Janssen Pharmaceutical Companies
U.S. Post-Marketing Requirements and Commitments
April 2019

Product	Due Date	Status	Description of Commitment or Requirement
DARZALEX (daratumumab) concentrate for solution for infusion	30-Nov-2018	Submitted	Submit the final report of a study conducted to assess the anti-drug antibody (ADA) response to daratumumab with the validated assay developed under PMR 3000-4.
DARZALEX (daratumumab) concentrate for solution for infusion	30-Nov-2018	Submitted	Conduct a study to validate an assay for binding antibodies to daratumumab to assess the product's potential for immunogenic reactions in treated patients. Submit a validation report for the validated, sensitive, and accurate assay for the detection of binding antibodies to daratumumab, including procedures for the accurate detection of binding antibodies to daratumumab in the presence of daratumumab levels expected in the serum or plasma at the time of patient sampling.
DARZALEX (daratumumab) concentrate for solution for infusion	30-Apr-2017	Submitted	Collect, analyze, and submit additional safety data from ongoing clinical trials to characterize the safety of daratumumab in patients with baseline hepatic impairment. Study Completion
DARZALEX (daratumumab) concentrate for solution for infusion	30-Jun-2017	Submitted	Conduct a study to validate an assay for neutralizing antibodies to daratumumab to assess the potential for increased adverse outcome from loss of product effect in treated patients. Submit a validation report for the validated, sensitive, and accurate assay for the detection of neutralizing antibodies to daratumumab, including procedures for the accurate detection of neutralizing antibodies to daratumumab in the presence of daratumumab levels that are expected in the serum or plasma at the time of patient sampling.
DURAGESIC® (fentanyl) transdermal patch	31-Mar-2020	Ongoing	A prospective, observational study designed to quantify the serious risks of misuse, abuse, and addiction associated with long-term use of opioid analgesics for management of chronic pain among patients prescribed ER/LA opioid analgesics. This study must address at a minimum the following specific objectives: a) Estimate the incidence of misuse, abuse, and addiction associated with longterm use of opioid analgesics for chronic pain. Examine the effect of product/formulation, dose and duration of opioid use, prescriber specialty, indication, and other clinical factors (e.g., concomitant psychotropic medications, personal or family history of substance abuse, history of psychiatric illness) on the risk of misuse, abuse, and addiction. b) Evaluate and quantify other risk factors for misuse, abuse, and addiction associated with long-term use of opioid analgesics for chronic pain, including but not limited to the following: demographic factors, psychosocial/behavioral factors, medical factors, and genetic factors. Identify confounders and effect modifiers of individual risk factor/outcome relationships."
DURAGESIC® (fentanyl) transdermal patch	30-Jun-2017	Submitted	An observational study using medical record review to evaluate the association between doctor/pharmacy shopping outcomes and patient behaviors suggestive of misuse, abuse and/or addiction.

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DURAGESIC® (fentanyl) transdermal patch	31-Aug-2019	Submitted	Conduct a clinical trial to estimate the serious risk for the development of hyperalgesia following the long-term use of high-dose ER/LA opioid analgesics for at least one year to treat chronic pain. Include an assessment of risk relative to efficacy.
DURAGESIC® (fentanyl) transdermal patch	30-Sep-2019	Ongoing	An observational study designed to measure the incidence and predictors of opioid overdose and death (OOD), as well as opioid abuse/addiction, using patient health records, insurance claims, and death records. This study must address at a minimum the following specific objectives: a) Estimate the incidence of abuse/addiction, overdose, and death associated with long-term use of opioid analgesics for chronic pain. Stratify overdose by intentionality wherever possible. Examine the effect of product/formulation, dose and duration of opioid use, prescriber specialty, indication, and other clinical factors (e.g., concomitant psychotropic medications, personal or abuse/addiction, overdose, and death. b) Evaluate and quantify other risk factors for abuse/addiction, overdose, and death associated with long-term use of opioid analgesics for chronic pain, including but not limited to the following: demographic factors, psychosocial/behavioral factors, medical factors, and genetic factors. Identify confounders and effect modifiers of individual risk factor/outcome relationships. Stratify overdose by intentionality wherever possible."
DURAGESIC® (fentanyl) transdermal patch	31-Jan-2016	Submitted	A prospective observational study designed to assess the content validity and patient interpretation of the Prescription Opioid Misuse and Abuse Questionnaire (POMAQ). Patient understanding of the concepts of misuse and abuse will also be obtained."
