U.S. Postmarketing Commitments Table:

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
ANDROGEL (testosterone)	NDA 22309	A hand washing trial following the application of testosterone. This clinical trial will measure the amount of residual testosterone before and after washing the primary user's hands.	April 29, 2011	Final Report Submission: July 31, 2012	Submitted
CREON (pancrelipase)	NDA 20725	A 10 year, observational study to prospectively evaluate the incidence of fibrosing colonopathy in patients with cystic fibrosis treated with pancrelipase Delayed-Release Capsules in the US and to assess potential risk factors for the event.	April 30, 2009	June 20, 2021	Pending
CREON (pancrelipase)	NDA 20725	A 10 year, observational study to prospectively evaluate the risk of transmission of selected porcine viruses in patients taking pancrelipase Delayed-Release Capsules.	April 30, 2009	Final Report Submission: June 20, 2021	Pending
DEPAKOTE (divalproex sodium)	NDA 22267	Conduct an adequate and well-controlled drug-drug interaction study to systematically evaluate whether an interaction occurs between olanzapine and divalproex sodium when they are co-administered.	October 15, 2009	Final Report Submission: October 16, 2011	Submitted
HUMIRA (adalimumab)	BLA 125057/0	Establish a pregnancy registry of patients with rheumatoid arthritis who become pregnant while on anti-rheumatic therapy, including adalimumab as well as other medications, which will run for 3 years.	December 31, 2002	Final Report Submission: December 31, 2015	Delayed
HUMIRA (adalimumab)	BLA 125057/89	Conduct study protocol P06-134, a 5-year, 5000 patient, multi-center, uncontrolled, observational study of adult patients with Crohn's disease treated in a routine clinical setting with adalimumab.	February 27, 2007	December 31, 2016	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
HUMIRA (adalimumab)	BLA 125057/89	Complete and submit data from study protocol M06-806, a one-year, multi-center, randomized, double-blind study designed to evaluate the safety, efficacy, and pharmacokinetics of adalimumab in the induction and maintenance of clinical remission in pediatric subjects 6 to 17 years of age with moderate to severe Crohn's disease. The study will include collection of baseline data on prior loss of response to or intolerance to infliximab, using definitions similar to those used in protocol M04-691.	February 27, 2007	December 31, 2012	Delayed
HUMIRA (adalimumab)	BLA 125057/114	PMC #1 - Conduct Study Protocol P10-262, an 800-patient observational study, with inclusion of a reference group, of pediatric patients 4 to 17 years of age with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA).	February 21, 2008	December 31, 2021	Ongoing
HUMIRA (adalimumab)	BLA 125057/114	PMC #2 - Conduct a compassionate use study in patients 2 to 4 years of age with moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) to collect pharmacokinetic data in 6 to 20 patients and to collect safety data in 30 patients according to the safety assessment specified in postmarketing commitment number 1.	February 21, 2008	December 31, 2021	Ongoing
HUMIRA (adalimumab)	BLA 125057/110	Conduct a prospective, multi-center registry including 5000 adult psoriasis patients treated with adalimumab in the United States. This registry will characterize and assess the incidence of serious adverse events (including serious infections,	January 18, 2008	January 31, 2023	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
		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 for a period of at least 10 years with comprehensive annual reports provided to the Agency. 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 titled *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment.*			
HUMIRA (adalimumab)	BLA 125057/110	Deferred pediatric study under PREA for the treatment of moderate to severe chronic plaque psoriasis in pediatric patients ages 4 to 17. The pediatric plan is to assess data anticipated from ongoing trials as well as further analysis and assessment of data, including data pertaining to the diagnosis and treatment of psoriasis in the pediatric population, and to establish a study plan that incorporates this new data.	January 18, 2008	January 31, 2013	Pending
HUMIRA (adalimumab)	BLA 125057	Enhanced pharmacovigilance program for reports of malignancy in pediatric, adolescent, and young adult (< 30 years of age) patients treated with adalimumab, for a period of up to 10 years after this notification to collect data that will be	November 02, 2011	March 31, 2020	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
		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 and young adult patients. Interim analyses and summaries of new and cumulative safety information in pediatric and young adult patients must be submitted annually, followed by the final report at the conclusion of the monitoring period.			
HUMIRA (adalimumab)	BLA 125057/232	PMR #1 - A study in inflammatory bowel disease (IBD) patients treated with Humira (adalimumab) in which you will bank tissue or blood samples (as appropriate) and then analyze them to identify genetic mutations and other biomarkers that predispose these patients to developing Hepatosplenic T-Cell Lymphoma (HSTCL).	September 28, 2012	Final Report Submission: September 30, 2020	Ongoing
HUMIRA (adalimumab)	BLA 125057/232	PMR #2 - A multi-center observational study of Humira (adalimumab) in adults with moderately to severely active ulcerative colitis treated in a routine clinical setting, to assess the long-term safety as measured by the incidence of opportunistic infections and malignancies. Long-term effectiveness should be assessed as a secondary goal. The proposed study should follow patients for a period of at least 10 years from time of enrollment in order to	September 28, 2012	Final Report Submission: December 31, 2029	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
		ascertain adverse events with longer latency periods such as malignancies. The primary analysis is to summarize safety data for patients on adalimumab and patients on non-biologic immunomodulator therapy. The study should be adequately sized to sufficiently detect a doubling of the risk of lymphoma events in each treatment group. A secondary analysis is to summarize safety data for patients on adalimumab and patients on the combination of adalimumab and non-biologic immunomodulator therapy. In addition, the study is to document and evaluate effects of withdrawal and re-treatment with adalimumab and “switching” with other tumor necrosis factor (TNF)-blockers or biologics.			
HUMIRA (adalimumab)	BLA 125057/232	PMR #3 - Develop, qualify, and implement improved validated anti-adalimumab antibody (AAA) assays with reduced sensitivity to product interference. Until assays have been developed and validated, patient blood samples collected from clinical studies and trials should be banked under appropriate storage conditions. You will provide assay SOPs, validation protocols, and validation final reports that include data demonstrating that the assay is specific, sensitive and reproducible, and capable of sensitively detecting AAA responses in the presence of adalimumab levels that are expected to be present at the time of patient sampling.	September 28, 2012	Final Report Submission: December 31, 2013	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
HUMIRA (adalimumab)	BLA 125057/232	PMR #4 - Utilizing a validated AAA assay as described in PMR #3 above, you should measure and analyze the immunogenicity profile based on post-dose patient samples from completed study M10-223, the trial conducted under PMR #5, the trial conducted under PMR #6, and the trial conducted under PMC #7.	September 28, 2012	Final Report Submission: March 31, 2019	Ongoing
HUMIRA (adalimumab)	BLA 125057/232	PMR #5 - Conduct a trial in moderately to severely active ulcerative colitis patients to evaluate the safety of induction regimens of adalimumab at doses higher than 160/80 mg. In this trial, the efficacy of Humira (adalimumab) should also be assessed, both during induction treatment as well as during continued treatment after induction, and pharmacokinetic measurements should be conducted for exposure-response analysis. In this trial, collecting samples for immunogenicity testing (utilizing a validated anti-adalimumab antibody assay as described in PMR #3 above) and conducting analyses of the impact of immunogenicity on safety, pharmacokinetics, and efficacy is important. The protocol should be agreed upon by the agency prior to the initiation of the trial.	September 28, 2012	Final Report Submission: March 31, 2019	Ongoing
HUMIRA (adalimumab)	BLA 125057/232	PMR #6 - A safety and pharmacokinetic trial as a sub-study of the trial described in PMR #5 above to evaluate trough concentrations of adalimumab and antibody levels (utilizing a validated anti-adalimumab antibody assay as described in PMR #3 above) at the time	September 28, 2012	Final Report Submission: March 31, 2019	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
		of loss of clinical remission in patients whose physicians plan to escalate the dose (e.g., decrease the dosing interval to weekly or increase the dosage) in response to loss of remission. Trough concentrations will be evaluated to determine whether patients who have low adalimumab exposures benefit from dose escalation without increasing risk of serious adverse events. The protocol should be agreed upon by the agency prior to initiation of the trial.			
HUMIRA (adalimumab)	BLA 125057/232	PMC #7 - Conduct a one-year, multi-center, randomized, double-blind placebo-controlled trial to evaluate the efficacy, safety and pharmacokinetics of adalimumab in pediatric patients 5 to 17 years of age with moderately to severely active ulcerative colitis. In this trial, the efficacy of adalimumab should be assessed during induction treatment as well as during continued treatment after induction, and pharmacokinetic measurements should be conducted for exposure-response analysis. Also, collect samples for immunogenicity testing (utilizing a validated AAA assay as described in PMR #3 above) and conduct analyses of the impact of immunogenicity on pharmacokinetics, efficacy and safety. The protocol should be agreed upon by the agency prior to the initiation of the trial.	September 28, 2012	Final Report Submission: December 31, 2019	Ongoing
KALETRA (lopinavir/ritonavir)	NDA 21906	Please submit the 24 week results of PENTA 18 evaluating the pharmacokinetic, safety and activity of twice daily and once	April 27, 2010	Final Report Submission: December 31,	Ongoing

