Increased pricing pressure and other restrictions in the U.S. and abroad from MCOs, institutional purchasers and government agencies and programs, among others, continue to negatively affect our revenues and profit margins.
Our products continue to be subject to increasing pressures across the portfolio from market access, pharmaceutical pricing controls and discounting and other restrictions in the U.S., the EU and other regions around the world that result in lower prices, lower reimbursement rates and smaller populations for whom payers will reimburse, which negatively impact our revenues and profit margins, including from (i) the impact of the increased pricing pressure from Medicare Part D formularies, Medicare Part B reimbursement rates (including the potential implementation of the pilot program by the Centers for Medicare & Medicaid Services ("CMS") that would, among other things, set payment amounts to physicians on Part B drugs based on international drug prices and would include fifty percent of Medicare Part B single source drugs), expanded utilization under the 340B Drug Pricing Program ("340B"), as well as commercial formularies in general; (ii) rules and practices of MCOs and institutional and governmental purchasers taking actions to control costs or shift the cost burden to manufacturers, including actions that could result in the exclusion of a product from, or the unfavorable placement of, a product on a MCO formulary; (iii) government administrative and policy changes and changes in laws and regulations for federal healthcare programs such as Medicare and Medicaid, other government actions and inquiries at the federal level (including the proposals contained in the "American Patient First Blueprint") that seek to amend pharmaceutical pricing and reimbursement practices such as using international pricing indexes, modifying the federal Anti-Kickback statute discount safe harbor, accelerating generic drug approval processes, promoting the use of biosimilar drugs and the option of applying step therapy, listing prices of products in DTC television advertisements and granting additional authority to governmental agencies to manage drug utilization and negotiate drug prices and laws at the state level (including laws that have recently been enacted in California, Vermont, Nevada and New York that are focused on drug pricing transparency and/or limiting state spending on drugs), including the proposed rule by the U.S. federal government to allow states or certain other non-federal government entities to submit proposals to the FDA allowing for the importation of certain prescription drugs from Canada; (iv) the potential impact of changes to U.S. federal pharmaceutical coverage and reimbursement policies and practices, including changes resulting from our implementation of the guidance in the 2016 final rule issued by the CMS on the calculation of average manufacturer price and best price (which also will require inclusion of sales in U.S. Territories in the calculation of average manufacturer price and best price beginning on April 1, 2022), as well as the scrutiny of drug manufacturers, including Celgene, by the House Oversight and Reform Committee in January 2019 seeking documents and detailed information about drug-pricing practices; (v) reimbursement delays; (vi) government price erosion mechanisms across Europe and in other countries resulting in deflation for pharmaceutical product pricing; (vii) the increased purchasing power of entities that negotiate on behalf of Medicare, Medicaid and private sector beneficiaries; (viii) collection delays or failures to pay in government-funded public hospitals outside the U.S.; (ix) the impact on pricing from parallel trade and drug importation across borders; (x) other developments in technology and/or industry practices that could impact the reimbursement policies and practices of third-party payers; and (xi) inhibited market access due to real or perceived differences in value propositions for our products compared to competing products. We expect that these market access constraints, pharmaceutical pricing controls and discounting and other restrictions will become more acute and will continue to negatively affect our future revenues and profit margins.

Additionally, in early 2016, Health Resources and Services Administration ("HRSA") finalized a regulation regarding the 340B pricing methodology and providing guidelines for when civil monetary penalties may be issued for "knowing and intentional" manufacturer overcharges of 340B covered entities. The effective date of this regulation was January 1, 2019. Following the effective date, manufacturers who are found to have knowingly and intentionally overcharged 340B covered entities could be subject to significant monetary penalties. Such findings could also result in negative publicity that could harm the manufacturer's reputation or cause business disruption. Over the course of the past few years, Celgene had received inquiries from HRSA regarding the limited distribution networks for Revlimid, Pomalyst, and Thalomid and compliance with the 340B program. We believe that we have complied with applicable legal requirements. If we are ultimately required to change our sales or pricing practices with regard to the distribution of these drugs under the 340B program, or if we were required to pay penalties under the applicable regulations, there would be an adverse effect on our revenues and profitability.

We may experience difficulties or delays in the development and commercialization of new products.
Compounds or products may appear promising in development but fail to reach market within the expected or optimal timeframe, or at all. In addition, product extensions or additional indications may not be approved. Furthermore, products or indications approved under the U.S. FDA's Accelerated Approval Program may be contingent upon verification and description of clinical benefit in confirmatory studies and such studies may not be successful. For example, in July 2019, we announced that Part 2 of the Phase III CheckMate-227 trial did not meet its primary endpoint of overall survival with Opdivo plus chemotherapy versus chemotherapy therapy in patients with first-line non-squamous NSCLC.

Developing and commercializing new compounds and products involve inherent risks and uncertainties, including (i) efficacy and safety concerns, delayed or denied regulatory approvals, delays or challenges with producing products on a commercial scale or excessive costs to manufacture products; (ii) inability to enroll patients and timely completion of the clinical trials; (iii) failure to enter into or implement optimal alliances for the development and/or commercialization of new products; (iv) failure to maintain a consistent scope and variety of promising late-stage products; (v) failure of one or more of our products to achieve or maintain commercial viability; and (vi) changes in regulatory approval processes may cause delays or denials of new product approvals.