DURAGESIC® (fentanyl) transdermal patch	30-Nov-2017	Submitted	An observational study to evaluate the validity and reproducibility of the Prescription Opioid Misuse and Abuse Questionnaire (POMAQ), which will be used to identify opioid abuse and misuse behaviors among participants who have chronic pain which requires long-term opioid analgesic use.
DURAGESIC® (fentanyl) transdermal patch	30-Nov-2017	Submitted	An observational study to validate measures of prescription opioid Substance Use Disorder and addiction in patients who have received or are receiving opioid analgesics for chronic pain.
DURAGESIC® (fentanyl) transdermal patch	31-Dec-2016	Submitted	An observational study to develop and validate an algorithm using coded medical terminologies and other electronic healthcare data to identify opioid-related overdose and death.
DURAGESIC® (fentanyl) transdermal patch	31-Jan-2017	Submitted	An observational study to develop and validate an algorithm using coded medical terminologies to identify patients experiencing prescription opioid abuse or addiction, among patients receiving an ER/LA opioid analgesic.
DURAGESIC® (fentanyl) transdermal patch	31-Jan-2018	Submitted	An observational study using coded medical terminologies and other electronic healthcare data to define and validate doctor and/or pharmacy shopping outcomes by examining their association with abuse and/or addiction.
DURAGESIC® (fentanyl) transdermal patch	31-Dec-2018	Submitted	An observational study using a validated patient survey to evaluate the association between doctor/pharmacy shopping outcomes and self-reported misuse and abuse.
EDURANT™ (rilpivirine hydrochloride) film-coated tablet	31-Mar-2023	Pending	A pediatric safety and antiviral activity study of rilpivirine with activity based on the results of virologic response over at least 48 weeks of dosing and safety monitored over 48 weeks in pediatric subjects from 4 weeks to <12 years of age.
ERLEADA™ (apulutamide) film-coated tablet	30-Jun-2023	Ongoing	Submit the analyses and datasets with the final report for the clinical trial entitled; "SPARTAN, a phase 3 double-blind, randomized study of apalutamide versus placebo in patients with nonmetastatic castration-resistant prostate cancer [ARN-509-003]

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INTELENCE® (etravirine) tablet	30-Jun-2014	Submitted	2919-1 Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric subjects from 2 years to 6 years of age. This study will determine the pharmacokinetic profile, safety, and activity of etravirine in pediatric subjects from 2 years to 6 years of age.
INTELENCE® (etravirine) tablet	31-Oct-2020	Ongoing	Deferred pediatric study under PREA for the treatment of HIV-1 infection in pediatric subjects from 2 months to 6 years of age. This study will determine the pharmacokinetic profile, safety, and activity of etravirine in pediatric subjects from 2 months to 6 years of age."
INVOKANA (canagliflozin hemihydrate) film-coated tablet	30-Jun-2024	Delayed	A 26-week, randomized double-blind, placebo-controlled study, followed by a 26-week double-blind, placebo- or active-controlled extension, to evaluate the efficacy and safety of canagliflozin compared to placebo in pediatric patients ages 10 to <18 years with type 2 diabetes mellitus, as add-on to metformin and as monotherapy.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	30-Nov-2023	Ongoing	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	01-Dec-2021	Ongoing	An enhanced pharmacovigilance study of ketoacidosis in patients treated with canagliflozin tablets. The study will include reports of ketoacidosis or diabetic ketoacidosis for a period of 5 years, and will include assessment and analysis of spontaneous reports of ketoacidosis in patients treated with Invokana (canagliflozin) tablets, with specialized follow-up to collect additional information on these cases.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-May-2018	Submitted	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-May-2019	Ongoing	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-May-2020	Ongoing	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-May-2021	Ongoing	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.

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INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-Dec-2017	Submitted	An enhanced pharmacovigilance study of ketoacidosis in patients treated with canagliflozin tablets. The study will include reports of ketoacidosis or diabetic ketoacidosis for a period of 5 years, and will include assessment and analysis of spontaneous reports of ketoacidosis in patients treated with Invokana (canagliflozin) tablets, with specialized follow-up to collect additional information on these cases.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-Dec-2018	Submitted	An enhanced pharmacovigilance study of ketoacidosis in patients treated with canagliflozin tablets. The study will include reports of ketoacidosis or diabetic ketoacidosis for a period of 5 years, and will include assessment and analysis of spontaneous reports of ketoacidosis in patients treated with Invokana (canagliflozin) tablets, with specialized follow-up to collect additional information on these cases.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-Dec-2019	Ongoing	An enhanced pharmacovigilance study of ketoacidosis in patients treated with canagliflozin tablets. The study will include reports of ketoacidosis or diabetic ketoacidosis for a period of 5 years, and will include assessment and analysis of spontaneous reports of ketoacidosis in patients treated with Invokana (canagliflozin) tablets, with specialized follow-up to collect additional information on these cases.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-Dec-2020	Ongoing	An enhanced pharmacovigilance study of ketoacidosis in patients treated with canagliflozin tablets. The study will include reports of ketoacidosis or diabetic ketoacidosis for a period of 5 years, and will include assessment and analysis of spontaneous reports of ketoacidosis in patients treated with Invokana (canagliflozin) tablets, with specialized follow-up to collect additional information on these cases.