Name of Product	NDA/BLA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
		daily dosing of lopinavir/ritonavir tablets in a reviewable format. Submit a final report that includes detailed summaries of pharmacokinetic, safety and activity data as well as electronic datasets.		2013	
TRILIPIX (fenofibric acid)	NDA 22224	A randomized, double-blind, placebo-controlled trial evaluating the effect of fenofibric acid on the incidence of major adverse cardiovascular events in high-risk men and women at LDL-C goal on statin therapy, but with residually high triglycerides and low HDL-C.	July 06, 2011	Final Report Submission: January 31, 2021	Pending
ZEMPLAR (paricalcitol)	NDA 21606	Deferred pediatric study under PREA for the treatment of Stage 3 and Stage 4 chronic kidney disease in pediatric patients ages twelve to sixteen years.	May 26, 2005	Final Report Submission: December 31, 2013	Delayed
ZEMPLAR (paricalcitol)	NDA 21606	Deferred pediatric study under PREA for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease (CKD) Stage 5 for patients receiving peritoneal dialysis in pediatric patients' ages ten to sixteen years.	June 29, 2009	Final Report Submission: December 31, 2013	Ongoing
ZEMPLAR (paricalcitol)	NDA 21606	Deferred pediatric study under PREA for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease (CKD) Stage 5 for patients receiving peritoneal dialysis in pediatric patients' ages zero to nine years.	June 29, 2009	April 30, 2014	Pending

Note: The PMC Summary Table includes all U.S. active postmarketing commitments as of September 30, 2012.