Sanofi
Form 20-F
March 08, 2019
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**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

# FORM 20-F

**(Mark One)**

**REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

**or**

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2018**

**Or**

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**Or**

**SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report

**For the transition period from to**

**Commission File Number: 001-31368**

**Sanofi**

(Exact name of registrant as specified in its charter)

**N/A**

(Translation of registrant s name into English)

**France**

(Jurisdiction of incorporation or organization)

**54, Rue La Boétie, 75008 Paris, France**

(Address of principal executive offices)

**Karen Linehan, Executive Vice President Legal Affairs and General Counsel**

**54, Rue La Boétie, 75008 Paris, France. Fax: 011 + 33 1 53 77 43 03. Tel: 011 + 33 1 53 77 40 00**

(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

**Securities registered or to be registered pursuant to Section 12(b) of the Act:**

| **Title of each class:** | **Name of each exchange on which registered:** |
|---|---|
| American Depositary Shares, each representing one half of one ordinary share, par value 2 per share | NASDAQ Global Select Market |
| Ordinary shares, par value 2 per share | NASDAQ Global Select Market* |
| Contingent Value Rights | NASDAQ Global Market |

**Securities registered pursuant to Section 12(g) of the Act: None**

**The number of outstanding shares of each of the issuer s classes of capital or common stock as of December 31, 2018 was:**

Ordinary shares: 1,245,454,385

**Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.** YES NO .

**If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. YES NO .**

**Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.** Yes No

**Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).** Yes No

**Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or an emerging growth company. See definition of large accelerated filer, accelerated filer or emerging growth company Rule 12b-2 of the Exchange Act.**

Large accelerated filer Accelerated filer Non-accelerated filer Emerging growth company

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**The term new or revised financial accounting standard refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.**

**Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:**

U.S. GAAP | International Financial Reporting Standards as issued by the International Accounting Standards Board | Other

**If Other has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.** Item 17 Item 18

**If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).** Yes No .

***Not for trading but only in connection with the registration of American Depositary Shares representing such ordinary shares.**

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**Presentation of financial and other information**

The consolidated financial statements contained in this annual report on Form 20-F have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB) and with IFRS as adopted by the European Union, as of December 31, 2018.

Unless the context requires otherwise, the terms Sanofi, the Company, the Group, we, our or us refer to Sano consolidated subsidiaries.

All references herein to United States or US are to the United States of America, references to dollars or $ are to currency of the United States, references to France are to the Republic of France, and references to euro and are to t currency of the European Union member states (including France) participating in the European Monetary Union.

Brand names appearing in this annual report are trademarks of Sanofi and/or its affiliates, with the exception of:

- trademarks used or that may be or have been used under license by Sanofi and/or its affiliates, such as Actonel®, a trademark of Actavis; Aldurazyme®, a trademark of the Joint Venture Biomarin/Genzyme LLC; Cialis® OTC, a trademark of Eli Lilly; Leukine®, a trademark of Alcafleu; UshStat®, a trademark of Oxford Biomedica; Vaxelis®, a trademark of MCM Vaccine Co (USA) and MCM Vaccine B.V. (Netherlands); and Zaltrap®, a trademark of Regeneron in the United States;

- trademarks sold by Sanofi and/or its affiliates to a third party, such as Altace®, a trademark of King Pharmaceuticals in the United States; Hyalgan®, a trademark of Fidia Farmaceutici S.p.A.; Insulia®, a trademark of Voluntis; LibertyLink® Rice 601, LibertyLink® Rice 604 and StarLink®, trademarks of Bayer; and

- other third party trademarks such as Aabasaglar®, Basaglar® and Humalog®, trademarks of Eli Lilly; Eylia®, a trademark of Regeneron; GLAAS®, a trademark of Immune Design ; Kyprolis®, a trademark of Onyx Pharmaceuticals Inc.; Revlimid® trademark of Celgene Corporation; Semglee, a trademark of Mylan Pharmaceuticals Inc.; Velcade®, a trademark of Millenium Pharmaceuticals Inc ; Xyzal® Allergy 24, a trademark of GSK in some countries and UCB Farchim in other countries; and Zantac®, a trademark of Glaxo Group Limited.

Not all trademarks related to investigational agents have been authorized as of the date of this annual report by the relevant health authorities; for instance, the Lyxumia® trade name has not been approved by the FDA.

The data relating to market shares and ranking information for pharmaceutical products, in particular as presented in Item 4. Information on the Company B. Business Overview B.6. Markets B.6.1. Marketing and distribution, are based mainly on sales data excluding vaccines and in constant euros (unless otherwise indicated) on a September 2018 MAT (Moving

Annual Total) basis. The data are mainly from IQVIA local sales audit, supplemented by country-specific sources.

Data relating to market shares and ranking information presented herein for our Consumer Healthcare products are based on sales data from Nicholas Hall.

Data relating to market shares and ranking information presented herein for our vaccines business are based on internal estimates unless stated otherwise.

Product indications described in this annual report are composite summaries of the major indications approved in the product s principal markets. Not all indications are necessarily available in each of the markets in which the products are approved. The summaries presented herein for the purpose of financial reporting do not substitute for careful consideration of the full labeling approved in each market.

**Cautionary statement regarding forward-looking statements**

This Annual Report contains certain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. We may also make written or oral forward-looking statements in our periodic reports to the Securities and Exchange Commission on Form 6-K, in our annual report to shareholders, in our offering circulars and prospectuses, in press releases and other written materials and in oral statements made by our officers, directors or employees to third parties. Examples of such forward-looking statements include:

- projections of operating revenues, net income, business net income, earnings per share, business earnings per share, capital expenditures, cost savings, restructuring costs, positive or negative synergies, dividends, capital structure or other financial items or ratios;
- statements of our profit forecasts, trends, plans, objectives or goals, including those relating to products, clinical trials, regulatory approvals and competition; and
- statements about our future events and economic performance or that of France, the United States or any other countries in which we operate.

This information is based on data, assumptions and estimates considered as reasonable by Sanofi as at the date of this annual report and undue reliance should not be placed on such statements.

Words such as believe, anticipate, plan, expect, intend, target, estimate, project, predict, forecas and similar expressions are intended to identify forward-looking statements but are not the exclusive means of identifying such statements.

Forward-looking statements involve inherent, known and unknown, risks and uncertainties associated with the regulatory, economic, financial and competitive environment, and other factors that could cause future results and objectives to differ materially from those expressed or implied in the forward-looking statements.

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Risk factors which could affect future results and cause actual results to differ materially from those contained in any forward-looking statements are discussed under Item 3. Key Information D. Risk Factors . Additional risks, not currently known or considered immaterial by the Group, may have the

same unfavorable effect and investors may lose all or part of their investment.

Forward-looking statements speak only as of the date they are made. Other than required by law, we do not undertake any obligation to update them in light of new information or future developments.

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## Abbreviations

**Principal abbreviations used in the Annual Report on Form 20-F**

| | |
|---|---|
| **ADR** | American Depositary Receipt |
| **ADS** | American Depositary Share |
| **AFEP** | *Association française des entreprises privées* (French Association of Large Companies) |
| **AMF** | *Autorité des marchés financiers* (the French market regulator) |
| **ANDA** | Abbreviated New Drug Application |
| **BLA** | Biologic License Application |
| **BMS** | Bristol-Myers Squibb |
| **CEO** | Chief Executive Officer |
| **CER** | Constant exchange rates |
| **CGU** | Cash generating unit |
| **CHC** | Consumer Healthcare |
| **CHMP** | Committee for Medicinal Products for Human Use |
| **CVR** | Contingent value right |
| **ECB** | European Central Bank |
| **EFPIA** | European Federation of Pharmaceutical Industries and Associations |
| **EMA** | European Medicines Agency |
| **EU** | European Union |
| **FDA** | US Food and Drug Administration |
| **GAVI** | Global Alliance for Vaccines and Immunisation |
| **GBU** | Global Business Unit |
| **GCP** | Good clinical practices |
| **GDP** | Good distribution practices |
| **GLP** | Good laboratory practices |
| **GLP-1** | Glucagon-like peptide-1 |
| **GMP** | Good manufacturing practices |
| **Hib** | Haemophilus influenzae type b |
| **HSE** | Health, Safety and Environment |
| **IASB** | International Accounting Standards Board |
| **ICH** | International Council for Harmonization |
| **IFPMA** | International Federation of Pharmaceutical Manufacturers & Associations |
| **IFRS** | International Financial Reporting Standards |
| **IPV** | Inactivated polio vaccine |
| **ISIN** | International Securities Identification Number |
| **J-MHLW** | Japanese Ministry of Health, Labor and Welfare |
| **LSD** | Lysosomal storage disorder |
| **MEDEF** | *Mouvement des entreprises de France* (French business confederation) |
| **MS** | Multiple sclerosis |
| **NASDAQ** | National Association of Securities Dealers Automated Quotations |
| **NDA** | New Drug Application |
| **NHI** | National Health Insurance (Japan) |

| | |
|---|---|
| **NYSE** | New York Stock Exchange |
| **OECD** | Organisation for Economic Co-operation and Development |
| **OPV** | Oral polio vaccine |
| **OTC** | Over the counter |
| **PhRMA** | Pharmaceutical Research and Manufacturers of America |
| **PMDA** | Pharmaceuticals and Medical Devices Agency (Japan) |
| **PRV** | Priority Review Voucher |
| **PTE** | Patent Term Extension |
| **QIV** | Quadrivalent influenza vaccine |
| **R&D** | Research and development |
| **ROA** | Return on assets |
| **SA** | *Société anonyme* (French public limited corporation) |
| **SEC** | US Securities and Exchange Commission |
| **SPC** | Supplementary Protection Certificate |
| **TSR** | Total shareholder return |
| **UNICEF** | United Nations Children s Emergency Fund |
| **US** | United States of America |
| **WHO** | World Health Organization |

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ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Part I

Item 1. **Identity of Directors, Senior Management and Advisers**

N/A

Item 2. **Offer Statistics and Expected Timetable**

N/A

Item 3. **Key Information**

**A. Selected financial data**

**Summary of selected financial data**

The tables below set forth selected consolidated financial data for Sanofi. These financial data are derived from the Sanofi consolidated financial statements. The Sanofi consolidated financial statements for the years ended December 31, 2018, 2017 and 2016 are included in Item 18 of this annual report.

The consolidated financial statements of Sanofi for the years ended December 31, 2018, 2017 and 2016 have been prepared in compliance with IFRS as issued by the International Accounting Standards Board (IASB) and with IFRS as adopted by the European Union as of December 31, 2018. The term IFRS refers collectively to international accounting and financial reporting standards (IAS and IFRS) and to interpretations of the interpretations committees (SIC and IFRIC) mandatorily applicable as of December 31, 2018.

Sanofi reports its financial results in euros.

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## ITEM 3. KEY INFORMATION

**Selected condensed financial information**

| | As of and for the year ended December 31, | | | | |
|---|---|---|---|---|---|
| *( million, except per share data)* | **2018** | **2017[a]** | **2016[a]** | **2015** | **2014** |
| **IFRS Income statement data[b]** | | | | | |
| Net sales[c] | 34,463 | 35,072 | 33,809 | 34,060 | 31,380 |
| Gross profit | 24,242 | 24,608 | 23,995 | 23,942 | 21,769 |
| Operating income | 4,676 | 5,804 | 6,531 | 5,624 | 6,064 |
| Net income excluding the exchanged/held-for-exchange Animal Health business | 4,423 | 3,894 | 4,486 | 4,512 | 4,392 |
| Net income attributable to equity holders of Sanofi | 4,306 | 8,416 | 4,709 | 4,287 | 4,390 |
| **Basic earnings per share ( [d]):** | | | | | |
| Net income excluding the exchanged/held-for-exchange Animal Health business | 3.46 | 3.00 | 3.42 | 3.38 | 3.25 |
| Net income attributable to equity holders of Sanofi | 3.45 | 6.70 | 3.66 | 3.28 | 3.34 |
| **Diluted earnings per share ( [d]):** | | | | | |
| Net income attributable to equity holders of Sanofi | 3.43 | 6.64 | 3.63 | 3.25 | 3.30 |
| **IFRS Balance sheet data** | | | | | |
| Goodwill and other intangible assets | 66,124 | 53,344[f] | 51,166[f] | 51,583[f] | 53,740 |
| Total assets | 111,408 | 99,813 | 104,679 | 102,321 | 97,392 |
| Outstanding share capital | 2,491 | 2,508 | 2,544 | 2,603 | 2,620 |
| Equity attributable to equity holders of Sanofi | 58,876 | 58,070 | 57,552 | 58,049 | 56,120 |
| Long term debt | 22,007 | 14,326[f] | 16,815[f] | 13,118[f] | 13,276 |
| Cash dividend paid per share ( [g] | 3.07[h] | 3.03 | 2.96 | 2.93 | 2.85 |
| Cash dividend paid per share ($)[g] / [i] | 3.52[h] | 3.63 | 3.12 | 3.19 | 3.46 |

*(a) Includes the effects of the first-time application of IFRS 15 on revenue recognition, effective January 1,2018.*

*(b) The results of the Animal Health business, and the gain on the divestment of that business, are presented separately in accordance with IFRS 5 (Non-Current Assets Held for Sale and Discontinued Operations), see Notes D.2. and D.36. to our consolidated financial statements.*

*(c) Following a change in accounting presentation in 2016, VaxServe sales of non-Sanofi products are included in* ***Other revenues****. The presentation of prior period* ***Net sales*** *and* ***Other revenues*** *has been amended accordingly (see note B.13. to our consolidated financial statements).*

*(d) Based on the weighted average number of shares outstanding in each period used to compute basic earnings per share, equal to 1,247.1 million shares in 2018, 1,256.9 million shares in 2017, 1,286.6 million shares in 2016, 1,306.2 million shares in 2015, and 1,315.8 million shares in 2014.*

*(e) Based on the weighted average in each period of the number of shares outstanding plus stock options and restricted shares with a potentially dilutive effect:1,255.2 million shares in 2018, 1,266.8 million shares in 2017, 1,296.0 million shares in 2016, 1,320.7 million shares in 2015, and 1,331.1 million shares in 2014.*

*(f) As reported, excluding the Animal Health business presented in the line items,* ***Assets held for sale or exchange*** *and* ***Liabilities related to assets held for sale or exchange*** *as of December 31, 2015, December 31, 2016 and December 31, 2017.*

*(g) Each American Depositary Share, or ADS, represents one half of one share.*

*(h) Dividends for 2018 will be proposed for approval at the annual general meeting scheduled for April 30, 2019.*

*(i) Based on the relevant year-end exchange rate.*

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ITEM 3. KEY INFORMATION

**Selected exchange rate information**

The following table sets forth, for the periods and dates indicated, certain information concerning the exchange rates for the euro from 2014 through March 2019 expressed in US dollars per euro. The information concerning the US dollar exchange rate is based on the noon buying rate in New York City for cable transfers in foreign currencies as certified for customs purposes by the

Federal Reserve Bank of New York (the Noon Buying Rate ). We provide the exchange rates below solely for your convenience. We do not represent that euros were, could have been, or could be, converted into US dollars at these rates or at any other rate. For information regarding the effect of currency fluctuations on our results of operations, see Item 5. Operating and Financial Review and Prospects and Item 11. Quantitative and Qualitative Disclosures about Market Risk.

| *(U.S. dollar per euro)* | Period-end Rate | Average Rate[(a)] | High | Low |
|---|---|---|---|---|
| 2014 | 1.21 | 1.32 | 1.39 | 1.21 |
| 2015 | 1.09 | 1.10 | 1.20 | 1.05 |
| 2016 | 1.06 | 1.10 | 1.15 | 1.04 |
| 2017 | 1.20 | 1.14 | 1.20 | 1.04 |
| 2018 | 1.15 | 1.18 | 1.25 | 1.13 |
| Last 6 months | | | | |
| 2018 | | | | |
| September | 1.16 | 1.17 | 1.18 | 1.16 |
| October | 1.13 | 1.15 | 1.16 | 1.13 |
| November | 1.13 | 1.14 | 1.15 | 1.13 |
| December | 1.15 | 1.14 | 1.15 | 1.13 |
| 2019 | | | | |
| January | 1.15 | 1.14 | 1.15 | 1.13 |
| February | 1.13 | 1.14 | 1.15 | 1.13 |
| March[(b)] | 1.13 | 1.13 | 1.14 | 1.13 |

*(a)*

*The average of the Noon Buying Rates on the last business day of each month during the relevant period for the full year average, and on each business day of the month for the monthly average. The latest available Noon Buying Rate being March 1, 2019, we have used European Central Bank Rates for the period from March 4, 2019 through March 7, 2019.*

*(b) In each case, measured through March 7, 2019.*

On March 7, 2019 the European Central Bank Rate was 1.13 per euro.

**B. Capitalization and indebtedness**

N/A

**C. Reasons for offer and use of proceeds**

N/A

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ITEM 3. KEY INFORMATION

**D. Risk factors**

Important factors that could cause actual financial, business, research or operating results to differ materially from expectations are disclosed in this annual report, including without limitation the following risk factors. Investors should carefully consider all the information set forth in the following risk factors before deciding to invest in any of the Company s securities. In addition to the risks listed below, we may be subject to other material risks that as of the date of this report are not currently known to us or that we deem immaterial at this time.

**Risks relating to legal and regulatory matters**

**We rely on our patents and other proprietary rights to provide exclusive rights to market certain of our products, and if such patents and other rights were limited, invalidated or circumvented, our financial results could be materially and adversely affected.**

Through patent and other proprietary rights such as data exclusivity or supplementary protection certificates in Europe, we hold exclusivity rights for a number of our research-based products. However, the protection that we are able to obtain varies in its duration and scope from product to product and country by country. This protection may not be sufficient to maintain effective product exclusivity because of local differences in the patents, in national laws, applicable legal systems or developments in law or jurisprudence, which may give rise to inconsistent judgments when we assert or defend our patents.

Moreover, patent and other proprietary rights do not always provide effective protection for our products. Manufacturers of generic products or biosimilars are increasingly seeking to challenge patent validity or coverage before the patents expire, and manufacturers of biosimilars or interchangeable versions of the products are seeking to have their version of the product approved before the exclusivity period ends. Furthermore, in an infringement suit against a third-party, we may not prevail and the decision rendered may not conclude that our patent or other proprietary rights are valid, enforceable or infringed. Our competitors may also successfully avoid patents, for example through design innovation, and we may not hold sufficient evidence of infringement to bring suit.

We are involved in litigation worldwide to enforce certain of our patent rights against generics, proposed generics and biosimilars of our small molecule and biological pharmaceutical products (see Item 8. Financial Information A. Consolidated Financial Statements and Other Financial Information Information on Legal or Arbitration Proceedings for additional information). Even in cases where we ultimately prevail in an infringement claim, legal remedies available for harm caused to us by infringing products may be inadequate to make us whole. A competitor may launch a generic or a biosimilar product at risk before the initiation or completion of the court proceedings, and the court may decline to grant us a preliminary injunction to halt

further at risk sales and order removal of the infringing product from the market. Additionally, while we would be entitled to obtain damages in such a case, the amount that we may ultimately be awarded and able to collect may be insufficient to compensate all harm caused to us. A successful result against a competing product for a given patent or

in a specific country is not necessarily predictive of our future success against another competing product or in another country because of local variations in the patents and patent laws.

In addition, if we lose patent protection as a result of an adverse court decision or a settlement, we face the risk that government and private third-party payers and purchasers of pharmaceutical products may claim damages alleging they have over-reimbursed or overpaid for a drug. For example, in Australia, our patent on clopidogrel was ultimately held invalid. Following this decision, the Australian Government is seeking damages for its alleged over-reimbursement of clopidogrel drugs due to the preliminary injunction we had secured against the sale of generic clopidogrel during the course of the litigation.

In certain cases to terminate or avoid patent litigation, we or our collaborators may be required to obtain licenses from the holders of third-party intellectual property rights that already cover aspects of our existing and future products in order to manufacture, use and/or sell them. Any payments under these licenses may reduce our profits from such products and we may not be able to obtain these licenses on favorable terms or at all.

Third parties may also request a preliminary or a permanent injunction in a country from a court of law to prevent us from marketing a product if they consider that we infringe their patent rights in that country. For example, Sanofi is currently party to patent infringement proceedings in several countries initiated against us and Regeneron by Amgen relating to Praluent® in which Amgen has requested injunctive relief (see Note D.22.b) to the consolidated financial statements included at Item 18 of this annual report for more information). If third parties obtain a preliminary or permanent injunction or if we fail to obtain a required license for a country where a valid third-party intellectual property rights as confirmed by a court of law exist, or if we are unable to alter the design of our technology to fall outside the scope of third-party intellectual property rights, we may be unable to market some of our products in certain countries, which may limit our profitability.

Also, some countries may consider granting a compulsory license to a third-party to use patents protecting an innovator s product, which limits the value of the patent protection granted to such products.

We have increased the proportion of biological therapeutics in our pipeline relative to traditional small molecule pharmaceutical products. Typically, the development, manufacture, sale and distribution of biological therapeutics is complicated by third-party intellectual property rights (otherwise known as freedom to operate (FTO) issues), to a greater extent than for the development, manufacture, sale and distribution of small molecule therapeutics, because of the types of patents allowed

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by national patent offices. Further, our ability to successfully challenge third-party patent rights is dependent on the laws of national courts. Certain countries have laws that provide stronger bases for challenging third-party patent rights compared to the laws that are available to challenge patents in other countries. Therefore, we may be able to invalidate a certain third-party patent in one country but not invalidate counterpart patents in other countries. In addition, we expect to face increasing competition from biosimilars in the future. With the accelerated regulatory pathways provided in the US and Europe for biosimilar drug approval, biosimilars can be a threat to the exclusivity of any biological therapeutics we sell or may market in the future and can pose the same issues as the small molecule generic threat described above. Governments may adopt more permissive approval frameworks (for example, shortening the duration of data exclusivity, or narrowing the scope of new products receiving data exclusivity) which could allow competitors to obtain broader marketing approval for biosimilars including as a substitutable product, increasing competition for our products (see also Changes in the laws or regulations that apply to us could affect our business, results of operations and financial condition below). If a biosimilar version of one of our products were to be approved, it could reduce our sales and/or profitability of that product.

However, through our presence as a manufacturer of generics and biosimilars, we will also utilize patent challenge strategies against other innovators patents similar to those of long-established generic companies, though there is no assurance that these strategies will be successful.

If our patents and/or proprietary rights to our products were limited or circumvented, our financial results could be materially and adversely affected.

**Product liability claims could adversely affect our business, results of operations and financial condition.**

Product liability is a significant risk for any pharmaceutical company and our product liability exposure could increase given that liability claims relating to our businesses may differ with regard to their nature, scope and level from the types of product liability claims that we have handled in the past. Substantial damages have been awarded and/or settlements agreed notably in the United States and other common law jurisdictions against pharmaceutical companies based on claims for injuries allegedly caused by the use of their products. Such claims can also be accompanied by consumer fraud claims by customers or third-party payers seeking reimbursement of the cost of the product.

We are currently defending a number of product liability claims (see Note D.22.a) to the consolidated financial statements included at Item 18 of this annual report) and there can be no assurance that the Company will be successful in defending against these claims or will not face additional claims in the future.

Often establishing the full side effect profile of a pharmaceutical drug goes beyond data derived from preapproval clinical studies which may only involve several hundred to several thousand patients. Routine review and analysis of the continually growing body of post-marketing safety surveillance and clinical trials provide additional information for example, potential evidence of rare, population-specific or long-term adverse reactions or of drug interactions that were not observed in preapproval clinical studies and may cause product labeling to evolve over time following

interactions with regulatory authorities, including restrictions of therapeutic indications, new contraindications, warnings or precautions and occasionally even the suspension or withdrawal of a product marketing authorization. Following any of these events, pharmaceutical companies can face significant product liability claims.

Furthermore, we commercialize several devices (some of which use new technologies) which, if they malfunction, could cause unexpected damage and lead to product liability claims (see Breaches of data security, disruptions of information technology systems and cyber threats could result in financial, legal, business or reputational harm ).

Although we continue to insure a portion of our product liability with third-party carriers, product liability coverage is increasingly difficult and costly to obtain, particularly in the United States. In the future, it is possible that self-insurance may become the sole commercially reasonable means available for managing the product liability financial risk of our pharmaceuticals and vaccines businesses (see Item 4. Information on the Company B. Business Overview B.9. Insurance and Risk Coverage ). In cases where we self-insure, the legal costs that we would bear for handling such claims and potential indemnifications to be paid to claimants could have a negative impact on our financial condition.

Due to insurance conditions, even when we have insurance coverage, recoveries from insurers may not be totally successful. Moreover, insolvency of an insurer could affect our ability to recover claims on policies for which we have already paid a premium.

Product liability claims, regardless of their merits or the ultimate success of the Company s defense, are costly, divert management s attention, may harm our reputation and can impact the demand for our products. Substantial product liability claims could materially adversely affect our business, results of operations and financial condition.

**Our products and manufacturing facilities are subject to significant government regulations and approvals, which are often costly and could result in adverse consequences to our business if we fail to anticipate the regulations, comply with them and/or maintain the required approvals.**

Obtaining marketing authorization is a long and highly regulated process requiring us to present extensive documentation and data to the regulatory authorities. Regulatory processes differ

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ITEM 3. KEY INFORMATION

from one jurisdiction and regulatory authority to another. Either at the time of the filing of the application for a marketing authorization or later during its review, each regulatory authority may impose its own requirements which can evolve over time, including requiring local clinical studies, and it may delay or refuse to grant approval even though a product has already been approved in another country. Health authorities are increasingly focusing on product safety and on the risk/benefit profile of pharmaceutical products. In particular, the FDA and the EMA have increased their requirements, particularly in terms of the volume of data needed to demonstrate a product s efficacy and safety. Even after regulatory approval, marketed products are subject to continual review, risk evaluations or comparative effectiveness studies including post-marketing studies to which at times we have committed as a condition of approval. In addition, following the implementation of European pharmacovigilance legislation in 2012, the Company and the European Regulatory Agencies (under the supervision of the PRAC (Pharmacovigilance Risk Assessment Committee)) have reinforced their systematic and intensive safety signal detection systems, which may detect safety issues even with mature products that have been on the market for a considerable time. This system may result in negative risk/benefit assessments and additional market authorization suspensions or withdrawals. All of these requirements have increased the costs associated with maintaining regulatory approvals and achieving reimbursement for our products. Post-regulatory approval reviews and data analyses can lead to the issuance of recommendations by government agencies, healthcare professional and patient or other specialized organizations regarding the use of products; for example, a recommendation to limit the patient population of a drug s indication, the imposition of marketing restrictions, or the suspension or withdrawal of the product can result in a reduction in sales volume as well as an increased risk of litigation.

