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| ***Item 1A.*** | ***Risk Factors*** |

In addition to the other information contained in this Form 10-K, the following risk factors should be considered carefully in evaluating our company. It is possible that our business, financial condition, liquidity, or results of operations could be materially adversely affected by any of these risks. Certain of these risks could also adversely affect the company's reputation.

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| • | **Pharmaceutical research and development is very costly and highly uncertain; we may not succeed in developing or acquiring commercially successful products sufficient in number or value to replace revenues of products that have lost or will soon lose intellectual property protection or are displaced by competing products or therapies.** |

There are many difficulties and uncertainties inherent in human pharmaceutical research and development and the introduction of new products. There is a high rate of failure inherent in new drug discovery and development. To bring a drug from the discovery phase to market can take over a decade and often costs in excess of $2 billion. Failure can occur at any point in the process, including in later stages after substantial investment. As a result, most funds invested in research programs will not generate financial returns. New product candidates that appear promising in development may fail to reach the market or may have only limited commercial success because of efficacy or safety concerns, inability to obtain or maintain necessary regulatory approvals or payer reimbursement or coverage, limited scope of approved uses, changes in the relevant treatment standards or the availability of new or better competitive products, difficulty or excessive costs to manufacture, or infringement of the patents or intellectual property rights of others. Regulatory agencies continue to establish increasingly high hurdles for the efficacy and safety of new products. Delays and uncertainties in drug approval processes can result in delays in product launches and lost market opportunity. In addition, it can be very difficult to predict revenue growth rates of new products.

We cannot state with certainty when or whether our products now under development will be approved or launched; whether, if initially granted, such approval will be maintained; whether we will be able to develop, license, or otherwise acquire additional product candidates or products; or whether our products, once launched, will be commercially successful. We must maintain a continuous flow of successful new products and successful new indications or brand extensions for existing products sufficient both to cover our substantial research and development costs and to replace revenues that are lost as profitable products lose intellectual property exclusivity or are displaced by competing products or therapies. Failure to do so in the short-term or long-term would have a material adverse effect on our business, results of operations, cash flows, financial position, and prospects. See Item 7, “Management’s Discussion and Analysis - Results of Operations - Executive Overview - Late-Stage Pipeline,” for more details.

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| • | **We depend on products with intellectual property protection for most of our revenues, cash flows, and earnings; we have lost or will lose effective intellectual property protection for many of those products in the next several years, which has resulted and is likely to continue to result in rapid and severe declines in revenues.** |

A number of our top-selling human pharmaceutical products have recently lost, or will lose in the next several years, significant patent protection and/or data protection in the U.S. as well as key countries outside the U.S., as illustrated in the tables below:

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| **Product** | **U.S. Revenues**  **(2018)**  **($ in millions)** | | | **Percent of Worldwide Revenues**  **(2018)** | **Patent / Data Protection - U.S.** |
| Alimta | 1,131.0 | |  | 5% | Vitamin regimen patent plus pediatric exclusivity will expire in 2022 |
| Cialis | 1,129.2 | |  | 5% | Compound patent plus pediatric exclusivity expired in May 2018 and unit dose patent expired in September 2018 |
| Forteo | 757.9 | |  | 3% | Formulation and related process patents expired in December 2018 and use patents will expire in August 2019 |
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| **Product** | **Revenues Outside U.S.**  **(2018)**  **($ in millions)** | | | **Percent of Worldwide Revenues**  **(2018)** | **Patent / Data Protection - Major Europe / Japan** |
| Alimta | $ | 1,001.9 |  | 4% | Major European countries: vitamin regimen patent will expire in 2021  Japan: use patents to treat cancer concomitantly with vitamins will expire in 2021 |
| Forteo | 817.7 | |  | 3% | Japan: data package protection expired in July 2018; formulation and use patents will expire in August 2019 |
| Cymbalta | 653.7 | |  | 3% | Japan: data package protection will expire in January 2020 |

