The odds ratios with 95% CIs are shown graphically below and listed in the table to the right for each demographic subgroup treated with elagolix with add-back. Odds ratios were determined by pooling the results from a logistic regression model including treatment and study as the main effects and baseline MBL volume as a covariate in each data set from multiple imputation under each subgroup level.

BMI, body mass index; CI, confidence interval; E2, estradiol; MBL, menstrual blood loss; NETA, norethindrone acetate.

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.
The proportion of responders to the primary endpoint are depicted graphically for women in the overall pooled study population and each disease severity and demographic subgroup treated with placebo or elagolix with add-back therapy. For the primary endpoint, the final month was defined as the last 28 days before and including the reference day. Missing final month MBL was imputed using multiple imputation for each subgroup level. Women who met the primary endpoint criteria but prematurely discontinued the study drug because of adverse events, lack of efficacy, or required surgery or invasive intervention for treatment of uterine fibroids were categorized as nonresponders for the primary endpoint. Confidence intervals were determined by pooling the results from a logistic regression model including treatment and study as the main effects and baseline MBL volume as a covariate in each data set from multiple imputation under each subgroup level. Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set. The asterisk symbol (***) indicates $P < .001$.

FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2.

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.
SUPPLEMENTAL FIGURE 3
Mean changes in UFS-QOL scores from baseline to month 6 for study demographic subgroups

A, The mean change in symptom severity score for each subgroup is depicted. B, The mean change in total HRQoL score for each subgroup is depicted. For symptom severity, a higher score indicates worse symptom severity. For HRQoL, a higher score indicates better quality of life. Data are presented as LS means with error bars representing the standard error of mean. The change from baseline to month 6 in each parameter was analyzed using an ANCOVA model with treatment as the main effect and baseline value as a covariate. The asterisk symbol (*** indicates $P < .001$.

ANCOVA, analysis of covariance; FIGO, International Federation of Gynecology and Obstetrics; HRQoL, health-related quality of life; LS, least-squares; UFS-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.
### Subgroup baseline characteristics

| Factors | Subgroup/treatment | N  | Age (y) | BMI (kg/m²) | Race | Ethnicity | Subgroup/ Treatment | Black/ African American | Not black/ African American | Hispanic/ Latino | Not Hispanic/ Latino | MBL (mL) | Primary fibroid volume (cm³) | Uterine volume (cm³) | FIGO classification |
|---------|-------------------|----|---------|-------------|------|-----------|---------------------|------------------------|--------------------------|-----------------|---------------------|---------|----------------------------|---------------------|------------------|
| Overall group | Placebo | 196 | 42.0 (5.6) | 33.8 (7.5) | 133 (67.9) | 63 (32.1) | 30 (15.3) | 166 (84.7) | 254.8 (83.8) | 87.7 (1.0) | 512.4 (73.3) | 25 (13.0) | 254.8 (83.8) | 87.7 (1.0) | 0–3 |
| Elagolix + E₂/NETA | 395 | 42.6 (5.3) | 33.3 (6.9) | 265 (67.3) | 129 (32.7) | 65 (16.5) | 330 (83.5) | 233.4 (83.8) | 75.6 (1.3) | 485.1 (71.6) | 47 (12.1) | 233.4 (83.8) | 75.6 (1.3) | 0–3 |
| Age (y) | < 35 | | | | | | | | | | | | | |
| Placebo | 18 | 30.6 (2.5) | 32.2 (6.7) | 14 (77.8) | 4 (22.2) | 3 (16.7) | 15 (83.3) | 228.3 (102.6) | 125.3 (3.8) | 476.3 (155.2) | 3 (16.7) | 228.3 (102.6) | 125.3 (3.8) | 0–3 |
| Elagolix + E₂/NETA | 37 | 31.6 (2.3) | 32.6 (6.9) | 29 (78.4) | 8 (21.6) | 6 (16.2) | 31 (83.8) | 177.5 (86.9) | 93.9 (2.7) | 377.2 (113.9) | 8 (22.2) | 177.5 (86.9) | 93.9 (2.7) | 0–3 |
| ≥35–<40 | | | | | | | | | | | | | | |
| Placebo | 41 | 37.6 (1.3) | 34.8 (7.3) | 30 (73.2) | 11 (26.8) | 6 (14.6) | 35 (85.4) | 215.7 (86.0) | 71.5 (3.2) | 502.8 (127.0) | 6 (14.6) | 215.7 (86.0) | 71.5 (3.2) | 0–3 |
| Elagolix + E₂/NETA | 66 | 37.5 (1.4) | 32.4 (7.0) | 46 (69.7) | 20 (30.3) | 7 (10.6) | 59 (89.4) | 247.9 (89.1) | 64.4 (1.4) | 417.0 (113.9) | 9 (13.8) | 247.9 (89.1) | 64.4 (1.4) | 0–3 |
| ≥40–<45 | | | | | | | | | | | | | | |
| Placebo | 68 | 41.8 (1.4) | 34.5 (8.3) | 43 (63.2) | 25 (36.8) | 13 (19.1) | 55 (80.9) | 243.8 (83.8) | 95.1 (1.0) | 496.2 (73.3) | 7 (10.8) | 243.8 (83.8) | 95.1 (1.0) | 0–3 |
| Elagolix + E₂/NETA | 130 | 42.3 (1.4) | 33.9 (6.5) | 81 (62.3) | 49 (37.7) | 23 (17.7) | 107 (82.3) | 242.3 (85.6) | 75.0 (1.3) | 485.8 (113.9) | 12 (9.4) | 242.3 (85.6) | 75.0 (1.3) | 0–3 |
| ≥45 | | | | | | | | | | | | | | |
| Placebo | 69 | 47.8 (2.1) | 32.9 (6.8) | 46 (66.7) | 23 (33.3) | 8 (11.6) | 61 (88.4) | 295.9 (88.8) | 80.4 (2.1) | 543.5 (104.0) | 9 (13.2) | 295.9 (88.8) | 80.4 (2.1) | 0–3 |
| Elagolix + E₂/NETA | 162 | 47.3 (2.0) | 33.3 (7.1) | 109 (67.7) | 52 (32.3) | 29 (17.9) | 133 (82.1) | 233.2 (83.8) | 76.4 (2.0) | 536.9 (107.9) | 18 (11.3) | 233.2 (83.8) | 76.4 (2.0) | 0–3 |
| BMI (kg/m²) | < 25 | | | | | | | | | | | | | | |
| Placebo | 21 | 40.2 (6.1) | 22.8 (1.6) | 9 (42.9) | 12 (57.1) | 9 (42.9) | 12 (57.1) | 252.9 (102.1) | 60.3 (5.7) | 506.3 (175.4) | 5 (23.8) | 252.9 (102.1) | 60.3 (5.7) | 0–3 |
| Elagolix + E₂/NETA | 49 | 42.0 (5.4) | 23.3 (1.5) | 32 (66.7) | 16 (33.3) | 8 (16.3) | 41 (83.7) | 270.1 (89.1) | 102.0 (3.0) | 535.1 (113.8) | 4 (8.2) | 270.1 (89.1) | 102.0 (3.0) | 0–3 |

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## SUPPLEMENTAL TABLE 1
Subgroup baseline characteristics (continued)

| Factors | Subgroup/treatment | N | Age (y) | BMI (kg/m²) | Race/Ethnicity | Factors | Subgroup/treatment | N | Age (y) | BMI (kg/m²) | Primary fibroid volume (cm³) | Uterine volume (cm³) | FIGO classification |
|---------|---------------------|---|---------|-------------|----------------|---------|---------------------|---|---------|-------------|------------------------|-----------------|------------------|
|         |                     |   |         |             | Black/African American | Not black/African American | Hispanic/Latino | Other Hispanic/Latino | MBL (mL) | 0–3 | 4 | 5–8 |
| ≥25–<30 | Placebo            | 42 | 43.6 (5.3) 27.6 (1.5) 22 (52.4) 20 (47.6) 7 (16.7) 35 (83.3) | 328.8 (86.0) | 7 (17.5) 16 (40.0) 17 (42.5) |
|         | Elagolix + E2/NETA | 86 | 42.7 (5.6) 27.8 (1.4) 51 (59.3) 35 (40.7) 21 (24.4) 65 (75.6) | 219.1 (86.6) 781.9) | 428.0 (74.5) | 35 (83.3) |
|         |                     |   |         |             | 0–3 | 4 | 5–8 |
| ≥30–<35 | Placebo            | 53 | 42.3 (4.9) 32.3 (1.3) 36 (67.9) 17 (32.1) 8 (15.1) 45 (84.9) | 236.6 (88.8) | 77.9 (1.0) 727.2 | 408.2 (100.4) | 1735.8 |
|         | Elagolix + E2/NETA | 113 | 42.9 (5.1) 32.4 (1.4) 71 (62.8) 42 (37.2) 17 (15.0) 96 (85.0) | 241.0 (86.9) 820.1) | 554.5 (96.3) | 2312.0 |
|         |                     |   |         |             | 0–3 | 4 | 5–8 |
| ≥35–<40 | Placebo            | 43 | 41.5 (6.7) 37.2 (1.5) 37 (86.0) 6 (14.0) 4 (9.3) 39 (90.7) | 239.9 (83.8) | 96.9 (3.5) 513.5 | 567.3 (73.3) | 1992.4 |
|         | Elagolix + E2/NETA | 79 | 42.6 (4.5) 37.3 (1.6) 52 (65.8) 27 (34.2) 13 (16.5) 66 (83.5) | 220.3 (85.6) | 74.7 (2.0) 1081.5 | 484.2 (107.9) | 2892.7 |
|         |                     |   |         |             | 0–3 | 4 | 5–8 |
| >40     | Placebo            | 37 | 41.3 (4.7) 45.2 (5.1) 29 (78.4) 8 (21.6) 2 (5.4) 35 (94.6) | 215.4 (94.1) | 99.5 (2.1) 1041.7 | 555.9 (116.9) | 2590.2 |
|         | Elagolix + E2/NETA | 67 | 42.9 (5.2) 44.3 (3.7) 58 (86.6) 9 (13.4) 6 (9.0) 61 (91.0) | 229.0 (83.8) | 60.7 (1.4) 849.6 | 403.6 (71.6) | 1387.8 |
|         |                     |   |         |             | 0–3 | 4 | 5–8 |
| Race    | Black/African American | 133 41.6 (5.7) 34.9 (6.9) — — 5 (3.8) 128 (96.2) | 244.3 (83.8) | 84.6 (3.2) 1041.7 | 535.7 (73.3) | 2590.2 | 11 (8.5) 50 (38.5) 69 (53.1) |
|         | Elagolix + E2/NETA | 265 42.4 (5.5) 34.0 (7.3) — — 11 (4.2) 254 (95.8) | 238.6 (83.8) | 85.1 (1.4) 1081.5 | 536.8 (71.6) | 2892.7 | 30 (11.4) 118 (44.9) 115 (43.7) |
|         |                     |   |         |             | 0–3 | 4 | 5–8 |
| Not black/African American | 63 42.9 (5.1) 31.6 (8.1) — — 25 (39.7) 38 (60.3) | 277.0 (86.0) | 94.2 (1.0) 727.2 | 463.2 (100.4) | 1642.5 | 14 (22.6) 35 (56.5) 13 (21.0) |
|         | Elagolix + E2/NETA | 129 42.9 (5.0) 31.8 (5.7) — — 54 (41.9) 75 (58.1) | 223.4 (85.6) | 55.4 (1.3) 350.9 | 377.6 (96.3) | 2029.5 | 17 (13.6) 59 (47.2) 49 (39.2) |

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| Factors | Subgroup/ treatment | N  | Age (y) | BMI (kg/m²) | Race Ethnicity | Ethnicity | MBL (mL) | Primary fibroid volume (cm³) | Uterine volume (cm³) | FIGO classification |
|--------|---------------------|----|---------|-------------|----------------|-----------|----------|----------------------------|---------------------|-------------------|
|        |                     | 45 | 41.2 (6.1) | 31.3 (6.5) | 26 (57.8) | 19 (42.2) | 8 (17.8) | 37 (82.2) | 263.9 (86.0) | 71.7 (3.4) | 447.0 (127.0) | 447.0 (127.0) | — | — | — | — |
|        |                     | 110| 42.5 (5.2) | 34.5 (8.0) | 73 (66.4) | 37 (33.6) | 18 (16.4) | 92 (83.6) | 254.5 (83.8) | 83.1 (1.0) | 526.1 (100.4) | 526.1 (100.4) | — | — | — | — |
|        |                     | 225| 42.7 (5.3) | 32.9 (6.8) | 155 (69.2) | 69 (30.8) | 34 (15.1) | 191 (84.9) | 221.3 (83.8) | 63.4 (1.3) | 466.3 (74.5) | 466.3 (74.5) | — | — | — | — |
|        |                     | 37 | 41.3 (5.9) | 34.9 (6.6) | 31 (83.8) | 6 (16.2) | 2 (5.4) | 35 (94.6) | 251.7 (96.5) | 120.7 (4.1) | 541.7 (73.3) | 541.7 (73.3) | — | — | — | — |
|        |                     | 69 | 43.1 (5.4) | 34.1 (7.2) | 40 (58.0) | 29 (42.0) | 13 (18.8) | 56 (81.2) | 216.8 (86.6) | 120.6 (2.4) | 557.2 (96.6) | 557.2 (96.6) | — | — | — | — |