Moreover, to monitor our compliance with applicable regulations, the FDA, the EMA and comparable agencies in other jurisdictions routinely conduct inspections of our facilities and may identify potential deficiencies. We have received notices of deficiencies and FDA Warning Letters in the past following the inspection of some of our facilities and may receive such letters in the future. More generally, if we fail to adequately respond to Regulatory Inspection observations identifying a deficiency during an inspection, or fail to comply with applicable regulatory requirements at all or within the targeted timeline, we could be subject to enforcement, remedial and/or punitive actions by the FDA (such as a Warning Letter), the EMA or other regulatory authorities.

In addition, in order to comply with our duty to report adverse events and safety signals to regulatory authorities, we must regularly train our employees and third parties (such as external sales forces and distributor employees) on regulatory matters. If we fail to train these people, or fail to train them appropriately, or they do not comply with contractual requirements, we may be exposed to the risk that safety events are not reported or not reported in a timely manner in breach of our reporting obligations.

To the extent that new regulations raise the costs of obtaining and maintaining product authorizations, or limit the economic value of a new product to its originator, the growth prospects of our industry and of Sanofi would be diminished. At least 50% of our current development portfolio consists of biological products that may in the future bring new therapeutic responses to current unmet medical needs, but that may also lead to more regulatory and

technical constraints. Regulations applicable to biologics are often more complex and extensive than the regulations applicable to other pharmaceutical products. Biologics are also costly investments from an industrial standpoint as biological products are complex to produce. These constraints and costs could adversely affect our business, results of operations and financial condition.

**Claims and investigations relating to compliance, ethics, competition law, marketing practices, pricing, human rights of workers, data protection and other legal matters could adversely affect our business, results of operations and financial condition.**

Our industry is heavily regulated. Our business covers an extremely wide range of activities worldwide and involves numerous partners. We are therefore obligated to comply with the laws of all countries in which we operate. However, legal requirements may vary from country to country and new requirements may be imposed on us from time to time. We have adopted a Code of Ethics (the Code ) that requires employees to comply with applicable laws and regulations, as well as the specific principles and rules of conduct set forth in the Code. We also have policies and procedures designed to help ensure that we, our employees, officers, agents, intermediaries and other third parties comply with applicable laws and regulations (including the US Foreign Corrupt Practices Act (FCPA), the UK Bribery Act, the OECD Anti-Bribery Convention, the French Anti-Corruption measures law (Sapin II) and the French duty of vigilance law and other anti-bribery laws and regulations).

Notwithstanding these efforts, non compliance with laws and regulations may occur and there can be no assurance that we, our officers and/or our directors will not face liability for actions taken with respect to our business.

Any failure to comply directly or indirectly (including as a result of a business partner s breach) with the laws and regulations applicable to us, including new regulations, could result in substantial liabilities for the Company and harm the Company s reputation. Governments and regulatory authorities around the world have been strengthening implementation and enforcement activities in recent years, including in relation to anti-bribery, anti-corruption, ethical requirements with respect to medical and scientific research, respect of human rights of workers and data protection legislation.

With respect to data protection legislation, the General Data Protection Regulation ( GDPR ) has created a range of compliance obligations since it came into force within the European Union in May 2018. Violations of the GDPR carry

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financial risks due to penalties for data breach or improper processing of personal data (including a possible fine of up to 4% of total worldwide annual turnover for the preceding financial year for the most serious infringements) and may also harm our reputation. Also some uncertainty remains around the legal and regulatory environment for these evolving privacy and data protection laws.

Sanofi and certain of its subsidiaries are under investigation or could become the subject of additional investigations or legal proceedings by various government entities and are defending a number of lawsuits relating to pricing and marketing practices (including, for example, whistleblower litigation in the United States). We also face litigation and government investigations or audits, including allegations of corruption, claims related to employment matters, patent and intellectual property disputes, consumer law claims and tax audits. See Item 8. Financial Information A. Consolidated Financial Statements and Other Financial Information Information on Legal or Arbitration Proceedings and Note D.22. to our consolidated financial statements included at Item 18 of this annual report. Responding to such investigations is costly and may divert management s attention from our business.

Unfavorable outcomes in any of these matters, or in similar matters that may arise in the future, could preclude the commercialization of our products, harm our reputation, negatively affect the profitability of existing products and subject us to substantial fines (including treble damages and fines based on our sales), punitive damages, penalties and injunctive or administrative remedies, potentially leading to the imposition of additional regulatory controls, monitoring or self-reporting obligations, or exclusion from government reimbursement programs or markets, all of which could have a material adverse effect on our business, results of operations or financial condition.

As such proceedings are unpredictable, we may, after consideration of all relevant factors, decide to enter into settlement agreements to settle certain claims. Such settlements may involve significant monetary payments and/or criminal penalties and may include admissions of wrongdoing. Settlement of healthcare fraud cases in the United States may require companies to enter into a Corporate Integrity Agreement, which is intended to regulate company behavior for a specified period of years.

In September 2018, Sanofi has reached a civil settlement with the US Securities and Exchange Commission (SEC) fully resolving the SEC s investigation into possible violation of the US Foreign Corrupt Practices Act. Sanofi did not admit any wrongdoing in connection with the settlement but agreed to pay $25 million in penalties and also agreed to a two-year period of self-reporting on the effectiveness of its enhanced internal controls. The DOJ has also completed its related investigation and has declined to pursue any action.

**Changes in the laws or regulations that apply to us could affect our business, results of operations and financial condition.**

All aspects of our business, including research and development, manufacturing, marketing, pricing and sales, are subject to extensive legislation and governmental regulation. Changes in applicable laws and the costs of compliance with such laws and regulations could have a material adverse effect on our business.

For example, governmental authorities are increasingly looking to facilitate generic and biosimilar competition to existing products through new regulatory proposals intended to achieve, or resulting in, changes to the scope of patent or data exclusivity rights and use of accelerated regulatory pathways for generic and biosimilar drug approvals. Such regulatory proposals could make patent prosecution for new products more difficult and time consuming or could adversely affect the exclusivity period for our products (see We rely on our patents and other proprietary rights to provide exclusive rights to market certain of our products, and if such patents and other rights were limited, invalidated or circumvented, our financial results could be materially and adversely affected above). Regarding the United States market, on December 11, 2018, in line with the Trump Administration s stated goal of enhancing competition for biologicals, the FDA released final guidance defining biologics, transitioning biological products approved under an NDA to a deemed biologics license application (BLA), and outlining an abbreviated pathway for biosimilar licensure. As part of the publication of the final guidance, the FDA is allowing for ongoing comments from the public, which may result in further changes or revisions to such guidance. The potential impact of ongoing comments that may result in revisions to the final guidance is unknown and may negatively affect our market exclusivity or impact pricing considerations in the future. As discussed below, however, the overall status of the Biologics Price Competition and Incentives Act (BPCIA) is uncertain, based on a December 14, 2018 federal court decision which declared the Affordable Care Act (ACA), of which the BPCIA is a part, to be unconstitutional. (see The pricing and reimbursement of our products is increasingly affected by decisions of governments and other third parties and cost reduction initiatives below)

This new competitive environment and the potential regulatory changes and agency guidance may further limit the exclusivity available to innovative products on the market and directly impact pricing, access and reimbursement levels, which may adversely affect our business and future results. See Item 4. Information on the Company B. Business Overview B.6. Markets B.6.2. Competition and B.6.3. Regulatory framework .

Also, in Europe, the implementation of new regulations on Medical Devices and In-Vitro Diagnostics that will apply respectively in May 2020 and May 2022, may cause delays in approvals (for new drug-device combination products and new drug-device combination products and new medical devices/IVDs), product discontinuation (for some legacy medical devices & IVDs), and non-compliance risks (regarding post

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marketing safety reporting, Unique Device Identification (UDI), European Databank on Medical Devices (EUDAMED)), due to increased requirements in terms of approval process, post-marketing surveillance, traceability and transparency.

In addition to international tax law and regulatory changes such as the OECD Base Erosion and Profit Shifting initiatives and EU directives being implemented (such as EU directive rules against tax avoidance practices or relating to the mandatory automatic exchange of information in relation to reportable cross-border arrangements) changes in tax frameworks, tax reforms and other changes to the way existing tax laws are applied in jurisdictions and major countries where Sanofi and its subsidiaries and affiliates operate could affect our income, our effective tax rate, and consequently our future net income. This particularly applies to French and US tax reforms enacted respectively in December 2018 and December 2017 for which French tax administration and some Internal Revenue Services comments, guidelines and regulations are still expected. Additional tax changes may be enacted in France for instance with respect to the corporate tax rate which could be increased back to 34.4%. These changes may cover matters such as taxation of our operations, intercompany transactions, internal restructuring and more generally taxable income, tax rates, indirect taxation, transfer pricing, R&D tax credits, taxation of intellectual property, dividend taxation, controlled companies or a restriction in certain forms of tax relief. Any of these changes could have a material adverse effect on our business and future results. Additionally, due to the complexity of the fiscal environment, the ultimate resolution of any tax matters may result in payments greater or lesser than amounts accrued.

For information regarding risks related to changes in environmental rules and regulations, see Environmental liabilities and costs related to compliance with applicable regulations may have a significant adverse effect on our results of operations below.

**Risks relating to our business**

**Our research and development efforts may not succeed in adequately renewing our product portfolio.**

Discovering and developing a new product is a costly, lengthy and uncertain process. To be successful in the highly competitive pharmaceutical industry, we must commit substantial resources each year to research and development in order to develop new products to compensate for decreasing sales of products facing patent expiration and termination of regulatory data exclusivity, introduction of lower-priced generics, increasingly aggressive generic commercialization tactics or competition from new products of competitors that are perceived as being superior or equivalent. We must pursue both early stage research and early and late development stages in order to propose a sustainable and well-balanced portfolio of products. In 2018, we spent 5,894 million on research and development, amounting to 17.1% of our net sales.

Our industry is driven by the need for constant innovation, but we may spread ourselves across too many areas of inquiry to be successful and may not be able to improve internal research productivity sufficiently to sustain our pipeline. We may also fail to invest in the right technology platforms, therapeutic areas, and product classes, or fail to build a robust pipeline and fulfill unmet medical needs in a timely manner. Also when we perform portfolio review we

may miscalculate the probabilities of success at each phase of the development. Fields of discovery, particularly biotechnology, are highly competitive and characterized by significant and rapid technological changes. Numerous companies are working on the same targets and a product considered as promising at the very beginning of its development may become less attractive if a competitor addressing the same unmet need reaches the market earlier.

The research and development process can generally take 12 to 15 years from discovery to commercial product launch. This process is conducted in various stages in order to test, along with other features, the efficacy, effectiveness and safety of a product. There can be no assurance that any of these product candidates will be proven safe or effective. See Item 4. Information on the Company B. Business Overview B.5. Global Research & Development . Accordingly, there is a substantial risk at each stage of development including clinical studies that we will not achieve our goals of safety and/or efficacy and that we will have to abandon a product in which we have invested substantial amounts of money and human resources, even in late stage development (Phase III). More and more trials are designed with clinical endpoints of superiority; failure to achieve those endpoints could damage the product s reputation and our overall program. Decisions concerning the studies to be carried out can have a significant impact on the marketing strategy for a given product. Multiple in-depth studies can demonstrate that a product has additional benefits, facilitating the product s marketing, but such studies are expensive and time consuming and may delay the product s submission to health authorities for approval. Our ongoing investments in new product launches and research and development for future products could therefore result in increased costs without a proportionate increase in revenues, which would negatively affect our operating results and profitability.

In 2015 we announced that we had up to 18 new medicines and vaccines on track to arrive on the market between 2014-2020, including six key launches. As of the end of 2018, all of those six products have already been approved and launched: Toujeo®, Praluent®, Dengvaxia®, Soliqua® 100/33 / Suliqua®, Kevzara® and Dupixent®. However, there can be no assurance that all of the products approved or launched will achieve commercial success.

In addition, following (or in some cases contemporaneously with) review of a product for a marketing authorization, the medical need served by the product and the corresponding reimbursement are evaluated by governmental agencies and/or third-party payers, requiring in some cases additional studies,

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including comparative studies, which may effectively delay marketing, change the population which the new product treats, and add to its development costs.

After marketing approval of our products, other companies or investigators, whether independently or with our authorization, may conduct studies or analysis beyond our control that may ultimately report results negatively affecting our sales either permanently or temporarily, it may take time for us to address these reported findings, leading among other things to a material adverse impact on sales.

**The pricing and reimbursement of our products is increasingly affected by decisions of governments and other third parties and cost reduction initiatives.**

The commercial success of our existing products and our product candidates depends in part on their pricing and the conditions under which our products are reimbursed. Our products continue to be subject to increasing price and reimbursement pressure due, inter alia, to:

- price controls imposed by governments in many countries;
- increased public attention to the price of drugs and particularly price increases, limiting our ability to set the price, or to manage or increase the price of our products based upon their value;
- removal of a number of drugs from government reimbursement schemes (for example products determined to be less cost-effective than alternatives);
- partial reimbursement of patient populations within a labelled indication;
- increased difficulty in obtaining and maintaining satisfactory drug reimbursement rates;
- increase in cost containment policies (including budget limitations) related to health expenses;
- governmental and private health care provider policies that favor prescription of generic medicines or substitution of branded products with generic medicines;

more demanding evaluation criteria applied by Health Technology Assessment (HTA) agencies when considering whether to cover new drugs at a certain price level;

more governments using international reference pricing to set or manage the price of drugs based on an external benchmark of a product s price in other countries;

aggressive pricing strategies by some of our competitors; and

entry of new consumer healthcare competitors offering online sales.

In addition to the pricing pressures they exert, governmental and private third-party payers and purchasers of pharmaceutical products may reduce volumes of sales by restricting access to formularies (including exclusive formularies), managing prescribing via various conditions (including prior authorisations

and step edits) or otherwise discouraging physicians from prescribing our products (see also The concentration of the US market exposes us to greater pricing pressure below).

In the United States, the Affordable Care Act (ACA) has increased the government s role with respect to price, reimbursement, and coverage levels for healthcare services and products. This law also imposed rebates and fees on pharmaceutical companies. In May 2018, the Trump Administration published its American Patients First proposal, which indicates its plans to investigate the ACA s impact on private market drug prices and potentially alter the ACA taxes and rebates for Medicaid and Medicaid managed care organizations. On December 14, 2018, a federal judge for the Northern District of Texas, Fort Worth Division, issued a ruling declaring the ACA unconstitutional, which sets the stage for another hearing on the law by the Federal Court of Appeals for the Fifth Circuit and possibly the United States Supreme Court thereafter. Included in the many parts of the ACA that could potentially be affected by the continued litigation is the Biologics Price Competition and Incentives Act. In addition to further judicial review of the ACA, the Trump Administration and other United States federal and state officials are continuing to focus on the cost of health coverage, health care and pharmaceuticals although future policy or the timing of any changes remains unclear, creating significant risks for the sector. At the federal level, legislation like the Bipartisan Budget Act of 2018 amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, and also increases in 2019 the percentage by which a drug manufacturer must discount the cost of prescription drugs from 50 percent under current law to 70 percent. Further, from 2017-2018, at least seven states enacted and an additional 22 states proposed legislation which will require price transparency and reporting of certain manufacturer information. This trend is anticipated to continue to 2019, where legislation is expected regarding pricing transparency, marketing, access to drugs and other measures related to pricing.

Government price reporting obligations are complex, and we face risks related to the reporting of pricing data that could affect the reimbursement of and discount provided for our products to US government healthcare programs.

We also encounter cost containment issues in countries outside the United States. In certain countries, including countries in the European Union, China and Canada, the coverage of prescription drugs, and pricing and levels of reimbursement, are subject to governmental control. For example, in Europe various authorities are developing the use of tenders for expensive products and are considering joint procurement mechanisms to negotiate lower prices. See also below Global economic conditions and an unfavorable financial environment could have negative consequences for our business .

In China, the health authorities continue to develop measures around post loss-of-exclusivity (LOE) brands including the selection of the generics validated through bioequivalence. The health authorities are testing new procurement systems targeting

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post LOE brands with generics demonstrating bioequivalence in four municipalities and seven major cities.

While we are trying to predict the availability or level of reimbursement and related restrictions for our product candidates, external events and unexpected decisions can occur that go against our expectations.

Price negotiations in a country may result in a price that is incompatible with the global price positioning of our products, which may lead us not to launch the product in that country, damaging our image and resulting in a decrease in initially anticipated sales.

Finally, our operating results may also be affected by parallel imports, particularly within the European Union, whereby distributors engage in arbitrage based on national price differences to buy products in low cost markets for resale in higher cost markets.

**The concentration of the US market exposes us to greater pricing pressure.**

In the United States, price is increasingly important to managed care organizations (MCOs) and pharmacy benefit managers (PBMs), and as the MCOs/PBMs grow in size following market consolidation, pharmaceutical companies have faced increased pressure in discounting and usage negotiations, and competition among pharmaceutical companies to have their products included in the payers formularies is robust. This can lead to price discounts or rebates in connection with the placement of products.

Exclusion of one of our drugs from a formulary can significantly reduce sales in the MCO/PBM patient population (for instance, effective 2017 Lantus®/Toujeo® were excluded from certain template formularies covering millions of people).

Also, some payers in the United States have put in place significant restrictions on the usage of Praluent®, which has resulted in significant out-of-pocket expenditures for patients. As a result in 2018 we reduced the net price of Praluent for US payers that agreed to reduce burdensome access barriers for patients.

Due to these pressures on our prices, our revenues and margins are, and could continue to be, negatively affected.

**We may lose market share to competing therapeutic options, biosimilar or generic products.**

We are faced with intense competition from generic products, biosimilars and brand-name drugs including from retail chains and distributors.

Doctors or patients may choose competitors products over ours or alternative therapeutic options such as surgery if they perceive them to be safer, more reliable, more effective, easier to administer or less expensive, which could cause our revenues to decline and adversely affect our results of operations.

The success of any product also depends on our ability to meet patient expectations and in certain areas such as diabetes to

deliver a positive patient experience. We need also to educate patients when permissible and promote our products to healthcare providers by providing them with innovative data about the product and its uses including through the use of digital tools. If these education efforts are not effective, we may not be able to increase the sales of our products or realize the full value of our investment in their development.

We may not be able to anticipate precisely the date of market entry of generics or biosimilars or the potential impact on our sales, both of which depend on numerous parameters. The introduction of a generic version of a branded medicine typically results in a significant and rapid reduction in net sales for the branded product because generic manufacturers typically offer their unbranded versions at significantly lower prices, resulting in adverse price and volume effects for our genericized products. For example, although we do not believe it is possible to state with certainty what level of net sales would have been achieved in the absence of generic competition, a comparison of our consolidated net sales for 2018 and 2017 for products affected by generic and biosimilar competition shows a loss of 1,749 million of net sales on a reported basis. However, other parameters may have contributed to the loss of sales, such as a fall in the average price of certain products (e.g. Lantus®). Also mandatory price regulations apply in certain countries to off-patent products and classes of products, and generics prices are taken into account for international reference pricing and tenders. Substitution is often permitted for generic products that are considered to be interchangeable or clinically identical. Competition, including from non-substitutable biosimilars, would likely result in a decrease in prices, additional rebates, increased promotion efforts and lower margins.

Approval of a generic or biosimilar that is substitutable for one of our products would increase the risk of accelerated market penetration by that generic or biosimilar to a greater extent than would be the case for a non-substitutable product.

These trends are exacerbated by applicable legislation which encourages the use of generic products to reduce spending on prescription drugs in many countries such as the United States, France and Germany. Therefore, the market for our products could also be affected if a competitor s innovative drug in the same market were to become available as a generic because a certain number of patients can be expected to switch to a lower-cost alternative therapy. We expect this generic competition to continue and to affect more of our products, including those with relatively modest sales.

**The manufacture of our products is technically complex, and supply interruptions, product recalls or inventory losses caused by unforeseen events may reduce sales, adversely affect our operating results and financial condition, delay the launch of new products and negatively impact our image.**

Many of our products are manufactured using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints and are heavily

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regulated by governmental health authorities around the world. Whether our products and the related raw materials are manufactured at our own dedicated manufacturing facilities or by third parties, we must ensure that all manufacturing processes comply with current Good Manufacturing Practices (cGMP) and other applicable regulations, as well as with our own quality standards. Third parties supply us with a portion of our raw materials, active ingredients and medical devices, which exposes us to the risk of a supply shortage or interruption in the event that these suppliers are unable to manufacture our products in line with quality standards or if they experience financial difficulties. Further, some raw materials essential to the manufacture of our products are not widely available from sources we consider reliable; for example, we have approved only a limited number of suppliers of heparins for use in the manufacture of Lovenox®. Any of these factors could adversely affect our business, operating results or financial condition. See Item 4. Information on the Company B. Business Overview B.8. Production and Raw Materials for a description of these outsourcing arrangements.

Our products are also increasingly reliant on the use of product-specific devices for administration which may result in technical issues. For example, Praluent® is administered with an auto-injector manufactured by a third party.

We must also be able to produce sufficient quantities of our products to satisfy demand. We may have difficulties transforming and adapting our existing plants to manufacture new products, including biologics, and scaling up production of our products currently under development once they are approved. We may fail to develop and maintain technology platforms for developing, launching and manufacturing our biological products. We also need to be and remain competitive in the biologic area in terms of manufacturing capabilities. Our biological products, in particular, are subject to the risk of manufacturing stoppages or the risk of loss of inventory because of the difficulties inherent in the processing of biological materials and the potential difficulties in accessing adequate amounts of raw materials meeting required standards. These difficulties may also be encountered during testing, which is a mandatory requirement for the products to be released. For example, in China, we encountered supply constraints of Pentaxim® vaccine in 2018 due to a problem with a supplier of a raw material used in the formulation of Pentaxim® vaccine for China. As a result we had to find an alternative raw material to meet the Chinese requirements. Effective insurance coverage for biological products may also be difficult to obtain in the event of contaminated batches as the cause of the contamination can be difficult to ascertain (for the impact on our financial statements see Impairment charges or write-downs in our books and changes in accounting standards could have a significant adverse effect on Sanofi s results of operations and financial results. below)

Additionally, specific conditions must be respected both by Sanofi and our customers for the storage and distribution of many of our

biological products. For example, cold storage is required for certain vaccines, insulin-based products and some hemophilia products. Failure to adhere to these requirements may result in lost product inventory or products becoming out of specification, which in turn may result in efficacy or safety issues for patients.

The complexity of these processes, as well as strict internal and health authority standards for the manufacture of our products, subject us to risks because the investigation and remediation of any identified or suspected problems can

cause production delays, substantial expense, product recalls or lost sales and inventories, and delay the launch of new products; this could adversely affect our operating results and financial condition, and cause reputational damage and the risk of product liability (see Product liability claims could adversely affect our business, results of operations and financial condition above).

When manufacturing disruptions occur, we may not have alternate manufacturing capacity, particularly for certain biologics. In the event of manufacturing disruptions, our ability to use backup facilities or set up new facilities is more limited because biologics are more complex to manufacture and generally require dedicated facilities. Even though we aim to have backup sources of supply whenever possible, including by manufacturing backup supplies of our principal active ingredients at additional facilities when practicable, we cannot be certain they will be sufficient if our principal sources become unavailable. Switching sources and manufacturing facilities requires significant time and prior approval by health authorities.

Supply shortages generate even greater negative reactions when they occur with respect to life saving medicines with limited or no viable therapeutic alternatives. Shortages of products can have a negative impact on the confidence of patients, customers and professional healthcare providers and the image of Sanofi and may lead to lower product revenues. Government authorities and regulators in the United States, in the European Union and other agencies worldwide are also considering measures to reduce these risks, such as through Supply Risk Management Plans for some products with high medical need, e.g. the French decree of July 2016 concerning the preparation of shortage management plans ( plans de gestion des pénuries ). It cannot be ruled out that these ongoing initiatives may generate additional costs for Sanofi if they result in a requirement to establish backup supply channels or to increase inventory levels to avoid shortages.

We are sometimes required to use animals to test our products in the development phase and to test our vaccines before distributing them. Animal testing activities have been the subject of controversy and adverse publicity. Testing on animals can be vital for the development or commercialization of a product. If applicable regulations were to ban this practice or if, due to pressure from animal welfare groups, we were no longer able to source animals to perform such tests, it would be difficult and in some cases impossible to develop or distribute our products in certain jurisdictions under the applicable marketing authorizations.

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**We rely on third parties for the discovery, manufacture and marketing of some of our products.**

Our industry is both highly collaborative and competitive, whether in the discovery and development of new products, in-licensing, the marketing and distribution of approved products, or manufacturing activities. We expect that we will continue to rely on third parties for key aspects of our business and we need to ensure our attractiveness as a potential partner.

We conduct a number of significant research and development programs and market some of our products in collaboration with other biotechnology and pharmaceutical companies. For example, we currently have a global strategic collaboration with Regeneron on monoclonal antibodies. In immuno-oncology, we have a global collaboration for the joint development and commercialization of cemiplimab, a programmed cell death protein 1 (PD-1) inhibitor antibody. We have also an immuno-oncology discovery and development agreement on the development of two clinical-stage bispecific antibody programs targeting respectively (i) BCMA and CD3 and (ii) MUC16 and CD3. (See Item 4. Information on the Company B. Business Overview ). In addition we may also rely on partners to design and manufacture medical devices, notably for the administration of our products.

As regards products recently launched or under development in our R&D portfolio for which we have an alliance arrangement with a partner, the terms of the alliance agreements may require us to share profits and losses arising from commercialization of such products with our partners. This differs from the treatment of revenue and costs generated by other products for which we have no alliance agreement, and such profit sharing may deliver a lower contribution to our financial results.

If disruptions or quality concerns were to arise in the third-party supply of raw materials, active ingredients or medical devices or if our partners were unable to manufacture a product, this could also adversely affect our ability to sell our products in the quantities demanded by the market and could damage our reputation and relationships with our customers. See also The manufacture of our products is technically complex, and supply interruptions, product recalls or inventory losses caused by unforeseen events may reduce sales, adversely affect our operating results and financial condition, delay the launch of new products and negatively impact our image above.