Certain other significant products no longer have effective exclusivity through patent protection or data protection. For non-biologic products, loss of exclusivity (whether by expiration or as a consequence of litigation) typically results in the entry of one or more generic competitors, leading to a rapid and severe decline in revenues, especially in the U.S. Historically, outside the U.S. the market penetration of generics following loss of exclusivity has not been as rapid or pervasive as in the U.S.; however, generic market penetration is increasing in many markets outside the U.S., including Japan, Europe, and many countries in the emerging markets. For biologics (such as Humalog, Humulin, Erbitux, Cyramza, Trulicity, Taltz, and Emgality), loss of exclusivity may or may not result in the near-term entry of competitor versions (i.e., biosimilars) due to development timelines, manufacturing challenges, and/or uncertainties in the regulatory pathways for approval of the competitor versions.

There is no assurance that the patents we are seeking will be granted or that the patents we hold will be found valid and enforceable if challenged. Moreover, patents relating to particular products, uses, formulations, or processes do not preclude other manufacturers from employing alternative processes or marketing alternative products or formulations that compete with our patented products. In addition, competitors or other third parties may assert claims that our activities infringe patents or other intellectual property rights held by them, or allege a third-party right of ownership in our existing intellectual property. See Item 7, “Management’s Discussion and Analysis - Results of Operations - Executive Overview - Other Matters - Patent Matters,” and Item 1, "Business - Patents, Trademarks, and Other Intellectual Property Rights," for more details.

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| **•** | **Our long-term success depends on intellectual property protection; if our intellectual property rights are invalidated, circumvented, or weakened, our business will be adversely affected.** |

Our long-term success depends on our ability to continually discover or acquire, develop, and commercialize innovative new pharmaceutical products. Without strong intellectual property protection, we would be unable to generate the returns necessary to support the enormous investments in research and development and capital as well as other expenditures required to bring new drugs to the market.

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Intellectual property protection varies throughout the world and is subject to change over time. In the U.S., in addition to the process for challenging patents which applies to our biologic products, the Hatch-Waxman Act provides generic companies powerful incentives to seek to invalidate our other human pharmaceutical patents. As a result, we expect that our U.S. patents on major pharmaceutical products will continue to be routinely challenged in litigation and administrative proceedings, and may not be upheld. In addition, a separateIPR process allows competitors to request review of issued patents by the USPTO without the protections of the Hatch-Waxman Act. Our patents may be invalidated via this review process. Although such a decision can be appealed to the courts, in certain circumstances a loss in such a proceeding could result in a competitor entering the market, while a win provides no precedential value - the same patent can still be challenged by other competitors. We face many generic manufacturer challenges to our patents outside the U.S. as well. The entry of generic competitors typically results in rapid and severe declines in revenues. In addition, competitors or other third parties may claim that our activities infringe patents or other intellectual property rights held by them. If successful, such claims could result in our being unable to market a product in a particular territory or being required to pay significant damages for past infringement or royalties on future sales. See Item 1, “Business - Patents, Trademarks, and Other Intellectual Property Rights,” Item 3, "Legal Proceedings," and Item 8, "Financial Statements and Supplementary Data - Note 15, Contingencies," for more details.

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| • | **Our human pharmaceutical business is subject to increasing government price controls and other public and private restrictions on pricing, reimbursement, and access for our drugs, which could have a material adverse effect on our reputation or business.** |

Public and private payers are taking increasingly aggressive steps to control their expenditures for human pharmaceuticals by placing restrictions on pricing and reimbursement for, and patient access to, our medications. These pressures could continue to negatively affect our future revenues and net income.

We expect pricing, reimbursement, and access pressures from both governments and private payers inside and outside the U.S. to become more severe. For more details, see Item 1, “Business - Regulations and Private Payer Actions Affecting Human Pharmaceutical Pricing, Reimbursement, and Access,” and Item 7, “Management’s Discussion and Analysis - Results of Operations - Executive Overview - Other Matters - Trends Affecting Pharmaceutical Pricing, Reimbursement, and Access.”