INVOKANA (canagliflozin hemihydrate) film-coated tablet	31-May-2022	Ongoing	An assessment and analysis of all foreign and domestic spontaneous reports of malignancy (pheochromocytoma, Leydig cell tumor, and renal cell carcinoma), fatal pancreatitis, hemorrhagic/necrotizing pancreatitis, severe hypersensitivity reactions (angioedema, anaphylaxis, Stevens-Johnson syndrome), photosensitivity reactions, serious hepatic abnormalities, and pregnancy in patients treated with canagliflozin. The enhanced pharmacovigilance should continue for 10 years from the date of approval for malignancies and 5 years for all other events.
LEVAQUIN (levofloxacin hemihydrate film-coated tablet	31-Dec-2099	No HA Due Date	A field study to evaluate the efficacy and safety of levofloxacin in the event of an attack with the intentional release of Yersinia pestis in the United States.
LEVAQUIN (levofloxacin hemihydrate) oral solution	31-Dec-2099	No HA Due Date	A field study to evaluate the efficacy and safety of levofloxacin in the event of an attack with the intentional release of Yersinia pestis in the United States.
LEVAQUIN (levofloxacin hemihydrate) solution for infusion	31-Dec-2099	No HA Due Date	A field study to evaluate the efficacy and safety of levofloxacin in the event of an attack with the intentional release of Yersinia pestis in the United States.
LEVAQUIN (levofloxacin hemihydrate) solution for infusion	31-Dec-2006	Submitted	Commitment to conduct post-marketing PK clinical trial in renally impaired patients
LEVAQUIN (levofloxacin hemihydrate) film-coated tablet	31-Dec-2006	Submitted	Commitment to conduct post-marketing PK clinical trial in renally impaired patients

Product	Due Date	Status	Description of Commitment or Requirement
LEVAQUIN (levofloxacin hemihydrate) oral solution	31-Dec-2006	Submitted	Commitment to conduct post-marketing PK clinical trial in renally impaired patients
LEVAQUIN (levofloxacin hemihydrate) film-coated tablet	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data from treatment greater than 28 days, if such data become available.
LEVAQUIN (levofloxacin hemihydrate) oral solution	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data in pediatric patients from treatment greater than 14 days, if such data become available.
LEVAQUIN (levofloxacin hemihydrate) oral solution	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data from treatment greater than 28 days, if such data become available.
LEVAQUIN (levofloxacin hemihydrate) solution for infusion	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data in pediatric patients from treatment greater than 14 days, if such data become available.
LEVAQUIN (levofloxacin hemihydrate) solution for infusion	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data from treatment greater than 28 days, if such data become available.
LEVAQUIN (levofloxacin hemihydrate) film-coated tablet	31-Dec-2099	No HA Due Date	Cooperation with U.S.-based public health agencies in evaluating data on the use of LEVAQUIN® (levofloxacin) in a large U.S. population for inhalational anthrax (post-exposure) prophylaxis, should an exposure occur. This includes long-term safety data in pediatric patients from treatment greater than 14 days, if such data become available.
OLYSIO® (simeprevir sodium) capsule, hard	31-Dec-2021	Terminated	A trial to evaluate the pharmacokinetics, safety and treatment response (using sustained virologic response) of OLYSIO™ (simeprevir) as a component of a combination antiviral treatment regimen in pediatric subjects 3 through 17 years of age with chronic hepatitis C.
OLYSIO® (simeprevir sodium) capsule, hard	31-Jan-2025	Terminated	Collection of long-term safety data for subjects enrolled in the pediatric simeprevir safety, pharmacokinetic and efficacy trial. Data collected should include at least 3 years of follow-up in order to characterize the long-term safety of OLYSIO™ (simeprevir) in pediatric subjects, including growth assessment, sexual maturation and characterization of OLYSIO™ (simeprevir) resistance-associated substitutions in viral isolates from subjects failing therapy.