When we research and market our products through collaboration agreements, we are also subject to the risk that we may not adequately manage our alliance. For instance, we may not properly manage the decision making process with our partners. Decisions may also be under the control of or subject to the approval of our collaboration partners, who may have views that differ from ours. We are also subject to the risk that our partners may not perform effectively, which could have a detrimental effect when the performance of certain key tasks or functions is the responsibility of our collaboration partners. Failures in the development process or differing priorities may adversely affect the activities conducted through the collaboration arrangements.

Any conflicts or difficulties that we may have with our partners during the course of these agreements or at the time of their renewal or renegotiation, or any disruption in the relationships with our partners, may affect the development, the launch and/or the marketing of certain of our products or product candidates and may cause a decline in our revenues

or otherwise negatively affect our results of operations.

**A substantial share of the revenue and income of Sanofi continues to depend on the performance of certain flagship products.**

We generate a substantial share of our revenues from the sale of certain key products (see Item 5. Operating and Financial Review and Prospects Results of Operations Year ended December 31, 2018 compared with year ended December 31, 2017 Net Sales Pharmaceuticals segment ).

Among our flagship products, Lantus®, Lovenox® and Plavix® already face generic competition on the market. Lantus® is particularly important; it was Sanofi s leading product with revenues of 3,565 million in 2018, representing 10.3% of Sanofi s net sales for the year. Aubagio®, following a settlement agreement entered into in 2017, is expected to face generic competition starting from August 2023. The launch of new medicines and vaccines in other therapeutic areas and the performance of our other businesses may not be sufficient to reduce the relative contribution of the products mentioned above to our overall performance. More generally expiration of effective intellectual property protections for our products typically results in the entry of one or more lower-priced generic competitors, often leading to a rapid and severe decline in revenues on those products (for information on the expected impact of biosimilar entry on the market see We may lose market share to competing therapeutic options, biosimilar or generic products above and for information regarding ongoing patent litigation see Note D.22. to the consolidated financial statements included at Item 18 of this annual report).

Furthermore, in general, if one or more of our flagship products were to encounter problems such as material product liability litigation, unexpected side effects, recall, regulatory proceedings, publicity affecting doctor or patient confidence, pressure from existing competitive products, exclusion from formularies or changes in labeling, or if a new, more effective treatment were introduced, or if there were a reduction in sales or a decline in sales growth of one or more of our flagship products, the adverse impact on our business, results of operations and financial condition could be significant.

**Breaches of data security, disruptions of information technology systems and cyber threats could result in financial, legal, business or reputational harm.**

Our business depends heavily on the use of interdependent information technology systems, including Internet-based systems and digital tools. Certain key areas such as research and development, production and sales are to a large extent dependent on our information systems (including cloud-based

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computing) or those of third-party providers (including for the storage and transfer of critical, confidential, sensitive or personal information regarding our patients, clinical trials, vendors, customers, employees, collaborators and others). We and our third-party service providers use secure information technology systems for the protection of data and threat detection. Like many companies, we may experience certain of these events given that the external cyber-attack threat continues to grow and there can be no assurance that our efforts or those of our third-party service providers to implement adequate security and control measures would be sufficient to protect against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyber-attack, security breach, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm.

Any such event could negatively impact important processes, such as the conduct of scientific research and clinical trials, the submission of the results of such efforts to health authorities in support of requests for product approvals, the functioning of our manufacturing and supply chain processes, our compliance with legal obligations and other key business activities, including our employees ability to communicate with one another and with third parties. (see Product liability claims could adversely affect our business, results of operations and financial condition above)

In addition, if we do not allocate and effectively manage the resources necessary to build and maintain our information systems, and require our third-party service providers, suppliers, contract manufacturers, distributors or other third parties to do the same, or if we or they fail to timely identify or appropriately respond to cyberattacks or other incidents, our business could be disrupted, potentially damaging our customers health or business and negatively impacting our reputation, business and results of operations.

Although we maintain insurance coverage, this insurance may not be sufficiently available in the future to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. For example, certain types of cyber-attacks could be considered as an Act of War subject to insurance exclusion.

**Failure of our business continuity planning in the event of a crisis incident may affect our results of operations and our reputation.**

We may not be adequately prepared and/or able to respond effectively to a crisis incident (for instance in the event of a pandemic, natural disaster, a manufacturing, logistics or information technology systems breakdown, or a cyber-attack).

This could result in a delay or interruption of supply, or a threat to our business and assets, as well as to the safety of our employees. If we cannot mitigate the impact of the incident because we cannot react rapidly or because we cannot implement a business continuity plan in line with the magnitude of the incident, we could be prevented from restoring our operations in a timely manner and our operating results may be negatively impacted, as well as our image and reputation.

**We are subject to the risk of non-payment by our customers.[(1)]**

We run the risk of delayed payments or even non-payment by our customers, which consist principally of wholesalers, distributors, pharmacies, hospitals, clinics and government agencies. This risk is accentuated by recent concentrations among distributors, as well as by uncertainties around global credit and economic conditions, in particular in emerging markets. The United States poses particular customer credit risk issues because of the concentrated distribution system: our three main customers represented respectively 9%, 6% and 4% of our consolidated net sales in 2018. We are also exposed to large wholesalers in other markets, particularly in Europe. Although we assigned receivables to factoring companies or banks, an inability of one or more of these wholesalers to honor their debts to us could adversely affect our financial condition (see Note D.34. to our consolidated financial statements included at Item 18 of this annual report).

In some countries, some customers are public or subsidized health systems. The economic and credit conditions in these countries may lead to an increase in the average length of time needed to collect on accounts receivable or the ability to collect 100% of receivables outstanding. Because of this context, we may need to reassess the recoverable amount of our debts in these countries during future financial years (see also Item 5. Operating and Financial Review and Prospects Liquidity and Capital Resources Liquidity. ).

**Global economic conditions and an unfavorable financial environment could have negative consequences for our business.[2]**

Over the past several years, growth of the global pharmaceutical market has become increasingly tied to global economic growth. In this context, a substantial and lasting slowdown of the global economy, major national economies or emerging markets could negatively affect growth in the global pharmaceutical market and, as a result, adversely affect our business.

Unfavorable economic conditions have reduced the sources of funding for national social security systems, leading to austerity measures including heightened pressure on drug prices,

*(1) Information in this section is supplementary to Notes B.8.8. (with respect to information required by IFRS 7), D.10 and D.34 to our consolidated financial statements included at Item 18 of this annual report.*

*(2) Information in this section is supplementary to Note B.8.8. to our consolidated financial statements included at Item 18 of this annual report, with respect to information required by IFRS 7.*

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increased substitution of generic drugs, and the exclusion of certain products from formularies.

Further, our net sales may be negatively impacted by the continuing challenging global economic environment, as high unemployment, increases in cost-sharing, and lack of developed third-party payer systems in certain regions may lead some patients to switch to generic products, delay treatments, skip doses or use other treatments to reduce their costs. In the United States there is a consistent increase in the number of patients in the Medicaid program, under which sales of pharmaceuticals are subject to substantial rebates and, in many US states, to formulary restrictions limiting access to brand-name drugs, including ours. Also, employers may seek to transfer a greater portion of healthcare costs to their employees due to rising costs.

Our Consumer Healthcare business could also be adversely impacted by difficult economic conditions that limit the financial resources of our customers.

If economic conditions worsen, or in the event of default or failure of major players including wholesalers or public sector buyers financed by insolvent states, the financial situation of the Company, its results of operations and the distribution channels of its products may be adversely affected. See also We are subject to the risk ofion-payment by our customers above.

Economic and financial difficulties may have an adverse impact on third parties who are important to our business, including collaboration partners and suppliers, which could cause such third parties to delay or disrupt performance of their obligations to us and could materially adversely affect our business or results of operations. See We rely on third parties for the discovery, manufacture and marketing of some of our products above. For more information see Item 5. Operating and Financial Review and Prospects Liquidity and Capital Resources Liquidity.

**The impact of Brexit could negatively affect our business**

Following the Brexit vote in the UK, the EU decided to move the headquarters of the EU s health authority, the EMA, from the UK to the Netherlands by March 2019. It is expected that a significant percentage of the current employees of the EMA will decide not to make the move to the Netherlands. This raises the possibility that new drug approvals in the EU could be delayed as a result. We are also addressing the impact of Brexit on our supply chain management and quality oversight between the UK and the EU and our internal Brexit Task Force is developing and deploying appropriate contingency plans aiming at avoiding interruption of supply to patients in the event of a hard Brexit see Item 4. Business Overview B.6.3.8. Other new legislation proposed or pending implementation Brexit and The globalization of our business exposes us to increased risks in specific areas below).

**Counterfeit versions of our products harm our business.**

Counterfeiting activities and the presence of counterfeit products in a number of markets and over the Internet continue to be a challenge for maintaining a safe drug supply. Counterfeit products are frequently unsafe or ineffective, and can be life-threatening. To distributors and users, counterfeit products may be visually

indistinguishable from the authentic version. Reports of adverse reactions to counterfeit drugs along with increased levels of counterfeiting could be mistakenly attributed to the authentic product, affect patient confidence in the authentic product, and harm the business of companies such as Sanofi. If one of our products were to be the subject of counterfeits, we could incur substantial reputational and financial harm. See Item 4. Information on the Company B. Business Overview B.6. Markets B.6.2. Competition.

**The expansion of social media platforms and new technologies present risks and challenges for our business and reputation.**

We increasingly rely on social media, new technologies and digital tools to communicate about our products and diseases or to provide health services. The use of these media requires specific attention, monitoring programs and moderation of comments. For example, patients may use these channels to comment on the effectiveness of a product and to report an alleged adverse event. When such questions arise, the nature of evidence-based health care and restrictions on what pharmaceutical manufacturers may say about their products are not always well suited to rapidly defending Sanofi or the public s legitimate interests in the face of the political and market pressures generated by social media and rapid news cycles, and this may result in commercial harm, overly restrictive regulatory actions and erratic share price performance. In addition, unauthorized communications, such as press releases or posts on social media, purported to be issued by Sanofi, may contain information that is false or otherwise damaging and could have an adverse impact on our stock price. Negative or inaccurate posts or comments about Sanofi, our business, directors or officers on any social networking website could seriously damage our reputation. In addition, our employees and partners may use social media and mobile technologies inappropriately, which may give rise to liability for Sanofi, or which could lead to breaches of data security, loss of trade secrets or other intellectual property or public disclosure of sensitive information, including information about our employees, clinical trials or customers or other information. Such uses of social media and mobile technologies could have a material adverse effect on our reputation, business, financial condition and results of operations.

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**Impairment charges or write-downs in our books and changes in accounting standards could have a significant adverse effect on Sanofi s results of operations and financial results.**

Substantial value is allocated to intangible assets and goodwill resulting from business combinations, as disclosed at Note D.4. to our consolidated financial statements included in this annual report at Item 18, which could be substantially written down in value upon indications of impairment (primarily relating to pharmacovigilance, discontinued research and development projects, patent litigation and the launch of competing products), with adverse effects on our financial condition and the value of our assets.

If any of our strategic equity investments decline in value and remain below cost for an extended period, we may be required to write down our investment. We own a significant stake in Regeneron Pharmaceuticals, Inc. (21.7% of its share capital as of December 31, 2018), which is listed on NASDAQ and has been accounted for using the equity method since 2014. Any material deterioration in Regeneron s share price or financial performance would be an indicator that the value of our investment might have become impaired. This would require us to perform an impairment test, which could have a negative impact on our financial statements.

In addition, the inherent variability of biologics manufacturing increases the risk of write-offs of these products. Due to the value of the materials used, the carrying amount of biological products is much higher than that of small-molecule products.

The financial environment and the economic difficulties affecting some countries could also negatively affect the value of our assets (see Global economic conditions and an unfavorable financial environment could have negative consequences for our business above and Fluctuations in currency exchange rates could adversely affect our results of operations and financial condition below).

Any new or revised accounting standards, rules and interpretations issued by the IASB (International Accounting Standards Board) could also result in changes to the recognition of income and expense that may materially and adversely affect Sanofi s financial results.

**Our pension liabilities are affected by factors such as the performance of plan assets, interest rates, actuarial data and experience and changes in laws and regulations.**

Our future funding obligations for our main defined-benefit pension plans depend on changes in the future performance of assets held in trust for these plans, the interest rates used to determine funding levels (or company liabilities), actuarial data and experience, inflation trends, the level of benefits provided for by the plans, as well as changes in laws and regulations. Adverse changes in those factors could increase our unfunded obligations under such plans, which would require more funds to be contributed and hence negatively affect our cash flow and results (see Note D.19.1. to our consolidated financial statements included at Item 18 of this annual report).

**Risks relating to Sanofi s structure and strategy**

**Our strategic objectives for long-term growth may not be fully realized.**

In November 2015, we outlined our strategic roadmap for the period 2015-2020. Our strategy rests on four pillars: reshape our portfolio, deliver outstanding launches, sustain innovation in R&D and simplify our organization.

We may not be able to fully realize our strategic objectives and, even if we are able to do so, these strategic objectives may not deliver the expected benefits or within the expected timeline.

We are looking to reshape our portfolio through acquisitions and divestitures and may not reach this objective if we are unable to identify opportunities, or enter into agreements in a timely manner or on sufficiently attractive terms. In addition, we may fail to (i) adopt the best strategy for our acquisitions / divestitures or (ii) compete successfully in an intensively competitive, increasingly focused market environment. (see We may fail to successfully identify external business opportunities or realize the anticipated benefits from our strategic investments or divestments below and Our research and development efforts may not succeed in adequately renewing our product portfolio above). We may also not have the necessary flexibility to appropriately reallocate resources toward our priority businesses.

The successful launch of a new pharmaceutical product involves substantial investment in sales and marketing activities. In 2015 we announced that we have up to 18 new medicines and vaccines on track to arrive on the market between 2014-2020 including six key launches. As of the end of 2018, all of those six products have already been approved and launched: Toujeo®, Praluent®, Dengvaxia® and Soliqua® 100/33 / Suliqua®, Kevzara® and Dupixent®. However there can be no assurance that all of these products will achieve commercial success. We may also encounter failures or delays in our launch strategy. For example, Dengvaxia® sales suffer from political changes and economic volatility in Latin America and also from the recommendation to update the label at the end of 2017 following new clinical studies. In addition, in the Philippines, Sanofi received a legal order revoking the Dengvaxia® License in early 2019. In addition, the implementation of utilization management restrictions by payers in the United States and limited market access in Europe hampered our launch strategy on Praluent®. The launch strategy we develop (in terms of timing, pricing, market access, marketing efforts and dedicated sales forces) may not deliver the benefits that we expect. The competitive environment for a given product may also have changed by the time of the actual launch, modifying our initial expectations. The need to prioritize the allocation of resources may also cause delays in or hamper the launch of some of our products.

Sustaining innovation in R&D is inherently risky due to the high rate of failure and we may not be able to allocate our resources to obtain optimal results (see also Our research and development efforts may not succeed in adequately renewing our product portfolio above).

Our global organization through the implementation from January 2016 of five global business units (GBUs), and their reorganization

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from 2019 to refocus two GBUs (Primary Care and China and Emerging Markets) to meet significant growth objectives, requires substantial attention from our management. There is no guarantee that this organization will enable Sanofi to concentrate its efforts around the businesses most likely to deliver growth, or that these GBUs will grow in line with anticipated growth rates or deliver the expected benefits. Also we need to simplify our organization to gain agility and generate savings. There is no certainty that we will manage to implement these changes within the appropriate time-frames to support our growth strategy.

We have also defined a focused, competitive digital strategy (see Item 4. Information on the Company B. Business Overview B.1. Strategy). Our seven priority digital initiatives use digital to create value in two ways: (i) helping us run our business better, faster, and cheaper as we use digital across our value chain to increase productivity, and (ii) introducing new business models (in diabetes). Nevertheless we may fail to capture the benefits of digital at an appropriate cost and/or in a timely manner. Competitors, including new entrants such as tech companies, may outpace us in this fast-moving area.

Failure to support and grow our marketed products, successfully execute the launches of newly approved products, advance our late-stage pipeline, manage the change of our organization or deliver digital transformation would have an adverse impact on our business, prospects and results of operations.

**We may fail to successfully identify external business opportunities or realize the anticipated benefits from our strategic investments or divestments.**

We pursue a strategy of selective acquisitions, in-licensing and collaborations in order to reinforce our pipeline and portfolio. We are also proceeding to selective divestments to focus on key business areas. The implementation of this strategy depends on our ability to identify transaction opportunities, mobilize the appropriate resources and execute these transactions on acceptable financing terms. Moreover, entering into in-licensing or collaboration agreements generally requires the payment of significant milestones well before the relevant products reach the market, without any assurance that such investments will ultimately become profitable in the long term (see Note D.21.1. to the consolidated financial statements included at Item 18 of this annual report and also We rely on third parties for the discovery, manufacture and marketing of some of our products above).

For newly acquired activities or businesses our growth objectives could be delayed or ultimately not realized, and expected synergies could be adversely impacted if:

- we are unable to quickly or efficiently integrate those activities or businesses;
- integration takes longer than expected;

key employees leave; or

we have higher than anticipated integration costs.

For divestments, the financial benefit could be impacted if we face significant financial claims or price adjustment post closing.

In March 2018 and June 2018, we completed the acquisitions of Bioverativ and Ablynx respectively, but the expected benefits of those transactions may never be fully realized or may take longer to realize than expected.

We may miscalculate the risks associated with business development transactions at the time they are made or not have the resources or ability to access all the relevant information to evaluate them properly, including with regard to the potential of research and development pipelines, manufacturing issues, compliance issues, or the outcome of ongoing legal and other proceedings. It may also take a considerable amount of time and be difficult to implement a risk analysis and risk mitigation plan after the acquisition of an activity or business is completed due to lack of historical data. As a result, risk management and coverage of such risks, particularly through insurance policies, may prove to be insufficient or ill-adapted.

Because of the active competition among pharmaceutical groups for such business development opportunities, there can be no assurance of our success in completing these transactions when such opportunities are identified.

**The globalization of our business exposes us to increased risks in specific areas.**

We continue to focus on emerging markets. However, difficulties in operating in emerging markets, a significant decline in the anticipated growth rate in these regions or an unfavorable movement of the exchange rates of these countries currencies against the euro could impair our ability to take advantage of these growth opportunities and could affect our business, results of operations or financial condition (see also Global economic conditions and an unfavorable financial environment could have negative consequences for our business above).

The expansion of our activities in emerging markets also exposes us to more volatile economic conditions, political instability (including a backlash in certain areas against free trade), competition from multinational or locally based companies that are already well established in these markets, the inability to adequately respond to the unique characteristics of emerging markets (particularly with respect to their underdeveloped judicial systems and regulatory frameworks), difficulties in recruiting qualified personnel or maintaining the necessary internal control systems, potential exchange controls, weaker intellectual property protection, higher crime levels (particularly with respect to counterfeit products (see Counterfeit versions of our products harm our business above)), and compliance issues including corruption and fraud (see Claims and investigations relating to compliance, ethics, competition law, marketing practices, pricing, human rights of workers, data protection and other legal matters could adversely affect our business, results of operations and financial condition above).

We may also face compliance and internal control systems issues in mature markets due to increased competition and more complex and stringent regulations.

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In Europe, there is a risk that barriers to free trade and the free movement of people may rise following the United Kingdom s Brexit vote and the rise of nationalist, separatist and populist sentiment in various countries. Also, international conflicts, barriers to free trade and related restrictions could collectively disturb the international flow of goods and increase the costs and difficulties of international transactions.

As a global healthcare leader, we are exposed to a number of risks inherent in sectors in which we were previously less active such as consumer healthcare. The business models and trade channels in consumer healthcare, in particular regarding promotional efforts and trade terms for example, are different from those in our traditional pharmaceuticals business.

**Our success depends in part on our senior management team and other key employees and our ability to attract, integrate and retain key personnel and qualified individuals in the face of intense competition.**

We depend on the expertise of our senior management team and other key employees. In addition, we rely heavily on recruiting and retaining talented people to help us meet our strategic objectives. We face intense competition for qualified individuals for senior management positions, or in specific geographic regions or in specialized fields such as clinical development, biosciences and devices, or digital and artificial intelligence. In addition, our ability to hire qualified personnel also depends in part on our ability to reward performance, incentivize our employees and to pay competitive compensation. Laws and regulations on executive compensation may restrict our ability to attract, motivate and retain the required level of talented people. The inability to attract, integrate and/or retain highly skilled personnel, in particular those in leadership positions, may weaken our succession plans, may materially adversely affect the implementation of our strategy and our ability to meet our strategic objectives and could ultimately adversely impact our business or results of operations.

**Environmental risks of our industrial activities**

**Risks from the handling of hazardous materials could adversely affect our results of operations.**

Manufacturing activities, such as the chemical manufacturing of the active ingredients in our products and the related storage and transportation of raw materials, products and waste, expose us to various risks, including:

- fires and/or explosions;
- storage tank leaks and ruptures; or
- discharges or releases of toxic or pathogen substances.

These operating risks can cause personal injury, property damage and environmental contamination, and may result in the shutdown of affected facilities and/or the imposition of civil, administrative, criminal penalties and/or civil damages.

The occurrence of any of these events may significantly reduce the productivity and profitability of a particular manufacturing facility and adversely affect our operating results and reputation.

Although we maintain property, business interruption and casualty insurance that we believe is in accordance with customary industry practices, this insurance may not be adequate to fully cover all potential hazards incidental to our business.

**Environmental liabilities and costs related to compliance with applicable regulations may have a significant adverse effect on our results of operations.**

The environmental laws of various jurisdictions impose actual and potential obligations on our Company to remediate contaminated sites. These obligations may relate to sites:

- that we currently own or operate;
- that we formerly owned or operated; or
- where waste from our operations was disposed.

These environmental remediation obligations could significantly reduce our operating results. Sanofi accrues provisions for remediation when our management believes the need is probable and that it is reasonably possible to estimate the cost. See Item 4. Information on the Company B. Business Overview B.10. Health, Safety and Environment (HSE) for additional information regarding our environmental policies. In particular, our provisions for these obligations may be insufficient if the assumptions underlying these provisions prove incorrect or if we are held responsible for additional, currently undiscovered contamination. These judgments and estimates may later prove inaccurate, and any shortfalls could have a material adverse effect on our results of operations and financial condition.

We are or may become involved in claims, lawsuits and administrative proceedings relating to environmental matters. Some current and former Sanofi subsidiaries have been named as potentially responsible parties or the equivalent under the US Comprehensive Environmental Response, Compensation and Liability Act of 1980, as amended (also known as Superfund ), and similar statutes in France, Germany, Italy, Brazil and elsewhere. As a matter of statutory or contractual obligation, we and/or our subsidiaries may retain responsibility for environmental liabilities at some of the sites of our predecessor companies, or of subsidiaries that we demerged, divested or may divest. We have disputes outstanding regarding certain sites no longer owned by the Company. An adverse outcome in such disputes might have a significant adverse effect on our operating results. See Note D.22.d) to the consolidated financial statements included at Item 18 of this annual report and Item 8. Financial Information A. Consolidated Financial Statements and Other Financial Information Information on Legal or Arbitration Proceedings .

Environmental regulations are evolving. For example, in Europe, new or evolving regulatory regimes include REACH, CLP/GHS, SEVESO, IPPC/IED, the Waste Framework Directive, the

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Emission Trading Scheme Directive, the Water Framework Directive, the Directive on Taxation of Energy Products and Electricity and several other regulations aimed at preventing global warming. Stricter environmental, safety and health laws and enforcement policies could result in substantial costs and liabilities to our Company and could subject our handling, manufacture, use, reuse or disposal of substances or pollutants, site restoration and compliance to more rigorous scrutiny than is currently the case. Consequently, compliance with these laws could result in significant capital expenditures as well as other costs and liabilities, thereby adversely affecting our business, results of operations or financial condition. For more detailed information on environmental issues, see Item 4. Information on the Company B. Business Overview B.10. Health, Safety and Environment (HSE).

**Natural disasters prevalent in certain regions in which we do business could affect our operations.**

Some of our production sites are located in areas exposed to natural disasters, such as earthquakes, floods and hurricanes. Such disasters could be exacerbated in a context of global warming. In the event of a major disaster we could experience severe destruction or interruption of our operations and production capacity. As a result, our operations and our employees could suffer serious harm which could have a material adverse effect on our business, financial condition and results of operations.

**Risks related to financial markets[1]**

**Fluctuations in currency exchange rates could adversely affect our results of operations and financial condition.**

Because we sell our products in numerous countries, our results of operations and financial condition could be adversely affected by fluctuations in currency exchange rates. We are particularly sensitive to movements in exchange rates between the euro and the US dollar, the Japanese yen, the Chinese Yuan and to currencies in emerging markets. In 2018, 33.5% of our net sales were generated in the United States; 22.2% in Emerging Markets other than China (see the definition in Item 5. Operating and Financial Review and Prospects A/ Operating results ), including countries that are, or may in future become, subject to exchange controls; 7.1% in China; and 5.0% in Japan. While we incur expenses in those currencies, the impact of currency exchange rates on these expenses does not fully offset the impact of currency exchange rates on our revenues. As a result, currency exchange rate movements can have a considerable impact on our earnings. When deemed appropriate and when technically feasible, we enter into transactions to hedge our exposure to foreign exchange risks. These efforts, when undertaken, may fail to offset the effect of adverse currency exchange rate fluctuations on our results of operations or financial condition. For more information concerning our

exchange rate exposure, see Item 11. Quantitative and Qualitative Disclosures about Market Risk.

**Risks relating to an investment in our shares or ADSs**

**Foreign exchange fluctuations may adversely affect the US dollar value of our ADSs and dividends (if any).**

Holders of ADSs face exchange rate risk. Our ADSs trade in US dollars and our shares trade in euros. The value of the ADSs and our shares could fluctuate as the exchange rates between these currencies fluctuate. If and when we pay dividends, they would be denominated in euros. Fluctuations in the exchange rate between the euro and the US dollar will affect the US dollar amounts received by owners of ADSs upon conversion by the depositary of cash dividends, if any. Moreover, these fluctuations may affect the US dollar price of the ADSs on the Nasdaq Global Select Market (Nasdaq) whether or not we pay dividends, in addition to any amounts that a holder would receive upon our liquidation or in the event of a sale of assets, merger, tender offer or similar transaction denominated in euros or any foreign currency other than US dollars.