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| • | **We face intense competition from multinational pharmaceutical companies, biotechnology companies, and lower-cost generic and biosimilar manufacturers, and such competition could have a material adverse effect on our business.** |

We compete with a large number of multinational pharmaceutical companies, biotechnology companies, and generic pharmaceutical companies. To compete successfully, we must continue to deliver to the market innovative, cost-effective products that meet important medical needs. Our product revenues can be adversely affected by the introduction by competitors of branded products that are perceived as superior by the marketplace, by generic or biosimilar versions of our branded products, and by generic or biosimilar versions of other products in the same therapeutic class as our branded products. Our revenues can also be adversely affected by treatment innovations that eliminate or minimize the need for treatment with our drugs. See Item 1, “Business - Competition” and "Business - Research and Development," for more details.

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| • | **Changes in foreign currency rates or devaluation of a foreign currency can materially affect our revenue, cost of sales, and operating expenses.** |

As a global company with substantial operations outside the U.S., we face foreign currency risk exposure from fluctuating currency exchange rates. While we seek to manage a portion of these exposures through hedging and other risk management techniques, significant fluctuations in currency rates can have a material impact, either positive or negative, on our revenue, cost of sales, and operating expenses. In the event of an extreme devaluation of local currency, the price of our products could become unsustainable in the relevant market. See Item 7, “Management’s Discussion and Analysis - Financial Condition” for more details.

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| **•** | **Unanticipated changes in our tax rates or exposure to additional tax liabilities could increase our income taxes and decrease our net income.** |

We are subject to income taxes in the U.S. and numerous foreign jurisdictions. Changes in the relevant tax laws, regulations, administrative practices, principles, and interpretations could adversely affect our future effective tax rates. The U.S. enacted tax reform legislation significantly revising the U.S. tax law, effective January 2018, and a number of other countries are actively considering or enacting tax changes. Modifications to key elements of the U.S. or international tax framework could have a material adverse effect on our consolidated operating results and cash flows. See Item 7, “Management’s Discussion and Analysis - Results of Operations - Executive Overview - Other Matters” and Item 8, "Financial Statements and Supplementary Data - Note 13, Income Taxes," for more details.

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| • | **Failure, inadequacy, or breach of our information technology systems, infrastructure, and business information or violations of data protection laws could result in material harm to our business and reputation.** |

A great deal of confidential information owned by both us and our business partners is stored in our information systems, networks, and facilities or those of third parties. This includes valuable trade secrets and intellectual property, clinical trial information, corporate strategic plans, marketing plans, customer information, and personally identifiable information, such as employee and patient information (collectively, “confidential information”). We also rely to a large extent on the efficient and uninterrupted operation of complex information technology systems, infrastructure, and hardware (together “IT systems”), some of which are within the company’s control and some of which are within the control of third parties, to accumulate, process, store, and transmit large amounts of confidential information and other data. Maintaining the confidentiality, integrity and availability of our IT systems and confidential information is vital to our business.

IT systems are vulnerable to system inadequacies, operating failures, service interruptions or failures, security breaches, malicious intrusions, or cyber-attacks from a variety of sources. Cyber-attacks are growing in their frequency, sophistication, and intensity, and are becoming increasingly difficult to detect, mitigate, or prevent. Cyber-attacks come in many forms, including the deployment of harmful malware, exploitation of vulnerabilities, denial-of-service attacks, the use of social engineering, and other means to compromise the confidentiality, integrity and availability of our IT systems, confidential information, and other data. Breaches resulting in the compromise, loss, theft, destruction, or unauthorized disclosure or use of confidential information, or the unauthorized access to, disruption of, or interference with our products and services, can occur in a variety of ways, including but not limited to, negligent or wrongful conduct by employees or others with permitted access to our systems and information, or wrongful conduct by hackers, competitors, certain governments, or other current or former company personnel. Our third party partners face similar risks.