PREZCOBIX® (darunavir ethanolate + cobicistat) film-coated tablet	31-Dec-2021	Pending	Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 3 years to less than 6 years of age and weighing at least 15 kg. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC age-appropriate formulation in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children ages 3 years to less than 6 years may not be required if the dosing recommendation for the FDC age-appropriate formulation can be supported by pediatric trials already conducted with the individual drug products and if the age-appropriate FDC produces similar exposures as the individual components.

Product	Due Date	Status	Description of Commitment or Requirement
PREZCOBIX® (darunavir ethanolate + cobicistat) film-coated tablet	31-Dec-2021	Pending	Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed dose combination (FDC) age-appropriate formulation in HIV-infected pediatric subjects 6 years to less than 12 years of age and weighing at least 15 kg. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC age-appropriate formulation in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children ages 6 years to less than 12 years may not be required if the dosing recommendation for the FDC age-appropriate formulation can be supported by pediatric trials already conducted with the individual drug products and if the age-appropriate FDC produces similar exposures as the individual components.
PREZCOBIX® (darunavir ethanolate + cobicistat) film-coated tablet	31-Dec-2021	Pending	Evaluate the pharmacokinetics, safety, and antiviral activity (efficacy) of darunavir and cobicistat fixed-dose combination (FDC) tablets in HIV-infected pediatric subjects 12 years to less than 18 years of age. The safety and antiviral activity (efficacy) of darunavir and cobicistat FDC tablets in pediatric subjects should be evaluated for a minimum of 24 weeks. A clinical trial in children 12 years to less than 18 years of age may not be required if the dosing recommendation for the FDC tablets can be supported by pediatric trials already conducted with the individual drug products and if the FDC produces similar exposures as the individual components.
REMICADE (infliximab) powder for concentrate for solution for infusion	01-Dec-2018	Delayed	A prospective, multi-center registry including 4000 adult psoriasis patients treated with commercial REMICADE® (infliximab) in the United States. This registry will characterize and assess the incidence of serious adverse events (including serious infection, tuberculosis, opportunistic infections, malignancies, hypersensitivity reactions, autoimmune reactions and deaths) as well as other adverse events of interest in the study cohort. All enrolled study patients will be evaluated twice yearly for a period of at least 8 years with comprehensive annual reports provided to the agency. We will to collect data on the patient characteristics, demographics and drug exposure (including dose, duration and time to onset of adverse event). The collection of data will be via active surveillance methods and data will be validated by a review of medical records as per the Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment.
REMICADE (infliximab) powder for concentrate for solution for infusion	30-Jun-2018	Delayed	A safety and pharmacokinetic trial as a substudy of the DEVELOP registry to evaluate whether trough concentrations at the time of loss of clinical response can be used to identify pediatric UC and Crohn's disease patients who have low infliximab exposures and would benefit from a dose increase above that approved without increasing risk of serious adverse events.
REMICADE (infliximab) powder for concentrate for solution for infusion	31-Dec-2045	Ongoing	A study to analyze samples from the pediatric inflammatory bowel disease (IBD) registry (DEVELOP) and the safety and pharmacokinetic trial as a substudy of the DEVELOP registry to determine the presence of anti-drug antibodies (ADA).
REMICADE (infliximab) powder for concentrate for solution for infusion	30-Jun-2019	Ongoing	A study to bank samples for future evaluation to identify genetic mutations and other biomarkers that predispose inflammatory bowel disease (IBD) patients to developing Hepatosplenic T-Cell Lymphoma (HSTCL).
REMICADE (infliximab) powder for concentrate for solution for infusion	30-Sep-2013	Submitted	Conduct a prospective, observational registry study of women with Crohn's disease, rheumatoid arthritis and psoriatic arthritis exposed to infliximab during pregnancy. This study will assess the pregnancy outcomes in women who were exposed to infliximab during pregnancy relative to background risk in similar patients not exposed to infliximab.

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REMICADE (infliximab) powder for concentrate for solution for infusion	30-Jun-2027	Ongoing	Conduct a registry of patients with pediatric Crohn's disease being treated with REMICADE® (infliximab) that will be established to obtain long-term clinical status and safety information. Information will be collected on patient demographics, disease characteristics, history of concomitant medications, dose and duration and frequency of REMICADE® (infliximab) administration, clinical status, adverse events including dysplasias and malignancies of all types, infections, autoimmune disease, assessment of immunogenicity, and potential effects of antibody formation. The age range should include patients ages 0 to 19 years. This registry will be designed so that detailed clinical status information is collected at registry entry and on a 6-month basis for at least 20 years. We commit to expand the currently existing Pediatric IBD Registry, and will actively encourage both patients and physicians to participate in the registry through an advertisement campaign, that includes a plan for proactive communication of associated risk. We also commit to recruiting at least 2,000 REMICADE® (infliximab)-treated pediatric Crohn's patients, which will provide an adequate number of patients to participate in the registry so that outcome measures will be collected and adequate risk assessment can be made. We will provide prompt risk communication for serious adverse events that are reported through the registry. The registry data will be analyzed at yearly intervals and the results will be submitted in annual reports for BB-IND 5389.
