Summary Basis of Regulatory Action

Date: October 6, 2016
From: Bharat Khurana, DVM, PhD, MBA, Chair of the Review Committee
BLA/ STN#: 125508/153

APPROVED

Applicant Name: Merck Sharpe & Dohme Corp.

Date of Submission: February 01, 2016
PDUFA Goal Date: December 01, 2016

Proprietary Name: GARDASIL 9
Established Name: Human Papillomavirus 9-valent Vaccine, Recombinant

Reason for the Submission:
To include a 2-dose schedule for administration of GARDASIL 9 as an alternative to the previously licensed 3-dose schedule in individuals 9 through 14 years of age.

Indication:
No change is proposed to the GARDASIL 9 indications in this supplement. Indications for the 2-dose schedule are the same as for the 3-dose schedule. GARDASIL 9 is indicated in girls and women 9 through 26 years of age for the prevention of the following diseases:

- Cervical, vulvar, vaginal, and anal cancer caused by Human Papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58.
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11.

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma in situ (AIS).
- Cervical intraepithelial neoplasia (CIN) grade 1.
- Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3.
- Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3.
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

GARDASIL 9 is indicated in boys and men 9 through 26 years of age for the prevention of the following diseases:

- Anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58.
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11.
- And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

Recommended Action: Approval

Signatory Authorities Action: Approval

Offices Signatory Authority: Wellington Sun, M.D., Director, DVRPA<ESIG>

☒ I concur with the summary review. APPROVED

☐ I concur with the summary review and include a separate review to add further analysis.

☐ I do not concur with the summary review and include a separate review.

Specific documentation used in developing the SBRA	**Reviewer Name**
Clinical Review	Joohee Lee, M.D.
Statistical Review	Lihan Yan, Ph.D.
Bioresearch Monitoring Review	Carla Jordan
Labeling – APLB review	Dana Jones
Pharmacovigilance Review	Adamma Mba-Jonas

Cross referenced applications:

- IND 9030, Human Papillomavirus Quadrivalent (Types 6, 11, 16 and 18; *S. cerevisiae*) L1 Capsid Virus-Like Particle Vaccine with Alum
- IND 13447, Human Papillomavirus Recombinant L1 Nine-Valent (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58; *Saccharomyces cerevisiae*) Virus-Like Particle Vaccine with Alum Adjuvant
- BLA 125126, Human Papillomavirus Quadrivalent (Types 6, 11, 16 and 18) Vaccine, Recombinant, GARDASIL®

1. Introduction

GARDASIL 9 is a non-infectious recombinant 9-valent Human Papillomavirus (HPV) vaccine consisting of purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58. The VLPs are adsorbed on amorphous aluminum hydroxyphosphate sulfate (AAHS) adjuvant. GARDASIL 9 is available as a suspension in 0.5 mL single-dose vials and prefilled syringes, for intramuscular administration in three 0.5 mL doses at months 0, 2, and 6 (3-dose schedule).

GARDASIL 9 was first licensed for use in the U.S. on December 10, 2014 in girls and women 9 through 26 years of age, and boys 9 through 15 years of age. On December 15, 2015, the indication for GARDASIL 9 was expanded to include boys and men 16 through 26 years of age.

In this supplemental Biologics Licensing Application (sBLA), submitted February 1, 2016, the applicant proposed a label change to include an alternative 2-dose schedule for administration of GARDASIL 9 in individuals 9 through 14 years of age at 0, and 6 to 12 months. Data from a Phase 3 clinical study, V503-010, were submitted to support the proposed label change. In this study, immunogenicity of a 2-dose regimen of GARDASIL 9, administered at 0 and 6 months or 0 and 12 months in girls and boys 9 to 14 years of age, was compared to that of the current licensed 3-dose regimen of GARDASIL 9 administered at 0, 2, and 6 months in young women 16 to 26 years of age. No change to the GARDASIL 9 formulation or indications was proposed in this application.