The failure or inadequacy of our IT systems, the compromise, loss, theft, destruction, or unauthorized disclosure or use of confidential information, or the unauthorized access to, disruption of, or interference with our products and services that rely on IT systems, could impair our ability to secure and maintain intellectual property rights; result in a product manufacturing interruption or failure, or in the interruption or failure of products or services that rely on IT systems; damage our operations, customer relationships, or reputation; or cause us to lose trade secrets or other competitive advantages. Unauthorized disclosure of personally identifiable information could expose us to significant sanctions for violations of data privacy laws and regulations around the world and could damage public trust in our company.

To date, system inadequacies, operating failures, unauthorized access, service interruptions or failures, security breaches, malicious intrusions, cyber-attacks, and the compromise, loss, theft, destruction, or unauthorized disclosure or use of confidential information have not had a material impact on our consolidated results of operations. We have implemented measures to protect, detect, respond to, and minimize or prevent these risks; however, these measures may not be successful. If they are not successful, any of these events could result in material financial, legal, business, or reputational harm to our business .

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| **•** | **Significant economic downturns or international trade disruptions or disputes could adversely affect our business and operating results.** |

While human pharmaceuticals and companion animal health products have not generally been sensitive to overall economic cycles, prolonged economic slowdowns could lead to decreased utilization of our products, affecting our sales volume. Our food animal business may be affected by depressed prices for our customers’ end products. Declining tax revenues attributable to economic downturns increase the pressure on governments to reduce human health care spending, leading to increasing government efforts to control drug prices and utilization. Additionally, some customers, including governments or other entities reliant upon government funding, may be unable to pay in a timely manner for our products. Also, if our customers, suppliers, or collaboration partners experience financial difficulties, we could experience slower customer collections, greater bad debt expense, and performance defaults by suppliers or collaboration partners. Similarly, in the event of a significant economic downturn, we could have difficulty accessing credit markets.

Significant portions of our business are conducted in Europe, including the U.K.; Asia; and other international geographies. Interruptions in international relationships such as the current negotiations between U.K. and the EU on the U.K.’s exit from the EU (“Brexit”), and trade disputes such as the current trade negotiations between the U.S. and China, could result in changes to regulations governing our products and our intellectual property, or otherwise affect our ability to do business. While we do not expect either circumstance to materially affect our business in a direct manner, these and similar events could adversely affect us, or our business partners or customers.

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| • | **Pharmaceutical products can develop unexpected safety or efficacy concerns, which could have a material adverse effect on revenues and income.** |

Human pharmaceutical products receive regulatory approval based on data obtained in controlled clinical trials of limited duration. After approval, the products are used for longer periods of time by much larger numbers of patients; we and others (including regulatory agencies and private payers) collect extensive information on the efficacy and safety of our marketed products by continuously monitoring the use of our products in the marketplace. In addition, we or others may conduct post-marketing clinical studies on efficacy and safety of our marketed products. New safety or efficacy data from both market surveillance and post-marketing clinical studies may result in product label changes or other measures that could reduce the product's market acceptance and result in declining sales. Serious safety or efficacy issues that arise after product approval could result in voluntary or mandatory product recalls or withdrawals from the market. Safety issues could also result in costly product liability claims.

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| **•** | **We face many product liability claims and are self-insured; we could face large numbers of claims in the future, which could adversely affect our business.** |

We are subject to a substantial number of product liability claims involving Actos*®*, Axiron®, Byetta*®*, Cialis, and Cymbalta among other products. See Item 8, “Financial Statements and Supplementary Data - Note 15, Contingencies,” and Item 3, “Legal Proceedings,” for more information on our current product liability litigation. Because of the nature of pharmaceutical products, we are and could in the future become subject to large numbers of product liability claims for these or other products in the future, which require substantial expenditures to resolve and, if involving marketed products, could adversely affect sales of the product. Due to a very restrictive market for product liability insurance, we are self-insured for product liability losses for all our currently marketed products.