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### SUPPLEMENTAL TABLE 1
Subgroup baseline characteristics (continued)

| Factors                      | Subgroup/treatment | N   | Age (y)       | BMI (kg/m²) | Race | Ethnicity | MBL (mL) | Primary fibroid volume (cm³) | Uterine volume (cm³) | FIGO classification |
|------------------------------|--------------------|-----|---------------|-------------|------|-----------|----------|-------------------------------|---------------------|---------------------|
|                              |                    |     |               |             | Black/African American | Not black/African American | Hispanic/Latino | Not Hispanic/Latino |                           |                     |                     |
|                              |                    |     |               |             | 0—3              | 4              | 5—8                          |                               |                     |                     |
| Highest FIGO type classification | Placebo            | 25  | 41.0 (6.2)    | 31.3 (6.9)  | 11 (44.0)         | 14 (56.0)       | 7 (28.0)         | 18 (72.0)         | 247.0 (86.0)                | 66.1 (3.4)            | 381.4 (127.0)        |
|                              | Elagolix + E2/NETA | 47  | 41.4 (5.7)    | 32.6 (6.6)  | 30 (63.8)         | 17 (36.2)       | 12 (25.5)        | 35 (74.5)         | 232.8 (96.8)                | 56.9 (3.0)            | 388.9 (71.6)         |
|                              |                    |     |               |             | 0                 | 4              | 5                           |                               |                     |                     |
| Placebo                      |                    | 85  | 42.1 (5.0)    | 34.2 (8.3)  | 50 (88.8)         | 35 (41.2)       | 13 (15.3)        | 72 (84.7)         | 260.9 (83.8)                | 83.1 (1.0)            | 532.2 (116.9)        |
| Elagolix + E2/NETA           |                    | 177 | 42.4 (5.5)    | 33.8 (7.1)  | 118 (66.7)        | 59 (33.3)       | 26 (14.7)        | 151 (85.3)        | 240.6 (83.8)                | 61.4 (1.3)            | 433.1 (96.3)         |
| Primary fibroid FIGO classification | Placebo            | 82  | 42.2 (6.1)    | 34.2 (6.7)  | 69 (84.1)         | 13 (15.9)       | 8 (9.8)          | 74 (90.2)         | 254.0 (88.8)                | 99.0 (4.1)            | 527.5 (73.3)         |
|                              | Elagolix + E2/NETA | 165 | 43.0 (4.9)    | 32.8 (6.6)  | 115 (70.1)        | 49 (29.9)       | 26 (15.8)        | 139 (84.2)        | 227.4 (86.6)                | 96.1 (2.4)            | 561.8 (74.5)         |
| Primary fibroid volume (cm³)  |                    |     |               |             | 0                 | 4              | 5                           |                               |                     |                     |
| Placebo                      |                    | 38  | 40.7 (5.9)    | 31.6 (6.1)  | 21 (55.3)         | 17 (44.7)       | 7 (18.4)         | 31 (81.6)         | 259.8 (86.0)                | 78.4 (3.4)            | 449.9 (127.0)        |
| Elagolix + E2/NETA           |                    | 78  | 41.4 (5.1)    | 32.9 (6.6)  | 54 (69.2)         | 24 (30.8)       | 17 (21.8)        | 61 (78.2)         | 276.6 (96.8)                | 75.8 (3.0)            | 447.6 (71.6)         |
| FIGO classification          |                    |     |               |             | 0—3              | 4              | 5—8                          |                               |                     |                     |
| Placebo                      |                    | 96  | 42.5 (5.2)    | 33.9 (8.2)  | 60 (62.5)         | 36 (37.5)       | 16 (16.7)        | 80 (83.3)         | 257.1 (83.8)                | 78.4 (1.0)            | 512.1 (100.4)        |
| Elagolix + E2/NETA           |                    | 191 | 42.6 (5.3)    | 33.4 (7.0)  | 135 (70.7)        | 56 (29.3)       | 26 (13.6)        | 165 (86.4)        | 228.4 (83.8)                | 61.2 (1.3)            | 460.1 (74.5)         |
| Placebo                      |                    | 58  | 42.0 (5.9)    | 35.2 (6.9)  | 49 (84.5)         | 9 (15.5)        | 5 (8.6)          | 53 (91.4)         | 252.1 (93.8)                | 109.2 (4.1)           | 547.7 (73.3)         |
| Elagolix + E2/NETA           |                    | 120 | 43.3 (5.2)    | 33.1 (6.8)  | 74 (62.2)         | 45 (37.8)       | 21 (17.5)        | 99 (82.5)         | 215.4 (86.6)                | 98.4 (2.4)            | 540.3 (96.6)         |
**SUPPLEMENTAL TABLE 1**

Subgroup baseline characteristics (continued)

| Factors                  | Subgroup/treatment          | N     | Age (y) | BMI (kg/m²) | Race/ethnicity | Uterine volume (cm³) | Primary fibroid volume (cm³) | FIGO classification |
|--------------------------|----------------------------|-------|---------|-------------|----------------|----------------------|--------------------------|---------------------|
| Uterine volume           | < Median (≤356.5 cm³)       |       |         |             |                |                      |                          |                     |
| Placebo                  | 88                         | 41.5  | 34.1    | 7.5         | 58 (65.9)      | 6 (12.5)            | 196.5 (83.8 - 675.5)        | 11 (12.5)           |
| Elagolix + E2/NETA       | 203                        | 42.1  | 33.8    | 7.2         | 120 (59.1)     | 168 (82.8)           | 202.1 (83.8 - 665.2)        | 27.3 (1.3)          |
| ≥Median (≥356.5 cm³)     |                            |       |         |             |                |                      |                          |                     |
| Placebo                  | 108                        | 42.4  | 33.6    | 7.4         | 75 (69.4)      | 89 (82.4)            | 302.3 (88.8 - 1207.1)       | 267.3 (1.3)         |
| Elagolix + E2/NETA       | 192                        | 43.1  | 32.7    | 6.5         | 145 (75.9)     | 162 (84.4)           | 266.6 (86.6 - 1118.0)       | 126.7 (4.9)         |
| Primary fibroid volume   | < Median (≤36.2 cm³)        |       |         |             |                |                      |                          |                     |
| Placebo                  | 92                         | 42.1  | 34.4    | 7.9         | 61 (66.3)      | 78 (84.8)            | 212.6 (83.8 - 828.6)        | 13.9 (1.3)          |
| Elagolix + E2/NETA       | 189                        | 42.5  | 33.8    | 6.9         | 114 (60.3)     | 155 (82.0)           | 210.0 (83.8 - 1118.0)       | 292.9 (71.6)        |
| ≥Median (≥36.2 cm³)      |                            |       |         |             |                |                      |                          |                     |
| Placebo                  | 100                        | 41.9  | 33.4    | 7.2         | 69 (69.0)      | 86 (86.0)            | 296.2 (88.8 - 1207.1)       | 153.9 (38.6)        |
| Elagolix + E2/NETA       | 200                        | 42.6  | 32.7    | 6.8         | 149 (74.9)     | 170 (85.0)           | 258.7 (87.6 - 930.8)        | 133.9 (36.6)        |

Percentages calculated on nonmissing values.

Data are mean (SD), n (%), or mean (minimum—maximum).

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; NETA, norethindrone acetate; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2.

\( N = 394; ^{1} N = 192; ^{2} N = 389; ^{3} N = 36; ^{4} N = 65; ^{5} N = 128; ^{6} N = 161; ^{7} N = 68; ^{8} N = 160; ^{9} N = 40; ^{10} N = 85; ^{11} N = 52; ^{12} N = 112; ^{13} N = 76; ^{14} N = 224; ^{15} N = 130; ^{16} N = 263; ^{17} N = 62; ^{18} N = 125; ^{19} N = 28; ^{20} N = 64; ^{21} N = 329; ^{22} N = 164; ^{23} N = 325; ^{24} N = 170; ^{25} N = 190; ^{26} N = 200; ^{27} N = 191; ^{28} N = 107; ^{29} N = 189. \)

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## SUPPLEMENTAL TABLE 2
Change in menstrual blood loss from baseline to final month by demographic subgroup

| Factors          | Subgroup/treatment | N  | Change from baseline in MBL volume to final month, mL (SE) | Difference from placebo, mL, (SE) | P value |
|------------------|--------------------|----|----------------------------------------------------------|----------------------------------|---------|
| **Age (y)**      |                    |    |                                                          |                                  |         |
| <35              | Placebo            | 18 | 19.8 (31.5)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 37 | -149.2 (22.1)                                            | -169.1 (38.8)                    | <.001   |
| ≥35              | Placebo            | 41 | -34.4 (19.1)                                             |                                  |         |
|                  | Elagolix+E2/NETA   | 66 | -167.5 (15.2)                                            | -133.1 (24.4)                    | <.001   |
| ≥40              | Placebo            | 68 | 24.2 (21.6)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 130| -175.8 (15.6)                                            | -200.1 (28.7)                    | <.001   |
| ≥45              | Placebo            | 69 | -4.4 (16.4)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 162| -179.9 (10.5)                                            | -175.5 (19.6)                    | <.001   |
| **BMI (kg/m²)**  | <25                |    |                                                          |                                  |         |
|                  | Placebo            | 21 | -4.1 (29.8)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 49 | -169.7 (19.9)                                            | -165.6 (35.7)                    | <.001   |
| ≥25              | Placebo            | 42 | 25.1 (32.7)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 86 | -151.0 (22.3)                                            | -176.1 (40.0)                    | <.001   |
| ≥30              | Placebo            | 53 | -6.6 (16.1)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 113| -195.1 (10.5)                                            | -188.5 (19.1)                    | <.001   |
| ≥35              | Placebo            | 43 | -30.6 (18.5)                                             |                                  |         |
|                  | Elagolix+E2/NETA   | 79 | -185.1 (13.8)                                            | -154.5 (23.1)                    | <.001   |
| ≥40              | Placebo            | 37 | -0.9 (24.3)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 67 | -145.9 (17.8)                                            | -145.0 (30.1)                    | <.001   |
| **Race**         | Black/African American | |                                                          |                                  |         |
|                  | Placebo            | 133| -4.7 (12.8)                                              |                                  |         |
|                  | Elagolix+E2/NETA   | 265| -177.1 (9.1)                                             | -172.4 (15.6)                    | <.001   |
| Not black/African American | | | | | |
|                  | Placebo            | 63 | 7.3 (19.6)                                               |                                  |         |
|                  | Elagolix+E2/NETA   | 129| -163.6 (13.7)                                            | -170.9 (23.9)                    | <.001   |

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021. (continued)
| Factors          | Subgroup/treatment | N  | Change from baseline in MBL volume to final month, mL (SE) | Difference from placebo, mL (SE) | P value |
|------------------|--------------------|----|------------------------------------------------------------|----------------------------------|---------|
| Ethnicity        | Hispanic/Latino    |    |                                                            |                                  |         |
|                  | Placebo            | 30 | 25.7 (25.2)                                                |                                  |         |
|                  | Elagolix + E2/NETA | 65 | -161.5 (16.9)                                              | -187.2 (30.4)                    | < .001  |
|                  | Not Hispanic/Latino|    |                                                            |                                  |         |
|                  | Placebo            | 166| -6.1 (11.8)                                                |                                  |         |
|                  | Elagolix + E2/NETA | 330| -174.4 (8.4)                                               | -168.3 (14.5)                    | < .001  |

Data are least-squares mean (SE).

Final month was defined as the last 28 days before and including the reference day.

Missing final month MBL was imputed using multiple imputation (subset of the data sets obtained by multiple imputation for the primary analysis for subjects with baseline demographic characteristics).

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo by pooling the results from an ANCOVA model with treatment and study as the main effects and baseline MBL volume as a covariate in each data set from multiple imputation.

ANCOVA, analysis of covariance; BMI, body mass index; E2, estradiol; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2.

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.
| Factors                      | Subgroup/treatment | n/N     | Proportion of women with amenorrhea during final month, % (95% CI) | Difference from placebo, % (95% CI) | P value |
|------------------------------|--------------------|---------|------------------------------------------------------------------|----------------------------------|---------|
| Overall pooled study population | Placebo            | 8/176   | 4.5 (1.5—7.62)                                                   |                                  |         |
|                              | Elagolix+E2/NETA   | 179/355 | 50.4 (45.2, 55.6)                                                | 45.9 (39.8, 51.9)                | <.001   |
| Age (y)                      |                    |         |                                                                  |                                  |         |
| <35                          | Placebo            | 1/16    | 6.3 (0.0—18.1)                                                  |                                  |         |
|                              | Elagolix+E2/NETA   | 18/33   | 54.5 (37.6—71.5)                                                | 48.3 (27.6—69.0)                | <.001   |
| ≥35—<40                      | Placebo            | 2/37    | 5.4 (0.0—12.7)                                                  |                                  |         |
|                              | Elagolix+E2/NETA   | 28/62   | 45.2 (32.8—57.6)                                                | 39.8 (25.4—54.1)                | <.001   |
| ≥40—<45                      | Placebo            | 1/59    | 1.7 (0.0—5.0)                                                   |                                  |         |
|                              | Elagolix+E2/NETA   | 63/115  | 54.8 (45.7—63.9)                                                | 53.1 (43.4—62.8)                | <.001   |
| ≥45                          | Placebo            | 4/64    | 6.3 (0.3—12.2)                                                  |                                  |         |
|                              | Elagolix+E2/NETA   | 70/145  | 48.3 (40.1, 56.4)                                               | 42.0 (32.0, 52.1)                | <.001   |
| BMI (kg/m²)                  |                     |         |                                                                  |                                  |         |
| <25                          | Placebo            | 3/19    | 15.8 (0.0—32.2)                                                 |                                  |         |
|                              | Elagolix+E2/NETA   | 19/40   | 47.5 (32.0—62.3)                                                | 31.7 (9.2—54.3)                 | .021    |
| ≥25—<30                      | Placebo            | 0/39    | 0.0 (0.0—0.0)                                                   |                                  |         |
|                              | Elagolix+E2/NETA   | 44/80   | 55.0 (44.1—65.9)                                                | 55.0 (44.1—65.9)                | <.001   |
| ≥30—<35                      | Placebo            | 3/47    | 6.4 (0.0—13.4)                                                  |                                  |         |
|                              | Elagolix+E2/NETA   | 51/100  | 51.0 (41.2—60.8)                                                | 44.6 (32.6—56.7)                | <.001   |
| ≥35—<40                      | Placebo            | 1/38    | 2.6 (0.0—7.7)                                                   |                                  |         |
|                              | Elagolix+E2/NETA   | 31/70   | 44.3 (32.7—55.9)                                                | 41.7 (29.0—54.4)                | <.001   |
| ≥40                          | Placebo            | 1/33    | 3.0 (0.0—8.9)                                                   |                                  | <.001   |
|                              | Elagolix+E2/NETA   | 33/64   | 51.6 (39.3, 63.8)                                               | 48.5 (35.0, 62.1)                | <.001   |

*Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.* (continued)
### SUPPLEMENTAL TABLE 3
Proportion of women with amenorrhea during the final month by subgroup (continued)

| Factors                        | Subgroup/treatment           | n/N     | Proportion of women with amenorrhea during final month, % (95% CI) | Difference from placebo, % (95% CI) | *P* value |
|-------------------------------|------------------------------|---------|---------------------------------------------------------------------|-------------------------------------|-----------|
| **Race**                      |                              |         |                                                                     |                                     |           |
| Black/African American        | Placebo                      | 6/117   | 5.1 (1.1—9.1)                                                       |                                     |           |
|                               | Elagolix + E2/NETA           | 120/239 | 50.2 (43.9—56.6)                                                   | 45.1 (37.6—52.6)                    | <.001     |
| Not black/African American    | Placebo                      | 2/59    | 3.4 (0.0—8.0)                                                       |                                     |           |
|                               | Elagolix + E2/NETA           | 59/115  | 51.3 (42.2, 60.4)                                                   | 47.9 (37.7, 58.2)                   | <.001     |
| **Ethnicity**                 |                              |         |                                                                     |                                     |           |
| Hispanic/Latino               | Placebo                      | 2/29    | 6.9 (0.0—16.1)                                                      |                                     |           |
|                               | Elagolix + E2/NETA           | 32/57   | 56.1 (43.3—69.0)                                                   | 49.2 (33.4—65.1)                    | <.001     |
| Not Hispanic/Latino           | Placebo                      | 6/147   | 4.1 (0.9—7.3)                                                       |                                     |           |
|                               | Elagolix + E2/NETA           | 147/298 | 49.3 (43.7, 55.0)                                                   | 45.2 (38.7, 51.8)                   | <.001     |
| **Lowest FIGO type classification** |                              |         |                                                                     |                                     |           |
| 0—3                           | Placebo                      | 1/36    | 2.8 (0.0—8.2)                                                       |                                     |           |
|                               | Elagolix + E2/NETA           | 44/92   | 47.8 (37.6—58.0)                                                   | 45.0 (33.5—56.6)                    | <.001     |
| 4                             | Placebo                      | 6/100   | 6.0 (1.4—10.7)                                                      |                                     |           |
|                               | Elagolix + E2/NETA           | 93/195  | 47.7 (40.7—54.7)                                                   | 41.7 (33.3—50.1)                    | <.001     |
| 5—8                           | Placebo                      | 1/36    | 2.8 (0.0—8.2)                                                       |                                     |           |
|                               | Elagolix + E2/NETA           | 37/62   | 59.7 (47.5—71.9)                                                   | 56.9 (43.6—70.2)                    | <.001     |

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## SUPPLEMENTAL TABLE 3
Proportion of women with amenorrhea during the final month by subgroup (continued)

| Factors                        | Subgroup/treatment | n/N     | Proportion of women with amenorrhea during final month, % (95% CI) | Difference from placebo, % (95% CI) | P-value |
|--------------------------------|--------------------|---------|---------------------------------------------------------------------|-------------------------------------|---------|
| Highest FIGO type classification | 0–3                |         |                                                                     |                                     |         |
| Placebo                        | 1/19               | 5.3 (0.0—15.3) |                                                                 |                                     |         |
| Elagolix+E2/NETA               | 22/45              | 48.9 (34.3—63.5) | 43.6 (25.9—61.4) | .002                              |         |
| Placebo                        | 5/78               | 6.4 (1.0—11.9) |                                                                 |                                     | <.001   |
| Elagolix+E2/NETA               | 77/155             | 49.7 (41.8—57.6) | 43.3 (33.7—52.8) | <.001                              |         |
| Placebo                        | 2/75               | 2.7 (0.0—6.3) |                                                                 |                                     | <.001   |
| Elagolix+E2/NETA               | 75/149             | 50.3 (42.3—58.4) | 47.7 (38.9—56.5) | <.001                              |         |
| Primary fibroid FIGO classification | 0–3                |         |                                                                     |                                     | <.001   |
| Placebo                        | 0/31               | 0.0                              |                                     |                          |         |
| Elagolix+E2/NETA               | 37/75              | 49.3 (38.0—60.7) | 49.3 (38.0—60.7) | <.001                              |         |
| Placebo                        | 6/88               | 6.8 (1.6—12.1) |                                                                 |                                     | <.001   |
| Elagolix+E2/NETA               | 83/169             | 49.1 (41.6—56.7) | 42.3 (33.1—51.5) | <.001                              |         |
| Placebo                        | 2/53               | 3.8 (0.0—8.9) |                                                                 |                                     | <.001   |
| Elagolix+E2/NETA               | 54/105             | 51.4 (41.9—61.0) | 47.7 (36.8—58.5) | <.001                              |         |
| Uterine volume (median=356.5 cm³) | < Median          |         |                                                                     |                                     |         |
| Placebo                        | 6/78               | 7.7 (1.8—13.6) |                                                                 |                                     |         |
| Elagolix+E2/NETA               | 100/180            | 55.6 (48.3—62.8) | 47.9 (38.5—57.2) | <.001                              |         |
| ≥ Median                       |                     |         |                                                                     |                                     |         |
| Placebo                        | 2/98               | 2.0 (0.0—4.8) |                                                                 |                                     | <.001   |
| Elagolix+E2/NETA               | 79/175             | 45.1 (37.8—52.5) | 43.1 (35.2—51.0) | <.001                              |         |

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### SUPPLEMENTAL TABLE 3
Proportion of women with amenorrhea during the final month by subgroup (continued)

| Factors                        | Subgroup/treatment | n/N   | Proportion of women with amenorrhea during final month, % (95% CI) | Difference from placebo, % (95% CI) | P value |
|--------------------------------|--------------------|-------|---------------------------------------------------------------------|-------------------------------------|---------|
| Primary fibroid volume (median¼36.2 cm³) | < Median           |       |                                                                     |                                     |         |
| Placebo                        | 5/83               | 6.0 (0.9—11.1)                      |                                     |                                     |         |
| Elagolix+E2/NETA               | 86/164             | 52.4 (44.8—60.1)                     | 46.4 (37.2—55.6)                     | <.001                              |         |
| ≥ Median                       |                    |                                 |                                     |                                     |         |
| Placebo                        | 3/89               | 3.4 (0.0—7.1)                       |                                     |                                     |         |
| Elagolix+E2/NETA               | 88/185             | 47.6 (40.4—54.8)                     | 44.2 (36.1—52.3)                     | <.001                              |         |

Data are presented as % (95% CI).

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

The denominator is the number of women with at least 38 days on elagolix with add-back before and including the reference day and having amenorrhea status at the final month of treatment for each subset.

CIs for the response rate and difference between response rates is based on the normal approximation.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo by the Cochran-Mantel-Haenszel test using study as the stratification factor.

BMI, body mass index; CI, confidence interval; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; NETA, norethindrone acetate; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2.

Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.
| Factors                     | Subgroup/treatment   | N  | Symptom severity Baseline | Month 6 | HRQoL total Baseline | Month 6 |
|-----------------------------|----------------------|----|---------------------------|---------|----------------------|---------|
|                             |                      |    |                           |         |                      |         |
| Overall pooled study population | Placebo             | 152| 60.8                      | 51.4    | 42.9                 | 52.1    |
|                             | Elagolix + E2/NETA   | 302| 59.2                      | 23.0    | 44.2                 | 83.6    |
| Age (y)                     |                      |    |                           |         |                      |         |
| <35                         | Placebo             | 15 | 61.9                      | 52.3    | 39.0                 | 46.6    |
|                             | Elagolix + E2/NETA   | 28 | 59.4                      | 23.3    | 47.3                 | 83.8    |
| ≥35 — < 40                  | Placebo             | 30 | 58.8                      | 51.0    | 43.3                 | 53.1    |
|                             | Elagolix + E2/NETA   | 52 | 64.7                      | 24.6    | 41.7                 | 82.5    |
| ≥40 — < 45                  | Placebo             | 48 | 58.3                      | 51.1    | 45.3                 | 53.3    |
|                             | Elagolix + E2/NETA   | 98 | 55.9                      | 20.4    | 45.3                 | 84.6    |
| ≥45                         | Placebo             | 59 | 63.5                      | 51.6    | 41.7                 | 52.1    |
|                             | Elagolix + E2/NETA   | 124| 59.5                      | 24.4    | 43.7                 | 83.2    |
| BMI (kg/m²)                 |                      |    |                           |         |                      |         |
| <25                         | Placebo             | 16 | 57.8                      | 51.0    | 46.5                 | 60.1    |
|                             | Elagolix + E2/NETA   | 30 | 57.9                      | 22.8    | 46.9                 | 84.9    |
| ≥25 — < 30                  | Placebo             | 37 | 58.6                      | 55.2    | 42.0                 | 46.2    |
|                             | Elagolix + E2/NETA   | 68 | 58.2                      | 22.2    | 46.0                 | 85.1    |
| ≥30 — < 35                  | Placebo             | 35 | 61.3                      | 51.1    | 41.7                 | 51.7    |
|                             | Elagolix + E2/NETA   | 85 | 60.5                      | 23.5    | 43.6                 | 82.8    |
| ≥35 — < 40                  | Placebo             | 35 | 64.1                      | 52.9    | 39.8                 | 49.3    |
|                             | Elagolix + E2/NETA   | 62 | 60.9                      | 21.2    | 43.1                 | 85.6    |
| ≥40                         | Placebo             | 29 | 60.5                      | 45.4    | 47.1                 | 59.1    |
|                             | Elagolix + E2/NETA   | 56 | 57.3                      | 25.3    | 42.7                 | 79.9    |

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### SUPPLEMENTAL TABLE 4
Mean scores at baseline and month 6 for symptom severity and HRQoL total (continued)

| Factors                              | Subgroup/treatment          | N   | Symptom severity | HRQoL total |
|--------------------------------------|-----------------------------|-----|------------------|-------------|
|                                      |                             |     | Baseline | Month 6 | Baseline | Month 6 |
| Race                                 | Black/African American      |     |          |          |           |          |
|                                      | Placebo                     | 103 | 58.9     | 49.9    | 43.4<sup>g</sup> | 52.5<sup>g</sup> |
|                                      | Elagolix + E2/NETA          | 206 | 59.1     | 25.1    | 44.7<sup>h</sup> | 82.2<sup>h</sup> |
|                                      |                             |     |          |          |           |          |
|                                      | Not black/African American  |     |          |          |           |          |
|                                      | Placebo                     | 49  | 64.7     | 54.5    | 41.8     | 51.4    |
|                                      | Elagolix + E2/NETA          | 95  | 59.6     | 18.2    | 43.6     | 86.6    |
|                                      |                             |     |          |          |           |          |
|                                      | MBL volume (median = 187.0 mL)<br>&/C21<br><Median |     |          |          |           |          |
|                                      | Placebo                     | 69  | 59.6     | 46.6    | 45.8     | 56.1    |
|                                      | Elagolix + E2/NETA          | 163 | 58.4     | 22.5    | 48.2     | 84.2    |
|                                      |                             |     |          |          |           |          |
|                                      | >Median                      |     |          |          |           |          |
|                                      | Placebo                     | 83  | 61.7     | 55.4    | 40.4<sup>i</sup> | 48.8<sup>i</sup> |
|                                      | Elagolix + E2/NETA          | 139 | 60.1     | 23.7    | 39.5<sup>j</sup> | 82.8<sup>j</sup> |
|                                      |                             |     |          |          |           |          |
|                                      | Lowest FIGO type classification<br>0–3<br><br>4<br><br>5–8 |     |          |          |           |          |
|                                      | Placebo                     | 32  | 59.2     | 58.7    | 45.7     | 49.0    |
|                                      | Elagolix + E2/NETA          | 79  | 61.3     | 22.4    | 45.3     | 84.7    |
|                                      |                             |     |          |          |           |          |
|                                      | 4                           |     |          |          |           |          |
|                                      | Placebo                     | 82  | 61.3     | 48.4    | 42.6<sup>k</sup> | 54.2<sup>k</sup> |
|                                      | Elagolix + E2/NETA          | 161 | 58.7     | 23.7    | 41.9<sup>l</sup> | 82.5<sup>l</sup> |
|                                      |                             |     |          |          |           |          |
|                                      | 5–8                         |     |          |          |           |          |
|                                      | Placebo                     | 34  | 61.0     | 53.2    | 41.6     | 49.6    |
|                                      | Elagolix + E2/NETA          | 57  | 58.5     | 21.6    | 48.8     | 85.4    |
|                                      |                             |     |          |          |           |          |
|                                      | Highest FIGO type classification<br>0–3<br><br>4 |     |          |          |           |          |
|                                      | Placebo                     | 18  | 57.1     | 54.3    | 50.5     | 56.2    |
|                                      | Elagolix + E2/NETA          | 39  | 63.2     | 22.9    | 47.7     | 87.2    |
|                                      |                             |     |          |          |           |          |
|                                      | 4                           |     |          |          |           |          |
|                                      | Placebo                     | 62  | 61.5     | 52.6    | 43.7<sup>m</sup> | 51.6<sup>m</sup> |
|                                      | Elagolix + E2/NETA          | 129 | 60.1     | 24.0    | 41.6<sup>n</sup> | 82.0<sup>n</sup> |

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### SUPPLEMENTAL TABLE 4
Mean scores at baseline and month 6 for symptom severity and HRQoL total (continued)

| Factors                                      | Subgroup/treatment | N  | Symptom severity | HRQoL total |
|----------------------------------------------|--------------------|----|------------------|-------------|
|                                              |                    |    | Baseline | Month 6 | Baseline | Month 6 |
| 5–8                                          |                    |    |           |         |           |         |
| Placebo                                      | 68                 |    | 61.1     | 50.3    | 40.5     | 51.3    |
| Elagolix + E2/NETA                          | 129                |    | 57.5     | 22.0    | 45.6     | 84.2    |
| Primary fibroid FIGO classification 0–3      |                    |    |           |         |           |         |
| Placebo                                      | 28                 |    | 60.6     | 59.0    | 45.5     | 49.7    |
| Elagolix + E2/NETA                          | 65                 |    | 63.6     | 22.1    | 44.2     | 85.3    |
| 4                                            |                    |    |           |         |           |         |
| Placebo                                      | 70                 |    | 62.5     | 51.1    | 40.4\(^\circ\) | 51.5\(^\circ\) |
| Elagolix + E2/NETA                          | 139                |    | 57.6     | 24.8    | 42.7\(^p\) | 81.7\(^p\) |
| 5–8                                          |                    |    |           |         |           |         |
| Placebo                                      | 50                 |    | 58.6     | 48.6    | 45.3     | 54.1    |
| Elagolix + E2/NETA                          | 93                 |    | 59.0     | 20.8    | 44.9     | 85.4    |
| Uterine volume (median = 356.5 cm\(^3\)) < Median |                |    |           |         |           |         |
| Placebo                                      | 65                 |    | 61.2     | 46.6    | 44.7\(^q\) | 55.6\(^q\) |
| Elagolix + E2/NETA                          | 155                |    | 58.1     | 21.9    | 44.1     | 83.9    |
| >Median                                      |                    |    |           |         |           |         |
| Placebo                                      | 87                 |    | 60.5     | 55.0    | 41.5     | 49.6    |
| Elagolix + E2/NETA                          | 147                |    | 60.4     | 24.2    | 44.4\(^l\) | 83.3\(^l\) |
| Primary fibroid volume (median = 36.2 cm\(^3\)) < Median |                |    |           |         |           |         |
| Placebo                                      | 71                 |    | 61.5     | 49.5    | 44.1\(^s\) | 54.7\(^s\) |
| Elagolix + E2/NETA                          | 141                |    | 57.6     | 20.8    | 45.0\(^i\) | 85.4\(^i\) |
| >Median                                      |                    |    |           |         |           |         |
| Placebo                                      | 77                 |    | 60.1     | 53.8    | 42.1     | 49.6    |
| Elagolix + E2/NETA                          | 156                |    | 61.0     | 24.9    | 43.5     | 82.1    |

Data are presented as mean scores.

