U.S. Postmarketing Commitments Table*

Name of Product	NDA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
IMBRUVICA®	NDA 205552 and NDA210563	Complete and submit the final results of the ongoing randomized, double-blind, placebo-controlled Phase 3 clinical trial (PCI-32765MCL3002) of ibrutinib in combination with bendamustine and rituximab in patients with newly diagnosed mantle cell lymphoma. Enrollment of approximately 520 patients is expected. The primary endpoint is progression-free survival as assessed by investigators. Overall survival is a key secondary endpoint.	13 November 2013	Final Report Submission: 03/2019 Updated Target Date: 09/2020	Ongoing
IMBRUVICA®	NDA 205552	Conduct an assessment and an analysis of data from clinical trials and all post-marketing sources in order to characterize the risk of serious bleeding in patients treated with Imbruvica®, (ibrutinib) Capsules. The risks of special interest are major hemorrhagic events and their potential association with concomitant use of anti-platelet and/or anticoagulant drugs (Final Report)	13 November 2013	Final Report Submission: 11/2018	Submitted
IMBRUVICA®	NDA 205552	Conduct a study to characterize the safety of long-term exposure to Imbruvica based on data and pooled analyses from trials of patients with mantle cell lymphoma and chronic lymphocytic leukemia. Submit 3-year, 4-year, and 5-year safety follow-up data and reports for a minimum population of 1000 patients treated with approved ibrutinib dosing regimens. Datasets should include patient level data on ibrutinib dosing, treatment-emergent adverse events, and treatment emergent laboratory information. This patient set may include approximately 350 patients who continue receiving long-term ibrutinib therapy after completion of primary analysis of the parent study, where study procedures are then limited to collect a minimum of Grade 3+ adverse events, available treatment emergent laboratory data, adverse events leading to treatment discontinuation and SAEs. Study reports should include analyses of adverse event categories listed in the current Warnings and Precautions section of the prescribing information, adverse events leading to treatment discontinuation, and serious adverse events.	04 March 2016	Final Data and Report Submission: 04/2019	Submitted
IMBRUVICA®	NDA 205552 and NDA210563	Submit the complete final report and data from a randomized, Phase 3 trial, comparing ibrutinib in combination with bendamustine and rituximab or rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone versus bendamustine and rituximab or rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone in subjects with previously treated follicular lymphoma or marginal zone lymphoma. At least 50 enrolled subjects need to have a diagnosis of marginal zone lymphoma. The primary endpoint is progression-free survival in the overall intent-to-treat population.	18 January 2017	Final Report Submission: 08/2019 Updated Target Date: 04/2021	Ongoing

Name of Product	NDA Number	Description of Commitment	Date Commitment Given	FDA Projected Completion Date	Commitment Status
IMBRUVICA®	NDA 205552	Conduct an analysis of safety in patients with chronic graft-versus-host-disease treated with ibrutinib. Submit the complete primary study report and datasets from Study PCYC-1140-IM: A Randomized, Double-Blind Phase 3 Study of Ibrutinib in Combination with Corticosteroids versus Placebo in Combination with Corticosteroids in Subjects with New Onset Chronic Graft-Versus-Host Disease (cGVHD). Include safety analyses that evaluate impact of concomitant medications (for example, corticosteroids and additional immunosuppressants) on the safety profile for ibrutinib	02 August 2017	Final Report Submission: 12/2022	Ongoing

*Chemistry Manufacturing and Controls (CMC) commitments are not included