**Persons holding ADSs rather than shares may have difficulty exercising certain rights as a shareholder.**

Holders of ADSs may have more difficulty exercising their rights as a shareholder than if they directly held shares. For example, if we issue new shares and existing shareholders have the right to subscribe for a pro rata portion of the new issuance, the depositary is allowed, at its own discretion, to sell this right to subscribe for new shares for the benefit of the ADS holders instead of making that right available to such holders. In that case, ADS holders could be substantially diluted. Holders of ADSs must also instruct the depositary how to vote their shares. Because of this additional procedural step involving the depositary, the process for exercising voting rights will take longer for holders of ADSs than for holders of shares. ADSs for which the depositary does not receive timely voting instructions will not be voted at any meeting.

**Our largest shareholder owns a significant percentage of the share capital and voting rights of Sanofi.**

As of December 31, 2018, L Oréal held approximately 9.48% of our issued share capital, accounting for approximately 16.95% of the voting rights (excluding treasury shares) of Sanofi. See Item 7. Major Shareholders and Related Party Transactions A. Major Shareholders. Affiliates of L Oréal currently serve on our Board of Directors. To the extent L Oréal continues to hold a large percentage of our share capital and voting rights, it will remain in a position to exert greater influence in the appointment of the directors and officers of Sanofi and in other corporate actions that require shareholders approval.



*(1) Information in this section is supplementary to Note B.8.8. to our consolidated financial statements included at Item 18 of this annual report with respect to information required by IFRS 7.*

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**Sales of our shares may cause the market price of our shares or ADSs to decline.**

Sales of large numbers of our shares, or a perception that such sales may occur, could adversely affect the market price for our shares and ADSs. To our knowledge, L Oréal, our largest shareholder, is not subject to any contractual restrictions on the sale of the shares it holds in our Company. L Oréal does not consider its stake in our Company as strategic.

**Risks relating to our Contingent Value Rights (CVRs)**

**In addition to the risks relating to our shares, CVR holders are subject to additional risks.**

In connection with our acquisition of Genzyme, we issued CVRs under a CVR agreement entered into by and between us and American Stock Transfer & Trust Company, the trustee (see also Note D.18. to the consolidated financial statements included at Item 18 of this annual report). A copy of the form of the CVR agreement is on file with the SEC as Annex B to Amendment No. 2 to the Registration Statement on Form F-4 filed with the Securities and Exchange Commission on March 24, 2011. Pursuant to the CVR agreement, each holder of a CVR is entitled to receive cash payments upon the achievement of certain milestones, if any, based on the achievement of certain cumulative net sales thresholds by Lemtrada® (alemtuzumab for treatment of multiple sclerosis). See Item 10. Additional Information C. Material Contracts The Contingent Value Rights Agreement.

CVR holders are subject to additional risks, including:

- the public market for the CVRs may not be active or the CVRs may trade at low volumes, both of which could have an adverse effect on the resale price, if any, of the CVRs;
- the market price and trading volume of the CVRs may be volatile;
- no payment will be made on the CVRs without the achievement of certain agreed upon milestones. As such, it may be difficult to value the CVRs and accordingly it may be difficult or impossible to resell the CVRs;
- if net sales do not exceed the thresholds set forth in the CVR agreement for any reason within the time periods specified therein, no payment will be made under the CVRs and the CVRs will expire without value;

since the US federal income tax treatment of the CVRs is unclear, any part of any CVR payment could be treated as ordinary income and required to be included in income prior to the receipt of the CVR payment;

any payments in respect of the CVRs rank at parity with our other unsecured unsubordinated indebtedness;

we are not prohibited from acquiring the CVRs, whether in open market transactions, private transactions or otherwise and we have already purchased CVRs on several occasions (for more information see Item 5. Operating and Financial Review and Prospects Liquidity and Capital Resources Liquidity. );

we may, under certain circumstances, purchase and cancel all outstanding CVRs; and

while we have agreed to use diligent efforts (as defined in the CVR agreement), until the CVR agreement is terminated, to achieve each of the remaining Lemtrada® related CVR milestones set forth in the CVR agreement, we are not required to take all possible actions to achieve these goals. On July 5, 2016 Sanofi disclosed that, based upon actual sales of Lemtrada® in Qualifying Major Markets and in other markets during the respective applicable periods since the Product Launch, Product Sales Milestone #1 has not been met. On February 7, 2018, Sanofi disclosed that, based upon actual sales trends to date, it does not expect that product sales milestones #2, #3 and #4 will be met. Failure to achieve the remaining sales milestones could have an adverse effect on the value of the CVRs (see also Note D.22.c to the consolidated financial statements included at Item 18 of the annual report regarding the ongoing CVR Trustee Claim).

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ITEM 4. INFORMATION ON THE COMPANY

Item 4. **Information on the Company**

**Introduction**

Sanofi is a leading global healthcare company, focused on patient needs and engaged in the research, development, manufacture and marketing of therapeutic solutions.

In the remainder of this section:

A product is referred to either by its international non-proprietary name (INN) or its brand name, which is generally exclusive to the company that markets it. In most cases, the brand names of our products, which may vary from country to country, are protected by specific registrations. In this document, products are identified by their brand names used in France and/or in the US.

For our Pharmaceuticals activity, unless otherwise stated, all market share percentages and rankings are calculated based on consolidated national pharmaceutical sales data, excluding vaccines and in constant euros, on a September 2018 MAT (Moving Annual Total) basis. The data are mainly from IQVIA local sales audit supplemented by various other country-specific sources including Knobloch (Mexico), GERS (France) and HMR (Portugal).

For our Vaccines activity, market share percentages and rankings are based on our own estimates. These estimates have been made from information in the public domain collated from various sources, including statistical data collected by industry associations and information published by our competitors.

Sanofi has three principal activities: Pharmaceuticals, Consumer Healthcare (CHC), and Vaccines via Sanofi Pasteur. These activities are operating segments within the meaning of the IFRS 8 accounting standard (see Note D.35. to our consolidated financial statements, included at Item 18 of this annual report).

We invest in the following activities: Rare Diseases, Multiple Sclerosis, Immunology, Rare Blood Disorder, Oncology, Diabetes, Cardiovascular, Established Prescription Products[(1)], Generics, Consumer Healthcare, and Vaccines. Unlike our Vaccines and Consumer Healthcare activities, which are operating segments within the meaning of IFRS 8, our Rare Diseases, Multiple Sclerosis, Immunology, Rare Blood Disorder, Oncology, Diabetes, Cardiovascular, Established Prescription Products and Generics activities are franchises whose performance is

monitored primarily on the basis of net sales; the

products sold by each of those franchises are included in our Pharmaceuticals operating segment. We are also active in emerging markets selling products from our three activities; the performance of our Emerging Markets(2) operations is monitored primarily on the basis of net sales.

For a presentation of the net sales of our activities for the year ended December 31, 2018, refer to Item 5 Results of Operations Year Ended December 31, 2018 Compared with Year Ended December 31, 2017 .

The most important pharmaceutical products marketed by us are described below.

Rare Diseases: a portfolio of enzyme replacement therapies including Cerezyme® for Gaucher disease, Myozyme® and Lumizyme® for Pompe disease, and Fabrazyme® for Fabry disease; Cerdelga®, an oral ceramide analog for Gaucher disease; and Aldurazyme® for mucopolysaccharidosis Type 1 (MPS 1).

Multiple sclerosis: Aubagio®, a once-daily oral immunomodulator; and Lemtrada®, a monoclonal antibody. Both products were developed to treat patients with relapsing forms of multiple sclerosis.

Immunology: Dupixent®, a monoclonal antibody against the Interleukin-4 receptor alpha, indicated for adults with moderate-to-severe atopic dermatitis and (in the US) for moderate-to-severe asthma; and Kevzara®, a monoclonal antibody against the Interleukin-6 receptor, indicated for adults with moderate to severe rheumatoid arthritis.

Rare Blood Disorder: Elocate® and Alprolix®, extended half-life clotting-factor therapies for the treatment of adults and children with hemophilia A and B, respectively; and Cablivi®, a bivalent nanobody for the treatment of adults experiencing an episode of acquired thrombotic thrombocytopenic purpura.

Oncology: Libtayo®, a fully human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1), for the treatment of certain patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC; Jevtana®, a taxane, indicated for patients with prostate cancer; Taxotere®, a taxane representing a cornerstone therapy for several cancer types; Eloxatin®, a platinum-based agent used as an adjuvant treatment for certain people with stage III colon cancer; Thymoglobulin®, a broad immuno-suppressive and immuno- modulating agent; Mozobil®, a hematopoietic stem cell mobilizer for patients with hematologic malignancies; and



*(1) Established Prescription Products comprises mature products including Plavix®, Lovenox®, Aprovel®, Renagel® and Renvela®.*

(2) *World excluding the US, Canada, Western & Eastern Europe (apart from Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

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Zaltrap®, a recombinant fusion protein, indicated for certain patients with metastatic colorectal cancer.

Diabetes: Lantus® (insulin glargine), a long-acting human insulin analog which is the world-leading brand in the insulin market; Toujeo® (insulin glargine 300 U/mL); Amaryl®, an oral once-daily sulfonylurea; Apidra®, a rapid-acting human insulin analog; Insuman®, a range of rapid-acting or intermediate-acting human insulins; Lyxumia®/Adlyxin® (lixisenatide), a once-daily GLP-1 receptor agonist; Soliqua® 100/33 / Suliqua®, a once-daily combination of insulin glargine and lixisenatide; and Admelog® / Insulin lispro Sanofi® (insulin lispro), a rapid-acting insulin.

Cardiovascular diseases: Praluent®, a cholesterol-lowering drug that inhibits PCSK9; and Multaq®, an anti-arrhythmic drug in atrial fibrillation.

Established Prescription Products: Plavix®, an anti-platelet agent indicated for a number of atherothrombotic conditions; Lovenox®, a low molecular weight heparin for the prophylaxis and treatment of venous thromboembolism and of acute coronary syndrome; Aprovel® and CoAprovel®, anti-hypertensives; Renagel® and Renvela®, oral phosphate binders for use in patients undergoing dialysis; Synvisc® and Synvisc-One®, viscosupplements used to reduce pain in patients suffering from osteoarthritis of certain joints; Stilnox®, for the short-term treatment of insomnia; and Allegra®, a long-lasting (12- and 24-hour) non-sedating anti-histamine for the treatment of seasonal allergic rhinitis (hay fever) and uncomplicated hives.

Generics: our pharmaceuticals portfolio also includes a wide range of generics. In September 2018, we completed the divestment of our European generics business Zentiva to Advent International, a US global private equity firm.

Our Consumer Healthcare (CHC) activity is focused around four strategic categories: Allergy Cough & Cold, Pain, Digestive and Nutritionals.

Our Vaccines activity is operated through Sanofi Pasteur. We sell vaccines in five areas: pediatric vaccines, influenza vaccines, adult and adolescent booster vaccines, meningitis vaccines, and travel and endemics vaccines.

In 2018, we obtained regulatory approval for two new products: Cablivi® in the EU and the US and Libtayo® in the US. We also obtained regulatory approval in the US for Dupixent® in an additional indication: moderate-to-severe asthma in certain patients.

Collaborations are essential to our business and a certain number of our products, whether on the market or under development, are in-licensed products relying on third-party rights or technologies.

**A/ History and development of the Company**

The current Sanofi corporation was incorporated under the laws of France in 1994 as a *société anonyme*, a form of limited liability company, for a term of 99 years. Since May 2011, we have operated under the commercial name Sanofi (formerly known as Sanofi-Aventis). Our registered office is located at 54, rue La Boétie, 75008 Paris, France, our main telephone number is +33 1 53 77 40 00 and our website is www.sanofi.com. Our principal US subsidiary s office is located at 55 Corporate Drive, Bridgewater, NJ 08807; telephone: +1 (908) 981 5000.

The SEC maintains an internet site at http://www.sec.gov that contains reports, information statements, and other information regarding issuers that file electronically with the SEC.

**Main changes over the last five years**

At the end of December 2016, Sanofi Pasteur and MSD ended their vaccines joint venture in Europe and integrated their respective European vaccines businesses into their own operations.

On January 1, 2017, Sanofi and Boehringer Ingelheim (BI) successfully closed in most markets a transaction to swap Sanofi s Animal Health business for BI s CHC business.

On March 8, 2018, following a tender offer, we acquired control of Bioverativ Inc., a US biopharmaceutical company headquartered in Waltham, Massachusetts. Bioverativ is engaged in the research, development and commercialization of therapies for people with hemophilia and other rare blood disorders.

On June 19, 2018, Sanofi finalized the acquisition of Ablynx, a Belgian biopharmaceutical company engaged in the development of Nanobodies® which combine the advantages of conventional antibody drugs with some of the features of small-molecule drugs in various therapeutic areas.

On September 30, 2018, we completed the divestment of our European generics business Zentiva to Advent International, a US global private equity firm.

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ITEM 4. INFORMATION ON THE COMPANY

**B/ Business overview**

**B.1. Strategy**

*The market context for Sanofi*

A number of fundamental trends point to a positive outlook for the pharmaceutical industry. The global population is growing and aging. Unmet medical needs remain high. The industry has increased R&D productivity, and is launching a high number of innovative medicines. Patients around the world, and a rising middle class in emerging markets, are demanding better care, empowered by access to new information. It is a particularly exciting time scientifically and technologically: the promise of genomics is being realized, immuno-oncology is transforming cancer treatments, and big data is generating new insights into disease. Digital technologies are having a transformative effect across sales, R&D and manufacturing, and acting as enablers for new businesses.

At the same time, increased geopolitical uncertainties, funding challenges, budget tightening and affordability will continue to put the entire healthcare value chain under significant pressure. Although we believe that pharmaceuticals will remain a fundamentally attractive business within that value chain, the bar for innovation will most likely continue to rise. Payers will continue to put scrutiny on prices and reimbursement, and demand demonstration of real life outcomes. This will be coupled with more innovative pricing and contracting practices; pricing pressure is already increasing in the US and China.

There are two other significant trends. Firstly, in the innovation race, good ideas are quickly recognized by competitors who can move fast to implement them. Secondly, biosimilars are now firmly part of the competitive landscape in both the US and Europe.

*Implementing the strategic roadmap*

To compete and win in this market, we announced our 2020 strategic roadmap in November 2015. We have made significant progress against each of the four pillars of that strategy: reshape the portfolio, deliver outstanding launches, sustain innovation in R&D, and simplify the organization.

*Reshape the portfolio*

To reshape the portfolio, we focused on three targets: sustaining our leadership, building competitive positions, and exploring strategic options. As a result, we have achieved several important milestones:

**Building a leading Rare Blood Disorder franchise**

We began the year by creating a new global Rare Blood Disorder franchise, with three strategic deals announced within the space of a month. The first was a reshaping of our alliance with Alnylam, under which we obtained global development and

commercialization rights to fitusiran, an investigational RNAi therapeutic currently in development for the treatment of hemophilia A and B. The second was the acquisition of Bioverativ, a biotechnology company focused on therapies for hemophilia and other rare blood disorders. Completed in early March 2018 at a price of $11.6 billion, this deal brought us a portfolio of products including the flagship hemophilia treatments Eloctate® and Alprolix®. The third was the acquisition of Ablynx, a company engaged in the discovery and development of Nanobodies®. This deal was completed in June 2018 at a price of 3.9 billion; it enhances our portfolio with the addition of Cablivi® (caplacizumab) - the first therapeutic specifically indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP) - which received marketing approval from the European Commission in September 2018 and from the FDA in February 2019.

**Rebuilding our competitive position in Oncology**

We have entered the Immuno-Oncology (IO) market with the US launch of Libtayo® (cemiplimab), the first anti PD-1 agent to be approved for metastatic cutaneous squamous cell carcinoma (CSCC) and certain locally advanced CSCCs. In January 2018, Sanofi and Regeneron announced that the two companies had more than doubled their investment in cemiplimab, to $1.6 billion. This will fund a broad clinical program in a range of cancers including basal cell carcinoma, cervical and non-small cell lung cancer.

As regards isatuximab, our fully-owned oncology asset, we see significant potential for the CD38 antibody in multiple myeloma and have several Phase III trials underway that address the entire disease continuum. In February 2019, we announced that the isatuximab Phase III trial in combination with standard of care therapies had met its primary endpoint of prolonging progression free survival in patients with relapsed/refractory multiple myeloma. We also believe strongly that isatuximab has potential beyond multiple myeloma.

In January 2019, we announced that we had restructured our IO collaboration with Regeneron. Under the revised agreement, our earlier stage IO efforts with Regeneron will now focus entirely on two bispecific antibodies. This gives us more flexibility to develop our own novel IO programs. Importantly, we will be able to focus on our platform of multi-specific T-cell engagers. This is a key milestone given our significantly enhanced capabilities in multi-specific biologics following the acquisition of Ablynx.

**Divesting our European Generics business**

In September, 2018, we completed the divestment of our European generics business Zentiva to Advent International, a US global private equity firm, for 1.9 billion (enterprise value).

**Bolstering our Consumer Healthcare operations**

In January 2017, Sanofi and Boehringer Ingelheim (BI) successfully closed a transaction to swap our Animal Health business for BI s Consumer Healthcare (CHC) business,

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enhancing our position in four strategic categories: Allergy Cough & Cold, Pain, Digestive and Nutritionals as well as our geographical footprint.

**Sustaining our leadership in Specialty Care, Vaccines and Emerging Markets**

In Rare Diseases, we are sustaining our market share leadership in rare genetic diseases through the patient-centered approach unique to Sanofi Genzyme, supported by product differentiation and market access. We continue to grow the market through screening expansion.

In Multiple Sclerosis, investing for the future, we have signed a licensing agreement with Principia to develop their experimental oral treatment (Bruton s tyrosine kinase inhibitor) that shows promise in multiple sclerosis and, potentially, other central nervous system diseases.

In Vaccines, the influenza vaccine market is highly competitive and to retain our leadership in this category we have built a differentiated product offering. This includes converting our influenza portfolio from trivalent to quadrivalent and offering age-specific products (such as Fluzone® High-Dose for the over-65s), and the recent US launch of Flublok®, the first recombinant protein-based influenza vaccine. Demand typically exceeds supply, so producing more is a key priority for us. We are investing to secure and expand influenza and pediatric vaccines capacity: in April 2018, we announced an investment of 350 million for the construction of a newstate-of-the-art vaccine manufacturing facility at the Sanofi Pasteur Canadian headquarters in Toronto, Ontario.

We are the pharmaceutical industry leader in Emerging Markets, and a major multinational player in Brazil, Russia, India, China and Mexico.

**Out-licensing our infectious disease research and development portfolio**

We have out-licensed most of our infectious disease research and early-stage development portfolio and transferred our infectious disease research unit to Evotec AG, though we continue to be involved in infectious diseases through our vaccine R&D and global health programs.

*Deliver outstanding launches*

**Launching our Immunology franchise**

We have the cornerstones of an important new franchise in immunology through Dupixent® (for atopic dermatitis, asthma) and Kevzara® (for rheumatoid arthritis). Both drugs were developed in collaboration with Regeneron and both were launched in 2017.

In 2017 we launched Dupixent®, the first and only biologic medicine for the treatment of adults with moderate-to-severe atopic dermatitis. In October 2018, Dupixent® was approved in

the US as an add-on maintenance therapy in some patients with moderate-to-severe asthma. In November 2018, the FDA accepted for Priority Review a supplemental application in certain adolescent patients with moderate-to-severe atopic dermatitis. Dupilumab is being evaluated in a broad range of clinical development programs for diseases that are driven by Type 2 inflammation. Dupixent® uptake to date is being driven by high patient need, healthcare professional engagement and market access. By the end of 2018, we had launched Dupixent® in the US and 16 other countries, including Japan.

**Other new launches**

In diabetes, we continued the global launch and ramp-up of Toujeo® and Soliqua® 100/33/ Suliqua®, a lixisenatide and insulin glargine combination treatment for diabetes.

In cardiovascular diseases, we continued the global launch and ramp-up of Praluent® for hypercholesterolemia. The European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending a new indication for Praluent® to reduce cardiovascular risk by lowering low-density lipoprotein cholesterol (LDL-C) levels as an adjunct to correction of other risk factors in adults with established atherosclerotic cardiovascular disease.

In December 2018, the European Commission granted marketing authorization for Dengvaxia® for use in European endemic areas in individuals aged 9 to 45 years with a documented prior dengue infection.

*Sustain innovation in R&D*

Our strategy depends on continued innovation in R&D. We continue to strengthen our R&D pipeline, increasing the number of high-quality projects in the early stage pipeline and replenishing the late development pipeline as products launch. We have aligned the R&D organization with the new Global Business Unit structure, reorganized research into thematic clusters, continued to build capability in translational science, and recruited important new talent. Sanofi has engaged a strong reshaping of its R&D strategy, strengthening the development of innovative products that promise to substantially elevate the standard of care for patients, and prioritizing the therapeutic areas where the patient need is most urgent and where the scientific and medical landscape is richest with opportunity. This shift in priorities translates into an increase in the proportion of R&D projects representing specialty care compared to primary care, while maintaining a strong commitment to Vaccines. In the long-term the aspiration is that roughly 80% of the Sanofi portfolio will consist of molecules with first-in-class or truly differentiated best-in-class potential, with two thirds of biologics compounds and two thirds of the pipeline directly derived from Sanofi internal research.

**Implementing rigorous portfolio prioritization processes**

To prioritize the most promising molecules in the pipeline, we undertook a rigorous portfolio review in 2018. This exercise

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resulted in termination of 13 development stage molecules. In addition, we discontinued 25 research projects. This illustrates Sanofi s commitment to managing a more focused portfolio to accelerate development of the most promising molecules in the pipeline.

**Developing technology platforms and an in-house Nanobody® platform**

R&D is leveraging the investments made a few years ago to establish competency in several therapeutic modalities, going beyond small molecules and conventional monoclonal antibodies, to produce differentiated molecules that tackle targets in novel and innovative ways. Besides the expansions of complex antibodies such as bi or tri specifics and the addition of nanobodies with the integration of the Ablynx platform, Sanofi has made important steps forward in genomic medicines. This includes enhancements to our internal capabilities in gene therapy based on the AAV platform, as well as new collaborations in virus based gene therapy, zinc finger based genome editing and mRNA therapeutics.

*Simplify the organization*

We are creating a more agile organization through:

A new Global Business Unit (GBU) structure, implemented in 2016, integrating global franchises and country-level commercial and medical organizations for each of our major businesses (Sanofi Genzyme; Diabetes and Cardiovascular; General Medicines and Emerging Markets; Sanofi Pasteur and Consumer Healthcare) and also saw the creation of Global Functions (Finance, Human Resources, Information Technology and Solutions, etc).

The refocusing of two of our GBUs, changing their organizational structure to provide greater focus on our operations in mature markets and across emerging markets. We have created a new Primary Care GBU, focused exclusively on mature markets, that combines the product portfolios of our previous Diabetes & Cardiovascular GBU and the Established Prescription Products franchise. Alongside this, we have created a second new GBU: China & Emerging Markets. The two new GBUs launched at the start of 2019.

In order to accelerate Sanofi s transformation, in 2018 we decided to combine all of our efforts into one new department: Business Transformation. This new department has been created to simplify our operating models, bring innovative practices to our organization, and create lasting, positive changes.

Dissolving our vaccines joint venture with MSD: at the end of 2016, Sanofi Pasteur and MSD ended their vaccines joint venture in Europe and integrated their respective European vaccines businesses into their own operations.

We have also defined a focused, competitive digital strategy with seven key initiatives to create value in two ways: help us run our

business better, faster, and cheaper; and pursue new business models.

For example, digital technologies offer the promise of speeding up our trials and getting our drugs to market faster; our plants will be connected with data flowing automatically from equipment sensors; and advanced analytics on supply chain data will enable real-time optimization. We are engaging physicians through a variety of channels, building precision marketing capabilities globally in CHC; and pursuing new business models to integrate drugs, devices, data, and service, and bring innovative solutions to people living with diabetes. Finally, digital transformation opens up the potential for Sanofi to become a much more data-driven organization.

**B.2. Main pharmaceutical products**

The sections below provide additional information on our main products. Our intellectual property rights over our pharmaceutical products are material to our operations and are described at B.7. Patents, Intellectual Property and Other Rights below. As disclosed in Item 8. Financial Information A. Consolidated Financial Statements and Other Financial Information Patents of this annual report, we are involved in significant litigation concerning the patent protection of a number of these products. For more information on sales performance, see Item 5. Operating and Financial Review and Prospects Results of Operations .

*a) Rare Diseases*

Our Rare Diseases business is focused on products for the treatment of rare genetic diseases and other rare chronic debilitating diseases, including lysosomal storage disorders (LSDs), a group of metabolic disorders caused by enzyme deficiencies.

**Cerezyme®**

Cerezyme® (imiglucerase, intravenous infusion) is an enzyme replacement therapy used to treat Gaucher disease, an inherited and potentially life-threatening LSD. It is estimated that Gaucher disease occurs in approximately one in 120,000 newborns in the general population and one in 850 in the Ashkenazi Jewish population worldwide, but the incidence and patient severity vary among regions. Cerezyme® has been marketed in the US since 1994, in the EU since 1997, in Japan since 1998 and in China since 2008, and is approved to treat Type 1 Gaucher disease in more than 85 countries. It has also been approved to treat the systemic symptoms of Type 3 Gaucher disease in most non-US markets, including the EU and Japan.

**Cerdelga®**

Cerdelga® (eliglustat) is the first and only first-line oral therapy for Gaucher disease Type 1 adult patients. A potent, highly specific ceramide analog inhibitor of GL-1 synthesis with broad tissue distribution, Cerdelga® has demonstrated efficacy in the treatment of naive Gaucher disease patients and in patients who

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switch from enzyme replacement therapy. Cerdelga® has been approved to treat Type 1 Gaucher disease in the US (2014), and in the EU and Japan (2015). Regulatory submissions are ongoing in other countries.

There are ongoing patent infringement proceedings in the US. For further information, see Item 8 Information on Legal or Arbitration Proceedings Cerdelga® Patent Litigation.