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; HRQoL, health-related quality of life; MBL, menstrual blood loss; NETA, norethindrone acetate; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2.

\(^a\) N=151; \(^b\) N=301; \(^c\) N=29; \(^d\) N=123; \(^e\) N=67; \(^f\) N=34; \(^g\) N=102; \(^h\) N=205; \(^i\) N=82; \(^j\) N=138; \(^k\) N=81; \(^l\) N=160; \(^m\) N=61; \(^n\) N=128; \(^o\) N=60; \(^p\) n=138; \(^q\) N=64; \(^r\) N=146; \(^s\) N=70; \(^t\) N=140.

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**SUPPLEMENTAL TABLE 5**
Overview of UFS-QOL Concern subscale at baseline and month 6 for the overall group and subgroups

| Factors       | Subgroup/treatment | N   | Baseline score<sup>a</sup> | Month 6 score<sup>a</sup> | Change in score from baseline to month 6<sup>b</sup> (SE) | Difference from placebo<sup>b</sup> (SE) | Pvalue  |
|---------------|--------------------|-----|-----------------------------|---------------------------|--------------------------------------------------------|---------------------------------------|---------|
| Overall pooled study population | Placebo            | 151 | 27.9                        | 38.2                      | 9.8 (2.0)                                              | 43.9 (2.5)                           | <.001   |
|               | Elagolix+E2/NETA   | 301 | 29.7                        | 82.6                      | 53.7 (1.4)                                              | 43.9 (2.5)                           | <.001   |
| Age (y)       |                    |     |                             |                           |                                                        |                                       |         |
| <35           | Placebo            | 15  | 28.3                        | 39.7                      | 10.1 (7.3)                                              |                                       | <.001   |
|               | Elagolix+E2/NETA   | 28  | 36.6                        | 83.6                      | 52.2 (5.5)                                              | 42.0 (9.2)                           | <.001   |
| ≥35—<40       | Placebo            | 29  | 27.4                        | 40.7                      | 14.3 (4.9)                                              |                                       | <.001   |
|               | Elagolix+E2/NETA   | 52  | 25.7                        | 82.6                      | 56.5 (3.7)                                              | 42.2 (6.1)                           | <.001   |
| ≥40—<45       | Placebo            | 48  | 30.8                        | 38.1                      | 7.6 (3.5)                                               |                                       | <.001   |
|               | Elagolix+E2/NETA   | 98  | 31.2                        | 84.0                      | 53.4 (2.4)                                              | 45.7 (4.3)                           | <.001   |
| ≥45           | Placebo            | 59  | 25.6                        | 36.8                      | 9.5 (3.2)                                               |                                       | <.001   |
|               | Elagolix+E2/NETA   | 123 | 28.7                        | 81.4                      | 53.1 (2.2)                                              | 43.6 (3.9)                           | <.001   |
| BMI (kg/m<sup>2</sup>) |                |     |                             |                           |                                                        |                                       |         |
| <25           | Placebo            | 16  | 39.7                        | 53.8                      | 18.3 (5.7)                                              |                                       | <.001   |
|               | Elagolix+E2/NETA   | 30  | 32.2                        | 85.7                      | 53.0 (4.1)                                              | 34.7 (7.1)                           | <.001   |
| ≥25—<30       | Placebo            | 37  | 28.2                        | 30.9                      | 1.8 (3.5)                                               |                                       | <.001   |
|               | Elagolix+E2/NETA   | 67  | 29.5                        | 83.5                      | 54.1 (2.6)                                              | 52.3 (4.4)                           | <.001   |
| ≥30—<35       | Placebo            | 35  | 24.9                        | 38.1                      | 10.3 (4.4)                                              |                                       | <.001   |
|               | Elagolix+E2/NETA   | 85  | 31.2                        | 81.6                      | 52.0 (2.8)                                              | 41.7 (5.3)                           | <.001   |
| ≥35—<40       | Placebo            | 34  | 24.7                        | 35.9                      | 9.3 (4.2)                                               |                                       | <.001   |
|               | Elagolix+E2/NETA   | 62  | 28.7                        | 86.8                      | 59.4 (3.1)                                              | 50.1 (5.2)                           | <.001   |
| ≥40           | Placebo            | 29  | 28.3                        | 41.9                      | 14.6 (5.2)                                              |                                       | <.001   |
|               | Elagolix+E2/NETA   | 56  | 27.5                        | 77.1                      | 50.0 (3.7)                                              | 35.4 (6.42)                          | <.001   |

*Al-Hendy et al. Predictors of response in elagolix-treated women with uterine fibroids. Am J Obstet Gynecol 2021.*

(continued)
### SUPPLEMENTAL TABLE 5
Overview of UFS-QOL Concern subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                        | Subgroup/treatment | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|-------------------------------|--------------------|----|----------------|---------------|-----------------------------------------------|-----------------------------|---------|
| Race                          | Black/African American |    |                |               |                                               |                             |         |
|                               | Placebo            | 102| 26.2           | 35.7          | 8.5 (2.6)                                     |                             |         |
|                               | Elagolix + E2/NETA | 205| 29.3           | 79.8          | 51.6 (1.9)                                    | 43.1 (3.2)                  | <.001   |
|                               | Not black/African American |     |                |               |                                               |                             |         |
|                               | Placebo            | 49 | 31.4           | 43.5          | 12.3 (3.0)                                    |                             |         |
|                               | Elagolix + E2/NETA | 95 | 30.9           | 88.9          | 57.9 (2.2)                                    | 45.5 (3.7)                  | <.001   |
| MBL volume (median = 187.0 mL) | < Median           |    |                |               |                                               |                             |         |
|                               | Placebo            | 69 | 30.7           | 42.8          | 10.0 (2.9)                                    |                             |         |
|                               | Elagolix + E2/NETA | 163| 35.5           | 84.0          | 50.0 (1.9)                                    | 40.0 (3.6)                  | <.001   |
|                               | ≥ Median           |    |                |               |                                               |                             |         |
|                               | Placebo            | 82 | 25.5           | 34.4          | 10.2 (2.9)                                    |                             |         |
|                               | Elagolix + E2/NETA | 138| 22.9           | 81.0          | 57.6 (2.2)                                    | 47.4 (3.5)                  | <.001   |
| Lowest FIGO type classification | 0–3                |    |                |               |                                               |                             |         |
|                               | Placebo            | 32 | 33.9           | 36.6          | 4.4 (4.2)                                     |                             |         |
|                               | Elagolix + E2/NETA | 79 | 30.1           | 82.9          | 52.1 (2.6)                                    | 47.8 (5.0)                  | <.001   |
|                               | 4                  |    |                |               |                                               |                             |         |
|                               | Placebo            | 81 | 26.7           | 40.1          | 13.3 (2.8)                                    |                             |         |
|                               | Elagolix + E2/NETA | 160| 27.3           | 81.3          | 54.3 (2.0)                                    | 41.0 (3.5)                  | <.001   |
|                               | 5–8                |    |                |               |                                               |                             |         |
|                               | Placebo            | 34 | 26.2           | 35.1          | 6.0 (4.1)                                     |                             |         |
|                               | Elagolix + E2/NETA | 57 | 34.4           | 85.1          | 53.9 (3.1)                                    | 47.9 (5.2)                  | <.001   |
| Highest FIGO type classification | 0–3                |    |                |               |                                               |                             |         |
|                               | Placebo            | 18 | 43.9           | 48.9          | 11.5 (5.8)                                    |                             |         |
|                               | Elagolix + E2/NETA | 39 | 31.4           | 85.0          | 52.3 (3.9)                                    | 40.8 (7.0)                  | <.001   |
|                               | 4                  |    |                |               |                                               |                             |         |
|                               | Placebo            | 61 | 26.3           | 35.1          | 8.3 (3.2)                                     |                             |         |
|                               | Elagolix + E2/NETA | 128| 27.7           | 80.8          | 53.7 (2.2)                                    | 45.4 (3.8)                  | <.001   |

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### SUPPLEMENTAL TABLE 5
Overview of UFS-QOL Concern subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                        | Subgroup/treatment | N   | Baseline score* | Month 6 score* | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|--------------------------------|--------------------|-----|-----------------|----------------|-----------------------------------------------|-----------------------------|---------|
|                                |                    |     |                 |                |                                               |                             |         |
| 5–8                            | Placebo            | 68  | 25.7            | 38.2           | 10.1 (3.1)                                   | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 129 | 30.6            | 83.4           | 53.9 (2.3)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 43.9 (3.8)                  |         |
| Primary fibroid FIGO classification 0–3 | Placebo     | 28  | 34.1            | 37.7           | 6.0 (4.4)                                    | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 65  | 29.5            | 84.0           | 54.1 (2.9)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 48.1 (5.3)                  |         |
|                                | Placebo            | 69  | 24.1            | 37.0           | 11.1 (3.1)                                   | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 138 | 28.4            | 79.9           | 52.5 (2.2)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 41.8 (3.9)                  |         |
| 5–8                            | Placebo            | 50  | 30.5            | 40.1           | 9.5 (3.3)                                    | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 93  | 31.0            | 85.3           | 54.5 (2.4)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 45.0 (4.1)                  |         |
| Uterine volume (median=356.5 cm³) | < Median       | 64  | 26.2            | 40.2           | 11.5 (3.1)                                   | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 155 | 30.2            | 83.0           | 53.2 (1.9)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 41.7 (3.7)                  |         |
|                                | ≥ Median           | 87  | 29.1            | 36.8           | 8.6 (7.1)                                    | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 146 | 29.2            | 82.3           | 54.0 (2.1)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 45.5 (3.4)                  |         |
| Primary fibroid volume (median=36.2 cm³) | < Median     | 70  | 28.4            | 41.2           | 11.6 (2.8)                                   | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 140 | 30.1            | 84.0           | 54.0 (1.9)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 42.3 (3.4)                  |         |
|                                | ≥ Median           | 77  | 28.0            | 35.5           | 8.1 (4.5)                                    | Elagolix + E2/NETA          | .001    |
|                                | Elagolix + E2/NETA | 156 | 28.9            | 81.1           | 53.5 (2.2)                                   |                             | .001    |
|                                |                    |     |                 |                |                                               | 45.4 (3.7)                  |         |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.
Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.
ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.
* Data are presented as means; † Data are presented as least-squares means (SE).
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### SUPPLEMENTAL TABLE 6
Overview of UFS-QOL Activities subscale at baseline and month 6 for the overall group and subgroups

| Factors          | Subgroup/treatment | N    | Baseline score a | Month 6 score a | Change in score from baseline to month 6 b (SE) | Difference from placebo b (SE) | P value |
|------------------|--------------------|------|------------------|-----------------|-----------------------------------------------|-------------------|---------|
|                  | Overall pooled study population | | | | | | |
|                  | Placebo           | 151  | 39.8            | 51.3            | 10.3 (1.8)                                  | 34.6 (2.1)         | <.001   |
|                  | Elagolix + E2/NETA| 301  | 42.8            | 42.8            | 45.0 (1.2)                                  | 34.6 (2.1)         | <.001   |
| Age (y)          | <35                | | | | | | |
|                  | Placebo           | 15   | 38.6            | 51.0            | 10.8 (6.5)                                  | 33.5 (8.2)         | <.001   |
|                  | Elagolix + E2/NETA| 28   | 46.4            | 85.3            | 44.3 (4.8)                                  | 33.5 (8.2)         | <.001   |
|                  | ≥35–<40           | | | | | | |
|                  | Placebo           | 29   | 40.8            | 51.4            | 11.7 (4.3)                                  | 34.0 (5.3)         | <.001   |
|                  | Elagolix + E2/NETA| 52   | 40.7            | 85.4            | 45.7 (3.2)                                  | 34.0 (5.3)         | <.001   |
|                  | ≥40–<45           | | | | | | |
|                  | Placebo           | 48   | 42.4            | 51.9            | 9.3 (3.1)                                   | 35.2 (3.8)         | <.001   |
|                  | Elagolix + E2/NETA| 98   | 44.6            | 87.8            | 44.5 (2.2)                                  | 35.2 (3.8)         | <.001   |
|                  | ≥45               | | | | | | |
|                  | Placebo           | 59   | 37.6            | 50.8            | 10.5 (2.6)                                  | 34.9 (3.2)         | <.001   |
|                  | Elagolix + E2/NETA| 123  | 41.5            | 86.7            | 45.4 (1.8)                                  | 34.9 (3.2)         | <.001   |
| BMI (kg/m²)      | <25               | | | | | | |
|                  | Placebo           | 16   | 42.4            | 59.6            | 16.8 (5.2)                                  | 26.1 (6.4)         | <.001   |
|                  | Elagolix + E2/NETA| 30   | 43.3            | 86.0            | 42.9 (3.8)                                  | 26.1 (6.4)         | <.001   |
|                  | ≥25–<30           | | | | | | |
|                  | Placebo           | 37   | 37.6            | 44.0            | 2.3 (3.4)                                   | 10.6 (3.4)         | <.001   |
|                  | Elagolix + E2/NETA| 67   | 45.5            | 88.4            | 45.1 (2.5)                                  | 42.8 (4.2)         | <.001   |
|                  | ≥30–<35           | | | | | | |
|                  | Placebo           | 35   | 41.7            | 53.0            | 10.5 (3.6)                                  | 30.0 (4.2)         | <.001   |
|                  | Elagolix + E2/NETA| 85   | 44.5            | 86.5            | 43.4 (2.3)                                  | 30.0 (4.2)         | <.001   |
|                  | ≥35–<40           | | | | | | |
|                  | Placebo           | 34   | 36.7            | 46.8            | 8.5 (3.9)                                   | 33.5 (4.8)         | <.001   |
|                  | Elagolix + E2/NETA| 62   | 41.1            | 89.4            | 48.3 (2.9)                                  | 41.6 (4.8)         | <.001   |
|                  | ≥40               | | | | | | |
|                  | Placebo           | 29   | 42.6            | 59.2            | 18.5 (4.2)                                  | 24.1 (5.2)         | <.001   |
|                  | Elagolix + E2/NETA| 56   | 38.7            | 82.0            | 42.6 (3.0)                                  | 24.1 (5.2)         | <.001   |