2. Background

HPV infection causes benign and malignant dysplastic anogenital disease in men and women. Nearly 100% of cervical cancers and 90% of anal cancers are caused by oncogenic HPV types. HPV is acquired most often through sexual activity, and acquisition of HPV infection typically occurs rapidly after sexual debut. Since HPV vaccines are most efficacious in those who have not previously been exposed to the virus, boys and girls aged 9-14 years, prior to becoming sexually active, represent the ideal HPV vaccination population. A higher rate of vaccination in this primary target population of boys and girls 9-14 years of age is needed. Using an effective 2-dose vaccine regimen in these younger cohorts may positively impact vaccination because of fewer number of visits required to deliver the HPV vaccine series and therefore, improve acceptability and compliance to the recommended vaccination regimen.

GARDASIL 9 is the second HPV vaccine manufactured by Merck Sharp & Dohme, approved for use in the U.S. Prior to the licensure of GARDASIL 9, Merck's 4-valent HPV vaccine, GARDASIL, was licensed in 2006. GARDASIL protects against disease caused by HPV Types 6, 11, 16, and 18. GARDASIL 9 includes the original four HPV types in GARDASIL, plus an additional five types, HPV 31, 33, 45, 52, and 58.

GARDASIL 9 was initially licensed on December 10, 2014 as a 3-dose regimen for girls and women 9 through 26 years of age, and boys 9 through 15 years of age, with an indication to prevent diseases related to the HPV types in the vaccine. On December 15, 2015, the

indication for GARDASIL 9 was extended to include boys and men 16 through 26 years of age.

In support of this sBLA, immunogenicity of the 2-dose regimen of GARDASIL 9 administered at 0 and 6 months (or 0 and 12 months) to girls and boys 9 to 14 years of age, was compared to that of the 3-dose regimen of GARDASIL 9 administered at 0, 2, and 6 months to young women 16 to 26 years of age. This study was designed to demonstrate noninferior antibody responses of a 2-dose regimen in boys and girls 9 through 14 years of age, compared to a 3-dose regimen in women 16 to 26 years of age.

3. Chemistry Manufacturing and Controls (CMC)

No manufacturing changes were proposed in this supplement, and no manufacturing information was needed or submitted for review.

4. Nonclinical Pharmacology/Toxicology

No nonclinical pharmacology/toxicology studies were needed or performed in support of this supplement.

5. Clinical Pharmacology

No clinical pharmacology information was needed or provided in this supplement.

6. Clinical/ Statistical

a) Clinical Program

In study V503-010, an immunological bridging strategy is used to infer effectiveness of 2-dose regimens (0, 6 months and 0, 12 months) of GARDASIL 9 in girls and boys 9 to 14 years of age by non-inferiority comparison with the 3-dose regimen (0, 2, and 6 months) of GARDASIL 9 in girls and women 9 through 26 years of age, the population in which efficacy of the 3-dose regimen has previously been established.

Study V503-010

Study V503-010 was designed as a phase 3, open-label international, multicenter clinical trial. A total of 1518 healthy subjects were enrolled in this study, including 301 girls 9 to 14 years old to receive the 2-dose regimen (0, 6 months), 301 boys 9 to 14 years old to receive the 2-dose regimen (0, 6 months), 301 girls and boys 9 to 14 years old to receive the 2-dose regimen (0, 12 months) (151 girls and 150 boys), 301 girls 9 to 14 years old to receive the 3-dose regimen (0, 2, 6 months), and 314 young women 16 to 26 years old to receive the 3-dose regimen (0, 2, 6 months). Fifty-three centers in 15 countries participated in the study, including 12 in the U.S.. Other centers were located in Canada, Chile, Colombia, Czech Republic, Denmark, Israel, Republic of Korea, Malaysia, Norway, South Africa, Spain, Taiwan, Thailand, and Turkey. Over 96% of girls and boys who

received the 2-dose regimen (0, 6 months or 0, 12 months) and women who received the 3-dose regimen (0, 2, 6 months) completed the last vaccination of their assigned vaccine series.

