## **Supplemental Table 5**: Studies of Endometrial Histology with Vaginal Prasterone/DHEA in Postmenopausal Women

| **Reference** | **Treatment(s)** | **Study design and population** | **Other endometrial data/comments** |
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| Bouchard et al 201658  Portman et al 201555  Duration: 52 weeks | * 0.50% (6.5 mg) DHEA (n = 530) [Intrarosa®, Endoceutics, Quebec City, Canada] * Intravaginal ovule inserted daily at bedtime | * Phase 3, long-term safety, open-label study conducted at 31 sites in the US and 10 sites in Canada * Nonhysterectomized postmenopausal women (40–75 years) with mild-to-severe vaginal dryness, “vaginal and/or irritation/itching” or “vaginal pain associated with sexual activity” * Women with undiagnosed abnormal genital bleeding, endometrial hyperplasia, cancer, or other abnormal endometrial histology on the endometrial biopsy at baseline were excluded * Endometrial biopsies performed at screening and at study end | * No endometrial hyperplasia or cancer were reported * Endometrial biopsies were atrophic (n = 389) or no tissue or insufficient tissue (n = 33) in women with 52 weeks of therapy * Endometrial biopsies were atrophic in women (n = 15) with >12 weeks but <52 weeks of therapy |
| Labrie et al, 200959  Portman et al, 201555  Duration: 12 weeks | * DHEA * 0.25% (3.25 mg) DHEA (n = 53) * 0.50% (6.5 mg) DHEA (n = 56) * 1.00% (13 mg) DHEA (n = 54) * Placebo (n = 53) * Intravaginal ovule inserted daily at bedtime | * Randomized, double-blind, placebo-controlled, multicenter trial * Postmenopausal women (40–75 years) with vaginal atrophy, and moderate-to-severe vaginal dryness or “vaginal and/or vulvar irritation/itching” or “vaginal pain associated with sexual activity” * Women with undiagnosed abnormal genital bleeding, endometrial cancer, or endometrial hyperplasia at baseline were excluded * Endometrial biopsies were taken at screening and at study end | * No endometrial hyperplasia or cancer were reported * At 12 weeks (as reported by Portman et al, 2015)   + Biopsies were rated as no tissue or insufficient tissue for diagnosis in no women with 0.25% DHEA, 1 with 0.50% DHEA, 0 with 1.0% DHEA, and 1 with placebo   + Atrophic endometrium was found in all women with evaluable biopsies: 0.25% DHEA (n = 27); 0.50% DHEA (n = 28); 1.0% DHEA (n = 30); placebo (n = 24) |
| Archer et al, 201560  Duration: 12 weeks | * DHEA * 0.25% (3.25 mg) DHEA (n = 87) * 0.50% (6.5 mg) DHEA (n = 87) * Placebo (n = 81) * Intravaginal ovule inserted daily at bedtime | * Randomized, double-blind, placebo-controlled, multicenter trial conducted at 24 sites in the US and 9 in Canada * Postmenopausal women (40–75 years) with vaginal atrophy and moderate-to-severe pain during sexual activity * Women with undiagnosed abnormal genital bleeding, endometrial hyperplasia, cancer, or other abnormal endometrial histology on the endometrial biopsy at baseline were excluded * Endometrial biopsy performed at screening and at study end | * No endometrial hyperplasia or cancer were reported * At 12 weeks   + Biopsies had no tissue or insufficient tissue for diagnosis in 2 women with 0.25% DHEA, and 5 with 0.50% DHEA, and 2 with placebo   + Atrophic endometrium was found in all women with evaluable biopsies: 0.25% DHEA (n = 23); 0.50% DHEA (n = 23); placebo (n = 25) |
| Bouchard et al, 201561  Duration: 12 weeks | * DHEA * 0.25% (3.25 mg) DHEA (n = 148) * 0.50% (6.5 mg) DHEA (n = 150) * Placebo (n = 152) * Intravaginal ovule inserted daily at bedtime for 2 weeks, then twice weekly for 10 weeks | * Randomized, double-blind, placebo-controlled, multicenter trial conducted at 32 sites in the US and 10 in Canada * Postmenopausal women (40–75 years) with vaginal atrophy and moderate to severe pain during sexual activity * Women with endometrial hyperplasia, cancer, or other abnormal endometrial histology on the endometrial biopsy at baseline were excluded * Endometrial biopsies taken at screening and end of the study | * No endometrial hyperplasia or cancer were reported * At 12 weeks   + Biopsies had no tissue or insufficient tissue for diagnosis in 9 women with placebo, 7 with 0.25% DHEA, and 6 with 0.50% DHEA   + Atrophic endometrium was found in all women with evaluable biopsies: 0.25% DHEA (n = 67); 0.50% DHEA (n = 66); placebo (n = 70) |

DHEA, dehydroepiandrosterone.