United States Clinical Postmarketing Commitments/Requirements

Corporate Integrity Agreement (CIA) - June 2023

Generic Name	Trade Name	Application Number	Commitment Date	PMC/PMR Identifier	Description of Commitment/Requirement	Current Status	Explanation of Status
adalimumab-atto	AMJEVITA	761024	23-Sep-2016	US PMR 3125-1	Assessment of Amjevita (adalimumab-atto) for the treatment of Polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years to less than 4 years of age.	Fulfilled	
adalimumab-atto	AMJEVITA	761024	23-Sep-2016	US PMR 3125-2	Assessment of Amjevita (adalimumab-atto) for the treatment of pediatric Crohn's disease in pediatric patients 6 years to 17 years of age.	Fulfilled	
adalimumab-atto	AMJEVITA	761024	23-Sep-2016	US PMR 3125-3	Assessment of Amjevita (adalimumab-atto) for the treatment of pediatric ulcerative colitis in pediatric patients 5 years to 17 years of age.	Ongoing	Amgen has requested and received a deferral of assessment of UC in patients 5 years of age and older, currently approved for Humira, until expiration of Humira orphan exclusivity on 24 February 2028. Amgen will propose extrapolation to this age group based on information reflected in the Humira prescribing information combined with a scientific justification for extrapolating the pediatric information upon expiration of above exclusivity.
adalimumab-atto	AMJEVITA	761024	23-Sep-2016	US PMR 3125-4	Develop a presentation that can be used to accurately administer Amjevita adalimumab-atto) to pediatric patients who weigh less than 15 kg.	Fulfilled	
apremilast	OTEZLA	205437	21-Mar-2014	US PMR 2135-1	Conduct a prospective, observational, controlled, pregnancy exposure registry study to monitor pregnancies exposed to apremilast with the primary objective to evaluate whether there is any increase in the risk of birth defects.	Delayed	The study completion and final report submission milestones are delayed due challenges with enrollment. On 12 April 2022, the FDA issued correspondence indicating that Amgen has good cause for not complying with the original PMR milestone dates for study completion and final report submission and acknowledged Amgen's revised milestone dates (Study Completion: 6/2026; Final Report Submission: 3/2027).
apremilast	OTEZLA	205437	23-Sep-2014	US PMR 2791-1	Conduct a dose finding, pharmacokinetics and safety trial in subjects with moderate to severe plaque psoriasis between the ages of 6 to 17 years.	Fulfilled	
apremilast	OTEZLA	205437	23-Sep-2014	US PMR 2791-2	Conduct a safety and efficacy trial in pediatric subjects with moderate to severe plaque psoriasis between the ages of 6 to 17 years.	Fulfilled	
apremilast	OTEZLA	205437	20-Dec-2021	US PMR 4207-1	Conduct a Phase 3, multicenter, open-label study to assess the safety of apremilast in approximately 50 pediatric subjects (6 through 17 years of age, inclusive) with mild-to-moderate plaque psoriasis.	Ongoing	First clinical site was activated on 28 August 2023. First subject was screened on 27 September 2023. First subject was enrolled on 24 October 2023.
blinatumomab	BLINCYTO	125557/0000	03-Dec-2014	US PMR 2836-01	Complete the trial and submit the final report and data to verify and describe the clinical benefit of blinatumomab, including efficacy and safety from Protocol 00103311, a Phase 3 randomized, open-label, active-controlled trial comparing blinatumomab to standard of care for treatment of patients with relapsed or refractory Ph-negative B-cell precursor acute lymphoblastic leukemia (ALL). Enrollment of approximately 400 patients is expected, and the primary endpoint is overall survival.	Fulfilled	
blinatumomab	BLINCYTO	125557/008	11-Jul-2017	US PMR 3230-1	Characterize the impact, if any, of administration of blinatumomab as salvage therapy prior to allogeneic hematopoietic stem cell transplantation (HSCT) on early safety outcomes after HSCT as compared to standard of care (SOC) chemotherapy. Conduct an analysis of registry data (for example the Center for International Blood and Marrow Transplantation Research registry) to determine whether or not prior treatment with blinatumomab increases the risk of day-100 mortality or acute graft-versus-host disease as compared to SOC chemotherapy.	Ongoing	
blinatumomab	BLINCYTO	125557/008	11-Jul-2017	US PMR 3230-2	Submit the final report and datasets for trial 00103311 (TOWER), a randomized trial of blinatumomab versus standard of care chemotherapy in patients with relapsed or refractory Philadelphia-negative acute lymphoblastic leukemia. Include final overall survival data, updated safety data, and quality of life data.	Fulfilled	
blinatumomab	BLINCYTO	125557/008	11-Jul-2017	US PMR 3230-3	Submit the final report and datasets for trial 20120216 (ALCANTARA), a single arm trial of blinatumomab in patients with relapsed or refractory Philadelphia positive acute lymphoblastic leukemia. Include final overall survival data, final relapse free survival, response rates, and safety data.	Fulfilled	
blinatumomab	BLINCYTO	125557/013	29-Mar-2018	US PMR 3366-1	Complete a randomized trial and submit the final study report and data sets to verify and describe the clinical benefit of blinatumomab in adults with acute lymphoblastic leukemia in morphologic complete remission with detectable minimal residual disease, including efficacy and safety from protocol E1910: Combination chemotherapy with or without blinatumomab in treating patients with newly-diagnosed BCR-ABL-negative B lineage acute lymphoblastic leukemia. Randomization of approximately 280 newly diagnosed patients is expected, and the primary endpoint is overall survival.	Released	FDA released this requirement on 20 June 2023 as it is no longer needed because the requirement was met with fulfillment of PMR 3366-2
blinatumomab	BLINCYTO	125557/013	29-Mar-2018	US PMR 3366-2	Complete a randomized trial and submit the final study report and data sets to verify and describe the clinical benefit of blinatumomab in pediatric patients in morphologic complete remission with detectable minimal residual disease, including efficacy and safety from protocol AALL1331: Risk-stratified Phase III testing of blinatumomab in first relapse of childhood B-lymphoblastic leukemia (B-ALL). Enrollment of approximately 598 patients is expected. The primary endpoint is disease-free survival.	Fulfilled	This requirement was fulfilled with the FDA approval of the S-023 supplement on 20 June 2023, which converted the MRD+ indication from accelerated approval to regular approval.