The primary objectives of the study were to demonstrate in the per protocol population that serum antibody responses to each HPV vaccine type (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58), as measured by geometric mean titers (GMTs) for each HPV vaccine type at 4 weeks post last dose, after a 2-dose schedule of GARDASIL 9 (Day 1 and Month 6, or Day 1 and Month 12) among girls and boys 9 to 14 years of age (P1 cohorts) were non-inferior to HPV antibody responses after a 3-dose schedule (Day 1, Month 2, and Month 6) in women 16 to 26 years of age (P2 cohorts). Non-inferiority was pre-specified as a lower limit of the two-sided 95% confidence interval of the GMT ratio (P1/P2) exceeding 0.67 for all 9 HPV types contained in the vaccine (Table 1).

Table 1: Summary of Anti-HPV cLIA Geometric Mean Titers in the PPI* Population at One Month After the Last Vaccine Dose Among Subjects Who Received 2 Doses† or 3 Doses† of GARDASIL 9 (Study 8)

Population (Regimen)	N	n	GMT mMU‡/mL	GMT Ratio relative to 3-dose regimen in 16- through 26-year-old girls and women (95% CI)
Anti-HPV 6				
9- to 14-year-old girls (0, 6)†	301	258	1657.9	2.15 (1.83, 2.53)§
9- to 14-year-old boys (0, 6)†	301	263	1557.4	2.02 (1.73, 2.36)§
9- to 14-year-old girls and boys (0, 12)†	300	257	2678.8	3.47 (2.93, 4.11)§
9- to 14-year-old girls (0, 2, 6)†	300	254	1496.1	1.94 (1.65, 2.29)¶
16- to 26-year-old women (0, 2, 6)†	314	238	770.9	1
Anti-HPV 11				
9- to 14-year-old girls (0, 6)†	301	258	1388.9	2.39 (2.03, 2.82)§
9- to 14-year-old boys (0, 6)†	301	264	1423.9	2.45 (2.09, 2.88)§
9- to 14-year-old girls and boys (0, 12)†	300	257	2941.8	5.07 (4.32, 5.94)§
9- to 14-year-old girls (0, 2, 6)†	300	254	1306.3	2.25 (1.90, 2.66)¶
16- to 26-year-old women (0, 2, 6)†	314	238	580.5	1
Anti-HPV 16				
9- to 14-year-old girls (0, 6)†	301	272	8004.9	2.54 (2.14, 3.00)§
9- to 14-year-old boys (0, 6)†	301	273	8474.8	2.69 (2.29, 3.15)§
9- to 14-year-old girls and boys (0, 12)†	300	264	14329.3	4.54 (3.84, 5.37)§
9- to 14-year-old girls (0, 2, 6)†	300	269	6996.0	2.22 (1.89, 2.61)¶
16- to 26-year-old women (0, 2, 6)†	314	249	3154.0	1
Anti-HPV 18				
9- to 14-year-old girls (0, 6)†	301	272	1872.8	2.46 (2.05, 2.96)§
9- to 14-year-old boys (0, 6)†	301	272	1860.9	2.44 (2.04, 2.92)§
9- to 14-year-old girls and boys (0, 12)†	300	266	2810.4	3.69 (3.06, 4.45)§
9- to 14-year-old girls (0, 2, 6)†	300	270	2049.3	2.69 (2.24, 3.24)¶
16- to 26-year-old women (0, 2, 6)†	314	267	761.5	1
Anti-HPV 31				
9- to 14-year-old girls (0, 6)†	301	272	1436.3	2.51 (2.10, 3.00)§
9- to 14-year-old boys (0, 6)†	301	271	1498.2	2.62 (2.20, 3.12)§
9- to 14-year-old girls and boys (0, 12)†	300	268	2117.5	3.70 (3.08, 4.45)§
9- to 14-year-old girls (0, 2, 6)†	300	271	1748.3	3.06 (2.54, 3.67)¶
16- to 26-year-old women (0, 2, 6)†	314	264	572.1	1