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## SUPPLEMENTAL TABLE 6
Overview of UFS-QOL Activities subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors | Subgroup/treatment       | N    | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|---------|--------------------------|------|----------------|---------------|-----------------------------------------------|-------------------------------|---------|
|         | Race                     |      |                |               |                                               |                               |         |
|         | Black/African American   |      |                |               |                                               |                               |         |
|         | Placebo                  | 102  | 41.9           | 51.8          | 9.6 (2.3)                                     |                               | <.001   |
|         | Elagolix+E2/NETA         | 205  | 43.6           | 85.4          | 42.8 (1.6)                                    | 33.2 (2.8)                    | <.001   |
|         |                           |      |                |               |                                               |                               |         |
|         | Not black/African American |   |                |               |                                               |                               |         |
|         | Placebo                  | 49   | 35.6           | 50.4          | 11.5 (2.7)                                    |                               | <.001   |
|         | Elagolix+E2/NETA         | 95   | 41.7           | 89.5          | 49.5 (1.9)                                    | 37.9 (3.3)                    | <.001   |
|         | MBL volume (median=187.0 mL) |  |                |               |                                               |                               |         |
|         | < Median                 |      |                |               |                                               |                               |         |
|         | Placebo                  | 69   | 44.8           | 57.6          | 10.3 (2.6)                                    |                               | <.001   |
|         | Elagolix+E2/NETA         | 163  | 49.9           | 87.6          | 39.1 (1.7)                                    | 28.7 (3.1)                    | <.001   |
|         |                           |      |                |               |                                               |                               |         |
|         | ≥ Median                 |      |                |               |                                               |                               |         |
|         | Placebo                  | 82   | 35.6           | 46.0          | 11.3 (2.3)                                    |                               | <.001   |
|         | Elagolix+E2/NETA         | 138  | 34.5           | 85.7          | 51.2 (1.8)                                    | 40.0 (3.0)                    | <.001   |
|         | Lowest FIGO type classification |  |                |               |                                               |                               |         |
|         | 0–3                      |      |                |               |                                               |                               |         |
|         | Placebo                  | 32   | 40.0           | 48.7          | 7.8 (3.8)                                     |                               | <.001   |
|         | Elagolix+E2/NETA         | 79   | 42.9           | 87.0          | 45.5 (2.4)                                    | 37.7 (4.5)                    | <.001   |
|         | 4                        |      |                |               |                                               |                               |         |
|         | Placebo                  | 81   | 39.9           | 53.5          | 13.4 (2.4)                                    |                               | <.001   |
|         | Elagolix+E2/NETA         | 160  | 40.2           | 85.7          | 45.5 (1.7)                                    | 32.1 (2.9)                    | <.001   |
|         | ≥8                       |      |                |               |                                               |                               |         |
|         | Placebo                  | 34   | 39.6           | 47.8          | 4.7 (3.5)                                     |                               | <.001   |
|         | Elagolix+E2/NETA         | 57   | 49.7           | 89.5          | 43.7 (2.7)                                    | 39.1 (4.4)                    | <.001   |
|         | Highest FIGO type classification | |                |               |                                               |                               |         |
|         | 0–3                      |      |                |               |                                               |                               |         |
|         | Placebo                  | 18   | 46.8           | 58.9          | 13. (5.4)                                     |                               | <.001   |
|         | Elagolix+E2/NETA         | 39   | 47.8           | 88.4          | 42.9 (3.7)                                    | 29.2 (6.5)                    | <.001   |
|         | 4                        |      |                |               |                                               |                               |         |
|         | Placebo                  | 61   | 39.1           | 50.7          | 11.9 (2.7)                                    |                               | <.001   |
|         | Elagolix+E2/NETA         | 128  | 38.9           | 85.1          | 46.4 (1.9)                                    | 34.4 (3.3)                    | <.001   |

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### SUPPLEMENTAL TABLE 6
Overview of UFS-QOL Activities subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors | Subgroup/treatment | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|---------|--------------------|----|----------------|---------------|-----------------------------------------------|-------------------------------|---------|
| 5–8     | Placebo            | 68 | 38.7           | 49.4          | 7.6 (2.6)                                     |                               |         |
|         | Elagolix + E2/NETA | 129| 45.1           | 88.0          | 44.5 (1.9)                                    | 36.8 (3.2)                   | <.001   |

| Primary fibroid FIGO classification | 0–3 | Placebo | 28 | 41.7 | 50.5 | 10.0 (4.2) | 36.8 (3.2) | <.001 |
|                                   |     | Elagolix + E2/NETA | 65 | 42.1 | 87.1 | 46.5 (2.7) | 36.5 (5.0) | <.001 |
|                                   |     | Placebo | 69 | 37.1 | 50.6 | 11.5 (2.6) | 33.4 (3.2) | <.001 |
|                                   |     | Elagolix + E2/NETA | 138| 41.4 | 84.9 | 44.9 (1.8) | 30.1 (3.0) | <.001 |

| 5–8     | Placebo            | 50 | 42.7           | 52.2          | 8.4 (2.8)                                     |                               |         |
|         | Elagolix + E2/NETA | 93 | 45.3           | 89.3          | 44.8 (2.0)                                    | 36.4 (3.4)                   | <.001   |

| Uterine volume (median = 356.5 cm³) | < Median | Placebo | 64 | 43.0 | 57.4 | 13.7 (2.6) | 30.1 (3.0) | <.001 |
|                                   | ≥ Median | Elagolix + E2/NETA | 155| 44.1 | 87.6 | 43.8 (1.6) | 37.6 (3.0) | <.001 |

| Primary fibroid volume (median = 36.2 cm³) | < Median | Placebo | 70 | 41.8 | 56.1 | 12.7 (2.3) | 32.2 (2.8) | <.001 |
|                                          | ≥ Median | Elagolix + E2/NETA | 140| 44.9 | 89.1 | 45.0 (1.6) | 37.5 (3.2) | <.001 |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.

ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

* Data are presented as least-squares means (SE).
* Data are presented as means; b Data are presented as least-squares means (SE).

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### SUPPLEMENTAL TABLE 7
Overview of UFS-QOL Energy/Mood subscale at baseline and month 6 for the overall group and subgroups

| Factors                | Subgroup/treatment | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|------------------------|--------------------|----|----------------|---------------|-----------------------------------------------|-------------------------------|---------|
| Overall pooled study population | Placebo           | 151| 47.5           | 57.4          | 9.6 (1.7)                                     | 23.3 (2.0)                   | <.001   |
|                        | Elagolix + E2/NETA | 301| 48.5           | 84.1          | 36.0 (1.2)                                    | 26.3 (2.0)                   | <.001   |
| Age (y)                |                    |    |                |               |                                               |                              |         |
| <35                    | Placebo            | 15 | 43.8           | 50.5          | 6.4 (6.0)                                     | 26.3 (2.0)                   | <.001   |
|                        | Elagolix + E2/NETA | 28 | 47.4           | 85.1          | 37.7 (5.4)                                    | 34.1 (7.5)                   | <.001   |
| ≥35 – <40              | Placebo            | 29 | 47.3           | 57.1          | 11.8 (4.0)                                    | 24.7 (5.0)                   | <.001   |
|                        | Elagolix + E2/NETA | 52 | 44.5           | 81.0          | 36.5 (3.0)                                    | 24.7 (5.0)                   | <.001   |
| ≥40 – <45              | Placebo            | 48 | 49.0           | 59.4          | 10.4 (2.8)                                    | 26.9 (3.5)                   | <.001   |
| ≥45                    | Placebo            | 59 | 47.3           | 57.7          | 8.5 (2.6)                                     | 24.8 (3.2)                   | <.001   |
| BMI (kg/m²)            |                    |    |                |               |                                               |                              |         |
| <25                    | Placebo            | 16 | 50.7           | 65.2          | 14.1 (4.4)                                    | 21.9 (5.5)                   | <.001   |
|                        | Elagolix + E2/NETA | 30 | 51.7           | 87.3          | 35.9 (3.2)                                    | 21.9 (5.5)                   | <.001   |
| ≥25 – <30              | Placebo            | 37 | 48.6           | 52.5          | 3.9 (3.3)                                     | 10.1 (3.3)                   | <.001   |
|                        | Elagolix + E2/NETA | 67 | 50.4           | 85.3          | 35.5 (2.5)                                    | 32.3 (4.1)                   | <.001   |
| ≥30 – <35              | Placebo            | 35 | 44.6           | 56.4          | 11.8 (3.6)                                    | 27.0 (4.3)                   | <.001   |
|                        | Elagolix + E2/NETA | 85 | 46.8           | 84.0          | 37.2 (2.3)                                    | 27.0 (4.3)                   | <.001   |
| ≥35 – <40              | Placebo            | 34 | 45.0           | 54.9          | 9.9 (3.5)                                     | 29.2 (4.4)                   | <.001   |
|                        | Elagolix + E2/NETA | 62 | 47.8           | 84.9          | 37.1 (2.6)                                    | 29.2 (4.4)                   | <.001   |
| ≥40                    | Placebo            | 29 | 50.6           | 63.5          | 12.9 (3.8)                                    | 15.1 (3.8)                   | <.001   |
|                        | Elagolix + E2/NETA | 56 | 47.5           | 80.0          | 32.6 (2.8)                                    | 17.4 (4.7)                   | <.001   |

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| Factors                        | Subgroup/treatment                        | N   | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | Pvalue |
|-------------------------------|-------------------------------------------|-----|----------------|---------------|-----------------------------------------------|-------------------------------|--------|
| Race                          | Black/African American                    |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 102 | 48.3           | 58.2          | 9.7 (3.0)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 205 | 49.6           | 83.4          | 64.6 (1.5)                                    | 24.9 (2.6)                    | <.001  |
|                               | Not black/African American                |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 49  | 45.7           | 55.8          | 9.2 (2.7)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 95  | 46.3           | 85.4          | 38.6 (1.9)                                    | 29.4 (3.3)                    | <.001  |
| MBL volume (median=187.0 mL)  | < Median                                  |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 69  | 48.7           | 58.9          | 9.1 (2.5)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 163 | 50.9           | 84.5          | 34.1 (1.6)                                    | 25.0 (2.9)                    | <.001  |
|                               | ≥ Median                                  |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 82  | 46.5           | 56.2          | 10.4 (2.2)                                    |                               |        |
|                               | Elagolix + E2/NETA                        | 138 | 45.6           | 83.5          | 37.9 (1.7)                                    | 27.5 (2.8)                    | <.001  |
| Lowest FIGO type classification | 0–3                                      |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 32  | 50.9           | 54.4          | 3.8 (3.5)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 79  | 50.5           | 85.8          | 35.5 (2.2)                                    | 31.6 (4.1)                    | <.001  |
|                               | 4                                         |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 81  | 47.1           | 59.2          | 12.6 (2.3)                                    |                               |        |
|                               | Elagolix + E2/NETA                        | 160 | 46.8           | 82.4          | 35.8 (1.6)                                    | 23.3 (2.9)                    | <.001  |
|                               | 5–8                                       |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 34  | 45.7           | 55.3          | 7.2 (3.0)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 57  | 50.4           | 86.7          | 37.3 (2.3)                                    | 30.1 (3.8)                    | <.001  |
| Highest FIGO type classification | 0–3                                     |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 18  | 51.2           | 56.5          | 5.8 (4.7)                                     |                               |        |
|                               | Elagolix + E2/NETA                        | 39  | 51.9           | 89.5          | 38.5 (3.2)                                    | 32.7 (5.7)                    | <.001  |
|                               | 4                                         |     |                |               |                                               |                               |        |
|                               | Placebo                                   | 61  | 48.8           | 57.1          | 10.6 (2.7)                                    |                               |        |
|                               | Elagolix + E2/NETA                        | 128 | 45.9           | 81.6          | 35.7 (1.8)                                    | 25.1 (3.2)                    | <.001  |

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### SUPPLEMENTAL TABLE 7
Overview of UFS-QOL Energy/Mood subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                          | Subgroup/treatment | N   | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | Pvalue  |
|----------------------------------|--------------------|-----|----------------|---------------|-----------------------------------------------|-------------------------------|---------|
| 5–8                              | Placebo            | 68  | 45.5           | 57.5          | 9.3 (2.4)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 129 | 50.0           | 85.1          | 35.6 (1.7)                                   | 26.4 (2.9)                   | <.001   |
| Primary fibroid FIGO classification | 0–3                |     |                |               |                                              |                              |         |
|                                  | Placebo            | 28  | 50.1           | 54.3          | 5.5 (3.8)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 65  | 49.3           | 86.5          | 37.9 (2.4)                                   | 32.4 (4.5)                   | <.001   |
|                                  | 4                  |     |                |               |                                              |                              |         |
|                                  | Placebo            | 69  | 44.6           | 56.0          | 9.8 (2.6)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 138 | 49.2           | 81.8          | 34.3 (1.9)                                   | 24.5 (3.2)                   | <.001   |
| 5–8                              | Placebo            | 50  | 50.3           | 60.6          | 11.1 (2.5)                                   |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 93  | 46.9           | 86.1          | 37.4 (1.8)                                   | 26.3 (3.1)                   | <.001   |
| Uterine volume (median=356.5 cm³) | <Median            |     |                |               |                                              |                              |         |
|                                  | Placebo            | 64  | 47.6           | 57.8          | 10.4 (2.5)                                   |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 155 | 46.8           | 84.4          | 37.2 (1.6)                                   | 26.8 (2.9)                   | <.001   |
|                                  | ≥Median            |     |                |               |                                              |                              |         |
|                                  | Placebo            | 87  | 47.4           | 57.2          | 9.0 (2.2)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 146 | 50.3           | 83.7          | 34.6 (1.7)                                   | 25.6 (2.8)                   | <.001   |
| Primary fibroid volume (median=36.2 cm³) | <Median            |     |                |               |                                              |                              |         |
|                                  | Placebo            | 70  | 46.3           | 56.9          | 8.9 (2.3)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 140 | 48.9           | 86.2          | 37.5 (1.6)                                   | 28.6 (2.8)                   | <.001   |
|                                  | ≥Median            |     |                |               |                                              |                              |         |
|                                  | Placebo            | 77  | 48.8           | 57.6          | 9.9 (2.4)                                    |                                | <.001   |
|                                  | Elagolix+E2/NETA   | 156 | 48.1           | 82.3          | 34.8 (1.7)                                   | 24.9 (2.9)                   | <.001   |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.

ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

* Data are presented as means; † Data are presented as least-squares means (SE).

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### SUPPLEMENTAL TABLE 8
Overview of UFS-QOL Control subscale at baseline and month 6 for the overall group and subgroups

| Factors          | Subgroup/treatment | N   | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | Pvalue |
|------------------|--------------------|-----|----------------|---------------|---------------------------------------------|----------------------------|--------|
| Overall pooled study population | Placebo            | 151 | 55.5           | 63.4          | 8.6 (1.7)                                   | 23.6 (2.0)                 | <.001  |
|                  | Elagolix + E2/NETA | 301 | 55.2           | 86.9          | 32.2 (1.2)                                   |                           |        |
| Age (y)          | <35                |     |                |               |                                             |                           |        |
|                  | Placebo            | 15  | 41.7           | 48.3          | 2.0 (5.7)                                   |                           |        |
|                  | Elagolix + E2/NETA | 28  | 54.3           | 85.9          | 39.7 (4.2)                                   | 36.7 (7.1)                 | <.001  |
|                  | >35—<40            |     |                |               |                                             |                           |        |
|                  | Placebo            | 29  | 52.9           | 63.3          | 10.0 (4.2)                                   |                           |        |
|                  | Elagolix + E2/NETA | 52  | 53.7           | 86.5          | 33.2 (3.2)                                   | 23.0 (5.3)                 | <.001  |
|                  | >40—<45            |     |                |               |                                             |                           |        |
|                  | Placebo            | 48  | 59.3           | 65.4          | 6.1 (3.0)                                   |                           |        |
|                  | Elagolix + E2/NETA | 98  | 57.8           | 87.1          | 30.0 (2.1)                                   | 22.2 (3.7)                 | <.001  |
|                  | >45                |     |                |               |                                             |                           |        |
|                  | Placebo            | 59  | 57.3           | 65.8          | 8.4 (2.4)                                   |                           |        |
|                  | Elagolix + E2/NETA | 123 | 53.9           | 87.2          | 33.3 (1.7)                                   | 22.4 (2.9)                 | <.001  |
| BMI (kg/m^2)     | <25                |     |                |               |                                             |                           |        |
|                  | Placebo            | 16  | 47.8           | 64.4          | 10.8 (4.5)                                   |                           |        |
|                  | Elagolix + E2/NETA | 30  | 59.3           | 89.5          | 33.1 (3.3)                                   | 22.3 (5.7)                 | <.001  |
|                  | >25—<30            |     |                |               |                                             |                           |        |
|                  | Placebo            | 37  | 54.5           | 59.6          | 4.3 (3.3)                                   |                           |        |
|                  | Elagolix + E2/NETA | 67  | 57.9           | 88.6          | 30.7 (2.5)                                   | 27.8 (4.2)                 | <.001  |
|                  | >30—<35            |     |                |               |                                             |                           |        |
|                  | Placebo            | 35  | 53.6           | 62.6          | 9.0 (3.4)                                   |                           |        |
|                  | Elagolix + E2/NETA | 85  | 53.2           | 87.6          | 34.4 (2.2)                                   | 25.2 (4.0)                 | <.001  |
|                  | >35—<40            |     |                |               |                                             |                           |        |
|                  | Placebo            | 34  | 54.6           | 61.6          | 7.7 (3.9)                                   |                           |        |
|                  | Elagolix + E2/NETA | 62  | 53.1           | 86.5          | 33.4 (2.9)                                   | 25.3 (4.9)                 | <.001  |
|                  | >40                |     |                |               |                                             |                           |        |
|                  | Placebo            | 29  | 64.7           | 71.0          | 6.3 (3.7)                                   |                           |        |
|                  | Elagolix + E2/NETA | 56  | 54.6           | 82.8          | 28.2 (2.7)                                   | 15.4 (4.6)                 | .001   |

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### Overview of UFS-QOL Control subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                              | Subgroup/treatment       | N     | Baseline score<sup>a</sup> | Month 6 score<sup>a</sup> | Change in score from baseline to month 6<sup>b</sup> (SE) | Difference from placebo<sup>c</sup> (SE) | Pvalue  |
|--------------------------------------|--------------------------|-------|----------------------------|---------------------------|----------------------------------------------------------|------------------------------------------|---------|
| **Race**                             |                          |       |                            |                           |                                                          |                                          |         |
| Black/African American                | Placebo                  | 102   | 57.5                       | 65.1                      | 9.5 (2.1)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 205   | 55.5                       | 85.9                      | 30.8 (1.5)                                                | 21.3 (2.6)                                | <.001   |
| Not black/African American            | Placebo                  | 49    | 51.4                       | 60.0                      | 6.5 (2.6)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 95    | 55.0                       | 89.3                      | 34.8 (1.8)                                                | 28.2 (3.2)                                | <.001   |
| **MBL volume (median = 187.0 mL)**    | < Median                 |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 69    | 59.8                       | 68.1                      | 8.9 (2.4)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 163   | 59.4                       | 87.1                      | 27.9 (1.6)                                                | 19.0 (2.9)                                | <.001   |
|                                      | ≥ Median                 |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 82    | 52.0                       | 59.5                      | 9.0 (2.3)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 138   | 50.1                       | 86.8                      | 36.8 (1.8)                                                | 27.8 (2.9)                                | <.001   |
| **Lowest FIGO type classification**   | 0–3                      |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 32    | 57.2                       | 58.9                      | 1.7 (3.7)                                                 |                                          | <.001   |
|                                      | Elagolix + E2/NETA       | 79    | 55.6                       | 87.7                      | 32.1 (2.4)                                                | 29.3 (4.4)                                | <.001   |
|                                      | 4                        |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 81    | 55.6                       | 65.4                      | 12.0 (2.3)                                                |                                          | <.001   |
|                                      | Elagolix + E2/NETA       | 160   | 52.2                       | 86.0                      | 33.5 (1.6)                                                | 21.3 (2.8)                                | <.001   |
|                                      | 5–8                      |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 34    | 54.3                       | 61.3                      | 6.9 (3.1)                                                 |                                          | <.001   |
|                                      | Elagolix + E2/NETA       | 57    | 62.7                       | 89.1                      | 29.1 (2.4)                                                | 25.2 (4.0)                                | <.001   |
| **Highest FIGO type classification**  | 0–3                      |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 18    | 58.9                       | 65.0                      | 6.1 (5.1)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 39    | 56.4                       | 89.9                      | 33.5 (3.5)                                                | 25.5 (6.2)                                | <.001   |
|                                      | 4                        |       |                            |                           |                                                          |                                          |         |
|                                      | Placebo                  | 61    | 57.3                       | 63.6                      | 6.3 (2.7)                                                 |                                          |         |
|                                      | Elagolix + E2/NETA       | 128   | 51.3                       | 84.9                      | 32.6 (1.9)                                                | 22.9 (3.3)                                | <.001   |

<sup>a</sup> Baseline and month 6 scores are reported as mean values. <sup>b</sup> Change in score from baseline to month 6 is reported as mean change (SE). <sup>c</sup> Difference from placebo is reported as mean difference (SE).

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### SUPPLEMENTAL TABLE 8
Overview of UFS-QOL Control subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                                      | Subgroup/treatment | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P-value |
|----------------------------------------------|--------------------|----|----------------|---------------|-----------------------------------------------|-------------------------------|---------|
| 5–8                                          | Placebo            | 68 | 53.3           | 62.1          | 6.7 (2.4)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 129| 58.6           | 88.4          | 31.4 (1.7)                                    | 24.7 (2.9)                    |         |
| Primary fibroid FIGO classification 0–3      | Placebo            | 28 | 55.7           | 58.4          | 4.4 (4.1)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 65 | 53.7           | 88.3          | 34.8 (2.7)                                    | 30.5 (5.0)                    | <.001   |
| 4                                            | Placebo            | 69 | 53.3           | 63.8          | 11.0 (2.5)                                    |                               | <.001   |
|                                              | Elagolix + E2/NETA | 138| 53.9           | 85.2          | 32.2 (1.8)                                    | 21.2 (3.1)                    | <.001   |
| 5–8                                          | Placebo            | 50 | 58.9           | 64.6          | 6.5 (2.5)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 93 | 58.0           | 89.0          | 31.2 (1.8)                                    | 24.6 (3.1)                    | <.001   |
| Uterine volume (median=356.5 cm³)            | <Median            | 64 | 61.6           | 70.9          | 13.1 (2.5)                                    |                               | <.001   |
|                                              | Elagolix + E2/NETA | 155| 54.5           | 86.6          | 30.5 (1.6)                                    | 17.5 (2.9)                    | <.001   |
|                                              | >Median            | 87 | 51.0           | 58.0          | 5.9 (2.2)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 146| 55.8           | 87.3          | 33.7 (1.7)                                    | 27.8 (2.8)                    | <.001   |
| Primary fibroid volume (median=36.2 cm³)     | <Median            | 70 | 60.2           | 67.4          | 9.6 (2.3)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 140| 55.7           | 87.4          | 30.9 (1.6)                                    | 21.3 (2.8)                    | <.001   |
|                                              | >Median            | 77 | 51.5           | 59.1          | 7.1 (2.5)                                     |                               | <.001   |
|                                              | Elagolix + E2/NETA | 156| 54.6           | 86.8          | 33.9 (1.7)                                    | 26.9 (3.0)                    | <.001   |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set. Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.

ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2; Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

* Data are presented as means; † Data are presented as least-squares means (SE).

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### SUPPLEMENTAL TABLE 9
Overview of UFS-QOL Self-conscious subscale at baseline and month 6 for the overall group and subgroups

| Factors          | Subgroup/treatment       | N  | Baseline score<sup>a</sup> | Month 6 score<sup>b</sup> | Change in score from baseline to month 6<sup>c</sup> (SE) | Difference from placebo<sup>d</sup> (SE) | P value |
|------------------|--------------------------|----|-----------------------------|---------------------------|----------------------------------------------------------|------------------------------------------|---------|
| **Overall pooled study population** | **Placebo** | 151 | 38.9                        | 44.4                      | 4.3 (2.2)                                                | 31.7 (2.6)                              | <.001   |
|                  | **Elagolix + E2/NETA**   | 301 | 41.6                        | 77.0                      | 35.9 (1.5)                                               | 31.7 (2.6)                              | <.001   |
| **Age (y)**      | <35                      |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 15  | 37.2                        | 30.0                      | 12.3 (7.4)                                               |                                          |         |
|                  | **Elagolix + E2/NETA**   | 28  | 53.0                        | 79.2                      | 31.6 (5.5)                                               | 44.0 (9.3)                              | <.001   |
|                  | ≥35–<40                  |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 29  | 39.7                        | 49.1                      | 9.4 (4.9)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 52  | 39.7                        | 76.6                      | 36.8 (3.7)                                               | 27.4 (6.2)                              | <.001   |
|                  | ≥40–<45                  |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 48  | 39.4                        | 46.5                      | 6.5 (3.7)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 98  | 40.8                        | 78.4                      | 37.9 (2.6)                                               | 31.4 (4.5)                              | <.001   |
|                  | ≥45                      |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 59  | 38.6                        | 44.1                      | 4.2 (3.5)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 123 | 40.4                        | 75.5                      | 35.0 (2.4)                                               | 30.8 (4.3)                              | <.001   |
| **BMI (kg/m<sup>2</sup>)** | <25                      |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 16  | 50.0                        | 53.6                      | 4.0 (5.7)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 30  | 49.2                        | 77.5                      | 28.4 (4.2)                                               | 24.4 (7.1)                              | .001    |
|                  | ≥25–<30                  |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 37  | 43.9                        | 47.0                      | 2.1 (5.3)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 67  | 46.3                        | 73.5                      | 27.6 (3.9)                                               | 25.5 (6.7)                              | <.001   |
|                  | ≥30–<35                  |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 35  | 36.7                        | 41.2                      | 4.3 (4.9)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 85  | 38.3                        | 72.4                      | 35.0 (3.2)                                               | 30.7 (5.9)                              | <.001   |
|                  | ≥35–<40                  |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 34  | 30.4                        | 38.7                      | 3.0 (4.5)                                                |                                          |         |
|                  | **Elagolix + E2/NETA**   | 62  | 40.3                        | 79.8                      | 41.2 (3.3)                                               | 38.2 (5.6)                              | <.001   |
|                  | ≥40                      |     |                             |                           |                                                         |                                          |         |
|                  | **Placebo**              | 29  | 47.7                        | 56.0                      | 11.1 (4.9)                                               |                                          |         |

