, month; DXA, dual energy X-ray absorptiometry.



Appendix 7. Number and Percentage of Women with Amenorrhea at Each Month in the Extension Studies

	Elaris EM-III		Elaris EM-IV	
Women with Amenorrhea,* n/N (%)	Elagolix 150mg QD	Elagolix 200mg BID	Elagolix 150mg QD	Elagolix 200mg BID
Extension study month				
1	33/146 (23)	88/136 (65)	33/140 (24)	95/139 (68)
2	43/137 (31)	88/128 (69)	38/138 (28)	93/134 (69)
3	41/131 (31)	80/123 (65)	34/134 (25)	87/127 (69)
4	38/127 (30)	78/119 (66)	27/127 (21)	85/124 (69)
5	36/124 (29)	72/114 (63)	32/125 (26)	74/118 (63)
6	25/94 (27)	57/90 (63)	18/89 (20)	59/97 (61)

Statistical comparisons between treatment groups were not predefined and not performed. *A woman was considered amenorrheic if she did not report menstrual period or any uterine bleeding in the e-Diary during each 28-day period of interest and answered in the e-Diary at least once. Days with missing electronic diary entries were considered 'no bleeding' days. QD = once daily, BID = twice daily.

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