Uptake of tLLO-HPV-E7 by APCs induces HPV-specific cytotoxic T-cell generation and HPV-specific immune responses. An interim analysis that will only assess futility will be performed when there is at least 40% progression-free survival (PFS) in any arm after treatment with AXAL. If objective response rates in any arm are determined to be less than 10% by blinded independent central review (BICR), the study will be stopped. The study will enroll approximately 450 patients at 150 sites. A pretreatment prophylaxis regimen consisting of nonsteroidal anti-inflammatory drugs (NSAIDs) and premedication with one or more of the following: a) biopsies through para-aortic node(s), b) ≥1 positive para-aortic node(s) by MRI/CT >1.5 cm diameter, or c) ≥1 positive para-aortic node(s) by PET with SUV >2.5

Completion of CCRT with curative intent, with:
- 24 weeks of cisplatin treatment and ≥40 Gy EBRT
- CCRT completed ≤10 weeks prior to the screening visit

Adequate hematologic, renal, and hepatic function

Key exclusion criteria

- FIGO stage IVA
- Residual disease following completion of CCRT with curative intent
- Histologies other than squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix
- Active autoimmune disease requiring systemic steroids or immunosuppressive agents
- Diagnosed with immunodeficiency, or received systemic steroid therapy/intravenous immunoglobulins for 2 years prior to first study treatment dose or, received a live vaccine within 30 days prior to first study treatment dose
- Underwent previous hysterectomy, or hysterectomy planned as part of the initial cervical cancer therapy
- Known contraindication (sensitivity or allergy) to thymophosphoramidate/sulfamethoxazole and/or ampicillin, known allergy to any component of the study drug's formulations
- Known clinically active bacterial, fungal, parasitic, or viral infection that requires therapy, or HIV-positive status

Patients will be stratified based on the presence of para-aortic lymph node metastases (yes vs no/unknown), region (US vs rest of the world), and FIGO stage (I-II or III-IV), and randomly assigned (2:1) to AXAL or placebo (Figure 2)

Patients will receive 1 infusion of placebo or AXAL (1x10⁹ vector-forming units [CFU]) every 3 weeks for 3 doses (weeks 1, 4, and 7) for the first 3 months (induction phase). Thereafter, patients will receive treatment every 8 weeks for 5 doses (weeks 15, 23, 31, 39, and 46) or until disease recurrence (maintenance phase).

The total treatment period will be approximately 1 year.

All patients will receive:
- A pretreatment prophylaxis regimen consisting of nonsteroidal anti-inflammatory drugs (NSAIDs), antihistamines, antivirals, and histamine H2 receptor antagonists at least 30 minutes prior to each infusion, if needed, additional doses of NSAIDs or antihistamines will be provided on days 1 and/or 2 following the infusion.
- A 7-day course of oral antibiotic therapy (eg, trimethoprim/sulfamethoxazole) or ampicillin (or matching placebo starting 72 hours after each infusion).

At the completion of study treatment or at the time of study discontinuation, patients will enter a 3-year surveillance period to ensure the eradication of Lm bacteria. Surveillance will consist of a 6-month course of trimethoprim/sulfamethoxazole, ampicillin, or matching placebo and a 2.5-year follow-up including routine monitoring (every 3 months) of complete blood count, comprehensive metabolic panel, and bone density to evaluate bone health.

Antibiotic therapy will begin either 72 hours following the last infusion of study treatment or immediately following study discontinuation.

Patients will be followed up for disease recurrence/progression after completion of study treatment for a total of 5 years or until death, whichever occurs earlier.

- Information regarding anticancer treatment(s) and interventions as well as survival following confirmed disease recurrence/progression will be collected.