**Myozyme® and Lumizyme®**

Myozyme® and Lumizyme® (alglucosidase alfa, intravenous infusion) are recombinant forms of the same human enzyme and are enzyme replacement therapies used to treat Infantile- and Late Onset Pompe disease (IOPD and LOPD), an inherited, progressive and often fatal neuromuscular disease. Pompe disease occurs in approximately one in 40,000 newborns worldwide, but incidence and patient severity vary among regions.

Myozyme® was first approved in 2006 in the EU and has since been approved in more than 70 countries. In the US, alglucosidase alfa has been marketed as Lumizyme® since 2010.

**Fabrazyme®**

Fabrazyme® (agalsidase beta, intravenous infusion) is an enzyme replacement therapy used to treat Fabry disease, an inherited, progressive and potentially life threatening LSD. Fabry disease occurs in approximately one in 35,000 newborns worldwide, but incidence and patient severity vary among regions. Fabrazyme® has been marketed in the EU since 2001 and in the US since 2003, and is approved in more than 70 countries.

**Aldurazyme®**

Aldurazyme® (laronidase, intravenous infusion) is the first and only approved treatment for mucopolysaccharidosis type 1 (MPS I). MPS I occurs in approximately one per 100,000 live births worldwide, but incidence and patient severity vary among regions. Aldurazyme® has been marketed in the EU and the US since 2003, and is approved in more than 75 countries.

*b) Multiple Sclerosis*

Multiple sclerosis (MS) is an autoimmune disease in which a person s immune system attacks the central nervous system, damaging myelin, the protective sheath that covers nerve fibers. This causes a break in communication between the brain and the rest of the body, ultimately destroying the nerves themselves, and causing irreversible damage. More than 2.5 million people suffer from MS worldwide.

Our MS franchise consists of Aubagio® (teriflunomide), a once-daily, oral immunomodulator, and Lemtrada® (alemtuzumab), a monoclonal antibody. Both products treat patients with relapsing forms of MS.

**Aubagio®**

Aubagio® (teriflunomide), a small molecule immunomodulatory agent with anti-inflammatory properties, is a once-daily oral therapy.

Aubagio® is approved in more than 70 countries around the world including the US (since September 2012) for the treatment of patients with relapsing forms of MS, the EU (since August 2013) for the treatment of adult patients with relapsing remitting MS), and China (since July 2018). Ongoing development efforts include the TeriKIDS study to assess the safety and efficacy of teriflunomide in children (see B.5. Global research & development ) and global post-marketing registries for pregnancy.

In 2017, Sanofi reached settlement with all 20 generic Aubagio® ANDA first filers, granting each a royalty-free license to enter the US market on March 12, 2023.

**Lemtrada®**

Lemtrada® (alemtuzumab) is a humanized monoclonal antibody targeting the CD52 antigen. Lemtrada® is administered by intravenous infusion as two short courses 12 months apart; for the majority of patients no further treatment is necessary, making Lemtrada® the only disease-modifying therapy (DMT) that can provide long term durable efficacy in the absence of continuous dosing.

Lemtrada® is approved in more than 60 countries including the EU (since September 2013) for the treatment of adult patients with relapsing forms of MS with active disease defined by clinical or imaging features, and the US (since November 2014) for the treatment of patients with relapsing forms of MS. Because of its safety profile, the FDA approval limited use of Lemtrada® to patients who have had an inadequate response to two or more drugs indicated for the treatment of MS, and included a black-box warning on potential side effects. In the US, Lemtrada® is only available through a restricted distribution program called the Lemtrada® Risk Evaluation and Mitigation Strategy (REMS) Program.

Alemtuzumab is being evaluated in a Phase III study in pediatric patients (see B.5. Global research & development ).

Bayer Healthcare receives contingent payments based on alemtuzumab global sales revenue. For additional information, see Note D.18. to our consolidated financial statements, included at Item 18 of this annual report.

*c) Immunology*

Our Immunology franchise consists of Dupixent® (dupilumab) for the treatment of adults with moderate-to-severe atopic dermatitis (AD) and as add-on maintenance therapy for some patients with moderate to severe asthma, and Kevzara® (sarilumab) for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA).

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ITEM 4. INFORMATION ON THE COMPANY

**Dupixent®**

Dupixent® (dupilumab), a human monoclonal antibody, binds to the interleukin-4 receptor (IL-4R) and has been shown to specifically inhibit overactive signaling of two key proteins (IL-4 and IL-13), which are believed to be major drivers of the persistent underlying inflammation in atopic dermatitis, and in certain other allergic or atopic diseases or that may underlie moderate-to-severe asthma. Dupixent® comes in a pre-filled syringe and can be self-administered as a subcutaneous injection.

Moderate-to-severe atopic dermatitis, a form of eczema and a chronic inflammatory disease, is characterized by rashes sometimes covering much of the body and can include intense, persistent itching and skin dryness, cracking, redness, crusting and oozing.

Dupixent® was granted marketing authorization by the FDA in March 2017 for the treatment of adults with moderate-to-severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies, or when those therapies are not advisable, and in October 2018 as an add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma. The European Commission approved Dupixent® in September 2017 for use in adults with moderate-to-severe AD who are candidates for systemic therapy, and is reviewing an application for authorization as an add-on maintenance therapy for moderate-to-severe asthma: the European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion in March 2019. Dupixent® is also approved for use in certain adult patients with moderate-to-severe atopic dermatitis in other countries including Canada and Japan.

Dupixent® is available in 17 countries including the US (since April 2017), several European Union countries (the first launch was in Germany in December 2017) and Japan (since April 2018). Applications for regulatory approval in certain patients with moderate to severe AD and in certain patients with moderate-to-severe asthma are being reviewed in several other countries. In November 2018, the FDA accepted for Priority Review a supplemental application in certain adolescent patients with moderate-to-severe atopic dermatitis.

Dupilumab is currently being evaluated in a broad range of clinical development programs for diseases that are driven by Type 2 inflammation, including pediatric atopic dermatitis, pediatric asthma, nasal polyps and eosinophilic esophagitis. See B.5. Global Research & Development .

Dupixent® is developed and commercialized in collaboration with Regeneron Pharmaceuticals, Inc. For additional information on the commercialization of this product, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Regeneron .

There are ongoing patent infringement proceedings in several countries initiated by Sanofi and Regeneron against Amgen and

Immunex relating to Dupixent®. See Note D.22.b) to the consolidated financial statements included at Item 18 of this annual report.

**Kevzara®**

Kevzara® (sarilumab) is a human monoclonal antibody that binds to the interleukin-6 receptor (IL-6R) and has been shown to inhibit IL-6R mediated signaling. IL-6 is a cytokine in the body that, in excess and over time, can contribute to the inflammation associated with rheumatoid arthritis.

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease causing inflammation, pain, and eventually joint damage and disability.

In May 2017, the FDA approved Kevzara® for the treatment of adult patients with moderately to severely active RA who have had an inadequate response or intolerance to one or more disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate. In June 2017, the European Commission granted marketing authorization for Kevzara® in combination with methotrexate for the treatment of moderately to severely active RA in adult patients who have responded inadequately to or who are intolerant to one or more DMARDs, such as methotrexate. Kevzara® is approved for use in certain adult patients with moderately to severely active RA in other countries including Canada, Russia, Taiwan, Israel, Hong Kong and Argentina. Additionally, Kevzara® is indicated in Japan for patients with inadequate response to conventional treatments irrespective of disease severity.

Kevzara® is available in 20 countries, including the US.

Sarilumab is being evaluated in children and adolescents with polyarticular-course juvenile idiopathic arthritis (JIA) or with systemic juvenile arthritis, and in adults with giant cell arteritis or with Polymyalgia Rheumatica. See B.5. Global Research & Development .

Kevzara® is developed and commercialized in collaboration with Regeneron Pharmaceuticals, Inc. For additional information on the commercialization of this product, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Regeneron .

*d) Rare Blood Disorder*

Rare Blood Disorder is a new franchise created in 2018 following the acquisition of Bioverativ. Bioverativ, including its two marketed products Eloctate® and Alprolix®, is being consolidated in our financial statements with effect from March 8, 2018 (see A. History and Development of the Company ).

**Eloctate®**

Eloctate® (antihemophilic factor (recombinant), Fc fusion protein), is an extended half-life clotting-factor therapy to control and prevent bleeding episodes in adults and children with hemophilia A. In the US, it is indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding

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episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes.

Hemophilia A is a rare, x-linked genetic bleeding disorder characterized by a deficiency of functional coagulation Factor VIII, resulting in a prolonged patient plasma-clotting time. As a consequence, people with hemophilia A bleed for a longer time than normal. Eloctate® temporarily replaces the missing coagulation Factor VIII by intravenous use.

We market Eloctate® primarily in the United States (since 2014), Japan, Canada, Australia, Colombia and Taiwan.

Eloctate® is developed and commercialized in collaboration with Swedish Orphan Biovitrum AB (publ), whose territories include Europe, Russia, Middle East and some countries in North Africa.

**Alprolix®**

Alprolix® (coagulation Factor IX (recombinant), Fc fusion protein) is an extended half-life clotting-factor therapy to control and prevent bleeding episodes in adults and children with hemophilia B. In the US, it is indicated for use in adults and children with hemophilia B for control and prevention of bleeding episodes, perioperative management, and routine prophylaxis to reduce the frequency of bleeding episodes.

Hemophilia B is a rare, x-linked genetic bleeding disorder characterized by a deficiency of functional coagulation Factor IX, which leads to a prolonged clotting time similar to hemophilia A. Hemophilia B is a less common type of hemophilia than hemophilia A. Alprolix® temporarily replaces the missing coagulation Factor IX, and is administered by intravenous injection.

We market Alprolix® primarily in the United States (since 2014), Japan, Canada, Australia and Colombia.

Alprolix® is developed and commercialized in collaboration with Swedish Orphan Biovitrum AB (publ), whose territories include Europe, Russia, Middle East and some countries in North Africa.

**Cablivi®**

Cablivi® (caplacizumab) is a bivalent anti-von Willebrand Factor (vWF) Nanobody® for the treatment of adults experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP). Cablivi® is the first therapeutic specifically indicated for the treatment of aTTP.

Acquired thrombotic thrombocytopenic purpura is a life-threatening, autoimmune-based blood clotting disorder characterized by extensive clot formation in small blood vessels throughout the body, leading to severe thrombocytopenia (very low platelet count), microangiopathic hemolytic anemia (loss of red blood cells through destruction), ischemia (restricted blood supply to parts of the body) and widespread organ damage especially in the brain and heart. Cablivi® has an immediate effect on platelet adhesion and the ensuing formation and accumulation of

the micro-clots.

Cablivi® was granted marketing authorization by the European Commission in September 2018 and by the FDA in February 2019.

Cablivi® is marketed in Germany and available in France under a temporary user license *(autorisation temporaire d´utilisation).*

Cablivi® was developed by Ablynx, a Sanofi company since mid 2018. See A. History and Development of the Company .

*e) Oncology*

**Libtayo®**

Libtayo® (cemiplimab-rwlc), an immune therapy drug, is a fully human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1). This may restore immune function through the activation of cytotoxic T cells, thereby avoiding tumor evasion from host immunity.

In September 2018, the FDA approved Libtayo® for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. Libtayo® is the only treatment specifically approved and available for advanced CSCC in the US. CSCC is the second most common form of skin cancer. Libtayo® is under regulatory review by the EMA and a number of other countries.

Cemiplimab is being investigated in several clinical development programs. See B.5. Global Research & Development .

Libtayo® is developed and commercialized in collaboration with Regeneron Pharmaceuticals, Inc. For additional information on the commercialization of this product, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Regeneron .

**Jevtana®**

Jevtana® (cabazitaxel), a chemotherapy drug and cytotoxic agent, is a semi-synthetic second-generation taxane promoting tubulin assembly and stabilizing microtubules; this prevents many cancer cells from dividing, which ultimately results in destroying many such cells. It is approved in combination with prednisone for the treatment of patients with castration resistant metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen.

Jevtana® was granted marketing authorization by the FDA in June 2010, by the European Commission in March 2011, and in Japan in July 2014. The product is marketed in over 75 countries.

**Thymoglobulin®**

Thymoglobulin® (anti-thymocyte Globulin) is a polyclonal anti-human thymocyte antibody preparation that acts as a broad immunosuppressive and immunomodulating agent. The product s primary mechanism of action is T-cell depletion, which is complemented by a host of other immunomodulating effects. In the US, Thymoglobulin® is indicated for for the prophylaxis and treatment of acute rejection in patients receiving a kidney transplant. Thymoglobulin® is to be used in conjunction with concomitant immunosuppression. Outside the US, depending on the country, Thymoglobulin® is indicated for the treatment and/or

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prevention of acute rejection in organ transplantation; immunosuppressive therapy in aplastic anemia; and the treatment and/or prevention of Graft-versus-Host Disease (GvHD) after allogeneic hematopoietic stem cell transplantation.

Thymoglobulin® is currently marketed in over 65 countries.

**Taxotere®**

Taxotere® (docetaxel), a chemotherapy drug and cytotoxic agent, is a semi-synthetic taxane promoting tubulin assembly and stabilizing microtubules. It has been approved for use in 11 indications in five different tumor types (breast, prostate, gastric, lung, and head and neck).

Taxotere® is available in more than 90 countries. Generics of docetaxel have been launched globally.

Sanofi is involved in Taxotere® product litigation in the US. See Note D.22.a) to our consolidated financial statements, included at Item 18 of this annual report.

**Eloxatin®**

Eloxatin® (oxaliplatin), a chemotherapy drug, is a platinum-based cytotoxic agent. In combination with the infusional administration of two other chemotherapy drugs (5-fluorouracil/leucovorin, in the FOLFOX regimen), Eloxatin® is approved by the FDA for adjuvant treatment of people with stage III colon cancer who have had their primary tumors surgically removed.

Eloxatin® is in-licensed from Debiopharm and is marketed in more than 70 countries worldwide. Generics of oxaliplatin have been launched globally.

**Mozobil®**

Mozobil® (plerixafor injection) is a hematopoietic stem cell mobilizer indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin s lymphoma (NHL) and multiple myeloma (MM). Mozobil® is marketed in over 50 countries.

**Zaltrap®**

Zaltrap® (aflibercept/ziv-aflibercept) is a recombinant fusion protein which acts as a soluble decoy receptor that binds to Vascular Endothelial Growth Factor-A (VEGF-A), Vascular Endothelial Growth Factor-B (VEGF-B) and placental growth factor (PIGF), preventing the bound VEGFs from binding to their native receptors. VEGF-A is one of the mediators contributing to tumor angiogenesis that helps provide the blood flow tumors need to grow. VEGF-B and

PlGF may also contribute to tumor angiogenesis.

The FDA approved Zaltrap® in August 2012 for use in combination with FOLFIRI (a chemotherapy regimen made up of 5-fluorouracil/leucovorin/irinotecan), in patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed

following an oxaliplatin-containing regimen. To avoid confusion with Eylea®, the FDA assigned a new name, ziv-aflibercept, to the active ingredient. The European Commission approved Zaltrap® (aflibercept) in February 2013 to treat mCRC that is resistant to or has progressed after an oxaliplatin-containing regimen.

Zaltrap® is now approved in more than 70 countries worldwide. For additional information on the commercialization of Zaltrap®, see Item 5 Financial Presentation of Alliances Alliance Arrangements with Regeneron .

*f) Diabetes*

**Lantus®**

Lantus® (insulin glargine 100 units/mL) is a long-acting analog of human insulin, indicated for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above. Approved in the US and in EU in 2000 and in Japan in 2008, Lantus® is available in over 130 countries worldwide.

A biosimilar of Lantus® from Eli Lilly and Company (Lilly) was launched in most European markets under the name Abasaglar® in 2015, and as Basaglar® in the US in December 2016. It has also been launched in Japan and in several other countries worldwide. In 2018, the FDA issued a complete response letter to Mylan for its biosimilar insulin glargine, which has been approved in Europe under the trade name of Semglee™ and is available in several European countries. In 2018, Merck & Co and Samsung Bioepis announced that they had abandoned global plans to commercialize Lusduna®, their biosimilar of Lantus®.

There are ongoing patent infringement proceedings in the US against Mylan. See Item 8. Financial Information B. Significant changes of this annual report for more information.

**Toujeo®**

Toujeo® (insulin glargine 300 units/mL) is a long-acting analog of human insulin, indicated for the treatment of diabetes mellitus in adults.

Toujeo® has been granted marketing authorization by the FDA (February 2015); the European Commission (April 2015); and the Ministry of Health, Labor and Welfare (J-MHLW) in Japan, where its approved brand name is Lantus® XR (June 2015). Toujeo® has now been launched in more than 40 countries.

Toujeo® is available in Toujeo® SoloSTAR®, a disposable prefilled pen which contains 450 units of insulin glargine and requires one third of the injection volume to deliver the same number of insulin units as Lantus® SoloSTAR®. In the US, since 2018, Toujeo® is also available in a disposable prefilled pen which contains 900 units of insulin glargine.

**Apidra®**

Apidra® (insulin glulisine) is a rapid-acting analog of human insulin, indicated for the treatment of diabetes mellitus in adults, for supplementary glycemic control. Apidra® has a more rapid

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onset and shorter duration of action than fast-acting human insulin and can be used in combination with long-acting insulins such as Toujeo® for supplementary glycemic control at mealtimes. Apidra® can be administered subcutaneously using syringes or specific pens including the Apidra® SoloSTAR® disposable pen. Apidra® is available in over 100 countries worldwide.

**Adlyxin®/Lyxumia®**

Adlyxin® or Lyxumia® (lixisenatide) is a once-daily injectable prandial GLP-1 receptor agonist and is indicated for the treatment of adults with type 2 diabetes to achieve glycemic control in combination with oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycemic control.

Lixisenatide was approved in the EU and in Japan in 2013 under the brand name of Lyxumia® and in the US in 2016 under the brand name of Adlyxin® . Lixisenatide is now marketed under the proprietary name Lyxumia® in more than 40 countries. Lixisenatide was in-licensed from Zealand Pharma A/S.

**Soliqua® 100/33 / Suliqua®**

Soliqua® 100/33 or Suliqua® is a once-daily fixed-ratio combination of insulin glargine 100 Units/mL, a long-acting analog of human insulin, and lixisenatide, a GLP-1 receptor agonist.

The FDA approved Soliqua® 100/33 in November 2016 for the treatment of adults with type 2 diabetes inadequately controlled on basal insulin (less than 60 units daily) or lixisenatide; and in February 2019, for patients uncontrolled on oral antidiabetic medicines. In January 2017, the European Commission granted marketing authorization in Europe for Suliqua® (the product s brand name in Europe) for use in combination with metformin for the treatment of adults with type 2 diabetes to improve glycemic control when this has not been provided by metformin alone or metformin combined with another oral glucose-lowering medicinal product or with basal insulin. In Europe, Suliqua® is available in two pens providing different dosing options. Suliqua® is approved in more than 30 countries and currently marketed in over 20.

**Admelog® / Insulin lispro Sanofi®**

Admelog® or Insulin lispro Sanofi® is a rapid-acting insulin similar to Humalog®, another insulin lispro 100 Units/mL. Admelog® was approved by the FDA in December 2017, and was also granted marketing authorization as a biosimilar (under the proprietary name Insulin lispro Sanofi®) by the European Commission in July 2017. It is used to improve blood sugar control in adults with Type 2 diabetes and adults and children (3 years and older) with Type 1 diabetes.

Admelog® comes in both vials and the SoloSTAR® pen, and was launched in the US and several European countries during 2018.

**Insuman®**

Insuman® (human insulin) is a range of insulin solutions and suspensions for injection and is indicated for diabetes patients when treatment with insulin is required. Human insulin is produced by recombinant DNA technology in Escherichia coli strains. Insuman® is supplied in vials, cartridges, and pre-filled disposable pens (SoloSTAR®). The Insuman® range is comprised of rapid-acting insulin solutions (Insuman® Rapid and Insuman® Infusat) that contain soluble insulin, an intermediate-acting insulin suspension (Insuman® Basal) that contains isophane insulin, and combinations of fast-acting and intermediate-acting insulins in various proportions (Insuman® Comb). Insuman® is principally sold in emerging markets.

**Integrated Care Solutions**

Sanofi and Verily Life Sciences LLC (formerly Google Life Sciences), an Alphabet company, announced in September 2016 the launch of Onduo, a joint venture created through Sanofi and Verily s diabetes-focused collaboration. Based in Cambridge, Massachusetts (United States), Onduo is a virtual care program with diabetes tools, coaching and clinical support. In 2018 Onduo started commercial pilots in several states in the US.

Sanofi, Sensile Medical and Verily Life Sciences LLC announced in June 2018 a joint development of an all-in-one pre-filled insulin patch pump, primarily to serve people living with type 2 diabetes. The alliance leverages Sanofi s expertise in patient-centered diabetes solutions and insulins, Sensile Medical s leadership in developing micro-pump technologies for medical use, and Verily s experience in micro-electronic integration and digital healthcare technology.

In France, Sanofi commercializes digital insulin titration solutions (under the names of Diabeo® and Insulia®), developed with Voluntis, a French company. Sanofi s digital titration solutions, embedded in a blood glucose meter (MyStarDoseCoach®) and a smartphone app (MyDoseCoach®), plus collaborations with Voluntis (including the Insulia® smartphone app), are being used by people with diabetes in ten pilot programs and some active commercial launches around the world. These tools use patients daily blood sugar measurements to recommend a dose that is aligned with a blood sugar target agreed with their physician.

*g) Cardiovascular Diseases*

**Praluent®**

Praluent® (alirocumab) is a human monoclonal antibody (mAb) for self-administered injection every two weeks that blocks the interaction of proprotein convertase subtilisin/kexin type 9 (PCSK9) with low-density lipoprotein (LDL) receptors, increasing the recycling of LDL receptors and reducing LDL cholesterol levels.

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ITEM 4. INFORMATION ON THE COMPANY

Praluent® is indicated as an adjunct to diet and maximally tolerated statin therapy in certain adult patients with uncontrolled LDL cholesterol.

Praluent® has been approved in more than 60 countries worldwide, including the US (in 2015), Japan (in 2016), Canada, Switzerland, Mexico and Brazil, as well as the European Union (in 2015).

In 2018, the FDA approved a Praluent® label update for some patients currently requiring LDL apheresis therapy. The FDA has also accepted a supplemental Biologics License Application (sBLA) which outlines a proposed update to the Prescribing Information to include the effect of Praluent® in reducing the overall risk of major adverse cardiovascular events with a target action date of April 28, 2019. The sBLA is supported by data from the ODYSSEY OUTCOMES trial that assessed the effect of Praluent® on cardiovascular morbidity and mortality within a post-acute coronary syndrome (ACS) patient population. In early February 2019, the European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion for Praluent® recommending a new indication to reduce cardiovascular risk in adults with established atherosclerotic cardiovascular disease.

On February 11, 2019, Sanofi and Regeneron announced that Praluent® will be made available at a new reduced US list price beginning in early March 2019. The new lower-priced Praluent® is expected to result in lower patient out-of-pocket costs and represents another step in Sanofi s efforts to help improve patient affordability and access.

Praluent® is developed and commercialized in collaboration with Regeneron Pharmaceuticals, Inc. For additional information on the commercialization of this product, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Regeneron .

There are ongoing patent infringement proceedings in several countries initiated against us and Regeneron Pharmaceuticals, Inc. by Amgen relating to Praluent® in which Amgen has requested injunctive reliefs. See Note D.22.b) to the consolidated financial statements included at Item 18 of this annual report.

**Multaq®**

Multaq® (dronedarone) is an oral multichannel blocker with anti-arrhythmic properties for prevention of atrial fibrillation recurrences in certain patients with a history of paroxysmal or persistent atrial fibrillation. Multaq® was approved in the US and in the EU in 2009. Multaq® is available in about 35 countries.

*h) Established Prescription Products*

**Plavix® / Iscover ®**

Plavix® or Iscover® (clopidogrel bisulfate), a platelet adenosine diphosphate (ADP) receptor antagonist with a rapid onset of action that selectively inhibits platelet aggregation induced by ADP, is indicated for the prevention of atherothrombotic events in

patients with a history of recent myocardial infarction (MI), recent ischemic stroke or established peripheral arterial disease (PAD)m and for patients with acute coronary syndrome (ACS).

Plavix® is also indicated in combination with acetylsalicylic acid (ASA) for the prevention of atherothrombotic and thromboembolic events in atrial fibrillation, including stroke.

CoPlavix® / DuoPlavin®, a fixed-dose combination of clopidogrel bisulfate and ASA, is indicated for the prevention of atherothrombotic events in adult patients with acute coronary syndrome who are already taking both clopidogrel and ASA.

Plavix® or Iscover® are marketed in more than 80 countries. For additional information on the commercialization of these products, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Bristol-Myers Squibb .

A number of generics have been launched in Europe, the US, Japan and other markets.

Sanofi is involved in Plavix® product litigation in the US. See Note D.22.a) to our consolidated financial statements, included at Item 18 of this annual report.

**Lovenox® / Clexane®**

Lovenox® or Clexane® (enoxaparin sodium) is a low molecular weight heparin (LMWH). Its comprehensive clinical dossier has demonstrated a favorable risk-benefit ratio, notably in the prophylaxis and treatment of venous thromboembolism and in the treatment of acute coronary syndrome.

Lovenox® or Clexane® is marketed in more than 100 countries. Enoxaparin generics are available in the US, and biosimilar enoxaparin products have gradually become available across various European countries since 2016: Poland, Germany, UK, Italy, Spain, France and Austria.

**Aprovel® / Avapro® / Karvea®**

Aprovel® or Avapro ® or Karvea® (irbesartan) is an angiotensin II receptor antagonist. We also market CoAprovel® / Avalide® / Karvezide®, a fixed-dose combination of irbesartan and the diuretic hydrochlorothiazide.

Aprovel® is indicated as a first-line treatment for hypertension and for the treatment of nephropathy in hypertensive patients with type 2 diabetes. CoAprovel® is indicated for patients whose blood pressure is not adequately controlled with a monotherapy, but also as initial therapy in patients at high risk or with markedly high baseline blood pressure or who are likely to need multiple drugs to achieve their blood pressure goals. A fixed-dose combination with amlodipine (Aprovasc®) has been launched in several emerging market countries.