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| **•** | **Regulatory compliance problems could be damaging to the company.** |

The marketing, promotional, and pricing practices of human pharmaceutical manufacturers, as well as the manner in which manufacturers interact with purchasers, prescribers, and patients, are subject to extensive regulation. Many companies, including us, have been subject to claims related to these practices asserted by federal, state, and foreign governmental authorities, private payers, and consumers. These claims have resulted in substantial expense and other significant consequences to us. We are and could in the future become subject to such investigations, the outcomes of which could include criminal charges and fines, penalties, or other monetary or non-monetary remedies, including exclusion from U.S. federal and other health care programs. In addition, regulatory issues concerning compliance with cGMP regulations (and comparable foreign regulations) for pharmaceutical products can lead to product recalls and seizures, fines and penalties, interruption of production leading to product shortages, and delays in the approvals of new products pending resolution of the issues. See Item 1, “Business - Government Regulation of Our Operations,” for more details.

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| **•** | **Manufacturing difficulties or disruptions could lead to product supply problems.** |

Pharmaceutical and animal health manufacturing is complex and highly regulated. Manufacturing difficulties at our facilities or contracted facilities, or the failure or refusal of a contract manufacturer to supply contracted quantities, could result in product shortages, leading to lost revenue. Such difficulties or disruptions could result from quality or regulatory compliance problems; natural disasters; mechanical or information technology system vulnerabilities, such as system inadequacies, operating failures, service interruptions or failures, security breaches, malicious intrusions, or cyber-attacks from a variety of sources; or inability to obtain sole-source raw or intermediate materials. In addition, given the difficulties in predicting sales of new products and the very long lead times necessary for the expansion and regulatory qualification of pharmaceutical manufacturing capacity, it is possible that we could have difficulty meeting unanticipated demand for new products. See Item 1, “Business - Raw Materials and Product Supply,” for more details.

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| **•** | **Reliance on third-party relationships and outsourcing arrangements could adversely affect our business.** |

We rely on third parties, including suppliers, distributors, alliances with other pharmaceutical and biotechnology companies, and third-party service providers, for selected aspects of product development, manufacture, commercialization, support for information technology systems, product distribution, and certain financial transactional processes. For example, we outsource the day-to-day management and oversight of our clinical trials to contract research organizations. Outsourcing these functions involves the risk that the third parties may not perform to our standards or legal requirements; may not produce reliable results; may not perform in a timely manner; may not maintain the confidentiality, integrity, and availability of our proprietary information; or may fail to perform at all. Failure of these third parties to meet their contractual, regulatory, confidentiality, or other obligations to us could have a material adverse effect on our business.

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| • | **Our animal health segment faces risks related to increased generic competition, food and animal safety concerns, factors affecting global agricultural markets, and other risks.** |

The animal health segment may be impacted by, among other things, emerging restrictions and bans on the use of antibacterials in food-producing animals; perceived adverse effects on human health linked to the consumption of food derived from animals that utilize our products; increased regulation or decreased governmental support relating to the raising, processing, or consumption of food-producing animals; an outbreak of infectious disease carried by animals; adverse weather conditions and the availability of natural resources; adverse global economic conditions affecting agricultural markets; and failure of our research and development, acquisition, and licensing efforts to generate new products. The failure to manage these risks could have a material adverse effect on our revenues and income.

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| • | **We may not realize the anticipated value or tax treatment for the divestiture of our interest in Elanco.** |

There are uncertainties and risks related to the timing and potential value to Elanco, Lilly, and our and their shareholders of the planned separation of the Elanco animal health business, including business, industry, and market risks, as well as risks involving realizing the anticipated tax-free nature of the separation. Failure to implement the separation effectively could result in a lower value to Lilly and to shareholders.