REMICADE (infliximab) powder for concentrate for solution for infusion	31-Dec-2045	Ongoing	Expand the Pediatric IBD Registry (DEVELOP) to include pediatric patients with ulcerative colitis (UC) and indeterminate colitis (IC).
REMICADE® (infliximab) powder for concentrate for solution for infusion	31-Mar-2020	Ongoing	Requirement of all TNF-αblockers including REMICADE® (infliximab) Enhanced pharmacovigilance program for reports of malignancy in pediatric, adolescent, and young adult (≤ 30 years of age) patients treated with Remicade (infliximab), for a period of up to 10 years to collect data that will be analyzed to better define the risk of this serious adverse event. The enhanced pharmacovigilance program includes the following: 1) active query of reporters to obtain additional clinical information related to malignancy diagnoses; 2) expedited reporting to FDA of all initial and follow-up reports of any malignancy in pediatric, adolescent, and young adult patients.
RISPERDAL CONSTA® (risperidone) powder and solvent for prolonged-release suspension for injection;	31-Dec-2099	Submitted	Submit your plans for tracking medication errors and product complaints involving the new kits and clarify how you will address the challenges of differentiating reports for the new kits from reports involving the currently marketed kits
SIMPONI ARIA® (golimumab) solution for injection	13-Sep-2019	Delayed	A trial to evaluate the safety, efficacy, PK/PD and immunogenicity of SIMPONI® ARIA™ (IV golimumab) in pediatric patients between the ages 2 to 17 years and 11 months with active juvenile idiopathic arthritis (JIA) despite standard therapy with methotrexate.
SIMPONI® (golimumab) solution for injection in pre-filled pen and pre-filled syringe	31-May-2030	Delayed	A prospective, multi-center, long-term, observational study of ulcerative colitis patients treated with SIMPONI®(golimumab) in a routine clinical setting, to assess the long-term safety of SIMPONI® (golimumab). The study's primary outcome should be the incidence of lymphoma. Design the study around a testable hypothesis to rule out a clinically meaningful increase in lymphoma above an estimated background risk in a suitable comparator. Secondary endpoints should be pre-specified and may include the incidence of other malignancies. Select and justify the choice of appropriate comparator population(s) and corresponding background rate(s) relative to SIMPONI® (golimumab)-exposed patients. Provide sample sizes and effect sizes that can be ruled out under various enrollment target scenarios and loss to follow-up assumptions. Patients should be enrolled over an initial 5-year period and then followed for a period of at least 10 years from the time of enrollment. Progress updates of patient accrual and a demographic summary should be provided in your annual reports. Safety data should be provided in periodic safety reports.

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SIMPONI® (golimumab) solution for injection in pre-filled pen and pre-filled syringe	28-Feb-2021	Ongoing	A study to bank samples from inflammatory bowel disease patients treated with SIMPONI® (golimumab) for future evaluation to identify genetic mutations and other biomarkers that may predispose them to developing Hepatosplenic T-Cell Lymphoma (HSTCL).
SIMPONI® (golimumab) solution for injection in pre-filled pen and pre-filled syringe	31-May-2022	Delayed	A study to evaluate the effectiveness and safety of SIMPONI® (golimumab) in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis. The study should be designed to establish that the dose regimen(s) of SIMPONI® (golimumab) identified in PMC#4 (pharmacokinetic pediatric UC study) are effective and safe for induction treatment, as well as for continued treatment after induction. Pharmacokinetic measurements should be conducted for exposure-response analysis. Collect serum samples for immunogenicity testing and conduct analyses of the impact of immunogenicity on pharmacokinetics, efficacy and safety.
SIMPONI® (golimumab) solution for injection in pre-filled pen and pre-filled syringe	01-Mar-2020	Ongoing	Enhanced pharmacovigilance (PV) for reports of malignancy in pediatric, adolescent, and young adult patients for a period of up to 10 years. These reports must be provided on an annual basis. The final annual report is due on 01 Mar 2020.
SPRAVATO™ (esketamine hydrochloride)	30-Apr-2019	Ongoing	Conduct a 3-year open-label safety study to characterize the long-term effects of esketamine on cognitive function and urinary symptoms. Ongoing trial TRD 3008 will be adapted to meet this requirement.