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-1	Conduct a randomized controlled trial per Protocol PX-171-009, as finalized, to compare carfilzomib-lenalidomide dexamethasone with lenalidomide dexamethasone in a population of patients with myeloma, whose disease has relapsed after previous response to at least one but not more than three prior therapies, to assess efficacy and safety. Patients' disease is required to show evidence of progression after prior therapy. The trial includes 792 patients. The randomization will balance known important prognostic factors. The goal of the trial is to evaluate the primary endpoint of progression-free survival (PFS) for the carfilzomib-containing arm, as determined by an independent review committee blinded to the treatment given.	Fulfilled	

carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-2	Conduct a randomized clinical trial in patients receiving carfilzomib to identify and characterize the cardiac toxicities associated with carfilzomib. You have agreed to conduct this trial as a cardiac sub-trial within your ongoing Protocol 2011-003 (ENDEAVOR). The primary objective is to compare changes in cardiac function between the group receiving carfilzomib and a control group not receiving carfilzomib in a parallel group trial. The main trial protocol (2011-003) must require a baseline resting ECG and transthoracic ECHO to assess left ventricular (LV) function on all patients. If transthoracic ECHO is not available at some sites, MUGA will be acceptable for baseline screening LVEF evaluation. For the cardiac sub-trial, a subset of patients from the main trial will be assessed for LV and right ventricular (RV) function with transthoracic ECHO (or MUGA for those sites using MUGA at baseline) periodically throughout trial treatment and at the time of the End-of-Treatment visit, using similar test procedures and equipment to allow serial intra-patient comparisons. This cardiac sub-trial must include a minimum of 100 patients and a maximum of 300 patients total (50 to 150 patients per treatment arm). Specific details regarding the interpretation of LVEF changes must be pre-specified and outlined in the SAP for this cardiac toxicity trial. For the sub-trial, readers of the ECHOs/MUGAs must be blinded to the protocol treatment given. In addition, any patient in the main trial who has a cardiac adverse event (AE) that is considered a clinically significant AE must have an ECHO performed to assess LV and RV function as part of the evaluation of that AE. Submit a complete cardiac sub-trial protocol for review and concurrence before commencing the sub-trial.	Fulfilled	
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-3	Conduct a randomized clinical trial in patients receiving carfilzomib to identify and characterize the pulmonary toxicities associated with carfilzomib. The primary objective is to compare pulmonary toxicities between the group receiving carfilzomib and a control group not receiving carfilzomib in a parallel group trial. You have agreed to conduct this pulmonary sub-trial within your ongoing Protocol 2011-003. On all patients enrolled in the main trial, 2011-003, during screening, obtain a baseline transthoracic ECHO to estimate the pulmonary artery pressures and to assess right ventricular size, thickness, and function, and to serve as the baseline ECHO for later comparisons on all patients. In the pulmonary sub-trial, among a minimum of 100 patients and a maximum of 300 patients total (50 to 150 patients per treatment arm), assess this sub-group periodically for pulmonary artery pressures and right ventricular function with repeat transthoracic ECHO throughout trial treatment and at the time of End-of-Treatment visit, using similar test procedures and equipment to allow serial intrapatient comparisons. Emergent pulmonary toxicities must be further characterized in all patients receiving carfilzomib in the main trial also, to include at least the following: time course of onset and resolution, oximetry and/or blood gases, and consultation with a pulmonary specialist, when clinically appropriate, to provide further documentation of the nature of the emergent condition. Document the response to oxygen supplementation and other treatment measures. For the subtrial, readers of the ECHOs/MUGAs must be blinded to the treatment given. In the pulmonary sub-trial protocol, pre-specify how comparisons will be performed for changes between the two groups for outcomes related to pulmonary hypertension, right ventricular function, and clinical pulmonary safety events. Additionally, for all patients enrolled in the main trial, any patient who has a cardiac or pulmonary AE that is considered a clinically significant AE must have a follow-up ECHO at the time of the event to assess LV, RV, and pulmonary artery function. Submit a complete pulmonary sub-trial protocol for review and concurrence before commencing the sub-trial.	Fulfilled	
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-4	Conduct a clinical trial (2011-003 ENDEAVOR) to evaluate the safety of a 30-minute intravenous infusion of carfilzomib at the dose of 20/56 mg/m2 in patients with multiple myeloma.	Fulfilled	
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-5	Conduct a clinical trial (PX-171-007) to evaluate the safety of a 30-minute intravenous infusion of carfilzomib at the dose of 20/56 mg/m2 in patients with multiple myeloma.	Fulfilled	
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-6	Conduct a clinical trial in patients with hepatic impairment to assess safety and PK characteristics of carfilzomib administered as a 30 minute infusion. The number of patients enrolled in the trial should be sufficient to detect PK differences that would warrant dosage adjustment recommendations in the labeling. The duration of the trial should be sufficient (several cycles) to reasonably characterize potential safety issues. The PK sampling scheme should be optimized to accurately estimate relevant PK parameters for the parent drug. A data analysis plan must be included in the protocol. Submit your protocol for Agency review and concurrence prior to initiation.	Fulfilled	
carfilzomib	Kyprolis	202714/0000	20-Jul-2012	US PMR 1908-7	Conduct one or more clinical trials including Phase 3 Protocol 2011-003, supplemented as needed by an additional trial, to evaluate the PK, safety, and efficacy of carfilzomib in patients with varying degrees of renal impairment and those on chronic dialysis following the administration of carfilzomib when given as a 30 minute intravenous infusion at a sufficient dose level that will likely produce comparable exposure and clinical response to those patients without renal impairment who receive carfilzomib doses of 20/56 mg/m2 using the 30 minute infusion as planned in your upcoming Phase 3 trial Protocol 2011-003. Collect PK samples following carfilzomib doses of 56 mg/m2 or highest clinical dose in the protocol. Submit your protocol for Agency review and concurrence prior to initiation.	Fulfilled	
carfilzomib	Kyprolis	202714/0010	21-Jan-2016	US PMC 3022-2	Characterize the comparative safety and efficacy of the 20/27 mg/m2 and the 20/56 mg/m2 regimens of carfilzomib. Submit a study report with safety and efficacy outcomes of SWOG Protocol S1304 and your analysis of what clinical parameters might affect the choice of carfilzomib regimen for a particular patient.	Submitted	Final Report was submitted 28 Jan 2019. FDA responded that data included in the final report does not adequately fulfill the PMC. Amgen proposed revised milestones on 11 Mar 2020. General Advice Letter received from FDA on 09 July 2020. Amgen submitted a Response to the General Advice Letter that included protocol 20200381, protocol 20200086, and SAP for study 20200381 on 29 October 2020. On 15 September 2021 Amgen received General Advice Letter from FDA and submitted response in December 2021, in which Amgen proposed to revise the milestone for the final report to January 2023, however FDA has not formally accepted this milestone. Final reports for Study 2020086 and Study 20200381 were submitted to the FDA on 30 January 2023. An Information Request was received from the FDA on 06 February 2024 requesting Amgen to provide the raw and analysis-ready datasets and SAS programs for Study 20200381. Amgen submitted a response to the FDA Information Request on 23 February 2024. Amgen is awaiting FDA response.
carfilzomib	Kyprolis	202714/0010	21-Jan-2016	US PMR 3022-1	Characterize safety of long-term use in patients treated with Kyprolis (carfilzomib) 20/56 mg/m2 plus dexamethasone. Submit a final report and datasets with safety and efficacy outcomes of current clinical trial 2011-003 (ENDEAVOR) with at least 3 years of follow-up data.	Fulfilled	

carfilzomib	Kyprolis	202714/0022	14-Dec-2018	US PMR 3558-1	Conduct an observational study to evaluate incidence rates of heart failure among U.S. racial and ethnic minority patients with multiple myeloma treated or not treated with carfilzomib. Select a data source that captures risk factors for cardiac failure that may differ by race.	Released	Amgen submitted the final study report for study 20190012 in support of fulfillment of the PMR 3558-1 on 26 June 2020 . Amgen received the "Release from Post-Marketing Requirement" letter on 22 August 2020.
carfilzomib	Kyprolis	202714/0030	20-Aug-2020	US PMC 3917-1	Submit the final progression free survival, overall survival analysis, safety results and datasets with the final study report from the ongoing multicenter, randomized, phase 3 clinical trial (CANDOR) comparing daratumumab in combination with carfilzomib and dexamethasone to carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy. The results from this report may inform product labeling.	Fulfilled	
carfilzomib	Kyprolis	202714/033	30-Nov-2021	US PMC 4183-1	Conduct an integrated study analysis containing data from clinical trials, post-marketing reports, compassionate use/expanded access programs, real-world evidence, and other sources to further characterize the safety and efficacy of daratumumab (SC) in combination with carfilzomib and dexamethasone among U.S. racial and ethnic minority patients with multiple myeloma.	Ongoing	This study is ongoing. The Final Report is due August 2026.
carfilzomib	Kyprolis	202714/S-034	30-Jun-2022	US PMR 4279-1	Conduct a clinical trial sufficient to characterize and determine the incidence of second primary malignancies in patients receiving carfilzomib in combination with isatuximab and dexamethasone (Isa-Kd). This data may come from Study EFC15246 (IKEMA), supported by data from other trials across the carfilzomib development program. Include incidence rates, time to onset, outcomes, and efficacy in the final report. Efficacy should include final progression-free survival and overall survival results.	Submitted	Final report for Study 20220146 was submitted on 25 September 2023 (Final Report Due September 2023). Amgen also included a cross-reference to the submission made by Sanofi Aventis LLC for the IKEMA final study report planned to be submitted to Sanofi BLA 761113 on 27 September 2023. Amgen received an information request from FDA on 15 February 2024 requesting Amgen to provide all the raw and analysis-ready datasets and SAS programs for Study 20220146 and to provide a summary of second primary malignancies (SPMs) in all trials conducted with carfilzomib except ASPIRE and ENDEAVOR during the development program including single arm trials. Amgen submitted response to the FDA information request on 28 February 2024 and 05 April 2024, respectively. Amgen received a clinical information request on 31 May 2024 to identify the time period used for SPM data collection for ASPIRE, ENDEAVOR, and IKEMA clinical trials. Amgen submitted response to the FDA information request on 10 June 2024. Amgen is awaiting FDA's response.