Population (Regimen)	N	n	GMT mMU[‡]/mL	GMT Ratio relative to 3-dose regimen in 16- through 26-year-old girls and women (95% CI)
Anti-HPV 33				
9- to 14-year-old girls (0, 6)[†]	301	273	1030.0	2.96 (2.50, 3.50)[§]
9- to 14-year-old boys (0, 6)[†]	301	271	1040.0	2.99 (2.55, 3.50)[§]
9- to 14-year-old girls and boys (0, 12)[†]	300	269	2197.5	6.31 (5.36, 7.43)[§]
9- to 14-year-old girls (0, 2, 6)[†]	300	275	796.4	2.29 (1.95, 2.68) [¶]
16- to 26-year-old women (0, 2, 6)[†]	314	279	348.1	1
Anti-HPV 45				
9- to 14-year-old girls (0, 6)[†]	301	274	357.6	1.67 (1.38, 2.03)[§]
9- to 14-year-old boys (0, 6)[†]	301	273	352.3	1.65 (1.37, 1.99)[§]
9- to 14-year-old girls and boys (0, 12)[†]	300	268	417.7	1.96 (1.61, 2.37)[§]
9- to 14-year-old girls (0, 2, 6)[†]	300	275	661.7	3.10 (2.54, 3.77)[¶]
16- to 26-year-old women (0, 2, 6)[†]	314	280	213.6	1
Anti-HPV 52				
9- to 14-year-old girls (0, 6)[†]	301	272	581.1	1.60 (1.36, 1.87)[§]
9- to 14-year-old boys (0, 6)[†]	301	273	640.4	1.76 (1.51, 2.05)[§]
9- to 14-year-old girls and boys (0, 12)[†]	300	268	1123.4	3.08 (2.64, 3.61)[§]
9- to 14-year-old girls (0, 2, 6)[†]	300	275	909.9	2.50 (2.12, 2.95)[¶]
16- to 26-year-old women (0, 2, 6)[†]	314	271	364.2	1
Anti-HPV 58				
9- to 14-year-old girls (0, 6)[†]	301	270	1251.2	2.55 (2.15, 3.01)[§]
9- to 14-year-old boys (0, 6)[†]	301	270	1325.7	2.70 (2.30, 3.16)[§]
9- to 14-year-old girls and boys (0, 12)[†]	300	265	2444.6	4.98 (4.23, 5.86)[§]
9- to 14-year-old girls (0, 2, 6)[†]	300	273	1229.3	2.50 (2.11, 2.97)[¶]
16- to 26-year-old women (0, 2, 6)[†]	314	261	491.1	1

*The PPI population consisted of individuals who received all assigned vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the last vaccination dose and blood collection for immunogenicity assessment, and were seronegative to the relevant HPV type(s) (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) prior to dose 1.

[†]2-dose regimen (0, 6): vaccination at Day 1 and Month 6; 2-dose regimen (0, 12): vaccination at Day 1 and Month 12; 3-dose regimen (0, 2, 6): vaccination at Day 1, Month 2, and Month 6. The data are from Study 8 (NCT01984697).

[‡]mMU=milli-Merck Units

[§]Demonstration of non-inferiority required that the lower bound of the 95% CI of the GMT ratio be greater than 0.67

[¶]Exploratory analysis; criterion for non-inferiority was not pre-specified

N = Number of individuals randomized to the respective vaccination group who received at least 1 injection

n = Number of individuals contributing to the analysis

CI=Confidence Interval

cLIA=competitive Luminex Immunoassay

GMT=Geometric Mean Titer

The secondary objectives were to demonstrate that serum antibody responses to each HPV vaccine type (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58), as measured by seroconversion rates for each HPV vaccine type at 4 weeks post last dose, following a 2-dose schedule of GARDASIL 9 in individuals 9 to 14 years of age (P1 cohorts) were non-inferior to antibody responses following a 3-dose schedule in young women 16 to 26 years of age (P2 cohorts). The statistical criterion for noninferiority was pre-specified as the lower bound of two-sided 95% confidence interval for the difference (P1-P2) in seroconversion

percentages be greater than -5 percentage points for all 9 HPV types contained in the vaccine.