SPRAVATO™ (esketamine hydrochloride)	31-Dec-2020	Ongoing	Conduct a 3-year open-label safety study to characterize the long-term effects of esketamine on cognitive function and urinary symptoms. Ongoing trial TRD 3008 will be adapted to meet this requirement.
SPRAVATO™ (esketamine hydrochloride)	31-May-2021	Ongoing	Conduct a 3-year open-label safety study to characterize the long-term effects of esketamine on cognitive function and urinary symptoms. Ongoing trial TRD 3008 will be adapted to meet this requirement.
SPRAVATO™ (esketamine hydrochloride)	30-Sep-2019	Pending	To further characterize the potential risk of increasing thyroid stimulating hormone levels, analyze biobank samples taken at screening and predose on Days 1, 8, 25 or early withdrawal visits from patients who participated in the TRD3001 and TRD3002 Phase 3 studies.
SPRAVATO™ (esketamine hydrochloride)	30-Sep-2019	Pending	Conduct a study to evaluate the efficacy of esketamine monotherapy for the treatment of treatment-resistant depression. The study design must be agreed to by the Division prior to initiating the study.
SPRAVATO™ (esketamine hydrochloride)	31-Mar-2022	Pending	Conduct a study to evaluate the efficacy of esketamine monotherapy for the treatment of treatment-resistant depression. The study design must be agreed to by the Division prior to initiating the study.
SPRAVATO™ (esketamine hydrochloride)	31-Aug-2022	Pending	Conduct a study to evaluate the efficacy of esketamine monotherapy for the treatment of treatment-resistant depression. The study design must be agreed to by the Division prior to initiating the study.
SIRTURO® (bedaquiline fumarate) tablet	31-Mar-2022	Ongoing	A confirmatory randomized double blind placebo controlled multicenter Phase 3 trial in subjects with sputum smear-positive pulmonary multidrug resistant tuberculosis (MDR-TB). This trial should assess long- term outcomes of failure or relapse or death at least 6 months after all MDR-TB treatment is completed.

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SIRTURO® (bedaquiline fumarate) tablet	31-Aug-2019	Ongoing	Develop a patient registry for bedaquiline-treated patients to assess incidence rates of serious adverse events, including death. The registry should capture the information listed below: a. Indication for use, including utilization of expert medical consultation. b. Minimum Inhibitory Concentration (MIC) data for baseline and any subsequent MDR-TB isolate (in patients who have relapsed/at end of treatment). c. Drug Utilization Data. d. Information on drug distribution mechanisms used. e. Information on how the drug was actually distributed to patients. f. Patient outcomes (clinical and microbiologic). g. Safety assessments in bedaquiline-treated patients, including deaths. h. Concomitant medications.
SIRTURO® (bedaquiline fumarate) tablet	31-Dec-2019	Ongoing	A prospective in vitro study over a five-year period after introduction of SIRTURO® (bedaquiline) to the market to determine MICs of MDR-TB isolates to bedaquiline for the first 5 years from marketing. Report interpretation of these MICs once additional quality control testing methods are developed as noted in the required post-marketing studies PMR 1988-03 and PMR 1988-004. Provide detailed protocol describing the study to the Agency for review and comment before commencing the study.