carfilzomib	Kyprolis	202714/S-034	30-Jun-2022	US PMC 4279-2	Conduct an integrated analysis that contains data from clinical trials, post- marketing reports, compassionate use/expanded access programs, real- world evidence, and other sources to further characterize the safety and efficacy of carfilzomib in combination with isatuximab and dexamethasone (Isa-Kd) a ong U.S. racial and ethnic minority patients with multiplemyeloma.	Ongoing	Final Report Submission is due Dec 2026.
cinacalcet HCl	Sensipar	021688/0000	15-Mar-2017	US PMR 3202-1	Conduct a hypothesis-testing observational study to provide data regarding the potential association between Sensipar (cinacalcet) and fatal and non-fatal gastrointestinal bleeding. The study should have a comparator group, be powered to detect the outcomes of interest, with justification for the proposed detectable differences in incidence rates. Special attention should be given to complete data availability in dialysis patients with secondary hyperparathyroidism above and below the age of 65 years, the ability to ascertain cause of death in a timely manner, and a statistical consideration of competing risks. Secondary analyses should aim to quantify the exposure-risk window, including periods after exposure discontinuation. The choice of study design, data source(s), and sample size should be supported by a feasibility analysis submitted to and reviewed by FDA prior to protocol finalization.	Fulfilled	
darbepoetin alfa	Aranesp	103951/5088	15-Dec-2005	US PMC 001	To conduct a study, such as a single-arm open-label study or a prospective patient registry, to evaluate the safety and usefulness of Aranesp for initial treatment for the correction of anemia in pediatric chronic renal failure patients.	Released	
darbepoetin alfa	Aranesp	103951/5097	23-Mar-2006	US PMC 004	To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol DE-2002-0015, being conducted in 1000 patients with breast cancer receiving adjuvant (ARA-03) chemotherapy assessing the safety of Darbepoetin alfa administered at 300 mcg QW followed by 300 mcg Q3W as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA).	Fulfilled	
darbepoetin alfa	Aranesp	103951/5097	24-Mar-2006	US PMC 005	To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol SE-2002-9001, being conducted in 600 patients with head-and-neck cancer DAHANCA- 10) assessing the safety of Darbepoetin alfa administered at 150 mcg QW as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA).	Released	
darbepoetin alfa	Aranesp	103951/5097	23-Mar-2006	US PMC 006	To obtain and submit a final study report, including the primary data and analyses, of the ongoing, randomized, observational-control, investigator-sponsored study, Protocol FR-2003-3005, being conducted in 600 patients with diffuse large B-Cell lymphoma (GELA LNH-03-6B) assessing the safety of Darbepoetin alfa administered at 2.25 mcg/kg QW as compared to transfusion support, for the treatment of chemotherapy-induced anemia (CIA).	Fulfilled	
darbepoetin alfa	Aranesp	103951/5097	24-Mar-2006	US PMC 007	To conduct and provide the data and results of a meta-analysis of adverse outcomes, utilizing the data from studies 20010145, DE-2001-0033, DE-2002-0015, DE-2002-9001, and FR-2003-3005.	Released	
darbepoetin alfa	Aranesp	103951/5137	18-May-2007	US PMC 2681-1	Re-evaluate the N-glycan mapping specifications to ensure stringent control of N-glycan branching and sialylation and to evaluate the current methods and alternative strategies for controlling these attributes to assure consistency of product quality. The evaluation will comprise an assessment of impact of changes in the distribution of N-glycan	Fulfilled	Fulfilled on 12 July 2019.
darbepoetin alfa	Aranesp	103951/5188/S-5378	23-Jun-2009	US PMR 001 (PMR 2592-1)	To conduct clinical trial 20070782 entitled "A Randomized,Double-blind, Placebo-controlled Study to Evaluate the Long-term'Safety and Efficacy of Darbepoetin AlfaAdministered at 500 mcg Once-Every-3-Weeks (Q3W) in Anemic Subjects with Advanced Stage Non-small Cell Lung Cancer Receiving Multi-cycle Chemotherapy" to evaluate the impact of darbepoetin alfa on overall survival, progression-free survival, and objective tumor response rate.	Fulfilled	
darbepoetin alfa	Aranesp	103951/5248	24-Jun-2011	US PMR 002 (PMR 2785-1)	In patients with CKD who are not on dialysis (NOD), conduct one or more trials to determine whether a dosing strategy (e.g. fixed dose strategy) different from that in the approved labeling can further reduce exposure to ESA while preserving the benefit of reducing transfusion use.	Fulfilled	
darbepoetin alfa	Aranesp	103951/5326	13-Dec-2012	US PMC 001	To conduct a randomized, double-blinded, multi-center trial to evaluate the safety and efficacy of Aranesp for initial treatment for the correction of anemia in pediatric chronic renal failure patients.	Fulfilled	
darbepoetin alfa	Aranesp	103951/5375	09-Mar-2017	US PMC 3198-1	To assess the utilization of Epogen/Procrit and Aranesp for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.	Fulfilled	FDA Fulfillment letter dated and received on 05 December 2024
denosumab	Prolia	125320/0000	01-Jun-2010	US PMR 001 (2399-1)	To conduct a retrospective cohort study using multiple existing observational databases to collect data from a 5-year period prior to the availability of denosumab. The study should identify women with postmenopausal osteoporosis and determine the occurrence of serious infection including skin infection, dermatologic adverse events, and over-suppression of bone turnover in each database in order to assess the background rates of those adverse events. The data obtained in this study will be used to inform the implementation of postmarketing requirement #2.	Fulfilled	
denosumab	Prolia	125320/0000	01-Jun-2010	US PMR 002 (2399-2)	To conduct a long-term observational study in administrative databases to prospectively evaluate the incidence of serious infection including skin infection, dermatologic adverse events, and over-suppression of bone turnover in postmenopausal women administered Prolia (denosumab).	Fulfilled	Fulfillment letter (reference ID: 5421794) was received on July 30th 2024

denosumab	Prolia	125320/0000	01-Jun-2010	US PMR 003 (2399-3)	To conduct a long-term surveillance study in postmenopausal women administered Prolia (denosumab) to prospectively evaluate the incidence of serious infection including skin infections, dermatologic adverse events, and over-suppression of bone turnover.	Fulfilled	
denosumab	Prolia	125320/0000	01-Jun-2010	US PMR 004 (2399-4)	To conduct an in vivo drug-drug interaction clinical trial with a CYP3A4 substrate (e.g., midazolam) in postmenopausal female patients with osteoporosis to characterize the potential risk of drug interactions of Prolia (denosumab) with CYP3A4 substrates.	Fulfilled	
denosumab	XGEVA	125320/0007	18-Nov-2010	US PMC 005	To submit a final report that includes updated results for overall survival for trials 20050103 entitled " A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa) in the Treatment of Bone Metastases in Men with Hormone-Refractory Prostate Cancer;" 200050136 entitled "A Randomized, Double-blind, Multicenter Study of Denosumab Compared With Zoledronic Acid (Zometa) in the Treatment of Bone Metastases in Subjects With Advanced Breast Cancer;" and 20050244 entitled "A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa) in the Treatment of Metastases in Subjects With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma." The final report should also include the primary and derived datasets and analysis programs used to generate the overall survival results reported.	Fulfilled	
denosumab	XGEVA	125320/0007	18-Nov-2010	US PMR 001	To conduct a phase 1, open-label, dose-finding pharmacokinetic, pharmacodynamic, and safety study in pediatric patients ages 0 to 18 years who are diagnosed with solid tumors metastatic to bone. The study will determine whether a safe dose can be administered to patients in subsequent phase 2 and phase 3 studies.	Released	
denosumab	XGEVA	125320/0007	18-Nov-2010	US PMR 002	To conduct a phase 2, open-label, single-arm study in pediatric patients ages 0 to 18 with solid tumors with bone metastases to determine the safety, including effects on growing bones, and activity of denosumab in the prevention of skeletal related events.	Released	
denosumab	XGEVA	125320/0007	18-Nov-2010	US PMR 003	To conduct a randomized and controlled pediatric study to evaluate the efficacy and safety of denosumab for the prevention of skeletal related events in pediatric patients ages 0 to 18 years with solid tumors and bone metastases.	Released	
denosumab	XGEVA	125320/0007	18-Nov-2010	US PMR 004	To conduct a clinical trial to determine the safety of Xgeva (denosumab) 120 mg administered every four weeks by subcutaneous injection in patients with severe renal insufficiency (creatinine clearance less than 30 mL/min) and in patients receiving dialysis. The number of patients enrolled in the trial and the frequency and duration of plasma sampling will be sufficient to estimate the incidence and severity of hypocalcemia, hypomagnesemia, and hypophoshatemia in this patient population. The final report should include the primary and derived datasets using the CDISC and ADaM data models and the analysis programs used to generate the safety and laboratory analyses.	Fulfilled	