Per-protocol analysis of immunogenicity (Table 1) conducted at 4 weeks following the completion of the assigned vaccination regimen showed that the pre-specified noninferiority criteria for the primary and secondary endpoints (> 0.67 fold for geometric mean titer ratios and >-5% for difference in seroconversion rate, respectively) were met for all 9 HPV vaccine types, in 9 to14 year old girls and boys from both 2-dose schedule cohorts (0, 6 months, and 0, 12 months). These results support the bridging of efficacy of the 2-dose schedule of GARDASIL 9 (0, 6-12 months) in 9 to 14 year old boys and girls to efficacy that was established in 16 to 26 year old girls and women in the original BLA submission.

Solicited adverse events (AEs) were not collected because the safety profile of GARDASIL 9 has been thoroughly investigated in clinical studies involving over 15,000 subjects. However, non-serious AEs occurring Day 1 to 15 following any vaccination and serious adverse events (SAEs) through 6 months following the last vaccination were collected in the study. Safety results for V503-010 are discussed in Section 7 of this document.

b) Pediatrics

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), an assessment of the safety and effectiveness of the product for the claimed indication in all pediatric age groups must be submitted at the time an application for a new active ingredient, new dosage form, new dosing regimen, new indication, or new route of administration is submitted, unless the requirement for assessment has been deferred or waived. This submission includes a new 2-dose regimen for GARDASIL 9 administered at 0 and 6 to 12 months for individuals 9 through 14 years of age.

The pediatric development plan for GARDASIL 9 was presented to the FDA's Pediatric Review Committee on June 22, 2016. The Committee concurred with the pediatric assessment and a partial waiver of pediatric assessment of GARDASIL 9 was granted. The pediatric study requirement was waived for individuals 0 to <9 years of age and 15 to <17 years of age because GARDASIL 9 administered as the 2-dose schedule does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in these age groups and is not likely to be used in a substantial number of pediatric patients in these age groups.

c) Bioresearch Monitoring Review

CBER Bioresearch Monitoring (BiMo) issued three inspections in support of this Biologics Licensing Application supplement (sBLA). The clinical sites inspected were located in Canada, Chile, and Norway. The BiMo inspections did not reveal significant problems that impacted the data submitted in this marketing application.

7. Safety

Information about non-serious AEs occurring Day 1 to 15 following any vaccination and SAEs occuring 6 months following the last vaccination was collected regardless of causality in this study. The safety analyses results were descriptive. Overall, administration of the GARDASIL 9 vaccine was well-tolerated among study subjects. Most injection-site adverse events were of mild or moderate intensity. The most frequently reported injection-site AE was pain; the most frequently reported systemic AE was headache. Only one of the subjects discontinued the study due to an adverse event, urticaria, which was of moderate intensity and was assessed as vaccine-related by the investigator. CBER clinical reviewer reviewed the narrative summary and concurred with the investigators' assessments. Twenty two (22) subjects reported SAEs during the period from Day 1 through visit cut-off date; however, none of these SAEs were considered to be vaccine-related by the study investigators. CBER concurred that the SAEs were unlikely related to the vaccine. No subject died during the study. The overall safety profile of the 2-dose schedule in boys and girls, 9 through 14 years of age, enrolled in this study did not reveal any notable new safety findings compared to previous studies in the GARDASIL 9 vaccine clinical program.

8. Advisory Committee Meeting

This submission was not discussed at a Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting because FDA review of this submission did not identify concerns or issues which would have benefitted from an advisory committee discussion.

9. Other Relevant Regulatory Issues

The issue of whether to retain the 3-dose regimen in boys and girls 9 through 14 years of age in the label was discussed. Because the 3-dose regimen has been demonstrated to be effective, CBER could not justify eliminating this as an option for girls and boys 9 through 14 years of age in whom there may be specific reasons that could make the additional dose at Month 2 more desirable. The review committee recommends approval of an alternative 2-dose regimen for girls and boys 9 through 14 years of age based on the results of the immunobridging data this age group compared to older adolescents and young women, in whom clinical efficacy is established.