Aprovel® and CoAprovel® are marketed in more than 80 countries. For additional information on the commercialization of this product, see Item 5. Financial Presentation of Alliances Alliance Arrangements with Bristol-Myers Squibb . In Japan, the product is licensed to Shionogi Co. Ltd and BMS KK. BMS KK has sublicensed the agreement to Dainippon Pharma Co. Ltd.

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A number of generics have been launched in Europe, the US and other markets.

**Renagel® and Renvela®**

Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate) are oral phosphate binders used by chronic kidney disease (CKD) patients on dialysis as well as late stage CKD patients in Europe to treat hyperphosphatemia, or elevated phosphorus levels, which is associated with heart and bone disease. Renvela® is a second-generation buffered phosphate binder.

Renagel® and Renvela® are marketed in more than 85 countries. In Japan and several Pacific Rim countries, Renagel® is marketed by Chugai Pharmaceutical Co., Ltd and its sublicensee, Kyowa Hakko Kirin Co., Ltd.

In the US, several sevelamer carbonate tablets generics and two sevelamer carbonate powder generics have been approved. Sanofi has launched authorized generics of Renvela® in the US market, in both tablet form (October 2017) and powder form (in January 2018). Generics of sevelamer carbonate are currently marketed in various European countries. As of December 31, 2018, there are no generics of sevelamer hydrochloride approved in either Europe or in the US. We anticipate the first approvals of generics of sevelamer hydrochloride in the US in 2019.

**Allegra® / Telfast®**

Allegra® or Telfast® (fexofenadine hydrochloride) is a long-lasting (12- and 24-hour) non-sedating anti-histamine for the treatment of seasonal allergic rhinitis (hay fever) and uncomplicated hives. We also market Allegra-D® 12 Hour and Allegra-D® 24 Hour, anti-histamine/decongestant combination products with an extended-release decongestant. This combination is marketed in Japan under the Dellegra® brand name.

Allegra® / Telfast® is marketed in approximately 80 countries. Generics of most forms of Allegra® / Telfast® have been approved in most markets.

The Allegra® family is also available for over-the-counter (OTC) use. See B.3. Consumer Healthcare below.

**Stilnox® / Ambien® / Myslee®**

Stilnox® (zolpidem tartrate) is indicated for the short-term treatment of insomnia. Stilnox® is marketed in over 100 countries. It is available under the brand name Ambien® / Ambien®CR in the US and Myslee® in Japan, where it is co-promoted jointly with Astellas.

Stilnox® and Ambien CR® are subject to generic competition in most markets, including the US, Europe and Japan.

**Synvisc® / Synvisc-One®**

Synvisc® and Synvisc-One® (hylan G-F 20) are viscosupplements used to treat pain associated with osteoarthritis. Synvisc® is indicated for the treatment of pain associated with osteoarthritis of the knee, hip, ankle, and shoulder joint in countries that have adopted CE marking, and for pain due to knee osteoarthritis in the US. Synvisc-One® is approved for use in patients with osteoarthritis of the knee in the US and countries that require CE marking.

Synvisc® and Synvisc-One® are administered directly into the intra-articular space of the joint to temporarily restore synovial fluid. Synvisc® and Synvisc-One® are marketed in over 60 countries.

**Depakine®**

Depakine® (sodium valproate) is a broad-spectrum anti-epileptic that has been prescribed for more than 40 years and remains a reference treatment for epilepsy worldwide. Depakine® is also a mood stabilizer, registered in the treatment of manic episodes associated with bipolar disorder[3].

Depakine® is marketed in over 100 countries. We hold no rights to Depakine® in the US, and sodium valproate generics are available in most markets.

Sanofi is involved in product litigation related to Depakine®. See Note D.22.a) to the consolidated financial statements included at Item 18 of this annual report.

*i) Generics*

On September 30, 2018, we completed the divestment of our European generics business Zentiva to Advent International, a US global private equity firm. We have retained our presence in Generics in Emerging Markets, especially in Latin America with two top-of-mind brands Medley (Brazil) and Genfar (Colombia, Peru, Ecuador and Central America) and also in Russia, South Africa and Turkey.

**B.3. Consumer healthcare**

Our CHC sales are supported by a range of products including the following brands:

*Allergy, Cough & Cold*

Allegra® is a range of fexofenadine HCl based products. Fexofenadine is an anti-histamine for relief from allergy symptoms including sneezing, runny nose, itchy nose or throat, and itchy, watery eyes. Allegra® OTC is sold in more than 80 countries across the world.



*(3) In some countries this indication is branded differently (e.g. Depakote® in France).*

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Mucosolvan® is a cough brand with many different formulations. It contains the mucoactive agent ambroxol; this stimulates synthesis and release of surfactant. It is sold in various countries in Europe and Asia and in Russia.

*Pain*

Doliprane® offers a range of paracetamol/acetaminophen-based products for pain and fever with a wide range of dosage options and pharmaceutical forms, and is sold mainly in France and various African countries.

The Buscopan® range (hyoscine butylbromide) has an antispasmodic action that specifically targets the source of abdominal pain and discomfort. It is sold across the globe.

*Digestive*

Dulcolax® products offer a range of constipation solutions from predictable overnight relief to comfortable natural-feeling relief. The products are sold in over 80 countries. Dulcolax® tablets contain the active ingredient bisacodyl, which works directly on the colon to produce a bowel movement.

Enterogermina® is a probiotic indicated for the maintenance and restoration of intestinal flora in the treatment of acute or chronic intestinal disorders. Enterogermina® is sold primarily in Europe and in Latin America and parts of Asia.

Essentiale® is a natural soybean remedy to improve liver health. It is composed of essential phospholipids extracted from highly purified soya and contains a high percentage of phosphatidylcholine, a major component of the cell membrane. Essentiale® is used in fatty liver disease and is sold mainly in Russia, Eastern Europe, various countries in Southeast Asia, and China.

Zantac® products are for the prevention and relief of heartburn. Zantac® is sold in the US and Canada.

*Nutritionals*

Nutritionals include a range of products to maintain general health, provide immune system support, or supplement vitamin deficiencies. These products help manage energy, stress, sleep and anxiety, and include a number of brands across the globe including Nature s Own® in Australia to improve and maintain health, Pharmaton® (mainly

in Europe and Latin America), and Magne B6® in Europe.

*Other*

Gold Bond® offers a broad range of products including daily body lotions, anti-itch products, moisturizing and soothing lotions, body and foot creams and powders for eczema. Gold Bond® is only sold in the US.

**B.4. Vaccine products**

Sanofi Pasteur, the Vaccines division of Sanofi, is a world leader in the vaccine industry and a key supplier of life-saving vaccines all over the world and in publicly funded international markets such as UNICEF, the Pan American Health Organization (PAHO) and the Global Alliance for Vaccines and Immunization (GAVI).

The Sanofi Pasteur portfolio includes the following vaccines:

*a) Poliomyelitis, Pertussis and Hib pediatric vaccines*

Sanofi Pasteur is one of the key players in pediatric vaccines in both developed and emerging markets, with a broad portfolio of standalone and combination vaccines protecting against up to six diseases in a single injection. Due to the diversity of immunization schedules throughout the world, vaccines vary in composition according to regional specificities.

Tetraxim®, a pediatric combination vaccine protecting against diphtheria, tetanus, pertussis and poliomyelitis (polio), was first marketed in 1998. To date, the vaccine has been launched in close to 90 countries outside the US.

Pentaxim®, a pediatric combination vaccine protecting against diphtheria, tetanus, pertussis, polio and Hemophilus influenzae type b (Hib), was first marketed in 1997. To date, the vaccine has been launched in more than 100 countries outside the US. In most European, Latin American and Middle Eastern markets, Pentaxim® is being gradually replaced by Hexaxim®.

Hexaxim® / Hexyon® / Hexacima® is a fully liquid, ready-to-use 6-in-1 (hexavalent) pediatric vaccine that provides protection against diphtheria, tetanus, pertussis, polio, Hib and hepatitis B. In December 2014 the WHO granted prequalification status to Hexaxim® in a one-dose vial presentation. Hexaxim® is the only combination vaccine including acellular pertussis (acP) and inactivated polio vaccines (IPV) currently prequalified by the WHO. Hexaxim® is now available in 100 countries outside the US.

Pentacel®, a pediatric combination vaccine protecting against diphtheria, tetanus, pertussis, polio and Hib, was launched in the US in 2008.

Shan5® is a 5-in-1 (whole-cell pertussis based) vaccine protecting against five diseases (diphtheria, tetanus, pertussis, polio and hepatitis B). It regained WHO pre-qualification (which provides access to the product in low-income countries) in May 2014, and was launched in the Indian market in the last quarter of 2014. Shan5® has been retained for the GAVI/UNICEF tender for the 2017-2019 period and in Thailand through local tender.

Act HiB® is a standalone vaccine protecting against Hib, and is mainly distributed in the US, Japan and China in conjunction with pertussis combination vaccines that do not contain the Hib valence.

Polio vaccines: Sanofi Pasteur is a leading provider of polio vaccines and has been a partner of the Global Polio Eradication Initiative (GPEI) for over 30 years, with more than 13 billion doses of oral polio vaccines (OPV) delivered during that time.

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Over the 2014-2017 period, Sanofi Pasteur provided 130 million doses of inactivated polio vaccine (IPV) to support the WHO Polio End Game strategy for the 73 world poorest countries, representing 80% of the total IPV volumes used in those countries. On October 1, 2018, the ShanIPV™ 5-dose vial received WHO pre-qualification.

Vaxelis®: In 2017, Sanofi Pasteur (in partnership with Merck) made its PR5i hexavalent combination vaccine protecting against diphtheria, tetanus, pertussis, polio, Hib and hepatitis B available on the market under the trademark Vaxelis®. This vaccine is approved and distributed in various EU countries and was approved by the FDA in December 2018. Sanofi and Merck are working to maximize production to allow for a sustainable supply to meet anticipated US demand. Commercial supply will not be available in the US prior to 2020.

*b) Influenza vaccines*

Sanofi Pasteur is a world leader in the production and marketing of influenza vaccines.

Sanofi Pasteur has several distinct vaccines that are sold globally to meet growing demand for influenza vaccines and innovative solutions in the market.

Fluzone® Quadrivalent is a quadrivalent inactivated influenza vaccine, produced in the US, containing two type A antigens and two type B antigens in order to provide increased protection against more circulating strains of influenza viruses. Fluzone® Quadrivalent/FluQuadri® is available in 27 countries (including the US) for children aged over six months, adolescents and adults. Fluzone® 0.5ml QIV is the currently-licensed standard dose (15 µg/strain) quadrivalent influenza vaccine for ages 3 years and older. A half dose (0.25mL or 7.5 µg) is licensed for children aged 6-35 months.In January 2019, the FDA has approved the use of the 0.5 mL dose to include children age 6 through 35 months.

Fluzone® High-Dose vaccine, launched in the US in 2010, was specifically designed to provide greater protection against influenza in people aged 65 and older. Fluzone® High-Dose is sold in the US, Canada and Australia.

Flublok® is a quadrivalent influenza vaccine for adults age 18 and older. It is the only recombinant protein-based influenza vaccine approved by the FDA. Flublok® is currently sold in the US, with global expansion planned over the next several years.

Vaxigrip® is licensed in over 150 countries globally for people aged six months and older. It is a trivalent influenza vaccine, containing two antigens against type A influenza viruses and one antigen against type B influenza viruses.

Vaxigrip® Tetra is the quadrivalent (QIV) version of Vaxigrip®, including 2 antigens against A strains of influenza viruses and 2 antigens against B strains. Compared to the trivalent influenza vaccine, the addition of a second B strain to the vaccine provides increased protection against more influenza virus circulating strains. This quadrivalent formulation, VaxigripTetra®, was licensed in 2016 and has been launched in more than 40 countries since 2017.

*c) Adult booster vaccines*

Adacel® is the first trivalent adolescent and adult booster offering protection against diphtheria, tetanus and pertussis. It also reduces exposure for infants who are not immunized or only partially immunized. It is available in 40 countries (including the United States, and otherwise mostly in Europe and Latin America).

Repevax® / Adacel®-Polio is a combination vaccine that provides protection against diphtheria, tetanus, pertussis and polio. It is currently marketed in 20 countries, with a strong focus on European markets (France, Germany, UK).

*d) Meningitis vaccines*

Menactra® is the first quadrivalent conjugate vaccine against meningococcal meningitis (serogroups: A, C, Y, and W-135), one of the deadliest forms of meningitis in the world. Menactra® is indicated for people aged 9 months through 55 years in the US, Canada, several Middle Eastern countries including Saudi Arabia, and numerous other countries in all regions of the world. It is a strong leader in the meningitis quadrivalent market in the US, and is licensed in 70 countries worldwide. More than 100 million doses of Menactra® have been distributed since launch. It is the only fully liquid (no reconstitution needed) meningitis quadrivalent conjugated vaccine available in the market.

*e) Travel and endemics vaccines*

Sanofi Pasteur provides a wide range of travel and endemics vaccines including hepatitis A, typhoid, cholera, yellow fever, Japanese encephalitis and dengue, as well as rabies vaccines and immunoglobulins. These products are used in endemic settings in the developing world and are the foundation for important partnerships with governments and organizations such as UNICEF. They are also used by travelers and military personnel in industrialized countries and in endemic areas.

Focus on Dengue:

Dengvaxia® is licensed in 19 countries. The Philippines FDA revoked the Dengvaxia® license in early 2019 and Sanofi has filed a motion for reconsideration which has been denied. For more information, please see Item 8. Financial information Information on legal or arbitration proceedings . In 2018, the European Commission granted marketing authorization for Dengvaxia® to prevent dengue disease in individuals 9-45 years of age with a documented prior dengue infection who are living in endemic areas, and the FDA granted Dengvaxia® a priority review.

In most countries where Dengvaxia® is approved, the indication is for individuals aged 9 years or older living in a dengue-endemic area. Based on new results from a supplemental analysis of the long term clinical data on the vaccine reported in November 2017, Sanofi Pasteur is recommending a label update

for Dengvaxia® to target its use at people with prior dengue infection: the review process is ongoing in three countries, is expected to start soon in another country and revised label content has been agreed in all other relevant countries.

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The WHO has recognized the public health value of introducing Dengvaxia® in public immunization programs. In September 2018, the WHO issued a recommendation indicating a preference for a pre-vaccination screening strategy to target those at risk of re-infection for protection, and increase the potential of such programs to reduce the overall burden of dengue and severe dengue. As part of our long-standing commitment to ensure access to vaccination in the global effort to reduce the dengue burden, we are pursuing potential collaborations with experienced dengue test manufacturers in order to develop a new, rapid point-of-care dengue test. The aim of the new test is to broaden access to vaccination for those with prior infection who could benefit from the prevention of secondary infections with dengue, which carry a higher risk of being severe.

**B.5. GLOBAL RESEARCH & DEVELOPMENT**

In 2018 Sanofi engaged in a strong reshaping of its R&D strategy, strengthening the development of innovative products that promise to substantially elevate the standard of care for patients, and prioritizing the therapeutic areas where the patient need is most urgent and where the scientific and medical landscape is richest with opportunity.

R&D is leveraging the investments made a few years ago to establish competency in several therapeutic modalities, going beyond small molecules and conventional monoclonal antibodies, to produce differentiated molecules that tackle targets in novel and innovative ways. Besides the expansions of complex antibodies such as bi or tri specifics and the addition of nanobodies with the integration of the Ablynx platform, Sanofi has made important steps forward in genomic medicines. This includes enhancements to our internal capabilities in gene therapy based on the AAV (adeno-associated vectors) platform, as well as, new collaborations in virus based gene therapy, zinc finger based genome editing and mRNA therapeutics.

In development, sustained efforts are being made to accelerate the pace of delivery for patients, adopting a quick win, fast-fail approach that is underpinned by streamlined governance and pushing decision-making downward with strong team empowerment.

In the long term the aspiration is that roughly 80% of the Sanofi portfolio will consist of molecules with first-in-class or truly differentiated best-in-class potential, with two thirds of biologics compounds and two thirds of the pipeline directly derived from Sanofi internal research.

*B.5.1. Pharmaceuticals*

**B.5.1.1. Organization**

Our Global R&D organization is committed to responding to the real needs of patients by providing them with safe, cost-effective and appropriate therapeutic solutions, improving their access to treatment and delivering better health outcomes. In offering new solutions to patients, it is vital to understand the complexity of

human diseases, to sustain innovation and to foster scientific excellence without losing sight of the need for operational efficiency.

To meet these challenges, Sanofi R&D has evolved towards an integrated organization encompassing a wide range of therapeutic areas aligned with the Global Business Units (GBUs), which are dedicated to supporting our commercial operations and reflect our strengths and expertise as well as the most pressing health issues.

For Pharmaceuticals, six therapeutic areas (TAs) have been rolled out:

- Diabetes and Cardiovascular
- Oncology
- Immunology & Inflammation
- Multiple Sclerosis and Neurology
- Rare Blood Disorders
- Rare Diseases

These TAs drive a portfolio of R&D projects, ensuring a strategically coherent approach and flawless implementation.

Each TA has its own experts who are responsible for analyzing medical needs, defining project strategy and development plans, and leading the Global Project Teams.

Our R&D Operations department handles all operational activities and delivers effective development through integrated, collaborative project teams. Those teams harness high caliber functional expertise and the most appropriate technologies across chemical, biological and pharmaceuticals operations, translational medicine and early development, and clinical sciences.

In Research, a dedicated, integrated platform working across multiple disease areas and methods drives collaboration with internal and external partners to translate human biology research and state-of-the art technologies and processes into novel drug targets and world-class safe and effective drugs.

Sanofi s R&D operations are concentrated in three major hubs: North America, Germany and France. These hubs help build our scientific intelligence network and facilitate connections and knowledge-sharing between in-house scientists, and with external partners and scientific communities, in order to accelerate our research activities.

**B.5.1.2. Governance**

Global Project Teams (GPTs) are responsible for developing project strategy and driving the execution of projects through functional sub-teams. GPTs are led by a Global Project Head (GPH) who works in collaboration with a Project Manager (PM), and are built around core functional team members representing each department collaborating in the development project.

Various committees assess product and project development across the R&D value chain, carry out in-depth scientific review, make go and no-go decisions and determine portfolio priorities.

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The Research Working Group (RWG) tracks progress on research programs, and endorses entry into preclinical and the path to the First in Human phase (Phase I).

The Benefit-Risk Assessment Committee (BRAC) reviews the preclinical and clinical data before dossier submission.

The Development Working Group (DWG) endorses the path to Proof of Concept (POC), generally before Phase I, and tracks the development of products all along the value chain. This group is also responsible for the portfolio prioritization exercise.

The Integrated Development and Commercialization Council (IDCC) gives prior input to proof of clinical and commercial concept criteria, and endorses go to late development (Phase III start) and go to file.

The clinical portfolio is the result of decisions taken by these committees during their reviews, plus compounds entering the portfolio from the discovery phase or from third parties via acquisition, collaboration or alliances.

As described at Item 3. Key Information D. Risk Factors Risks Relating to Our Business research and development efforts may not succeed in adequately renewing the product portfolio and Risks Relating to the Group Structure and Strategy We may fail to successfully identify external business opportunities or realize the anticipated benefits from our strategic investments , our product development efforts are subject to the risks and uncertainties inherent in any new product development program.

**B.5.1.3. Products**

For 2018, the main events related to the pharmaceuticals portfolio were:

**Regulatory Approvals:**

In 2018, Sanofi obtained regulatory approval for caplacizumab (Cablivi®) in Europe and the US for the treatment of acquired thrombotic thrombocytopenic purpura and cemiplimab (Libtayo®) in the US for the treatment of cutaneous squamous cell carcinoma. Dupilumab (Dupixent®) was also approved in the US for asthma in adults and adolescents (12 to 17 years old), and for atopic dermatitis (adults) in Japan.

**Regulatory Submissions:**

- sotaglifozin (Zinquista ) was submitted for type I diabetes in Europe and the US;

cemiplimab (Libtayo®) was submitted for the treatment of cutaneous squamous cell carcinoma in Europe and the US (now approved in the US);

dupilumab (Dupixent®) was submitted in the US for the treatment of chronic rhinosinusitis with nasal polyposis. It was also submitted for the treatment of atopic dermatitis (adolescents 12 to 17 years old) in Europe and the US;

Praluent® was submitted in Europe and the US in the reduction of cardiovascular events after acute coronary syndrome.

**Phase III starts**

In 2018, the following products moved into Phase III:

fitusiran, indicated for the treatment of:

hemophilia A/B in adults;

dupilumab (Dupixent®) for the treatment of:

eosinophilic esophagitis;

sarilumab (Kevzara®) for the treatment of:

giant cell arteritis;

polymyalgia rheumatica;

isatuximab:

in combination with lenalidomide, bortezomib, and dexamethasone (VRd) for induction treatment in patients with newly diagnosed multiple myeloma who are eligible for transplant;

sotaglifozin (Zinquista ) for the treatment of:

worsening heart failure.

**Phase II starts**

In 2018, the following products moved into Phase II:

SAR440340, an anti-IL33 monoclonal antibody for the treatment of :

asthma;

chronic obstructive pulmonary disease (COPD);

atopic dermatitis;

dupilumab (Dupixent®) as an adjunct therapy for:

peanut allergy;

grass allergy;

sarilumab (Kevzara®) for the treatment of:

systemic juvenile idiopathic arthritis (sJiA);

isatuximab,

in combination with cemiplimab for the treatment of relapsed refractory multiple myeloma (RRMM) and solid tumors;

In combination with atezolizumab for the treatment of solid tumors and advanced malignancies.

**Phase I Starts**

In 2018, the following products entered Phase I:

SAR441344, an anti-CD40L mAb indicated for the treatment of multiple sclerosis;

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SAR440234, a T-Cell engaging bispecific (CD3/CD123) antibody for the treatment of acute myeloid leukemia;

SAR442720, an SHP2 inhibitor for the treatment of advanced non-small cell lung cancer;

SAR 441000, a cytokine mRNA for the treatment of melanoma.

**Entries to the Portfolio**

In 2018, the following products entered the R&D Portfolio:

From our deal with Bioverativ:

Sutimlimab (BIVV009), an anti-complement C1s mAb in Phase III for the treatment of cold agglutin disease and Phase I for the treatment of idiopathic thrombocytopenic purpura;
BIVV001, an investigational von Willebrand factor (VWF)-independent factor VIII therapy in Phase I for the treatment of hemophilia A;

ST400, a zinc finger nuclease (ZFN) gene editing technology in Phase I for the treatment of ß thalassemia;

BIVV003, a zinc finger nuclease (ZFN) gene editing technology for the treatment of sickle cell disease.

From our collaboration with Regulus: SAR339375, an anti-miR21 RNA in Phase II for the treatment of Alport syndrome.

From our deal with Denali: SAR443060 (DNL747), an RIPK1 inhibitor in Phase I for the treatment of amyotrophic lateral sclerosis and Alzheimer s disease.

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The clinical portfolio for new products as of March 8, 2019 can be summarized as follows; where several indications are being developed for one product, each indication is regarded as a separate project and specified individually in the table below.

For more information on Dupixent®, Kevzara®, Praluent®, Aubagio® , Cerdelga® and Lemtrada®, see also Item 4. Information on the Company B. Business Overview B.2. Main Pharmaceutical Products .

| | Phase I | Phase II | Phase III/registration |
|---|---|---|---|
| **Diabetes & Cardiovascular** | | | SAR341402 (T1 & T2 diabetes) |
| | | | sotagliflozin (T1 & T2 diabetes) |
| | | | sotagliflozin (WHF[a] in diabetes) |
| | | | efpeglenatide (T2 diabetes) |
| | | | Praluent® (LDL-C reduction HoFH[b]) |
| | | | Praluent® (LDL-C reduction pediatric) |
| | | | Praluent® (CV events after ACS[c]) |
| **Oncology** | SAR439459 | cemiplimab (BCC[d]) | isatuximab (3L RRMM[e] ICARIA) |
| | SAR438859 | isatuximab+cemiplimab (RRMM[f]) | isatuximab (1-3L RRMM[g] IKEMA) |
| | SAR441000 | | |
| | SAR442720 | isatuximab+cemiplimab (advanced malignancies[j]) | isatuximab (1L NDMM[h] Ti IMROZ) |
| | SAR440234 | isatuximab+cemiplimab (lymphoma) | isatuximab (1L NDMM[h] Te GMMG) |
| | SAR408701 | | |

| | | | |
|---|---|---|---|
| | | isatuximab+atezolizumab (advanced malignancies | cemiplimab (2L CC[i]) |
| | | | cemiplimab (1L NSCLC[j]) |
| | | isatuximab+atezolizumab | |
| | | (solid tumours)) | cemiplimab + chemotherapy (1LNSCLC [j]) |
| **Rare Blood Disorders** | BIVV003 (Sickle Cell disease) | | fitusiran (Hemophilia A&B) |
| | ST400 (ß thalassemia) | | sutimlimab BIVV009 (Cold Agglutinin Disease ) |
| | sutimlimab (ITP[k]) | | |
| | BIVV001 (Hemophilia A) | | |
| **Immunology &** | SAR441344 (Multiple Sclerosis) | Kevzara® (pcJiA[l]) | Dupixent® (asthma, 6-11 years) |
| **Inflammation** | | Kevzara® (sJiA[m]) | Dupixent® (Atopic Dermatitis adolescent & pediatric) |
| | | dupilumab (peanut allergy Pediatric) | dupilumab (EE[n]) |
| | | dupilumab (grass immunotherapy) | dupilumab (Nasal Polyposis) |
| | | | Kevzara® (Giant Cell Arteritis) |
| | | SAR440340 (Asthma) | |
| | | SAR440340 (COPD[o]) | Kevzara® (Polymyalgia Rheumatica) |
| | | SAR440340 (Atopic Dermatitis) | |
| | | SAR156597 (Systemic Scleroderma) | |
| **Multiple Sclerosis** | SAR443060 (ALS and AD[p]) | venglustat (GPD[q]) | Aubagio® (RMS pediatric.[r]) |
| **Neurology** | | SAR422459 (Stargardt) | Lemtrada® (RRMS pediatric.[s]) |
| | SAR442168 (Multiple Sclerosis) | | |
| **Rare diseases** | | olipudase alfa (Niemann Pick) | Avalglocosidase alfa (Pompe) |
| | | | venglustat (ADPKD[t]) |
| | | venglustat (Gaucher type3) | Cerdelga® (Gaucher Type I switching from ERT pediatric) |
| | | venglustat (Fabry) | |
| | | SAR339375 (Alport syndrome) | |

*(a) Worsening Heart Failure*

*(b) Homozygous Familial Hypercholesterolemia*

*(c) Acute Coronary Syndrome*

*(d) Basal Cell Carcinoma*

*(e) 3rd Line Relapsing and/or Refractory Multiple Myeloma*

*(f) Relapsing and/or Refractory Multiple Myeloma*

*(g) 1st-3rd Line Relapsing and/or Refractory Multiple Myeloma*

*(h) 1st Line Newly Diagnosed Multiple Myeloma*

*(i) 2nd Line Cervical Cancer*

*(j) 1st Line Non-Small Cell Lung Cancer*

*(k) Idiopathic Thrombocytopenic Purpura*

*(l) Polyarticular Juvenile Idiopathic Arthritis*

*(m) Systemic Juvenile Idiopathic Arthritis*

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*(n) Eosinophilic Esophagitis*

*(o) Chronic Obstructive Pulmonary Disease*

*(p) Amyotrophic Lateral Sclerosis and Alzheimer s disease*

*(q) Gaucher related Parkinson s Disease*

*(r) Relapsing Multiple Sclerosis pediatric*

*(s) Relapsing Remitting Multiple Sclerosis pediatric*

*(t) Autosomal Dominant Polycystic Kidney Disease*

Phase I studies are the first studies performed in humans, who are mainly healthy volunteers, except for studies in oncology, where Phase I studies are performed in patients. Their main objective is to assess the tolerability, the pharmacokinetic profile (the way the product is distributed and metabolized in the body and the manner by which it is eliminated) and where possible the pharmacodynamic profiles of the new drug (i.e. how the product may react on some receptors).