denosumab	XGEVA	125320/0094	13-Jun-2013	US PMC 002	Submit the final report including primary datasets, derived datasets, and analysis programs used to generate the safety and efficacy results for the ongoing single arm multicenter trial of denosumab in patients with giant cell tumor of bone. Include an analysis of radiographic response as determined by the local investigator in evaluable patients who received at least one dose of denosumab and underwent at least one postbaseline Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) tumor assessment during the trial. The primary analysis should be conducted after patients enrolled through November 2012 have had the opportunity to complete 12 months of treatment.	Fulfilled	PMC fulfillment letter received 09 June 2020
denosumab	XGEVA	125320/0094	13-Jun-2013	US PMC 003	Provide a detailed and thoughtful analysis of the risk factors associated with malignant transformation of GCTB and development of new sarcoma and the lifetime and annual incidences of these events in denosumab naïve patients. For this analysis, use data from a minimum of two representative databases in addition to information from published literature. Include subset analyses based on specific risk factors identified from the comprehensive investigation.	Fulfilled	Submitted FA CSR on 18 Dec 2018 and it takes ~3 mths for FDA to issue fulfilment letter; plan to follow-up with FDA last week of Mar'2019 re: fulfilment letter
denosumab	XGEVA	125320/0094	13-Jun-2013	US PMR 001	Submit a final report of follow-up safety data of Xgeva (denosumab) in patients with giant cell tumor of bone enrolled in the ongoing single arm trial through November 2012 for a minimum of five years or until death or lost to follow-up, whichever comes first. Comprehensively collect information regarding survival status, disease progression, serious adverse events, and adverse events of special interest including osteonecrosis of the jaw, pregnancy-related complications, atypical fractures, malignant transformation of giant cell tumor of bone, and secondary malignancies. Perform descriptive analyses of these safety data, including a subset analysis comparing the long-term safety of denosumab in adolescent and adult patients.	Fulfilled	PMR fulfillment letter received 09 June 2020
denosumab	Prolia	125320/51	20-Sep-2012	US PMR 001 (2957-1)	Inclusion of a new target population, men with osteoporosis, in the required postmarketing study entitled, "The Denosumab Global Postmarketing Safety Observational Study" (Study 20090522), designated as PMR #2 in the June 1, 2010 approval letter for BLA 125320/0.	Fulfilled	Fulfillment letter (reference ID: 5421794) was received on July 30th 2024
denosumab	Prolia	125320/51	20-Sep-2012	US PMR 002 (2957-2)	Inclusion of a new target population, men with osteoporosis, in the required postmarketing study entitled, "The Prolia Postmarketing Active Safety Surveillance Program" (Study 20090601), designated as PMR #3 in the June 1, 2010 approval letter for BLA 125320/0.	Fulfilled	Final study report was submitted in June 2022.
denosumab	Prolia	125320/51	20-Sep-2012	US PMR 003 (2957-3)	To conduct a postmarketing required clinical trial to investigate the levels of denosumab in the semen of men treated with Prolia.	Fulfilled	
denosumab	XGEVA	125320/185	24-Jan-2018	US PMR 001 (3333-1)	Perform a retrospective analysis in Metastatic-Related and Non Metastatic-Related Fractures in clinical trials 20050136, 20050244 and 20050103, leading to Xgeva approval in patients with bone metastases from solid tumors, during the active treatment period, and characterize the non-metastatic fractures. Submit the final report with labeling.	Fulfilled	PMC fulfillment letter received 11 May 2021.
denosumab	Prolia	125320/186	18-May-2018	US PMR 3422-1	To conduct a Phase 3 Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Safety and Efficacy of Denosumab in Pediatric Subjects With Glucocorticoid-induced Osteoporosis (Study 20140444)	Fulfilled	The fulfillment letter was received on May 22, 2025.
denosumab	Prolia	125320/186	18-May-2018	US PMR 3396-1	To include a new target population, adults with glucocorticoid-induced osteoporosis (GIOP), in the required postmarketing study entitled, "The Denosumab Global Postmarketing Safety Observational Study" (Study 20090522), designated as PMR 2399-#2 (or PMR #2).	Fulfilled	Fulfillment letter (reference ID: 5421794) was received on July 30th 2024.

denosumab	Prolia	125320/186	18-May-2018	US PMR 3396-2	To include a new target population, adults with glucocorticoid-induced osteoporosis, in the required postmarketing study entitled, "The Prolia Postmarketing Active Safety Surveillance Program" (Study 20090601), designated as PMR 2399-#3 (or PMR #3).	Fulfilled	Final study report was submitted in June 2022.
epoetin alfa	Epogen	103234/5189	23-Jun-2009	US PMC 001	To conduct clinical trial EPO-ANE-3010 entitled "A Randomized, Open-Label, Multicenter, Phase 3 Study of Epoetin Alfa plus Standard Supportive Care in Anemic Patients With Metastatic Breast Cancer Receiving Standard Chemotherapy" to evaluate the impact of Epoetin alfa on overall survival, progression free survival, time to tumor progression and objective tumor response rate. (Trial Completion for the J&J PRD Trial EPO-ANE-3010 is defined as the time-point when approximately 1,650 subjects have died).	Fulfilled	
epoetin alfa	Epogen	103234/5256	21-Jun-2011	US PMR 2786-1	In patients with CKD on dialysis, conduct one or more trials to identify an optimal strategy of ESA dose and schedule. These trials should identify the optimal dosing strategy which will demonstrate the superiority of the ESA dosingstrategy to minimize hemoglobin (Hg) variability, excursions, rate of change of Hb, and explore providing symptom benefit.	Fulfilled	
epoetin alfa	Epogen	103234/5360	09-Mar-2017	US PMR 3198-1	To assess the utilization of Epogen/Procrit and Aranesp for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.	Fulfilled	FDA Fulfillment letter dated and received on 05 December 2024
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 01 (3392-1)	To conduct a Juvenile monkey toxicology study to evaluate effects of erenumab-aooe on growth, reproductive development, and neurological and neurobehavioral development.	Fulfilled	
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 02 (3392-2)	To conduct an open-label pharmacokinetic, safety, and tolerability study in pediatric migraine patients ages 6 through 11 years. Dosing will depend on body weight, according to two weight bands: <40 kg and ≥40 kg. The study should identify doses that provide exposures that match those observed with the 70-mg and 140-mg doses of Aimovig in adults.	Submitted	
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 03 (3392-3)	To conduct a pediatric randomized, double-blind, placebo-controlled efficacy and safety study under PREA for the preventive treatment of chronic migraine in adolescents ages 12 through 17 years. This study includes a double-blind treatment phase (of at least 12 weeks duration), with an open-label extension (of at least 40 weeks duration). Two weight bands should be utilized for dosing. In each weight band, two different dosing levels of Aimovig should be tested. Dosing should provide exposures matching those observed with the 70-mg dose and with the 140-mg dose of Aimovig in adults.	Ongoing	
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 04 (3392-4)	To conduct a pediatric randomized, double-blind, placebo-controlled efficacy and safety study under PREA for the preventive treatment of episodic migraine in children and adolescents ages 6 through 17 years. This study includes a doubleblind treatment phase (of at least 12 weeks duration), with an open-label extension (of at least 40 weeks duration). Two weight bands should be utilized for dosing. In each weight band, two different dosing levels of Aimovig should be tested. Dosing should provide exposures matching those observed with the 70-mg dose and with the 140-mg dose of Aimovig in adults.	Ongoing	
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 05 (3392-5)	Conduct prospective pregnancy exposure registry cohort analyses in the United States that compare the maternal, fetal, and infant outcomes of women with migraine exposed to Aimovig during pregnancy with two unexposed control populations: one consisting of women with migraine who have not been exposed to Aimovig before or during pregnancy and the other consisting of women without migraine. The registry will identify and record pregnancy complications, major and minor congenital malformations, spontaneous abortions, stillbirths, elective terminations, preterm births, small-for-gestational-age births, and any other adverse outcomes, including postnatal growth and development. Outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, will be assessed through at least the first year of life.	Delayed	Delayed due to postponement of the study start date as a result of negotiation of the protocol content. The protocol content was finalized after final protocol submission due dates.