10. Labeling

The package insert (PI) and patient package insert (PPI) with all changes necessitated by inclusion of the data in support of the alternative 2-dose schedule (0, 6 to 12 months) of GARDASIL 9 for individuals 9 through 14 years of age were reviewed by relevant members of the review committee, including clinical, statistical, and APLB reviewers. The revised GARDASIL 9 PI approved with this supplement incorporates information from V503-010 study into the "Dosage and Administration" and "Clinical Studies" sections.

The content and format of the "Use In Specific Populations" section of the PI was also revised to comply with the Requirements for Pregnancy and Lactation Labeling, referred to as the "Pregnancy and Lactation Labeling Rule" (PLLR rule), published by FDA in December 2014.

The PPI was revised to reflect the inclusion of the alternative 2-dose schedule of GARDASIL 9 for individuals 9 through 14 years of age. Minor changes to improve clarity and consistency were made throughout the PI and PPI. The committee concurs that the PI and PPI submitted on October 6, 2016 are acceptable.

No changes to the carton/container labels were proposed in this supplement.

11. Recommendations and Risk/ Benefit Assessment

a) Recommended Regulatory Action

It is the consensus of the review committee to approve this supplemental application to include a 2-dose schedule (0, 6 to 12 months) for administration of GARDASIL 9 in individuals 9 through 14 years of age as an alternative schedule to the previously licensed 3-dose schedule.

b) Risk/ Benefit Assessment

Data submitted to the BLA supplement establish a substantial likelihood of benefit with respect to the effectiveness of the 2-dose schedule of GARDASIL 9 in individuals 9 through 14 years of age. The elimination of the second dose (at 2 months) of the licensed 3-dose schedule of GARDASIL 9 does not compromise the immunogenicity of the vaccine in 9 to 14 year-old boys and girls after the second dose. The data demonstrated non-inferiority of immune responses (as measured by GMTs and seroconversion percentages for the nine HPV types contained in the vaccine) of the 2-dose regimens (0, 6 months, or 0, 12 months) in girls and boys 9 through 14 years of age compared to the 3-dose schedule (0, 2, 6 months) in young women 16 to 26 year old. Data on the duration of immune response following a 2-dose schedule as compared to the 3-dose schedule of vaccination with GARDASIL 9 is currently not available. The safety profile of GARDASIL 9 vaccine (3-dose regimen) has been extensively characterized in previous Phase 3 clinical studies and post-marketing monitoring. A reduction in number of doses administered has an advantage in reducing local or systemic adverse events. The unsolicited safety data from V503-010 support this general statement. Administration of a 2-dose regimen of the GARDASIL 9 vaccine was well-tolerated in 9 to 14 year old girls and boys.

The overall risk-benefit profile of the 2-dose regimen was determined to be favorable since the risks of vaccination with 2-dose schedule of GARDASIL 9 in 9 to 14 year old girls and boys have been found to be minimal, there is a substantial likelihood of benefit in the prevention of diseases caused by the nine HPV types contained in the vaccine. The alternative 2-dose vaccination series given at 0, and 6 to 12 months in 9 through 14 year old boys and girls is effective and: 1) compliance can be improved with a schedule consisting of a fewer number of doses and 2) a longer interval between vaccinations is unlikely to increase the risk of HPV infection in this younger age group during the 6 to 12 month interval. The review committee concludes that the benefit offered by the 2-dose schedule of GARDASIL 9 in boys and girls 9 through 14 years of age outweighs its risks.

c) Recommendation for Postmarketing Risk Management Activities
No safety issues have been identified that would have warranted a Risk Evaluation and Mitigation Strategy (REMS) or a new Postmarketing Requirement (PMR).

d) Recommendation for Postmarketing Activities
Merck agreed to complete the ongoing study V503-010-01 to evaluate the persistence of antibody titers up to 36 months after vaccination to the nine vaccine-HPV types in GARDASIL 9 in males and females who received 2-dose and 3-dose regimens of GARDASIL 9. Merck will complete this study by August 18, 2017, and submit a final study report by June 30, 2018.