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| Factors                              | Subgroup/treatment     | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 \(^2\) (SE) | Difference from placebo \(^2\) (SE) | \(P\) value |
|-------------------------------------|------------------------|----|----------------|---------------|---------------------------------------------------|---------------------------------|-------------|
| Elagolix + E2/NETA                  |                        | 56 | 40.3           | 75.7          | 33.6 (3.6)                                        | 22.6 (6.2)                      | <.001       |
| Race                                | Black/African American |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 102| 37.3           | 43.9          | 5.4 (2.8)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 205| 40.8           | 75.9          | 36.2 (1.9)                                        | 30.8 (3.4)                      | <.001       |
| Not black/African American         |                        |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 49 | 42.3           | 45.6          | 1.5 (3.3)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 95 | 43.7           | 79.9          | 35.4 (2.4)                                        | 33.9 (4.1)                      | <.001       |
| MBL volume (median = 187.0 mL)     | < Median               |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 69 | 41.8           | 49.0          | 7.3 (3.2)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 163| 41.3           | 77.5          | 36.0 (2.1)                                        | 28.6 (3.8)                      | <.001       |
| ≥ Median                           |                        |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 82 | 36.5           | 40.5          | 1.9 (2.9)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 138| 41.9           | 76.4          | 35.8 (2.2)                                        | 33.9 (3.7)                      | <.001       |
| Lowest FIGO type classification    | 0–3                    |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 32 | 44.5           | 39.3          | −6.5 (4.5)                                        |                                 |             |
| Elagolix + E2/NETA                 |                        | 79 | 46.7           | 75.8          | 29.1 (2.8)                                        | 35.7 (5.3)                      | <.001       |
| 4                                  |                        |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 81 | 38.5           | 47.6          | 8.8 (3.0)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 160| 38.5           | 77.4          | 38.6 (2.1)                                        | 29.8 (3.7)                      | <.001       |
| 5–8                                |                        |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 34 | 35.8           | 41.9          | 4.1 (4.2)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 57 | 42.7           | 77.9          | 38.0 (3.2)                                        | 33.9 (5.3)                      | <.001       |
| Highest FIGO type classification   | 0–3                    |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 18 | 55.6           | 49.1          | −3.6 (6.2)                                        |                                 |             |
| Elagolix + E2/NETA                 |                        | 39 | 52.1           | 80.3          | 29.1 (4.2)                                        | 32.7 (7.5)                      | <.001       |
| 4                                  |                        |    |                |               |                                                   |                                |             |
| Placebo                            |                        | 61 | 40.0           | 46.0          | 5.3 (3.3)                                         |                                 |             |
| Elagolix + E2/NETA                 |                        | 128| 41.0           | 77.2          | 36.1 (2.2)                                        | 30.8 (3.9)                      | <.001       |

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SUPPLEMENTAL TABLE 9
Overview of UFS-QOL Self-conscious subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                                      | Subgroup/treatment | N  | Baseline score<sup>a</sup> | Month 6 score<sup>a</sup> | Change in score from baseline to month 6<sup>b</sup> (SE) | Difference from placebo<sup>c</sup> (SE) | Pvalue |
|----------------------------------------------|--------------------|----|-----------------------------|---------------------------|---------------------------------------------------------|------------------------------------------|--------|
| 5–8                                          | Placebo            | 68 | 34.1                        | 41.9                      | 5.2 (3.4)                                               |                                          |        |
|                                              | Elagolix + E2/NETA | 129| 38.7                        | 76.0                      | 37.8 (2.4)                                              | 32.6 (4.1)                               | <.001  |
| Primary fibroid FIGO classification 0–3      | Placebo            | 28 | 42.0                        | 39.0                      | −4.8 (4.9)                                              |                                          |        |
|                                              | Elagolix + E2/NETA | 65 | 46.7                        | 77.2                      | 31.4 (3.2)                                              | 36.2 (5.8)                               | <.001  |
| 4                                            | Placebo            | 69 | 38.8                        | 45.9                      | 5.9 (3.3)                                               |                                          |        |
|                                              | Elagolix + E2/NETA | 138| 40.6                        | 76.6                      | 36.0 (2.3)                                              | 30.1 (4.0)                               | <.001  |
| 5–8                                          | Placebo            | 50 | 38.2                        | 45.7                      | 7.2 (3.5)                                               |                                          |        |
|                                              | Elagolix + E2/NETA | 93 | 39.2                        | 77.9                      | 39.1 (2.6)                                              | 31.9 (4.4)                               | <.001  |
| Uterine volume (median = 356.5 cm<sup>3</sup>) | < Median            | Placebo            | 64 | 43.9                        | 49.6                      | 5.3 (3.2)                                               |                                          | <.001  |
|                                              | Elagolix + E2/NETA | 155| 44.0                        | 77.4                      | 33.1 (2.0)                                              | 27.8 (3.8)                               | <.001  |
|                                              | > Median            | Placebo            | 87 | 35.2                        | 40.6                      | 4.1 (2.9)                                               |                                          | <.001  |
|                                              | Elagolix + E2/NETA | 146| 39.0                        | 76.5                      | 38.6 (2.3)                                              | 34.5 (3.7)                               | <.001  |
| Primary fibroid volume (median = 36.2 cm<sup>3</sup>) | < Median            | Placebo            | 70 | 41.9                        | 47.7                      | 4.3 (3.0)                                               |                                          | <.001  |
|                                              | Elagolix + E2/NETA | 140| 43.3                        | 79.6                      | 35.7 (2.1)                                              | 31.4 (3.7)                               | <.001  |
|                                              | > Median            | Placebo            | 77 | 36.7                        | 41.6                      | 4.3 (3.2)                                               |                                          | <.001  |
|                                              | Elagolix + E2/NETA | 156| 39.9                        | 74.9                      | 36.6 (2.2)                                              | 32.2 (3.9)                               | <.001  |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.

ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

<sup>a</sup> Data are presented as means; <sup>b</sup> Data are presented as least-squares means (SE).

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**SUPPLEMENTAL TABLE 10**  
Overview of UFS-QOL Sexual Function subscale at baseline and month 6 for the overall group and subgroups

| Factors | Subgroup/treatment | N  | Baseline score | Month 6 score | Change in score from baseline to month 6 (SE) | Difference from placebo (SE) | P value |
|---------|--------------------|----|----------------|--------------|-----------------------------------------------|-----------------------------|---------|
| Overall pooled study population | Placebo | 150 | 49.2 | 54.9 | 6.6 (2.6) | 20.7 (3.1) | <.001 |
| | Elagolix + E2/NETA | 301 | 47.1 | 74.9 | 27.2 (1.8) | 20.7 (3.1) | <.001 |
| Age (y) | Placebo | <35 | 46.7 | 55.8 | 7.6 (7.7) | 19.0 (9.5) | .052 |
| | Elagolix + E2/NETA | 28 | 50.4 | 76.3 | 26.6 (5.6) | 22.2 (7.8) | .005 |
| | ≥35 – <40 | | | | | | |
| | Placebo | 29 | 58.6 | 56.9 | 3.0 (6.2) | 22.2 (7.8) | .005 |
| | Elagolix + E2/NETA | 52 | 48.3 | 76.0 | 25.2 (4.6) | 22.2 (7.8) | .005 |
| | ≥40 – <45 | | | | | | |
| | Placebo | 48 | 53.1 | 54.7 | 5.8 (4.4) | 20.2 (5.3) | <.001 |
| | Elagolix + E2/NETA | 98 | 46.2 | 72.6 | 26.0 (3.0) | 20.2 (5.3) | <.001 |
| | ≥45 | | | | | | |
| | Placebo | 58 | 41.8 | 53.9 | 8.9 (4.2) | 20.3 (5.1) | <.001 |
| | Elagolix + E2/NETA | 123 | 46.4 | 75.9 | 29.2 (2.9) | 20.3 (5.1) | <.001 |
| BMI (kg/m²) | Placebo | <25 | 54.7 | 58.6 | 7.4 (8.1) | 14.8 (10.0) | .144 |
| | Elagolix + E2/NETA | 30 | 44.6 | 70.8 | 22.2 (5.9) | 14.8 (10.0) | .144 |
| | ≥25 – <30 | | | | | | |
| | Placebo | 37 | 43.9 | 47.0 | 3.1 (5.3) | 14.8 (10.0) | .144 |
| | Elagolix + E2/NETA | 67 | 46.3 | 73.5 | 27.6 (3.9) | 25.5 (6.7) | <.001 |
| | ≥30 – <35 | | | | | | |
| | Placebo | 35 | 51.1 | 52.5 | 5.7 (5.5) | 18.4 (6.2) | <.001 |
| | Elagolix + E2/NETA | 85 | 43.2 | 72.5 | 28.4 (3.5) | 25.5 (6.7) | <.001 |
| | ≥35 – <40 | | | | | | |
| | Placebo | 33 | 47.0 | 59.1 | 10.1 (5.0) | 18.4 (6.2) | <.001 |
| | Elagolix + E2/NETA | 62 | 49.0 | 78.0 | 28.4 (3.5) | 25.5 (6.7) | <.001 |
| | ≥40 | | | | | | |
| | Placebo | 29 | 53.0 | 61.2 | 9.3 (5.8) | 17.6 (7.1) | .014 |
| | Elagolix + E2/NETA | 56 | 52.2 | 78.6 | 26.9 (4.1) | 17.6 (7.1) | .014 |

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| Factors                        | Subgroup/treatment | N   | Baseline score a | Month 6 score a | Change in score from baseline to month 6 b (SE) | Difference from placebo c (SE) | *P* value |
|-------------------------------|--------------------|-----|------------------|-----------------|-----------------------------------------------|--------------------------------|-----------|
| Race                          | Black/African American |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 101 | 48.5             | 59.0            | 10.6 (3.2)                                    |                                | <.001     |
|                               | Elagolix + E2/NETA | 205 | 48.3             | 73.7            | 25.3 (2.2)                                    | 14.8 (3.9)                     |           |
| Not black/African American    | Placebo            | 49  | 50.5             | 46.4            | −2.1 (4.2)                                    |                                 | <.001     |
|                               | Elagolix + E2/NETA | 95  | 44.6             | 77.2            | 30.9 (3.0)                                    | 33.1 (5.2)                     | <.001     |
| MBL volume (median = 187.0 mL)| < Median           |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 68  | 47.4             | 55.5            | 7.0 (3.8)                                     |                                 | <.001     |
|                               | Elagolix + E2/NETA | 163 | 47.4             | 74.9            | 26.4 (2.4)                                    | 19.4 (4.5)                     | <.001     |
|                               | ≥ Median           |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 82  | 50.6             | 54.4            | 6.6 (3.5)                                     |                                 | <.001     |
|                               | Elagolix + E2/NETA | 138 | 46.6             | 74.8            | 28.2 (2.7)                                    | 21.6 (4.4)                     | <.001     |
| Lowest FIGO type classification | 0–3                |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 32  | 50.0             | 52.7            | 4.9 (5.3)                                     |                                 | <.001     |
|                               | Elagolix + E2/NETA | 79  | 46.0             | 82.1            | 35.5 (3.4)                                    | 30.6 (6.3)                     | <.001     |
|                               | 4                  |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 81  | 49.4             | 56.8            | 8.6 (3.4)                                     |                                 | <.001     |
|                               | Elagolix + E2/NETA | 160 | 47.0             | 74.0            | 26.6 (2.4)                                    | 18.0 (4.3)                     | <.001     |
|                               | 5–8                |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 33  | 50.0             | 55.7            | 4.9 (5.5)                                     |                                 | <.001     |
|                               | Elagolix + E2/NETA | 57  | 50.4             | 69.5            | 18.5 (4.2)                                    | 13.7 (6.9)                     | .052      |
| Highest FIGO type classification | 0–3                |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 18  | 48.6             | 52.1            | 5.6 (7.1)                                     |                                 |           |
|                               | Elagolix + E2/NETA | 39  | 45.5             | 84.9            | 39.3 (4.8)                                    | 33.7 (8.6)                     | <.001     |
|                               | 4                  |     |                  |                 |                                               |                                 |           |
|                               | Placebo            | 61  | 56.6             | 54.9            | 3.7 (3.9)                                     |                                 |           |
|                               | Elagolix + E2/NETA | 128 | 48.1             | 75.8            | 27.4 (2.7)                                    | 23.7 (4.7)                     | <.001     |
### SUPPLEMENTAL TABLE 10
Overview of UFS-QOL Sexual Function subscale at baseline and month 6 for the overall group and subgroups (continued)

| Factors                                                                 | Subgroup/treatment | N   | Baseline score<sup>a</sup> | Month 6 score<sup>a</sup> | Change in score from baseline to month 6<sup>b</sup> (SE) | Difference from placebo<sup>c</sup> (SE) | P-value |
|------------------------------------------------------------------------|-------------------|-----|-----------------------------|----------------------------|----------------------------------------------------------|------------------------------------------|---------|
| 5 e 8                                                                  | Placebo           | 67  | 43.7                        | 57.3                       | 10.6 (3.9)                                               |                                          |         |
|                                                                        | Elagolix + E2/NETA| 129 | 47.2                        | 71.9                       | 23.9 (2.8)                                               | 13.3 (4.8)                               | .006    |
| Primary fibroid FIGO classification                                     | 0 e 3             |     |                             |                            |                                                          |                                          |         |
|                                                                        | Placebo           | 28  | 51.3                        | 54.5                       | 8.6 (5.8)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 65  | 42.5                        | 83.5                       | 40.1 (3.8)                                               | 31.4 (6.9)                               | <.001   |
|                                                                        | Placebo           | 69  | 48.6                        | 52.4                       | 3.6 (3.6)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 138 | 50.4                        | 73.8                       | 24.5 (2.6)                                               | 20.8 (4.5)                               | <.001   |
|                                                                        | Placebo           | 49  | 50.3                        | 61.0                       | 11.0 (4.5)                                               |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 93  | 46.4                        | 71.8                       | 23.2 (3.3)                                               | 12.2 (5.6)                               | .031    |
| Uterine volume (median = 356.5 cm<sup>3</sup>)                          | < Median          |     |                             |                            |                                                          |                                          |         |
|                                                                        | Placebo           | 64  | 45.7                        | 51.6                       | 6.2 (4.0)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 155 | 43.1                        | 73.6                       | 29.1 (2.6)                                               | 22.9 (4.7)                               | <.001   |
|                                                                        | Placebo           | 86  | 51.7                        | 57.4                       | 6.5 (3.3)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 146 | 51.2                        | 76.2                       | 25.4 (2.6)                                               | 19.0 (4.2)                               | <.001   |
| Primary fibroid volume (median = 36.2 cm<sup>3</sup>)                   | < Median          |     |                             |                            |                                                          |                                          |         |
|                                                                        | Placebo           | 70  | 46.1                        | 53.8                       | 7.6 (3.6)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 140 | 44.2                        | 76.3                       | 30.8 (2.5)                                               | 23.2 (4.4)                               | <.001   |
|                                                                        | Placebo           | 76  | 53.0                        | 57.4                       | 6.5 (3.7)                                                |                                          | <.001   |
|                                                                        | Elagolix + E2/NETA| 156 | 50.2                        | 74.4                       | 24.4 (2.6)                                               | 17.8 (4.6)                               | <.001   |

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

Statistical significance was determined for the difference between the elagolix with add-back dose group and placebo at month 6 from an ANOVA model with treatment as the main effect and baseline as a covariate.