erenumab-aooe	Aimovig	761077/0000	17-May-2018	US PMR 06 (3392-6)	Conduct a pregnancy outcomes study using a different study design than provided for in PMR 3392-5 (for example, a retrospective cohort study using claims or electronic medical record data or a case control study) to assess major congenital malformations, spontaneous abortions, stillbirths, and small-for-gestational-age births in women exposed to Aimovig during pregnancy compared to an unexposed control population.	Delayed	Delayed due to postponement of the study start date as a result of negotiation of the protocol content. The protocol content was finalized after final protocol submission due dates.
etanercept	Enbrel	103795/5099	09-Oct-2003	US PMC 001	Continue surveillance of lymphoma incidence in 7000 RA etanercept patients through ongoing EU registries, studies 16.0018, 16.023, and the RADIUS II observational study.	Fulfilled	
etanercept	Enbrel	103795/5149	30-Apr-2004	US PMC 003	To conduct a prospective, multicenter, surveillance study of 2500 adult patients with chronic plaque psoriasis who will be treated with commercial Etanercept but who have not previously enrolled in an Etanercept study. The surveillance study will be performed to assess the incidence of serious adverse events including all malignancies and serious infections.	Fulfilled	
etanercept	Enbrel	103795/5149	30-Apr-2004	US PMC 004	Conduct a prospective, observational registry study of women with rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis and plaque psoriasis exposed to Etanercept during pregnancy or within two weeks prior to conception. This study will assess the outcomes in the offspring born to those women who were exposed to Etanercept during pregnancy relative to background risk in similar patients not exposed to Etanercept.	Fulfilled	
etanercept	Enbrel	103795/5162	24-Sep-2004	US PMC 003	To obtain 10-year data on the development of cancer and autoimmune diseases for all patients who are enrolled in Protocols 16.0018 (long term follow-up study from prior RA or JRA studies) and 16.0023 (long term follow-up study for patients enrolled in Protocol 16.0012). Ten-year safety and efficacy data will be submitted in a license supplement.	Fulfilled	

etanercept	Enbrel	103795/5488	14-Feb-2017	US PMR 001	Enhanced pharmacovigilance program for reports of malignancy in pediatric, adolescent, and young adult (<30 years of age) patients treated with Enbrel (etanercept), 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.	Fulfilled	
etanercept	Enbrel	103795/5488	02-Nov-2011	US PMR 001	Enhanced pharmacovigilance program for reports of malignancy in pediatric, adolescent, and young adult (< 30 years of age) patients treated with Enbrel (etanercept), for a period of up to 10 years after this notification 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 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.	Released	
etelcalcetide	Parsabiv	208325	07-Feb-2017	US 3108 001	Conduct a pharmacokinetic/pharmacodynamics (PK/PD) modeling study evaluating Parsabiv (etelcalcetide) injection in adults with secondary hyperparathyroidism receiving hemodialysis to determine a safe starting dose in children.	Fulfilled	
etelcalcetide	Parsabiv	208325	07-Feb-2017	US 3108 002	Conduct a 26-week Phase 3, randomized, multiple-dose titration safety and PK study evaluating Parsabiv (etelcalcetide) injection with a comparator control arm in patients aged 2 to 17 years (inclusive) (Part 1), and subjects aged 1 month to 2 years (Part 2), both with secondary hyperparathyroidism receiving hemodialysis.	Delayed	FDA considered submission of Final Protocol late due to protocol negotiations
etelcalcetide	Parsabiv	208325	07-Feb-2017	US 3108 003	Conduct a comparative pharmacokinetic/pharmacodynamics (PK/PD) modeling study evaluating Parsabiv (etelcalcetide) injection in adult and pediatric subjects with secondary hyperparathyroidism receiving maintenance hemodialysis.	Pending	
etelcalcetide	Parsabiv	208325+C86	07-Feb-2017	US 3108 004	Conduct a hypothesis-testing observational study to provide data regarding the potential association between Parsabiv (etelcalcetide) and fatal and non-fatal gastrointestinal bleeding. The study should have a comparator group, be powered to detect the outcomes of interest, with justification for the proposed detectable differences in incidence rates. Special attention should be given to complete data availability in dialysis patients with secondary hyperparathyroidism above and below the age of 65 years, the ability to ascertain cause of death in a timely manner, and a statistical consideration of competing risks. Secondary analyses should aim to quantify the exposure-risk window, including periods after exposure discontinuation. The choice of study design, data source(s), and sample size should be supported by a feasibility analysis submitted to and reviewed by FDA prior to protocol finalization.	Fulfilled	FDA Fulfillment letter received on 29 January 2024
evolocumab	Repatha	125522/0000	27-Aug-2015	US PMR 2946-1	Conduct an efficacy and safety study evaluating Repatha (evolocumab) in patients with heterozygous familial hypercholesterolemia (HeFH) ages 10 years to less than 18 years. The study will be a randomized, 6-month, double-blind, placebocontrolled, parallel-group, multicenter efficacy and safety study (Part A) followed by an 18-month open-label extension in patients 10 years to less than 18 years with HeFH on stable lipid-modifying therapy with LDL-C ≥ 130 mg/dL (Part B).	Fulfilled	Fulfilled letter from the FDA on 22 August 2022
evolocumab	Repatha	125522/0000	27-Aug-2015	US PMR 2946-2	Conduct a prospective observational study of pregnant women exposed to Repatha (evolocumab) to evaluate fetal, infant, and childhood outcomes of pregnant women exposed to evolocumab and their live born offspring through the first 5 years of life to estimate incidence rates for the potential safety signals of adverse pregnancy outcomes, embryo-fetal growth and development, and adverse infant and childhood outcomes related to humoral immune suppression. The study should have validated/adjudicated outcomes, a comparator group, be powered to detect the outcomes of interest, and include the justification for the proposed detectable differences in incidence rates.	Released	FDA released Amgen from PMR 2946-2 on 03 Sep 2020 due to infeasibility and implemented PMR 2946-10.