STELARA (ustekinumab) solution for infusion	31-Aug-2030	Ongoing	Conduct a long-term, postmarketing, observational study to assess the long-term safety of STELARA (ustekinumab) versus other therapies used in the treatment of adults with moderate to severe Crohn's disease. The study's primary outcome is malignancy. Secondary outcomes include, but are not limited to, opportunistic infections (e.g., tuberculosis [TB]). Specify concise case definitions, and provide outcome validation for both primary and secondary outcomes. Describe and justify the choice of appropriate comparator population(s) and estimated background rate(s) relative to ustekinumab-exposed patients; clearly define the primary comparator population for the primary objective. Design the study around a testable hypothesis to assess, with sufficient sample size and power, a clinically meaningful increase in malignancy risk above the comparator background rate, with a pre-specified statistical analysis method. For the ustekinumab-exposed and comparator(s), the study drug initiation period should be clearly defined, including any exclusion and inclusion criteria. Ensure adequate number of patients with at least 18 months of ustekinumab exposure at the end of the study. Follow for a period of at least 7 years. (Draft Protocol Submission: February 2017 Final Protocol Submission: September 2017 Interim Report: December 2025 Study Completion: August 2029 Final Report Submission: August 2030)
STELARA (ustekinumab) solution for infusion	31-Aug-2019	Ongoing	Conduct a dose-ranging trial to determine the pharmacokinetics/pharmacodynamics, safety, and tolerability of STELARA (ustekinumab) induction dosing in pediatric patients 2 to 17 years of age with moderately to severely active Crohn's disease despite conventional therapy. (Final Protocol Submission: December 2016 Study Completion: February 2019 Final Report Submission: August 2019)
STELARA (ustekinumab) solution for infusion	30-Sep-2024	Pending	Conduct a randomized, controlled, blinded, multicenter trial to evaluate the safety and efficacy of STELARA (ustekinumab) in pediatric patients 2 to 17 years of age with moderately to severely active Crohn's disease despite conventional therapy. (Draft Protocol Submission: December 2019 Final Protocol Submission: June 2020 Study Completion: February 2024 Final Report Submission: September 2024)
STELARA (ustekinumab) solution for infusion	31-Mar-2020	Ongoing	Conduct a clinical trial to assess whether STELARA (ustekinumab) alters the metabolism or pharmacokinetics of cytochrome P450 (CYP) substrates in Crohn's disease (CD) patients treated with ustekinumab (e.g., using a cocktail of relevant CYP probe drugs). (Final Protocol Submission: March 2017 Trial Completion: September 2019 Final Report Submission: March 2020)

Product	Due Date	Status	Description of Commitment or Requirement
STELARA (ustekinumab) solution for injection; solution for injection in pre-filled syringe	31-Aug-2019	Ongoing	Conduct studies to evaluate the safety and efficacy of ustekinumab in pediatric subjects with plaque psoriasis.
STELARA (ustekinumab) solution for injection; solution for injection in pre-filled syringe	01-Dec-2020	Ongoing	Enroll 4,000 STELARA® (ustekinumab)-treated subjects into the Psoriasis Longitudinal Assessment Registry, (PSOLAR) and follow for 8 years from the time of enrollment. Subjects will be followed for the occurrence of serious infection, tuberculosis, opportunistic infections, malignancy, hypersensitivity reactions, autoimmune disease, neurologic or demyelinating disease, cardiovascular, gastrointestinal or hematologic adverse events.
STELARA (ustekinumab) solution for injection; solution for injection in pre-filled syringe	15-Jul-2014	Ongoing	Establish a U.S.-based prospective, observational pregnancy exposure registry that compares the pregnancy and fetal outcomes of women exposed to STELARA® (ustekinumab) during pregnancy to an unexposed control population. Outcomes of the registry should include major and minor congenital anomalies, spontaneous abortions, stillbirths, elective terminations, adverse effects on immune system development, and other serious adverse pregnancy outcomes. These outcomes should be assessed throughout pregnancy. Infant outcomes should be assessed through at least the first year of life.
STELARA (ustekinumab) solution for injection; solution for injection in pre-filled syringe	15-Dec-2020	Ongoing	Provide data analyses from the Nordic Database Initiative regarding the occurrence of serious infection, tuberculosis, opportunistic infections, malignancy, hypersensitivity reactions, autoimmune disease, neurologic or demyelinating disease, cardiovascular, gastrointestinal or hematologic adverse events with exposure to ustekinumab.
STELARA (ustekinumab) solution for injection; solution for injection in pre-filled syringe	15-Dec-2021	Ongoing	Provide data analyses from the Pregnancy Research Initiative (study C0168T71).
SYMTUZA™ (cobicistat + darunavir ethanolate + emtricitabine + tenofovir alafenamide fumarate)	01-Sep-2024	Ongoing	Conduct your deferred pediatric trial in HIV-1 infected patients weighing at least 40 kg to assess the pharmacokinetics, safety and tolerability, and antiviral activity of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide fixed-dose combination (FDC). Study participants should be monitored for 24 weeks to assess safety and durability of antiviral response. A clinical trial may not be required if the dosing recommendation for the FDC tablets can be supported by pediatric trials already conducted with the individual components and if the FDC produces similar exposures as the individual components.
TOPAMAX (topiramate) film-coated tablet	31-Jul-2022	Ongoing	A one year prospective, randomized, parallel, active-control arm trial to compare the safety of TOPAMAX® (topiramate) with regard to metabolic acidosis, renal stone formation, bone mineral density, and development (i.e. height, weight and sexual) with that of an alternate treatment in pediatric patients ages 2 to 15 years. Dosing for this study should be based on the pediatric monotherapy dosing recommendations in the approved labeling for TOPAMAX® (topiramate) and an expected efficacious dose for the comparator.
