**Lay Description of Important Outcomes**

Based on our current retrospective study evaluating the mRNA expression of XCL1 in 65 HR+/HER2- patients’ primary tumors treated in the preoperative palbociclib (POP) Randomized Clinical trial, we did not find a significant association between treatment response and baseline XCL1 mRNA tumor expression (p-value = 0.738).

Subpopulation Treatment Effect Pattern Plot (STEPP) analysis of the PALOMA3, Phase 3 trial, comparing the efficacy of PAL+FUL versus PBO+FUL and evaluation of treatment effect across the continuum of XCL1 values indicated that:

• Better PAL+FUL combination treatment independently of XCL1 values.

• Better 6-month PFS in patients treated with PAL+FUL compared to the PBO+FUL treatment within all subpopulations of XCL1 values.

• There was no systematic interaction found between treatment groups across the continuum of XCL1 values.

• Absolute and ratio measures of the treatment effect in terms of PFS at 6 months generally favored the PAL+FUL combination.

• It is relevant now to establish the role of tumor microenvironment by evaluation of XCL1 and IL24 because it is likely that the contribution of immune factors on a palbociclib response would be better assessed by a dynamic, prospective evaluation of immune cells (e.g. NK cells or cDC1 or T cells) interacting with cancer cells.