evolocumab	Repatha	125522/0000	27-Aug-2015	US PMR 2946-3	Conduct a large, randomized, controlled, long-term trial in which the incidence and severity of new-onset diabetes mellitus, injection site reactions, hypersensitivity, immunogenicity, and adverse events potentially related to demyelination with Repatha (evolocumab) will be evaluated.	Fulfilled	
evolocumab	Repatha	125522/0000	27-Aug-2015	US PMR 2946-4	Conduct a randomized, controlled, long-term trial that prospectively evaluates changes in neurocognitive function with Repatha (evolocumab) treatment. The trial must be adequately powered to exclude a clinically meaningful adverse effect.	Fulfilled	
evolocumab	Repatha	125522/0020	11-Apr-2019	US PMC 3586-1	Provide a report tracking the incidence of needle clogging as well as an analysis on whether the labeling updates have reduced the complaints, adverse events, and medication errors associated with injection failures as a result of needle clogging based on the post market tracking. These U.S. reports should be submitted in 6- month intervals for 2 years.	Fulfilled	FDA agreed to Amgen's proposed update to delay the milestone dates by one year in order to enable the relevant labeling components to enter the market, and thus enable the PMR to be assessed.
evolocumab	Repatha	125522/0000	03-Sep-2020	US PMR 2946-10	Conduct a worldwide, single-arm, descriptive study that actively collects prospective and retrospective data in women exposed to Repatha (evolocumab) during pregnancy to assess risk of pregnancy and maternal complicaitons, adverse effects on the developing fetus and neonate, and adverse effects on the infant in all exposed pregnancies of which you become aware. Infant outcomes should be assessed through at least the first year of life. The single arm pregnancy study will collect information for a minimum of 10 years from the date of market approval for Repatha.	Ongoing	
filgrastim	Neupogen	103353/5183	30-Mar-2015	US PMR 2893-1	Conduct a phase 4 observational study to evaluate the efficacy and safety of Neupogen (filgrastim) in the setting of Hematopoietic syndrome (HS) following acute radiation exposure.	Pending	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 001	To submit a final study report for study 20050181, entitled, "A Randomized, Multicenter Phase 3 Study to Compare the Efficacy of Panitumumab in combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastatic Colorectal Cancer" which is intended to verify the clinical benefit of Panitumumab through demonstration of an effect on overall survival (OS).	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 002	To conduct a Phase 1 study, Protocol 20050252 entitled, "A Phase 1 Study to Evaluate the Safety and Pharmacokinetics of Panitumumab in Children with Refractory Solid Tumors" in children and adolescents (up to 18 yr of age) to provide the initial safety assessment and establish the pharmacokinetics in pediatric patients with solid tumors in which, based on clinical study and published literature information, an EGFr inhibitor drug has been shown to have clinical activity.	Fulfilled	

panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 003	Based on the results of the Phase I protocol 20050252 (i.e., provided that a safe and tolerable dose of Panitumumab can be determined for children), Amgen will conduct a Phase 2 study to further assess the safety and to estimate the anti-tumor activity of Panitumumab in pediatric patients with solid tumors in which, based on clinical study and published literature information, an EGFr inhibitor drug has been shown to have clinical activity.	Released	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 004	To submit a summary of the final results of overall survival (OS), with 12-month minimal follow up from Study 20020408, entitled, "An Open Label Randomized, Phase 3 Clinical Trial of ABX -EGF Plus Best Supportive Care Versus Best Supportive Care in Subjects With Metastatic Colorectal Cancer." The submission wil include only the survival data. The final clinical study report will include 4-month follow up of overall survivaL.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 005	To submit interim and final clinical study reports based on data obtained in study 20050181, entitled, " A Randomized Multicenter Phase 3 Study to compare the Efficacy of Panitumumab in Combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastic Colorectal Cancer," that addressess clinical utility of EGFr testing with the Dako PharmDx EGFr kit as a means for selecting patients who will benefit when treated with Panitumumab. The report will include both summary analyses of safety and efficacy as a function of EGFr test results and primary datasets.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 006	To submit interim and final clinical study reports based on data obtained in Study 20050181, entitled, "A Randomized, Multicenter Phase 3 Study to Compare the Efficacy of Panitumumab in Combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastatic Colorectal Cancer", characterizing the toxicity profile of the commercially marketed product. The report will include comparative analyses of safety between study arms, case report forms for all patients with deaths during treatment or who discontinued treatment or underwent dose modification of panitumumab for adverse events, narrative summaries for all serious adverse events, and summary data characterizing panitumumab and chemotherapy drug exposure (e.g., dose intensity over fixed time periods). In addition, primary data will be provided in SAS-compatible electronic datasets.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 007	To submit interim and final clinical study reports based on data obtained in study 20050181, entitled, "A Randomized, Multicenter Phase 3 Study to Compare the Efficacy of Panitumumab in Combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastatic Colorectal Cancer" characterizing the immunogenicity profile of the commercial product, and impact of anti-Panitumumab binding and neutralizing antibodies on the pharmacokinetic, safety and efficacy profile of Panitumumab. The report will include both summary analyses and the primary datasets used to generate the summary analyses, in electronic, SAS-compatible format. This protocol was accepted for Special Protocol Assessment on May 3, 2006. Patient accrual began on June 30, 2006, the study will be completed (PFS data cut off) by February 28, 2008. An interim study report will be provided by August 30, 2008, and a final study report will be submitted by March 30, 2010.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 008	To submit a final study report for study 20050184, entitled "A Phase 2, Open-label, Randomized Clinical Trial of Skin Toxicity Treatment of Subjects Receiving Second-line FOLFIRI or Irinotecan Only Chemotherapy Concomitantly with Panitumumab" containing an evaluation of the clinical management of Panitumumab-induced skin toxicities. The report will include both summary analyses of safety as a function of medical management and primary datasets from this study and from any reference studies used for comparative safety analyses, which will include information on medical interventions and toxicity onset, severity and clinical course. The final protocol was submitted on March 28, 2006. Patient accrual began on April 19, 2006, and the study will be completed by May 15, 2008. A final study report will be submitted by November 30, 2008.	Released	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 009	To conduct a Phase 1 drug interaction study 20062010, entitled "Open Label, 2-Cohort, Randomized Study to Assess the Potential Pharmacokinetic Drug-Drug Interaction between Irinotecan and Panitumumab in Subjects with Colorectal Cancer" wih will provide a formal assessment of pharmacokinetic (PK) drug-drug interactions. The final study report will provide summary analyses of pharmacokinetic and safety information and primary data used to generate the analyses in an electronic, SAS-compatible dataset. The final protocol will be submitted by August 31, 2007. Patient accrual will begin by December 31, 2007, and the study will be completed (last PK sample for last enrolled patient) by April 1, 2009. The final study report will be submitted by August 30, 2009.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 010	To submit a final study report for study 20040192 entitled, "A Phase 1 Clinical Study of ABX-EGF (Panitumumab) Evaluation of the Safety and PK of ABX-EGF in Japanese Subjects with Advanced Solid Tumors" that characterizes the pharmacokinetic profile of Panitumumab in the Japanese population. The final study report should provide summary analyses and primary data, including pharmacokinetic data, in both the Japanese and non- Asian population that will permit an assessment of differences in pharmacokinetics, if any, based on race/ethnicity. The study will be completed (database lock) by June 30, 2006, and the final study report will be submitted by April 1, 2007.	Fulfilled	
panitumumab	Vectibix	125147/0000	27-Sep-2006	US PMC 011	To submit an assessment and the following information regarding the role of EGFr in post-natal lung, gastrointestinal, neurologic, bone, or pancreatic development in humans. a. Copies of all published literature reports of nonclinical or clinical data addressing the role of EGFr in post-natal human respiratory and gastrointestinal tract, neurologic, skeletal, and endocrine development. b. Identification (by Study Number) of any previously submitted final study reports, and submission of any additional data (including primary data) from non-clinical studies of Panitumumab conducted by, or under a contractual arrangement for, Amgen in young (pre-pubertal) non-human primates. These data, including all findings in respiratory and gastrointestinal tract, and neurologic, bone, and endocrine organs from any Panitumumab-treated juvenile animals from the . aforementioned studies, will be summarized and discussed in context of toxicities observed in adult human respiratory and gastrointestinal tract, neurologic, skeletal, and endocrine organ systems. The assessment, including all literature references, will be submitted by November 30, 2006.	Fulfilled	
pegfilgrastim	Neulasta	125031/0180	13-Nov-2015	US PMR 2997-1	Conduct a phase 4 observational study evaluating the efficacy and safety of Neulasta (pegfilgrastim) in the setting of Hematopoietic Syndrome (HS) following acute radiation exposure.	Pending	
pegfilgrastim	Neulasta	125031/197	10-Oct-2019	US PMR 3731-1	Submit pediatric assessments for Neulasta (pegfilgrastim) as described in section 505B(a)(2)(A) of the FD&C Act, including development of an "appropriate formulation" (presentation) that can be used to directly and accurately administer Neulasta (pegfilgrastim) to pediatric patients who weigh less than 45 kg and require doses that are less than 0.6 mL (6 mg), and conducting any necessary human factors studies to evaluate the ability of healthcare providers and/or caregivers to measure the appropriate doses.	Ongoing	Original Final Report Due Date: October 2022. Deferral Extension granted by the FDA on 9/28/2022; Final Report Due Date extended to 4/2025.