Phase II studies are early controlled studies in a limited number of patients under closely monitored conditions to show efficacy and short-term safety and to determine the dose and regimen for Phase III studies.

Phase III studies have the primary objective of demonstrating or confirming the therapeutic benefit and the safety of the new drug in the intended indication and population. They are designed to provide an adequate basis for registration.

a) Diabetes & Cardiovascular

Diabetes

**Sotagliflozin (SAR439954)**, an oral dual inhibitor of SGLT1/2, is in-licensed from Lexicon. Results of the Phase III program in type 1 diabetes were released in 2017. An NDA for sotagliflozin was filed in the US and EU in type 1

diabetes in March 2018. The European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion in March 2019. A large Phase III program including a Cardiovascular Outcome Trial is currently ongoing to investigate the use of sotagliflozin for the treatment of type 2 diabetes. A Phase III study in patients with worsening heart failure was initiated in the second quarter of 2018.

**Efpeglenatide (SAR439977)** is a long-acting GLP1 receptor agonist derived from our license agreement with Hanmi Pharmaceuticals. A Phase III development program in type 2 diabetes is ongoing. A cardiovascular outcome study, AMPLITUDE-O, evaluating efpeglenatide was initiated in the second quarter of 2018.

**Rapid Acting Insulin (SAR341402)** is in Phase III for the treatment of type 1 and type 2 diabetes.

**Admelog® (a rapid acting insulin SAR342434)** was approved in the US in October 2018.

Products removed from the portfolio in 2018

**SAR425899,** a dual GLP-1/glucagon receptors was terminated in November 2018

**SAR438335,** a dual GLP-1/GIP receptor agonists was terminated in November 2018

Cardiovascular

**Praluent®** (collaboration with Regeneron)**:** The results of the ODYSSEY OUTCOMES study, which showed Praluent® significantly reduced the risk of major adverse cardiovascular events in patients who had suffered a recent acute coronary syndrome, were submitted to the FDA and EMA in the second quarter of 2018. A Praluent® treatment regimen (administration every 4 weeks) was approved in Japan in Nov 2018. A study evaluating Praluent® in children with heterozygous familial hypercholesterolemia (HeFH) was initiated.

Products removed from the portfolio in 2018

**SAR407899**, a novel Rho-kinase inhibitor, was discontinued in Nov 2018

**SAR247799**, a S1P1 agonist, was discontinued in Nov 2018.

Further to the termination in January 2019 of the agreement with MyoKardia to jointly develop small-molecule therapeutics targeting genetic mutations associated with certain heart diseases, the following two projects were removed from the portfolio:

**SAR439152** (Mavacamten), a myosin inhibitor;

**SAR440181**, an allosteric activator of cardiac myosin ATPase .

b) Oncology

Products in development

**Isatuximab (SAR650984)**, in-licensed from ImmunoGen, is a monoclonal antibody which selectively binds to CD38, a cell surface antigen expressed in multiple myeloma cancer cells, and other hematological malignancies. Isatuximab kills tumor cells via multiple biological mechanisms including:

antibody-dependent cellular-mediated cytotoxicity (ADCC);

complement-dependent cytotoxicity (CDC);

antibody-dependent cellular phagocytosis (ADCP); and

direct induction of apoptosis (pro-apoptosis) without cross-linking.

Isatuximab also inhibits CD38 ectoenzymatic activity and the expansion of immune-suppressive regulatory T cells and myeloid derived suppressor cells.

The program is currently in Phase III clinical development, with multiple studies ongoing in multiple myeloma (MM), including four pivotal Phase III trials.

The Phase III **ICARIA-MM** trial is a randomized, open label, multicenter study comparing isatuximab in combination with

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pomalidomide and dexamethasone against pomalidomide and dexamethasone in patients with relapsed and refractory multiple myeloma.

The Phase III **IKEMA** trial is a randomized, open label, multicenter study assessing the clinical benefit of isatuximab combined with carfilzomib (Kyprolis®) and dexamethasone versus carfilzomib with dexamethasone in patients with relapsed and/or refractory multiple myeloma previously treated with one to three prior lines.

The Phase III **IMROZ** trial is a randomized, open-label, multicenter study assessing the clinical benefit of isatuximab in combination with bortezomib (Velcade®), lenalidomide (Revlimid®) and dexamethasone versus bortezomib, lenalidomide and dexamethasone in patients with newly diagnosed multiple myeloma not eligible for transplant.

The Phase III **GMMG HD7** trial is a randomized, open-label, multicenter study assessing the clinical benefit of isatuximab in combination with lenalidomide, bortezomib, and dexamethasone (RVd) for induction and with lenalidomide for maintenance in patients with newly diagnosed multiple myeloma. This study is conducted in collaboration with the German-speaking Myeloma Multicenter Group (GMMG) and was initiated in the last quarter of 2018.

A Phase I study in combination with cyclophosphamide, bortezomib and dexamethasone is ongoing in the treatment of adult patients newly diagnosed with multiple myeloma not eligible for transplant.

A Phase I/II study in combination with cemiplimab in the treatment of patients suffering from RRMM (relapsing and/or refractory multiple myeloma) was initiated in 2018.

In addition, early development studies in solid tumors are ongoing.

- A Phase I/II study with isatuximab in combination with cemiplimab in patients with advanced malignancies (prostate and non-small cell lung cancer),

- A Phase II study in combination with cemiplimab in the treatment of lymphoma,

- A Phase I/II study with isatuximab alone or in combination with atezolizumab in patients with advanced malignancies (hepatocellular carcinoma, squamous cell carcinoma of the head and neck, epithelial ovarian cancer or glioblastoma multiform),

- A Phase II study in combination with atezolizumab in the treatment of solid tumors.

**Libtayo® cemiplimab (SAR439684)**, a PD-1 inhibitor derived from our alliance with Regeneron, was approved by the FDA for the treatment of advanced CSCC (Sept 2018) and is anticipated to be approved in EU by the second quarter of 2019.

A Phase II program in the treatment of basal cell carcinoma was initiated in July 2017 and is ongoing.

Additional Phase III studies are also running in different indications:

- in the first-line treatment of patients with advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1, versus Platinum Based Chemotherapy; and

- in the treatment of patients with recurrent or metastatic platinum-refractory cervical cancer. In this study, cemiplimab is assessed versus investigator s choice chemotherapy.

**SAR439859** is a potent, orally bioavailable, and selective estrogen receptor (ER) inhibitor that belongs to the SERD class of compounds. SAR439859 antagonizes the binding of estradiol to ER but also promotes the transition of ER to an inactive conformation that leads to receptor degradation (98%) at sub-nanomolar concentrations in tumor cells harboring either wild type or mutant ER. The compound is in Phase I in the treatment of metastatic breast cancer, in monotherapy and in combination with palbociclib.

**SAR439459** is a monoclonal antibody which inhibits the activity of transforming growth factor beta (TGFß). TGFß regulates several biological processes (including wound healing, embryonic development, and malignant transformation) by controlling many key cellular functions including proliferation, differentiation, survival, migration, and epithelial mesenchyme transition. TGFß is expected to alleviate the suppressive tumor microenvironment and allow checkpoint modulators, such as anti-programmed cell death 1 (PD-1), to better induce immune responses and thus increase the proportion of patients benefitting from anti-PD-1 treatment. The compound is in Phase I in the treatment of advanced solid tumors in monotherapy and in combination with cemiplimab.

**SAR408701** is an antibody drug conjugate (ADC) that binds to CEACAM-5, a membrane glycoprotein originally identified as a surface marker on adenocarcinomas of the human gastrointestinal tract. A study is ongoing to evaluate the activity of the drug in the treatment of non-small-cell lung cancer, colorectal cancer and gastric cancer. In addition, there is an active Phase I trial in Japan.

**SAR440234**: is a novel bispecific T-cell engager (TCE) that has been engineered incorporating the proprietary Cross-Over-Dual-Variable-Domain (CODV) format, a fully humanized Fc-silenced IgG1 backbone, and variable domains from two antibodies, targeting CD3 (T-cell co-receptor) and CD123, respectively with the goal of developing a therapeutic molecule active against leukemic stem cells and blasts. The First in Human testing of dose-escalation of SAR440234 in patients with acute myeloid leukemia, acute lymphoid leukemia and myelodysplastic syndrome was initiated in 2018.

**SAR441000**: is an immunostimulatory mRNA mixture designed to stimulate both innate and adaptive arms of the immune system to maximize anti-tumor activity. It is developed in collaboration with BioNTech. The set-up phase of the First in Human study in patients with advanced melanoma is ongoing.

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**SAR442720** is an inhibitor of SHP2 designed to reduce cell growth signaling that is overactive in patients with non-small cell lung cancer and other types of cancers having specific types of genetic mutations. This compound is developed jointly by Sanofi and Revolution Medicines and the First in Human study in advanced non-small cell lung cancer with mutations (KRAS or in NF1) was initiated in 2018.

Products removed from the portfolio in 2018

**SAR566658** is an antibody drug conjugate (ADC) loaded with a maytansinoid derivative DM4 (huDS6-SPDB-DM4) targeting CA6. It was discontinued in April 2018. The product was in Phase II in the treatment of triple-negative breast cancer.

c) Immunology & Inflammation

Main products in Phase III and in the registration phase

**Dupixent® dupilumab (SAR231893)**, an interleukin-4 receptor alpha antagonist, is a human monoclonal antibody of the IgG4 subclass that binds to the IL-4Ra subunit and inhibits IL-4 and IL-13 signaling. Dupilumab is jointly developed with Regeneron in several indications:

**atopic dermatitis**: the product was approved for adults by the FDA in March 2017, by the European Commission in September 2017, and by the Japanese PMDA in January 2018, and launched under the trade name Dupixent®. A supplemental filing for the adolescent population has been accepted for priority review by the FDA, with a target action date of March 11, 2019. Several Phase III pediatric studies (6 months to 5 years and 6 to 11 years) are currently ongoing;

**asthma**: the product was approved for adults & adolescents by the FDA in October 2018, and the CHMP adopted a positive opinion in March 2019. A Phase III study in children (6-11 years) is ongoing;

**nasal polyposis**: positive Phase III results were announced in October 2018;

**eosinophilic esophagitis**: Phase II/III study started screening in September 2018;

**adjunct to immunotherapy:** Proof-of-concept studies were initiated in 2018 to evaluate dupilumab as an adjunct to immunotherapy (peanut and grass allergies);

**chronic obstructive pulmonary disease:** a Phase III study is on track to start early 2019.

**Kevzara® sarilumab (SAR153191)**, a monoclonal antibody against the Interleukin-6 Receptor derived from our alliance with Regeneron, already marketed in the treatment of moderate to severe rheumatoid arthritis.

The product is in Phase IIb in pediatric populations for two indications: polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis.

Two Phase III studies were initiated in 2018 for the treatment of polymyalgia rheumatic and giant cell arteritis.

Main products in early stage

**SAR441344,** an anti-CD40L mAb, is in Phase I for the treatment of multiple sclerosis.

**SAR156597** a humanized bi-specific monoclonal antibody targeting the cytokines IL-4 and IL-13, is in Phase IIa for the treatment of diffuse systemic sclerosis.

**SAR440340**, a human anti-IL33 monoclonal antibody derived from our alliance with Regeneron, has completed Phase I. Three Phase II studies started in 2018, in moderate-to-severe asthma, in atopic dermatitis and in chronic obstructive pulmonary disease.

Products removed from the portfolio in 2018

**SAR439794**, a TLR4 agonist, was discontinued in October 2018**.**

**GZ389988** (TrKA), a small molecule which inhibits binding of nerve growth factor (NGF), was terminated in November 2018.

**Ferroquine** (OZ439) is a first in class combination for malaria, developed in collaboration with the Medicines for Malaria Venture (MMV). In December 2018, Sanofi and MMV agreed to transfer operational responsibility to MMV such that MMV assumes leadership while Sanofi remains the sponsor of the studies and also retains responsibility for fulfilling drug supply, regulatory and legal obligations.

d) Multiple Sclerosis and Neurology

**SAR442168 (PRN2246)**, an orally administered Bruton s tyrosine kinase (BTK) inhibitor which was designed to access the brain and spinal cord by crossing the blood-brain barrier and impact immune cell and brain cell signaling. The Phase I studies were completed in the second half of 2018. The investigational new drug (IND) application was submitted December 2018, and a Phase IIb Proof of Concept/dose-ranging study in relapsing multiple sclerosis patients is planned to be initiated in early 2019.

**SAR443060 (DNL747)** is a best-in-class orally administered receptor-interacting serine/threonine protein kinases (RIPK1) inhibitor. It was designed to be brain penetrant and inhibit two major components of neurodegenerative diseases (inflammation and necroptosis), and is being developed for multiple sclerosis and neurodegenerative diseases. A Phase I study was completed in 2018 and two Phase Ib studies in amyotrophic lateral sclerosis and Alzheimer s disease were started in late 2018.

**Venglustat (GZ402671)**, an orally administered brain penetrant glucosylceramide synthase (GCS) inhibitor, has completed Part 1 (dose escalation phase) of a Phase II study in patients with early-stage Parkinson s disease carrying a ß-glucocerebrosidase (GBA) gene mutation (GBA-PD) or other prespecified variant. Part 2 (treatment phase) of the

study was started in early 2018. The product is also being developed in other rare disease indications (Gaucher disease type 3, Fabry disease and autosomal dominant polycystic kidney disease see Rare Diseases section).

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**Aubagio®** (teriflunomide) is currently marketed for the treatment of relapsing forms of multiple sclerosis and relapsing remitting multiple sclerosis. Teriflunomide is being evaluated in a Phase III study to assess safety and efficacy in pediatric patients with relapsing forms of multiple sclerosis.

**Lemtrada®** (alemtuzumab) is currently marketed for the treatment of relapsing forms of multiple sclerosis. Alemtuzumab is being evaluated in a Phase III study to assess safety and efficacy in pediatric patients with the relapsing remitting form of multiple sclerosis.

**SAR422459** is a gene therapy product which uses a lentivector gene delivery technology to introduce a functional ABCR gene into photoreceptors in patients with autosomal recessive Stargardt s disease. an orphan inherited condition that leads to progressive vision loss from childhood. The product is currently in Phase IIa.

Products removed from the portfolio in 2018

**SAR228810,** an anti-protofibrillar Abeta monoclonal antibody, completed a Phase I study in mild cognitive impairment due to Alzheimer s Disease (AD) and in mild AD. The project has been discontinued.

**UshStat® (SAR421869),** a gene therapy product which uses a lentivector gene delivery technology to introduce a functional MYO7A gene into the photoreceptors and retinal pigment epithelium (RPE) cells in patients with Usher 1B syndrome, an orphan inherited condition that leads to progressive visual field constriction and vision loss from childhood. The product, in Phase I/IIa, will be discontinued contingent upon identification of out-licensing partner.

e) Rare Diseases

Main products in Phase III and in the registration phase

**Avalglucosidase alfa (GZ402666 Neo GAA)** is a second generation enzyme replacement therapy targeting the treatment of Pompe disease. The Phase III program was launched in November 2016, with the COMET study targeting treatment naïve late onset Pompe disease patients. The Phase IIb/III mini-COMET study started in 2017, targeting treatment experienced infantile onset Pompe disease patients.

**GZ402665 (rhASM) olipudase alfa** is an enzyme replacement therapy targeting the treatment of non-neurological manifestations of acid sphingomyelinase deficiency (ASMD), also known as Niemann-Pick B disease. Both the open label pivotal Phase I/II trial in the pediatric population and the Phase II/III trial in the adult population have successfully completed enrollment for the target number of patients. Data from the pediatric and adult patients will be assessed one year after enrollment to support registration.

**Cerdelga®** (eliglustat) is already marketed as a first line oral therapy for Gaucher disease Type 1. It is also currently in Phase III for the treatment of Gaucher disease Type I in pediatric patients.

Main products in early stage

**Venglustat (GZ402671 GCS inhibitor)** is in development in Fabry disease, Gaucher disease type 3 (GD3) and Autosomal Dominant Polycystic Kidney Disease (ADPKD). The extension study of the Phase II trial for the treatment of Fabry disease to understand the long term effects of venglustat therapy in Fabry patients is completed. A Phase II study in Gaucher disease type 3 (LEAP) is ongoing; the first enrolled patient is about to reach two-year treatment and preliminary results have shown pharmacokinetic evidence that venglustat crosses the blood  CSF barrier. A Phase III pivotal study (STAGED-PKD) in rapidly progressive Autosomal Dominant Polycystic Kidney Disease (ADPKD) patients was initiated in 2018.

**SAR339375,** an anti-miR21 RNA is being developed in collaboration with Regulus. It is in Phase II for the treatment of Alport syndrome.

f) Rare Blood Disorders

Main products in Phase III and in the registration phase

**Sutimlimab (formerly BIVV009/TNT009)** is a monoclonal antibody targeting C1. It is a product candidate intended to selectively inhibit the classical complement pathway of the immune system. The Phase III program includes two parallel Phase III trials which are evaluating the efficacy and safety of Sutimlimab in adult patients with primary Cold Agglutinin Disease (CAD/CAgD). Sutimlimab was awarded Breakthrough Therapy Designation by the US Food and Drug Administration in 2018. Sutimlimab is also currently enrolling an open-label Phase Ib trial to evaluate the safety and tolerability of multi-dose in adult patients with Idiopathic Thrombocytopenic Purpura (ITP).

**Fitusiran (SAR439774** ALN-AT3) is a program in collaboration with Alnylam for the development of a siRNA therapeutic agent to treat hemophilia (A and B). It uses a novel approach targeting antithrombin (AT), with AT knockdown leading to increase in thrombin generation. The Phase III program (ATLAS) started in 2018.

Main products in early stage

**BIVV001 (rFVIIIFc-VWF-XTEN)** is an investigational von Willebrand factor (VWF)-independent factor VIII therapy for people with hemophilia A designed to potentially extend protection from bleeds with prophylactic dosing of once weekly or longer. Bioverativ recently dosed the last patient in EXTEN-A, a Phase I/IIa study to evaluate the safety and pharmacokinetic (PK) of BIVV001 in both a 25 IU/kg dose and 65 IU/kg dose cohort of subjects aged 18-65 years with severe hemophilia A. A Phase I repeat dose study to inform the selection of the Phase III dose and regimen started in October 2018.

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**Sangamo Collaboration (BIVV003, ST-400)** Bioverativ and Sangamo Therapeutics are working in collaboration to research, develop and commercialize treatments for sickle cell disease and beta thalassemia, two inherited blood disorders that result from the abnormal structure or underproduction of hemoglobin. The collaboration combines the extensive expertise of Sangamo in developing their genome editing technology with Bioverativ s deep understanding of hematology. The collaboration is focused on the goal of providing a single, lasting treatment for both sickle cell disease and beta thalassemia. Currently, Bioverativ is responsible for execution of the sickle cell disease Phase I/II program, BIVV003, while Sangamo is responsible for the beta thalassemia Phase I/II program, ST-400. Both programs are entering the recruiting phase of these first-in-human trials.

### *B.5.2. Vaccines*

The Vaccines R&D portfolio includes 11 vaccines and antibodies currently in advanced development, as shown in the table below. The portfolio is well balanced, with five vaccine products for novel targets and six vaccines which are enhancements of existing vaccine products.

In 2018, we obtained regulatory approval in the US for Vaxelis®, a pediatric hexavalent combination vaccine protecting against diphtheria, tetanus, pertussis, polio, Hemophilus influenza b and hepatitis B. In the EU, Vaxigrip Tetra® has been extended to childen aged 6 to 35 months. The Pneumoconjugate vaccine entered our Phase I portfolio in late 2018 and we announced in July 2018 that we had decided to discontinue clinical development of our experimental tuberculosis vaccine.

| Phase I | Phase II | Phase III | Registration |
|---|---|---|---|
| **Respiratory Syncytial Virus (RSV) vaccine**<br><br>Prevention of RSV infections in infants aged 4 months and older | **Human Immunodeficiency Virus (HIV) vaccine[a]**<br><br>Prevention of HIV infections in at-risk adults | **Fluzone® QIV HD**<br><br>**Quadrivalent** inactivated influenza vaccine High dose | |
| **Herpes Simplex Virus (HSV) vaccine[a]**<br><br>HSV-2 therapeutic vaccine | **SP0232 mAb[a]**<br><br>Passive prevention of respiratory syncytial virus infections for all infants | **MenQuadTT (ACYW)**<br><br>Advanced generation meningococcal ACYW conjugate vaccine | |
| **Pneumoconjugate Vaccine (PCV)[a]** | **VerorabVax®** (VRVg) | **Pediatric pentavalent vaccine[a]** | |

| | | |
|---|---|---|
| Prophylactic vaccine against pneumococcal pneumonia | Purified vero rabies vaccine | DTP-Polio-Hib[(b)] |
| | **SP0173** | Japan |
| | Tdap[(b)] booster vaccine | **Shan6** |
| | US, for persons aged over 64 | DTP-HepB-Polio-Hib[(b)] Pediatric hexavalent vaccine |

*(a) Partnered and/or in collaboration: Sanofi may have limited or shared rights to some of these products.*

*(b) D=Diphtheria, T=Tetanus, P=Pertussis, Hib=Hemophilus influenzae b, HepB=Hepatitis B, ap=acellular pertussis.*

**Enhancements of existing vaccines**

Fluzone® QIV HD is a higher dose quadrivalent influenza vaccine for the elderly (aged 65 years and older), who do not respond as well to standard dose influenza vaccines due to aging of the immune system (immunosenescence). A Phase III study has demonstrated non-inferior immunogenicity and comparable safety to the licensed trivalent Fluzone® High-Dose vaccine, which has shown greater protection versus standard dose.

Pediatric pentavalent vaccine for the Japanese market: Sanofi Pasteur, in partnership with Kitasato and Daiichi Sankyo (KDSV), is developing a pediatric pentavalent vaccine (primary series and booster vaccine) for the Japanese market. The vaccine includes diphtheria, tetanus and acellular pertussis (DTaP) from KDSV, and inactivated polio (IPV) and Hib from Sanofi Pasteur.

Shan6 is a cost-effective, all-in-one liquid hexavalent combination vaccine being developed for the Indian market and other low and middle income countries (WHO pre-qualification). It comprises a detoxified whole-cell pertussis component as well as diphtheria toxoid, tetanus toxoid, Hemophilus influenza type b PRP-T,

inactivated poliovirus types 1, 2, and 3 and hepatitis B virus components.

SP0173: The current Adacel® (Tdap booster vaccine containing tetanus toxoid, diphtheria toxoid, and 5-component acellular pertussis) is not indicated in the US for persons aged over 64. This development is specifically designed to bridge this indication gap.

MenQuadTT: Sanofi Pasteur s MenACYW-TT vaccine candidate is our latest advance in meningococcal quadrivalent conjugate vaccination, designed to help protect an expanded patient group including infants and adolescents through older adults. Phase II and initial Phase III trials have been performed in the US and the EU. Additional Phase III trials are ongoing in the EU, Asia and Latin America. The safety and immunogenicity profiles of the vaccine candidate are encouraging.

VerorabVax® (VRVg) is a next-generation purified human rabies vaccine under development, aimed at replacing both of Sanofi Pasteur s currently commercialized rabies vaccines (Imovax® Rabies and Verorab®). It will be cultured on Vero cells without animal or human material.

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**New vaccine targets**

SP0232 mAb: In March 2017 Sanofi Pasteur announced an agreement with MedImmune/AstraZeneca to develop and commercialize a monoclonal antibody (SP0232, also known as MEDI8897) which has been engineered to have a long half-life, so that only one dose would be needed for the entire RSV season to provide passive immunity and prevent RSV infection in all infants for their first RSV season (and in high-risk infants for their first and second RSV seasons). Positive primary analysis of the Phase IIb trial has demonstrated the safety and efficacy of SP0232. The product received fast-track designation from the FDA in 2015 and is currently under review for EMA PRIME priority medicines designation and for FDA Breakthrough Therapy designation.

Respiratory Syncytial Virus (RSV) infant vaccine: Sanofi Pasteur has a Cooperative Research and Development Agreement (CRADA) with the US National Institutes of Health (NIH) to develop a live attenuated RSV vaccine for immunization in infants aged 4 months and older. The lead candidate(s) are currently under Phase I evaluation in healthy infants without previous RSV exposure.

Pneumoconjugate Vaccine (PCV): Sanofi Pasteur is developing with SK chemicals (South Korea) a pneumococcal conjugate vaccine with broader coverage. This vaccine entered Phase I in December 2018.