ANOVA, analysis of variance; BMI, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

<sup>a</sup> Data are presented as means; <sup>b</sup> Data are presented as least-squares means (SE).

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### SUPPLEMENTAL TABLE 11
Overview of adverse events by subgroup

| Factors | Subgroup/treatment | TE AEs | Any AE | Any serious AE | Any severe AE | Any AE leading to discontinuation | Death |
|---------|--------------------|--------|--------|---------------|---------------|-----------------------------------|--------|
|         |                    |        |        |               |               |                                   |        |
| Age (y) | <35                |        |        |               |               |                                   |        |
| Placebo (N=8) |                  | 14 (77.8) | 1 (5.6) | 2 (11.1) | 3 (16.7) | 0                                  |        |
| Elagolix + E2/NETA (N=37) |         | 26 (70.3) | 0       | 5 (13.5) | 3 (8.1)  | 0                                  |        |
| ≥35−<40 |                    |        |        |               |               |                                   |        |
| Placebo (N=41) |                  | 27 (65.9) | 0       | 1 (2.4)  | 1 (2.4)  | 0                                  |        |
| Elagolix + E2/NETA (N=66) |         | 49 (74.2) | 0       | 7 (10.6) | 7 (10.6) | 0                                  |        |
| ≥40−<45 |                    |        |        |               |               |                                   |        |
| Placebo (N=68) |                  | 45 (66.2) | 2 (2.9)  | 5 (7.4)  | 6 (8.8)  | 0                                  |        |
| Elagolix + E2/NETA (N=130) |          | 93 (71.5) | 2 (1.5)  | 11 (8.5) | 11 (8.5) | 0                                  |        |
| ≥45     |                    |        |        |               |               |                                   |        |
| Placebo (N=69) |                  | 44 (63.8) | 3 (4.3)  | 2 (2.9)  | 3 (4.3)  | 0                                  |        |
| Elagolix + E2/NETA (N=163) |         | 115 (71.0) | 8 (4.9)  | 13 (8.0) | 17 (10.5) | 0                                  |        |
| BMI (kg/m²) |                 |        |        |               |               |                                   |        |
| <25     |                    |        |        |               |               |                                   |        |
| Placebo (N=21) |                  | 10 (47.6) | 0       | 3 (14.3) | 2 (9.5)  | 0                                  |        |
| Elagolix + E2/NETA (N=49) |         | 34 (69.4) | 0       | 6 (12.2) | 9 (18.4) | 0                                  |        |
| ≥25−<30 |                    |        |        |               |               |                                   |        |
| Placebo (N=42) |                  | 29 (69.0) | 2 (4.8)  | 4 (9.5)  | 2 (4.8)  | 0                                  |        |
| Elagolix + E2/NETA (N=86) |         | 62 (72.1) | 6 (7.0)  | 7 (8.1)  | 8 (9.3)  | 0                                  |        |
| ≥30−<35 |                    |        |        |               |               |                                   |        |
| Placebo (N=53) |                  | 35 (66.0) | 2 (3.8)  | 1 (1.9)  | 2 (3.8)  | 0                                  |        |
| Elagolix + E2/NETA (N=113) |        | 81 (71.7) | 0       | 9 (8.0)  | 13 (11.5) | 0                                  |        |
| ≥35−<40 |                    |        |        |               |               |                                   |        |
| Placebo (N=43) |                  | 30 (69.8) | 1 (2.3)  | 2 (4.7)  | 3 (7.0)  | 0                                  |        |
| Elagolix + E2/NETA (N=79) |         | 57 (72.2) | 1 (1.3)  | 6 (7.6)  | 4 (5.1)  | 0                                  |        |
| ≥40     |                    |        |        |               |               |                                   |        |
| Placebo (N=37) |                  | 26 (70.3) | 1 (2.7)  | 0       | 4 (10.8) | 0                                  |        |
| Elagolix + E2/NETA (N=67) |         | 49 (73.1) | 3 (4.5)  | 8 (11.9) | 4 (6.0)  | 0                                  |        |
### SUPPLEMENTAL TABLE 11
Overview of adverse events by subgroup (continued)

| Factors                        | Subgroup/treatment                  | TE AEs                                      |
|-------------------------------|-------------------------------------|---------------------------------------------|
|                               |                                     | Any AE  | Any serious AE<sup>a</sup> | Any severe AE<sup>b</sup> | Any AE leading to discontinuation | Death |
| Race                          | Black or African American           |         |                           |                          |                                     |       |
|                               | Placebo (N=133)                     | 85 (63.9)| 5 (3.8)                  | 6 (4.5)                  | 9 (6.8)                          | 0     |
|                               | Elagolix+E2/NETA (N=265)            | 193 (72.8)| 8 (3.0)                  | 29 (10.9)                | 26 (9.8)                         | 0     |
|                               | Not black or African American       |         |                           |                          |                                     |       |
|                               | Placebo (N=63)                      | 45 (71.4)| 1 (1.6)                  | 4 (6.3)                  | 4 (6.3)                          | 0     |
|                               | Elagolix+E2/NETA (N=129)            | 89 (69.0)| 2 (1.6)                  | 7 (5.4)                  | 12 (9.3)                         | 0     |
| Ethnicity                     | Hispanic/Latino                     |         |                           |                          |                                     |       |
|                               | Placebo (N=30)                      | 21 (70.0)| 1 (3.3)                  | 2 (6.7)                  | 1 (3.3)                          | 0     |
|                               | Elagolix+E2/NETA (N=65)             | 44 (67.7)| 2 (3.1)                  | 6 (9.2)                  | 5 (7.7)                          | 0     |
|                               | Not Hispanic/Latino                 |         |                           |                          |                                     |       |
|                               | Placebo (N=166)                     | 21 (70.0)| 5 (3.0)                  | 8 (4.8)                  | 12 (7.2)                         | 0     |
|                               | Elagolix+E2/NETA (N=330)            | 44 (67.7)| 8 (2.4)                  | 30 (9.1)                 | 33 (10.0)                        | 0     |
| Lowest FIGO type classification |                                     |         |                           |                          |                                     |       |
|                               | 0–3                                 |         |                           |                          |                                     |       |
|                               | Placebo (N=45)                      | 30 (66.7)| 1 (2.2)                  | 2 (4.4)                  | 6 (13.3)                         | 0     |
|                               | Elagolix+E2/NETA (N=95)             | 58 (61.1)| 2 (2.1)                  | 5 (5.3)                  | 3 (3.2)                          | 0     |
|                               | 4                                   |         |                           |                          |                                     |       |
|                               | Placebo (N=110)                     | 73 (66.4)| 4 (3.6)                  | 7 (6.4)                  | 6 (5.5)                          | 0     |
|                               | Elagolix+E2/NETA (N=225)            | 176 (78.2)| 8 (3.6)                  | 30 (13.3)                | 27 (12.0)                        | 0     |
|                               | 5–8                                 |         |                           |                          |                                     |       |
|                               | Placebo (N=37)                      | 25 (67.6)| 1 (2.7)                  | 1 (2.7)                  | 1 (2.7)                          | 0     |
|                               | Elagolix+E2/NETA (N=69)             | 45 (65.2)| 0                        | 1 (1.4)                  | 8 (11.6)                         | 0     |

<sup>a</sup> Includes any AE leading to discontinuation

<sup>b</sup> Includes any AE leading to discontinuation and death

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## SUPPLEMENTAL TABLE 11
Overview of adverse events by subgroup (continued)

| Factors                                      | Subgroup/treatment | TE AEs |  |
|----------------------------------------------|--------------------|--------|---|
| Highest FIGO type classification 0–3         |                    |        |   |
| Placebo (N=25)                               | 15 (60.0)          | 1 (4.0)| 1 (4.0)| 2 (8.0)| 0 |
| Elagolix+E2/NETA (N=47)                      | 24 (51.1)          | 2 (4.3)| 2 (4.3)| 2 (4.3)| 0 |
| 4                                             |                    |        |   |
| Placebo (N=85)                               | 55 (64.7)          | 2 (2.4)| 5 (5.9)| 7 (8.2)| 0 |
| Elagolix+E2/NETA (N=177)                     | 138 (78.0)         | 7 (4.0)| 23 (13.0)| 19 (10.7)| 0 |
| 5–8                                          |                    |        |   |
| Placebo (N=82)                               | 58 (70.7)          | 3 (3.7)| 4 (4.9)| 4 (4.9)| 0 |
| Elagolix+E2/NETA (N=165)                     | 117 (70.9)         | 1 (0.6)| 11 (6.7)| 17 (10.3)| 0 |
| Primary fibroid FIGO classification 0–3       |                    |        |   |
| Placebo (N=38)                               | 26 (68.4)          | 1 (2.6)| 1 (2.6)| 4 (10.5)| 0 |
| Elagolix+E2/NETA (N=78)                      | 47 (60.3)          | 2 (2.6)| 5 (6.4)| 3 (3.8)| 0 |
| 4                                             |                    |        |   |
| Placebo (N=96)                               | 63 (65.6)          | 4 (4.2)| 5 (5.2)| 6 (6.3)| 0 |
| Elagolix+E2/NETA (N=191)                     | 151 (79.1)         | 7 (3.7)| 22 (11.5)| 20 (10.5)| 0 |
| 5–8                                          |                    |        |   |
| Placebo (N=58)                               | 39 (67.2)          | 1 (1.7)| 4 (6.9)| 3 (5.2)| 0 |
| Elagolix+E2/NETA (N=120)                     | 81 (67.5)          | 1 (0.8)| 9 (7.5)| 15 (12.5)| 0 |
| Uterine volume (median=356.5 cm³)            | < Median           |        |   |
| Placebo (N=88)                               | 57 (54.8)          | 2 (2.3)| 4 (4.5)| 5 (5.7)| 0 |
| Elagolix+E2/NETA (N=104)                     | 147 (72.4)         | 6 (3.0)| 17 (8.4)| 20 (9.9)| 0 |
| ≥ Median                                      |                    |        |   |
| Placebo (N=108)                              | 73 (67.6)          | 4 (3.7)| 6 (5.6)| 8 (7.4)| 0 |
| Elagolix+E2/NETA (N=192)                     | 136 (70.8)         | 4 (2.1)| 19 (9.9)| 18 (9.4)| 0 |

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### SUPPLEMENTAL TABLE 11
Overview of adverse events by subgroup (continued)

| Factors                      | Subgroup/treatment | TE AEs                                      |
|------------------------------|--------------------|---------------------------------------------|
| Primary fibroid volume       | ≤ Median           | Any AE | Any serious AE | Any severe AE | Any AE leading to discontinuation | Death |
| (median = 36.2 cm³)          |                    |        |                |              |                               |       |
| Placebo (N = 92)             |                    | 61 (66.3) | 2 (2.2)       | 2 (2.2)      | 4 (4.3)                        | 0     |
| Elagolix + E2/NETA (N = 189) |                    | 133 (70.4) | 6 (3.2)       | 18 (9.5)     | 19 (10.1)                      | 0     |
| > Median                     |                    | 67 (67.0) | 4 (4.0)       | 8 (8.0)      | 9 (9.0)                        | 0     |
| Placebo (N = 100)            |                    | 146 (73.0) | 4 (2.0)       | 18 (9.0)     | 19 (9.5)                       | 0     |
| Elagolix + E2/NETA (N = 200) |                    |        |                |              |                               |       |

Data are presented as n (%).

Median values for uterine and primary fibroid volumes were based on the overall median of the pooled Elaris UF-1 and UF-2 data set.

All AEs were summarized with MedDRA version 21.0 and are listed in descending order by elagolix with add-back therapy.

The Breslow-Day test was only performed for statistical significance of homogeneity of treatment effect across subgroups for each event type if there were at least 10 women per treatment group with an event within each subgroup. No statistical significance was seen across subgroups.

ANOVA, analysis of variance; BM, body mass index; E2, estradiol; FIGO, International Federation of Gynecology and Obstetrics; MBL, menstrual blood loss; NETA, norethindrone acetate; SE, standard error; UF-1, Uterine Fibroids 1; UF-2, Uterine Fibroids 2; USF-QOL, Uterine Fibroid Symptom and Health-Related Quality of Life.

* Serious AEs were defined as life-threatening, requiring hospitalization or medical or surgical intervention to prevent a serious outcome, or resulting in persistent disability or death; † Severity of each AE was rated by investigators as mild, moderate, or severe.

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### SUPPLEMENTAL TABLE 12
Overview of TE adverse events from overall pooled study population

| Factors                                        | Placebo (N=196) | Elagolix + E2/NETA (N=395) |
|------------------------------------------------|-----------------|-----------------------------|
| Any AE                                         | 130 (66.3)      | 283 (71.6)                  |
| Any serious AE<sup>a</sup>                     | 6 (3.1)         | 10 (2.5)                    |
| Any severe AE<sup>b</sup>                      | 10 (5.1)        | 36 (9.1)                    |
| Any AE leading to study drug discontinuation   | 13 (6.6)        | 38 (9.6)                    |
| Death                                          | 0               | 0                           |

AEs that occurred in ≥5% of women within the elagolix-treated group

| Factor             | Placebo (N=196) | Elagolix + E2/NETA (N=395) |
|--------------------|-----------------|-----------------------------|
| Hot flash          | 13 (6.6)        | 79 (20.0)                   |
| Headache           | 14 (7.1)        | 37 (9.4)                    |
| Nausea             | 19 (9.7)        | 37 (9.4)                    |
| Night sweats       | 8 (4.1)         | 34 (8.6)                    |
| Fatigue            | 7 (3.6)         | 24 (6.1)                    |
| Dysmenorrhea       | 10 (5.1)        | 20 (5.1)                    |
| Metrorrhagia       | 1 (0.5)         | 20 (5.1)                    |
| Nasopharyngitis    | 12 (6.1)        | 20 (5.1)                    |

Data are presented as n (%).

All AEs were summarized with MedDRA version 21.0 and are listed in descending order by elagolix with add-back therapy.

AE, adverse event; E2, estradiol; NETA, norethindrone acetate; TE, treatment emergent.

<sup>a</sup>Serious AEs were defined as life-threatening, requiring hospitalization or medical or surgical intervention to prevent a serious outcome, or resulting in persistent disability or death;<sup>b</sup> Severity of each AE was rated by investigators as mild, moderate, or severe.

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