romiplostim	Nplate	125268/0	22-Aug-2008	US PMR 001 (PMR 2396-1)	Conduct an "Antibody Registry Study" that will enroll subjects who have received romiplostim and whose blood samples contain antibodies to either romiplostim or thrombopoietin. The antibody assays wil be performed by Amgen in response to spontaneously submitted requests for the post-marketing blood tests. As described in the romiplostim prescribing information, a lack or loss of response to romiplostim should prompt the healthcare provider to search for causative factors, including neutralizing antibodies toromiplostim. In these situations, healthcare providers are to submit blood samples to Amgen for detection of antinodies to romiplostim and thrombopoietin. The Antibody Registry Study wil collect follow-up platelet count and other clinical data sufficient to assess the long term consequences of the detected antibodies. Patients wil be followed until the detected antibodies resolve or stabilze in titer over a several month period of time.	Fulfilled	
romiplostim	Nplate	125268/0	22-Aug-2008	US PMR 002	To develop and maintain a prospective, observational pregnancy exposure registry study conducted in the United States that compares the pregnancy and fetal outcomes of women exposed to romiplostim during pregnancy to an unexposed control population. The registry will detect and record major and minor congenital anomalies, spontaneous abortions, stillbirths, elective terminations, adverse effects on immune system development, platelet number and function, neoplasm formation, bone marrow reticulin formation, thrombotic events, and any serious adverse pregnancy outcomes. These events will be assessed among the enrolled women throughout the pregnancy. The events will also be assessed among infants through at least the first year of life. Annual interim reports wil be submitted until FDA has acknowledged that sufficient data have been collected.	Released	
romiplostim	Nplate	125268/0	22-Aug-2008	US PMR 003	To conduct trial 20080009, "A Prospective Phase IV, Open-Label, Multi-Center, Study Evaluating the Changes in Bone Marrow Morphology in Subjects Receiving Romiplostim for the Treatment of Thrombocytopenia associated with Immune (Idiopathic) Thrombocytopenia Purpura (ITP)." In this trial, at least 150 patients will receive romiplostim and undergo bone marrow evaluations prior to, during and following the completion of romiplostim administration. A similar evaluation schedule will apply to the detection of antibody formation to romiplostim and thrombopoietin as well as the electrocardiographic (ECG) detection of cardiac conduction abnormalities. A first interim report will contain, in addition to any other items, ECG and the results of bone marrow evaluations for patients who have completed 12 months of trial participation. This information will be updated for patients who have completed 24 months of trial participation and submitted in a second interim report.	Released	
romiplostim	Nplate	125268/0	22-Aug-2008	US PMR 005	To conduct a milk only lactation study in the subset of women enrolled in the pregnancy registry who choose to breastfeed their infants. This study will be designed to detect the presence and concentration of romiplostim in breast milk and, when feasible, in the blood of the infants. The study will include a symptom diary for mothers to record any adverse effects in the breastfeeding infants. Annual interim reports wil be submitted until FDA has acknowledged that sufficient data has been collected.	Released	
romiplostim	Nplate	125268/0142	24-Jan-2014	US PMR 142-1	To develop and maintain a Pregnancy Surveillance Program that collects pregnancy and fetal outcomes of women exposed to romiplostim during pregnancy. Reports from the program will include an analysis of reports on major and minor congenital anomalies, spontaneous abortions, stillbirths, elective terminations, adverse effects on immune system development, platelet number and function, neoplasm formation, bone marrow reticulin formation, thrombotic events, and any serious adverse pregnancy outcomes.Amgen has created Addenda Questionnaires for mother and for infant to enable a request for this data as part of the Case Management process.	Fulfilled	
romiplostim	Nplate	125268	28-Jan-2021	PMC 4008-1	A phase 4 observational study to evaluate the efficacy and safety of Nplate (romiplostim) in the setting of Hematopoietic syndrome of Acute Radiation Syndrome (HS-ARS) following acute exposure to myelosuppressive doses of radiation.	Submitted	
romosozumab	Evenity	761062	09-Apr-2019	PMR 3595-1	To evaluate the feasibility of a required post-marketing study or trial assessing the cardiovascular safety of Evenity, conduct a study using a sequential analysis design (e.g., repeated analyses within five 1-year blocks of calendar time following marketing approval of Evenity) to assess utilization patterns and channeling bias. Using an appropriate lookback period for each characteristic, compare relevant patient characteristics measured at baseline, including patient demographics, history of stroke or myocardial infarction (MI) in the 1 year prior to initiation of therapy, history of fractures or falls, fracture risk scores, pertinent comorbidities (e.g., other history of MI, stroke, other cardiovascular diseases), pertinent medication use (e.g., other osteoporosis medications, glucocorticoids), healthcare utilization, and prescribing provider specialty among new users of Evenity compared to new users of other anti-osteoporosis therapies.	Submitted	The Final Report for this PMR was submitted on 26 February 2025.
Sotorasib	Lumakras	214665	28-May-2021	PMR 4071-1	Conduct a multicenter, randomized clinical trial and submit the final progression-free survival (PFS) results that verify and describe the clinical benefit of sotorasib in patients with locally advanced or metastatic non-small cell lung cancer with a history of prior systemic therapy for advanced disease and whose tumors harbor Kirsten rat sarcoma (KRAS) G12C mutation.	Fulfilled	
Sotorasib	Lumakras	214665	28-May-2021	PMR 4071-2	Conduct a multicenter, randomized clinical trial to further characterize serious adverse events, including gastro-intestinal toxicity and compare the safety and efficacy of sotorasib 960 mg daily versus a lower daily dose in patients with locally advanced or metastatic, KRAS G12C mutated, nonsmall cell lung cancer who have received at least one prior systemic therapy.	Fulfilled	
Sotorasib	Lumakras	214665	28-May-2021	PMR 4071-3	Conduct a hepatic impairment clinical trial to determine a safe and appropriate dose of sotorasib in patients with moderate and severe hepatic impairment. Design and conduct the trial in accordance with the FDA Guidance for Industry titled "Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling".	Fulfilled	
Sotorasib	Lumakras	214665	28-May-2021	PMR 4071-4	Conduct a clinical drug interaction study to assess the effect of concomitant sotorasib administration on the systemic exposure of BCRP transporter substrates. Refer to FDA Guidance for Industry for additional details: "Clinical Drug Interaction Studies - Cytochrome P450 Enzyme and Transporter- Mediated Drug Interactions."	Fulfilled	
Sotorasib	Lumakras	214665	28-May-2021	PMC 4071-5	Submit a final report containing data from clinical trials enrolling a sufficient representation of African American patients that is reflective of the US population of patients with KRAS G12C mutated non-small cell lung cancer to further characterize the safety and efficacy of sotorasib in African American patients with KRAS G12C mutated non-small cell lung cancer.	Fulfilled	

Sotorasib	Lumakras	214665	22-Dec-2023	PMR 4071-6	Complete a multicenter,randomized clinical trial intended to verify and describe the clinical benefit of sotorasib in patients with locally advanced or metastatic non-small cell lung cancer and whose tumors harbor Kirsten rat sarcoma (KRAS) G12C mutation. The primary endpoint(s) will be progression free survival as assessed by a Blinded Independent Review Committee and/or overall survival.	Ongoing	
talimogene laherparepvec	Imlygic	125518/0000	27-Oct-2015	US PMR 001	To conduct a prospective observational cohort study of 920 IMLYGIC-treated patients to characterize the risk of herpetic infection among patients, close contacts, and healthcare providers; each subject will be followed for 5 years after initiating IMLYGIC (study Protocol #20130193).	Released	Released as follow up to the Good Cause Request submitted on May 31, 2024 to request extension to the milestone dates.