TOPAMAX (topiramate) capsule, hard	31-Jul-2022	Ongoing	A one year prospective, randomized, parallel, active-control arm trial to compare the safety of TOPAMAX® (topiramate) with regard to metabolic acidosis, renal stone formation, bone mineral density, and development (i.e. height, weight and sexual) with that of an alternate treatment in pediatric patients ages 2 to 15 years. Dosing for this study should be based on the pediatric monotherapy dosing recommendations in the approved labeling for TOPAMAX® (topiramate) and an expected efficacious dose for the comparator.

Product	Due Date	Status	Description of Commitment or Requirement
TREMFYA (guselkumab) solution for injection in pre-filled syringe	30-Apr-2024	Ongoing	Conduct a Pharmacokinetics (PK), Safety and Efficacy Study in pediatric subjects 6 years to less than18 years of age with moderate to severe plaque psoriasis (with a duration of exposure to guselkumab of at least one year).
TREMFYA (guselkumab) solution for injection in pre-filled syringe	31-Dec-2026	Delayed	A prospective, registry-based observational exposure cohort study that compares the maternal, fetal, and infant outcomes of women exposed to guselkumab during pregnancy to an unexposed control population
TREMFYA (guselkumab) solution for injection in pre-filled syringe	31-Dec-2025	Delayed	Conduct a retrospective cohort study using claims or electronic medical record data or a case control study to assess adverse pregnancy outcomes such as major congenital malformations, spontaneous abortions, stillbirths, small for gestational age, neonatal deaths, and infant infections in women exposed to guselkumab during pregnancy compared to an unexposed control population
TREMFYA (guselkumab) solution for injection in pre-filled syringe	31-Dec-2031	Pending	Conduct an observational study to assess the long-term safety of guselkumab compared to other therapies used in the treatment of adults with moderate-tosevere plaque psoriasis who are candidates for systemic therapy or phototherapy in the course of actual clinical care. The study's primary outcome is the long-term risk of malignancy. Secondary outcomes include, but are not limited to, serious infections, tuberculosis, opportunistic infections, hypersensitivity reactions, autoimmune disease, neurologic or demyelinating disease, cardiovascular, gastrointestinal and hematologic adverse events
ULTRACET® (paracetamol + tramadol hydrochloride) film-coated tablet	15-May-2005	Submitted	Pediatric study commitment; final study report for TRAMAP-PEDS-001. Study TRAMAP-PEDS-001 compared the safety and clinical effectiveness of single doses of tramadol 75 mg/APAP 650 mg, tramadol 37.5 mg/APAP 325 mg, and placebo in pediatric participants, aged 8 to 17 years, with post-surgical pain. This study enrolled 150 participants at 20 study centers in the United States and Costa Rica.
XARELTO® (rivaroxaban) film-coated tablet	30-Jun-2020	Submitted	A single-dose PK/PD and tolerability trial in pediatric patients age birth to < 6 months with VTE to determine doses of rivaroxaban (oral suspension) that provide similar exposure and/or PD effect to those seen in older pediatric cohorts.
XARELTO® (rivaroxaban) film-coated tablet	30-Jun-2020	Submitted	A dose-exploration, multicenter clinical trial evaluating the multiple dose PK/PD profile and safety of oral rivaroxaban (oral suspension) in pediatric patients aged birth to <6 months with VTE.
XARELTO® (rivaroxaban) film-coated tablet	30-Jun-2020	Ongoing	A randomized, active-controlled, multicenter clinical trial evaluating the safety, efficacy and PK/PD (sparse sampling) of at least 3 months of treatment with oral rivaroxaban (tablets or oral suspension) in pediatric patients aged birth to < 17 years of age who have acute VTE. Patients who require treatment for longer than 3 months will be offered continuation of treatment in an open label extension of this study with treatment duration of up to 12 months. Patients from birth to <6 months of age may be enrolled only after data from a planned interim analysis have shown efficacy and safety of rivaroxaban in the older pediatric age groups. Age distribution of patients in the study should reflect the occurrence of VTE in the pediatric population.
ZYTIGA (abiraterone acetate) film-coated tablet	01-Feb-2019	Submitted	Submit the final analysis for overall survival, datasets, and labeling with the final report for the ongoing clinical trial, 212082PCR3011, entitled; "A Randomized, Double-blind, Comparative Study of Abiraterone Acetate Plus Low dose Prednisone Plus Androgen Deprivation Therapy (ADT) Versus ADT Alone in Newly Diagnosed Subjects With High Risk, Metastatic Hormone-Naive Prostate Cancer. Schedule Milestones: Final Report Submission"