talimogene laherparepvec	Imlygic	125518/0000	27-Oct-2015	US PMR 002	To complete the ongoing single-arm trial to evaluate the biodistribution and shedding of IMLYGIC in 60 IMLYGIC-treated subjects (study Protcol #20120324).	Fulfilled	10 Oct 2019 FDA PMR Fulfilled letter received
avacopan	Tavneos	214487	07-Oct-2021	4155-1 (combined as one study with PMR 4155-3)	Conduct a randomized controlled clinical trial of at least five years duration in patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis to evaluate safety outcomes, including hepatotoxicity and drug-induced liver injury, and serious hypersensitivity reactions, including angioedema and anaphylaxis.	Ongoing	
avacopan	Tavneos	214487	07-Oct-2021	PMR 4155-2	Conduct a clinical drug interaction trial to evaluate the effect of repeated doses of avacopan 30 mg twice daily with food at steady state on the pharmacokinetics of a sensitive substrate of CYP3A4 (e.g., simvastatin) to inform appropriate dosing strategies for coadministration of avacopan with CYP3A4 substrates.	Fulfilled	Fulfilled letter received from the FDA on 04 Jun 2024
avacopan	Tavneos	214487	07-Oct-2021	4155-3 (combined as one study with PMR 4155-1)	Conduct a randomized controlled clinical trial of at least five years duration in patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis to evaluate efficacy outcomes with long-term avacopan treatment.	Ongoing	
Teprotumumab	Tepezza	761142	21-Jan-2020	PMR 3780-8	A descriptive clinical trial to evaluate the safety, efficacy and need for retreatment of three different teprotumumab treatment durations for the treatment of Thyroid Eye Disease.	Ongoing	
Tarlatamab	Imdelltra	761344	16-May-2024	PMC 4635-3	Conduct an integrated analysis from ongoing, completed, or planned clinical trials and other potential data sources as appropriate enrolling a sufficient representation of United States (U.S.) racial and ethnic minority patients that is reflective of the U.S. population of patients with SCLC, to further characterize the efficacy, safety and pharmacokinetics of Tarlatamab in these patients. In the analysis, include a sufficient number of patients enrolled in the U.S. and a sufficient number of racial and ethnic minority patients reflective of the incidence of SCLC in each subpopulation to allow for interpretation of the results. The analyses should support comparative efficacy and safety outcome analyses between the aforementioned populations and White patients.	Ongoing	
Tarlatamab	Imdelltra	761344	16-May-2024	PMR 4635-2	Conduct an integrated safety analysis of data from patients with extensive stage small cell lung cancer to further characterize the long-term incidence, severity, and outcome of the known serious risks of cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, and neurologic toxicity. Include a comprehensive analysis from all available data sources including but not limited to patient-level and pooled analyses of ongoing and completed clinical trials. These data could also be obtained from the confirmatory trial titled "A Randomized, Open-label, Phase 3 Study of Tarlatamab Compared with Standard of Care in Subjects with Relapsed Small Cell Lung Cancer After Platinum-based First-line Chemotherapy (DeLLphi-304).	Ongoing	
Tarlatamab	Imdelltra	761344	16-May-2024	PMR 4635-1	Conduct a multicenter randomized clinical trial intended to verify and describe the clinical benefit of Tarlatamab in patients with extensive stage small cell lung cancer (ES-SCLC) who have had disease progression on or after platinum-based chemotherapy.	Ongoing	

Description	Commitment Type	Agency Number	Commitment Activity	Related PMR info	Product Family	Due Date	Status
In vitro study to assess the amount of Ravicti (glycerol phenylbutyrate) delivered through nasogastric and gastric tubes for dosing volumes less than 1 ml.	Other	3214-1	PMR	PMR 3214-1	glycerol phenylbutyrate		Fullfilled
Analysis of clinical data to evaluate associations between elevations in plasma PAA concentration and PAA/PAGN ratio with the development of serious neurological adverse reactions, and the risk of hyperammonemia in patients.	Safety	3527-1	PMR	PMR 3527-1	glycerol phenylbutyrate	9/30/2020	Fullfilled
A randomized, controlled clinical trial to assess the safety and efficacy of Ravicti (glycerol phenylbutyrate) in patients with Urea Cycle Disorders who are treatment naïve to phenylbutyrate.	Other	2013-4	PMR	PMR 2013-4	glycerol phenylbutyrate	12/31/2023	Submitted
A clinical trial to assess the safety, efficacy, and pharmacokinetics of RAVICTI (glycerol phenylbutyrate) and its metabolites (PBA, PAA and PAGN) during RAVICTI (glycerol phenylbutyrate) treatment in pediatric patients with Urea Cycle Disorders who are under 2 months of age.	Other	2013-1	PMR	PMR 2013-1	glycerol phenylbutyrate		Fullfilled
A descriptive clinical trial to evaluate the safety, efficacy and need for retreatment of three different teprotumumab treatment durations for the treatment of Thyroid Eye Disease.	Safety	BLA 761143	PMR	PMR 3780-8	teprotumumab	11/30/2026	Ongoing
Completion of the ongoing study, HZNP-TEP-302 (OPTIC-X).	Safety	BLA 761143	PMR	PMR 3780-9	teprotumumab	1/31/2021	Fullfilled
A worldwide single-arm pregnancy safety study to collect and analyze information for a minimum of 10 years on pregnancy complications and birth outcomes in women exposed to UPLIZNA (inebilizumab-cdon) during pregnancy in patients with neuromyelitis optica spectrum disorder (NMOSD). Provide a complete protocol which includes details regarding how you plan to encourage patients and providers to report pregnancy exposures (e.g., telephone contact number and/or website in prescribing information), measures to ensure complete data capture regarding pregnancy outcomes and any adverse effects in offspring, and plans for comprehensive data analysis and yearly reporting.	Safety	BLA 761142	PMR	PMR 3869-1	Inebilizumab	8/31/2033	Ongoing
A safety trial to monitor serum immunoglobulin G and M levels in patients with neuromyelitis optica spectrum disorder (NMOSD) during treatment with UPLIZNA (inebilizumab-cdon) to establish the nadir in circulating immunoglobulins during chronic treatment, and to monitor patients after discontinuation of treatment with UPLIZNA (inebilizumab-cdon) in order to ascertain the time needed to ensure restoration of pre-treatment baseline circulating serum levels of immunoglobulins G and M. This trial also should be designed to capture rates of infections, especially opportunistic and recurrent infections associated with immune suppression, and there should be monitoring of B-cell counts throughout treatment and after discontinuation until repletion of immunoglobulin levels.	Safety	BLA 761142	PMR	PMR 3869-2	Inebilizumab	8/31/2028	Ongoing
An observational safety study enrolling 500 patients treated with Krystexxa (pegloticase) for one year duration. Patients enrolled should have hyperuricemia and gout and be refractory to standard uric acid-lowering therapies (e.g., allopurinol). The study should include the following objectives: a. An evaluation of the frequency and severity of infusion reactions, anaphylaxis, and immune complex-related adverse events. b. Identification of serious adverse events associated with Krystexxa (pegloticase) therapy.	Safety	BLA 125293	PMR		pegloticase		Fullfilled