Herpes Simplex Virus (HSV) type 2 is a member of the herpes virus family and as such establishes life-long infections mainly genital herpes with latent virus established in neural ganglia. Although antivirals currently exist to treat these infections, no vaccine exists. Our vaccine candidate is a live attenuated virus and is being assessed as a therapeutic vaccine to reduce recurrence and transmission. It is currently in Phase I. In 2014, Sanofi Pasteur signed a contract with Immune Design Corp. to

collaborate on the development of this therapeutic herpes simplex virus vaccine candidate by exploring the potential of various combinations of agents.

Human Immunodeficiency Virus (HIV): Sanofi Pasteur is working in a pox-protein public-private partnership (P5) to document efficacy of a pox-protein based HIV prophylactic vaccine regimen in South Africa. Specifically, following the modest success of RV144 (the first trial to show supporting evidence that a vaccine could lower the risk of HIV acquisition, the P5 partnership adopted a pox-protein based vaccine regimen to potentially provide greater protection. This is currently being tested in a Phase IIb study in South Africa.

*B.5.3. R&D expenditures for late stage development*

Expenditures on research and development amounted to 5,894 million in 2018, comprising 4,572 million in the Pharmaceuticals segment; 143 million in the Consumer Healthcare segment; 555 million in the Vaccines segment; and 624 million allocated to Other , representing the R&D support function. Research and development expenditures were the equivalent of about 17,1% of net sales in 2018, compared to about 15.6% in 2017 and about 15.3% in 2016. The increase in R&D expenditures as a percentage of sales in 2018 is mainly due to a greater proportion of products being

in late stage development. It is also due to the integration of Ablynx and Bioverativ in 2018. Preclinical research in the Pharmaceuticals segment amounted to 983 million in 2018, compared to 1,086 million in 2017 and 1,077 million in 2016. Of the remaining 3,589 million relating to clinical development in the Pharmaceuticals segment ( 2,969 million in 2017 and 3,124 million in 2016), the largest portion was generated by Phase III or post-marketing studies, reflecting the cost of monitoring large scale clinical trials.

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| Compound | Entry into Phase III[a] (month/year) | Compound Patent Term[b] US | EU | Japan | Comments |
|---|---|---|---|---|---|
| SAR341402 | August 2017 | N/A | N/A | N/A | Phase III program ongoing in type 1 and 2 diabetes. |
| insulin aspart sotagliflozin (SAR439954) | November 2015 | 2028 | 2027 | 2027 | NDA filed in Type 1 diabetes. Phase III program ongoing in Type 2 diabetes and in worsening heart failure. |
| efpeglenatide (SAR439977) | December 2017 | 2028 | 2028 | 2028 | Phase III program ongoing in Type 2 diabetes. |
| dupilumab Dupixent® (SAR231893) | October 2014 | 2027 | 2029 | 2029 | Dossier approved in atopic dermatitis (AD) in adults, and in asthma for adults and children over 12 years old. Dossier filed in AD in adolescents (12-17 years old). Phase III program ongoing in AD (children: 6 months-11 years old) and in asthma (children: 6  11 years old). Phase III program ongoing in nasal polyposis and eosinophilic esophagitis. Phase II program ongoing in grass immunotherapy and peanut allergy. |
| sarilumab Kevzara® (SAR153191) | August 2011 | 2028[c] | 2027 | 2027 | Dossier approved in rheumatoid arthritis. Phase III program ongoing in giant cell arteritis and polymyalgia rheumatica. Phase II program ongoing in systemic juvenile arthritis and polyarticular juvenile idiopathic arthritis. |
| avalglucosidase alfa (GZ402666) | November 2016 | 2030 | 2028 | 2028 | Phase III program ongoing in Pompe disease. |
| Venglustat (GZ402671) | February 2019 | 2032 | 2032 | 2032 | Phase III study in autosomal dominant polycystic kidney disease (ADPKD) initiated. Phase II program ongoing in Fabry disease, Gaucher disease Type 3 and Gaucher related Parkinson  s disease. |
| fitusiran (SAR439774) | March 2018 | 2033 | 2033 | 2033 | Phase III program ongoing for the treatment of hemophilia A&B. |
| sutimlimab (BIVV009) | March 2018 | 2033 | 2033 | 2033 | Phase III program ongoing in Cold Agglutinin Disease. |
| isatuximab (SAR650984) | December 2016 | 2028 | 2027 | 2027 | Phase Ill program ongoing in relapsing refractory multiple myeloma (RRMM) and in newly diagnosed multiple myeloma. Phase II |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | program ongoing in combination with atezolizumab in advanced malignancies and solid tumors and in combination with cemiplimab in RRMM, advanced malignancies and lymphoma. |
| cemiplimab (SAR439684) | May 2017 | 2035 | 2035 | 2035 | Dossier approved for the treatment of advanced cutaneous squamous cell carcinoma. Phase III program ongoing in 1L non-small cell lung cancer (monotherapy and combination) and 2L cervical cancer. Registration Phase II study ongoing in advanced basal cell carcinoma. |

*(a) First patient included in Phase III in any indication.*

*(b) Subject to any future supplementary protection certificates and patent term extensions.*

*(c) With Patent Term Adjustment.*

With respect to the compound patent information set out above, investors should bear in mind the following additional factors:

The listed compound patent expiration dates do not reflect possible extensions of up to five years available in the US, the EU, and Japan for pharmaceutical products. See B.7. Patents, Intellectual Property and Other Rights Patent Protection for a description of supplementary protection certificates and patent term extensions.
Depending on the circumstances surrounding any final regulatory approval of the compound, there may be other listed patents or patent applications pending that could have relevance to the product as finally approved; the relevance of any such application would depend upon the claims that ultimately may be granted and the nature of the final regulatory approval of the product.

Regulatory exclusivity tied to the protection of clinical data is complementary to patent protection, and may provide more

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efficacious or longer lasting marketing exclusivity than a compound s patent estate. See B.7. Patents, Intellectual Property and Other Rights Regulatory Exclusivity for additional information. In the United States the data protection generally runs five years from first marketing approval of a new chemical entity, extended to seven years for an orphan drug indication and twelve years from first marketing approval of a biological product. In the EU and Japan the corresponding data protection periods are generally ten years and eight years, respectively.

**B.6. Markets**

A breakdown of revenues by business segment and by geographical region for 2018, 2017, and 2016 can be found at Note D.35. to our consolidated financial statements, included at Item 18 of this annual report.

The following market shares and ranking information are based on consolidated national pharmaceutical sales data (excluding vaccines), in constant euros, on a September 2018 MAT (Moving Annual Total) basis. The data are mainly from IQVIA local sales audit supplemented by various other country-specific sources including Knobloch (Mexico), GERS (France) and HMR (Portugal). For more information on market shares and rankings see Presentation of Financial and Other Information at the beginning of this Annual Report on Form 20-F.

*B.6.1. Marketing and distribution*

We have a commercial presence in approximately 100 countries, and our products are available in more than 170 countries. Sanofi is the sixth largest pharmaceutical company globally by sales. Our main markets in terms of net sales are respectively:

Emerging Markets (see definition in Information on the Company Introduction above): Sanofi is the leading healthcare company in emerging markets, and the fifth largest pharmaceutical company in China.

The US: we rank twelfth with a market share of 3.4%.

Europe: we are the third largest pharmaceutical company in France where our market share is 6.4% and we rank third in Germany with a 4.5% market share.

Other countries: our market share in Japan is 1.7%.

A breakdown of our aggregate net sales by geographical region is presented in Item 5. Operating and Financial Review and Prospects Results of Operations Year Ended December 31, 2018 Compared with Year Ended December 31, 2017.

Although specific distribution patterns vary by country, we sell prescription drugs primarily to wholesale drug distributors, independent and chain retail drug outlets, hospitals, clinics, managed-care organizations and government institutions. Rare disease products are also sold directly to physicians. With the exception of Consumer Healthcare products, our drugs are ordinarily dispensed to patients by pharmacies upon presentation of a doctor s prescription. Our Consumer Healthcare products are

also sold and distributed through e-commerce, which is a growing trend in consumer behavior. Our vaccines are sold and distributed through multiple channels including physicians, pharmacies, hospitals, private companies and distributors in the private sector, and governmental entities and non-governmental organizations in the public and international donor markets.

We use a range of channels from in-person to digital to disseminate information about and promote our products among healthcare professionals, ensuring that the channels not only cover our latest therapeutic advances but also our established prescription products, which satisfy patient needs in some therapy areas. We regularly exhibit at major medical congresses. In some countries, products are also marketed directly to patients by way of television, radio, newspapers and magazines, and digital channels (such as the internet). National education and prevention campaigns can be used to improve patients knowledge of their conditions.

Our sales representatives, who work closely with healthcare professionals, use their expertise to promote and provide information on our drugs. They represent our values on a day-to-day basis and are required to adhere to a code of ethics and to internal policies in which they receive training.

Although we market most of our products through our own sales forces, we have entered into and continue to form partnerships to co-promote/co-market certain products in specific geographical areas. Our major alliances are detailed at Item 5. Operating and Financial Review and Prospects Financial Presentation of Alliances. See also Item 3. Key Information D. Risk Factors We rely on third parties for the discovery, manufacture and marketing of some of our products.

*B.6.2. Competition*

The pharmaceutical industry continues to experience significant changes in its competitive environment.

There are four types of competition in the prescription pharmaceutical market:

- competition between pharmaceutical companies to research and develop new patented products or address unmet medical needs;
- competition between different patented pharmaceutical products marketed for the same therapeutic indication;
- competition between original and generic products or between original biological products and biosimilars, at the end of regulatory exclusivity or patent protection; and
- competition between generic or biosimilar products.

We compete with other pharmaceutical companies in all major markets to develop innovative new products. We may develop new technologies and new patented products wholly in-house, but we also enter into collaborative R&D agreements in order to access new technologies. See Note D.21. to our consolidated financial statements, included at

Item 18 of this annual report.

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Our prescription drugs compete in all major markets against patented drugs from major pharmaceutical companies. Our competitors in key businesses include: Novo Nordisk, Boehringer Ingelheim and Merck in diabetes; Eli Lilly in diabetes, immunology and oncology; Bristol-Myers Squibb in immunology and oncology; Novartis in diabetes, multiple sclerosis, and oncology; Shire in rare diseases and hemophilia; Pfizer in rare diseases, hemophilia and oncology; Biogen Idec, Teva and Merck Serono in multiple sclerosis; Bayer in multiple sclerosis and hemophilia; Roche in multiple sclerosis, hemophilia, immunology and oncology; AstraZeneca in diabetes, cardiovascular disease and oncology; and Amgen in cardiovascular disease.

In our Consumer Healthcare business, key competitors include Johnson & Johnson, Pfizer, GlaxoSmithKline, Bayer and Reckitt Benckiser as well as local players, especially in emerging markets.

Our generics business competes with multinational corporations such as Teva, Sandoz (a division of Novartis), Mylan and local players, especially in emerging markets.

In our Vaccines business we are one of the top four players, competing primarily with large multinational players including Merck, GlaxoSmithKline, and Pfizer.

We also face competition from generic drugs that enter the market when our patent protection or regulatory exclusivity expires, or when we lose a patent infringement lawsuit (see B.7. Patents, Intellectual Property and Other Rights below). Similarly, when a competing patented drug from another pharmaceutical company faces generic competition, those generic products can also affect the competitive environment of our own patented product. See Item 3. Key Information D. Risk factors Risks relating to our business .

Competition from producers of generics has increased sharply in response to healthcare cost containment measures and to the increased number of products for which patents or regulatory exclusivity have expired.

Generics manufacturers who have received all necessary regulatory approvals for a product may decide to launch a generic version before the patent expiry date, even in cases where the owner of the original product has already commenced patent infringement litigation against the generics manufacturer. Such launches are said to be at risk for the promoter of the generic product because it may be required to pay damages to the owner of the original product in the context of patent infringement litigation; however, such launches may also significantly impair the profitability of the pharmaceutical company whose product is challenged.

Drug manufacturers also face competition through parallel trading, also known as reimportation. This takes place when drugs sold abroad under the same brand name as in a domestic market are imported into that domestic market by parallel traders, who may repackage or resize the original product or sell it through alternative channels such as mail order or the internet.

This situation is of particular relevance to the EU, where such practices have been encouraged by the current regulatory framework. Parallel traders take advantage of the price differentials between markets arising from factors

including sales costs, market conditions (such as intermediate trading stages), tax rates, or national regulation of prices.

Finally, pharmaceutical companies face illegal competition from falsified drugs. The WHO estimates that falsified products account for 10% of the market worldwide, rising to 30% in some countries. All therapeutic areas are affected, also including vaccines. However, in markets where powerful regulatory controls are in place, falsified drugs are estimated to represent less than 1% of market value.

*B.6.3. Regulatory framework*

**B.6.3.1. Overview**

The pharmaceutical and health-related biotechnology sectors are highly regulated. National and supranational health authorities administer a vast array of legal and regulatory requirements that dictate pre-approval testing and quality standards to maximize the safety and efficacy of a new medical product. These authorities also regulate product labeling, manufacturing, importation/exportation and marketing, as well as mandatory post-approval commitments that may include pediatric development.

The submission of an application to a regulatory authority does not guarantee that a license to market will be granted. Furthermore, each regulatory authority may impose its own requirements during the course of the product development and application review. It may refuse to grant approval and require additional data before granting approval, even though the same product has already been approved in other countries. Regulatory authorities also have the authority to request product recalls and product withdrawals, and to impose penalties for violations of regulations based on data that are made available to them.

Product review and approval can vary from six months or less to several years from the date of application depending upon the country. Factors such as the quality of data, the degree of control exercised by the regulatory authority, the review procedures, the nature of the product and the condition to be treated, play a major role in the length of time a product is under review.

The International Council for Harmonization (ICH) continues to implement its reform mandate.

The aims are to reinforce the foundations of the ICH; expand harmonization globally beyond the traditional ICH members, i.e. the three founding members (EU, Japan, US) plus Canada and Switzerland as standing members; and facilitate the involvement of additional regulators and industry associations around the world. Since the reform started much progress has been made. There are now 10 regulatory agencies (Brazil, China, Chinese Taipei, Singapore and South Korea in addition to the three

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founding members and the two standing members) and 28 ICH organizations (including 13 regulatory authorities from around the world) with observer status.

International collaboration between regulatory authorities continues to develop with the implementation of confidentiality arrangements and memoranda of understanding between both ICH and non-ICH regulatory authorities. Examples include work-sharing on Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP) inspections, as well as regular interactions between the US and the EU in the form of clusters (pediatrics, oncology, advanced therapy medicinal products, vaccines, pharmacogenomics, orphan drugs, biosimilars, and blood products). In 2017 the United States and the EU completed an exchange of letters to amend the Pharmaceutical Annex to the 1998 US-EU Mutual Recognition Agreement. Under this agreement, US and EU regulators will be able to utilize each other s good manufacturing practice for inspections of pharmaceutical manufacturing facilities.

In addition to the joint efforts listed above, Free Trade Agreements (FTAs) have proven to be one of the best ways to open up foreign markets to exporters and to allow for discussions on harmonization topics for regulatory authorities. Some agreements, such as the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), are international in nature, while others are between specific countries. The requirements of many countries (including Japan and several EU Member States) to negotiate selling prices or reimbursement rates for pharmaceutical products with government regulators significantly extend the time to market entry beyond the initial marketing approval. While marketing authorizations for new pharmaceutical products in the EU have been largely centralized within the European Commission in collaboration with the EMA, pricing and reimbursement remain a matter of national competence.

**In the EU**, there are three main procedures for applying for marketing authorization:

The centralized procedure is mandatory for drugs derived from biotechnologies; new active substances designed for human use to treat HIV, viral diseases, cancer, neurodegenerative diseases, diabetes and auto-immune diseases; orphan drugs; and innovative products for veterinary use. When an application is submitted to the EMA, the scientific evaluation of the application is carried out by the Committee for Medicinal Products for Human Use (CHMP) and a scientific opinion is prepared. This opinion is sent to the European Commission which adopts the final decision and grants an EU marketing authorization. Such a marketing authorization is valid throughout the EU and the drug may be marketed within all EU Member States.

If a company is seeking a national marketing authorization in more than one Member State, two procedures are available to facilitate the granting of harmonized national authorizations across member states: the mutual recognition procedure or the decentralized procedure. Both procedures are based on the recognition by national competent authorities of a first assessment performed by the regulatory authority of one Member State.

National authorizations are still possible, but are only for products intended for commercialization in a single EU Member State or for line extensions to existing national product licenses.

In the EU, vaccines are treated as pharmaceutical products, and therefore have to obtain marketing authorization under the same procedures and conditions for registration described above.

On April 26, 2018, the European Commission published its Proposal for a Council Recommendation on strengthened cooperation against vaccine-preventable diseases in Europe and a Communication to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. The Recommendation was adopted by the EU Council on December 7, 2018. The text sets recommendations for action by national governments and the EU to address major vaccination challenges such as vaccination hesitancy, low vaccine uptake and supply issues. Suggested actions include the setting up of a coalition of healthcare professionals for vaccination, an EU vaccination information portal and an EU vaccination card.

The European Trade Association, Vaccines Europe and Sanofi have been working for the past year in support of the adoption of this recommendation as it will be a key lever to increase vaccination coverage rates across Europe.

In parallel, the European Parliament adopted the Resolution on vaccine hesitancy and the drop in vaccination rates in Europe on April 19, 2018; and the European Joint Action on vaccination, co-funded by the Health Programme, was launched on September 4, 2018. It will address vaccine hesitancy and seek to increase vaccination coverage in the EU. It is coordinated by INSERM (France) and involves 23 countries (including 20 EU countries). It will also work towards strengthening cooperation of national immunization advisory groups (NITAGs) with a view to increasing transparency and trust in the decision-making process regarding the introduction of new vaccines, and on finding options to better anticipate vaccine demand and secure sustainability of vaccine supply across Europe.

Vaccines industry representatives, via Vaccines Europe (including Sanofi), are involved in Work Packages in areas where industry can contribute such as Research, Development and supply. The European Commission is reinforcing its support for national vaccination efforts to increase coverage, including through the recent publication of three reports: State of vaccine confidence in the EU 2018 , Organisation and delivery of vaccination services in the European Union and Vaccination programmes and health systems in the EU .

Generic products are subject to the same marketing authorization procedures. A generic product must contain the same active medicinal substance as a reference product approved in the EU. Generic applications are abridged: generic manufacturers only need to submit quality data and demonstrate that the generic drug is bioequivalent to the originator product (i.e. performs in the same manner in the patient s body), but do not need to submit safety or efficacy data since regulatory authorities can refer to the reference product s dossier. Generic product

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applications can be filed and approved in the EU only after the originator product s eight-year data exclusivity period has expired. Further, generic manufacturers can only market their generic products after a 10- or 11-year period has elapsed from the date of approval of the originator product. In the case of orphan drugs, generic product applications may not be filed before the expiry of a 10- or 12-year period from the date of approval of the originator product.

Another relevant aspect in the EU regulatory framework is the sunset clause under which any marketing authorization ceases to be valid if it is not followed by marketing within three years, or if marketing is interrupted for a period of three consecutive years.

In 2018, the EMA recommended 84 medicines for marketing authorization (versus 92 in 2017), including 42 new active substances (versus 35 in 2017).

Among the 84 medicines recommended, 21 (25%) had an orphan designation (versus 19 in 2017 and 17 in 2016), providing medicines for patients with rare diseases. Four medicines were evaluated under accelerated assessment in 2018 (versus seven in both 2016 and 2017); this mechanism is reserved for medicines that have the potential to address unmet medical needs. One medicine was recommended for a conditional marketing authorization; this is one of the EMA s early access routes to patients, and is intended for medicines that address an unmet medical need and that target seriously debilitating, life-threatening or rare diseases, or are intended for use in emergency situations in response to a public health threat.

Post-authorization safety monitoring of pharmaceutical products is carefully regulated in Europe. EU pharmaceutical legislation for medicinal products describes the respective obligations of the marketing authorization holder (MAH) and of the regulatory authorities to set up a system for pharmacovigilance in order to collect, collate and evaluate information about suspected adverse reactions.

It is possible for the regulatory authorities to withdraw products from the market for safety reasons. Responsibilities for pharmacovigilance rest with the regulatory authorities of all the EU Member States in which the marketing authorizations are held. In accordance with applicable legislation, each EU Member State has a pharmacovigilance system for the collection and evaluation of information relevant to the risk-benefit balance of medicinal products. The regulatory authority regularly monitors the safety profile of the products available in its territory, takes appropriate action where necessary, and monitors the compliance of MAHs with their pharmacovigilance obligations. All relevant information is shared between the regulatory authorities and the MAH, in order to allow all parties involved in pharmacovigilance activities to fulfill their obligations and responsibilities.

Pharmacovigilance legislation in Europe was amended to strengthen the protection of patient health by promoting prompt and appropriate regulatory action on European medicines.

The measures included the creation of the Pharmacovigilance Risk Assessment Committee (PRAC), a scientific advisory committee at EMA level with a key role in the assessment of all

aspects of risk management relating to the use of medicinal products for human use approved in the European Economic Area (EEA). The PRAC performs reviews of marketed products (by class or on ad hoc basis) through various procedures. For Sanofi, 209 products underwent PRAC review through signal and referral procedures from July 2012 to December 2018, generating 136 safety labeling variations (24 new variations in 2018) and 7 additional risk minimization measures. In only two cases for Sanofi (Myolastan®, and methadone oral solutions containing povidone) did the review lead to the product being withdrawn from the EU market.

On November 22, 2017, as part of the ongoing implementation of EU legislation, the EMA launched a new and improved version of EudraVigilance (the system for managing and analyzing information on suspected adverse reactions to medicines which have been authorized or are being studied in clinical trials within the EEA), with enhanced functionalities to support the fulfilment of pharmacovigilance obligations. Alongside the launch, it became mandatory for national Competent Authorities and MAHs to use simplified electronic reporting to notify EudraVigilance of suspected adverse reactions related to medicines. The EMA and the European Commission have agreed transitional arrangements to streamline the monitoring of EudraVigilance by MAHs. A pilot period started on February 22, 2018 in which MAHs of the active substances included in a dedicated list have to monitor them in EudraVigilance and inform EMA and national competent authorities of validated signals with their medicines. The pilot was initially planned for one year but has been extended until further notice. The EMA will finalize a report at the end of 2019 on the experience of signal monitoring in EudraVigilance since February 2018.

The European database of medicinal products aims to deliver structured and quality assured information on medicinal products authorized in the EU that incorporates the terminology adopted in the EU for products, substances, and organizations underpinning pharmacovigilance and regulatory systems. Since January 1, 2015, MAHs have been required to notify the EMA of any new marketing authorizations and any change in the terms of a marketing authorization. Since July 2018, the EMA has made this list publicly available.

Public hearings are a new tool allowing the EMA to engage with EU citizens in the supervision of medicines and listen to their views and experiences. Public hearings are expected to give EU citizens a voice in the evaluation of the safety of medicines and empower them to express their views on issues related to the safety of certain medicines and the management of risks. Public hearings were held on valproate and related substances in 2017 (with Sanofi participation), and on quinolone and fluoroquinolone antibiotics in 2018.

**In the US**, applications for approval are submitted for review to the FDA, which has broad regulatory powers over all pharmaceutical and biological products that are intended for sale and marketing in the US. To commercialize a product in the US, a new drug application (NDA) under the Food, Drug and Cosmetic (FD&C) Act, or a Biological License Application (BLA) under the Public Health Service (PHS) Act, must be submitted to

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the FDA for filing and pre-market review. Specifically, the FDA must decide whether the product is safe and effective for its proposed use; if the benefits of the drug s use outweigh its risks; whether the drug s labeling is adequate; and if the manufacturing of the drug and the controls used for maintaining quality are adequate to preserve the drug s identity, strength, quality and purity. Based upon this review, the FDA can stipulate post-approval commitments and requirements. Approval for a new indication of a previously approved product requires submission of a supplemental NDA (sNDA) for a drug or a supplemental BLA (sBLA) for a biological product.

Sponsors wishing to market a generic drug can file an Abbreviated NDA (ANDA) under 505(j) of the FD&C Act. These applications are abbreviated because they are generally not required to include data to establish safety and effectiveness, but need only demonstrate that their product is bioequivalent (i.e. performs in humans in the same manner as the originator s product). Consequently, the length of time and cost required for development of generics can be considerably less than for the innovator s drug. The ANDA pathway in the US can only be used for generics of drugs approved under the FD&C Act.

The FD&C Act provides another abbreviated option for NDA approved products, which is a hybrid between an NDA and ANDA called the 505(b)(2) pathway. This 505(b)(2) pathway enables a sponsor to rely on the FDA s findings that the reference product is safe and effective, based on the innovator s preclinical and clinical data.

The FDA Center for Drug Evaluation and Research (CDER) approved 59 novel drugs in 2018 (versus 46 in 2017, 22 in 2016, 45 in 2015, 41 in 2014, and 27 in 2013). Designations and pathways to expedite drug development and review include Fast Track (24/59 = 41%), Breakthrough Therapy (14/59 = 24%), Accelerated approval (4/59 = 7%), and Priority Review (43/59 = 73%). Of the 59 novel drugs approved in 2018, 73% were designated in one or more expedited categories. No new vaccines were approved by the FDA in 2018, although three products (Gardasil 9, Afluira, and Fluarix Quadravalent) had their licenses expanded.

CDER identified 19 of the 59 novel drugs approved in 2018 as First-in-Class (32%) (as compared to 33% in 2017), one indicator of the innovative nature of a drug. Approximately 58% of the novel drugs approved in 2018 were approved to treat rare or orphan diseases that affect 200,000 or fewer Americans.

**In Japan**, the regulatory authorities can require local clinical studies, though they also accept multi-national studies. In some cases, bridging studies have been conducted to verify that foreign clinical data are applicable to Japanese patients and obtain data to determine the appropriateness of the dosages for Japanese patients. The Japanese Ministry of Health, Labor and Welfare (J-MHLW) has introduced a new National Health Insurance (NHI) pricing system. Reductions in NHI prices of new drugs every two years are compensated by a Premium for a maximum of 15 years. A Premium is granted in exchange for the development of unapproved drugs or off-label indications with

high medical needs. Once an official request for development of an unapproved drug or off-label indication has been made, pharmaceutical companies must file literature-based reports within six months or submit a clinical trial notification for registration within one year after the official development request. For unapproved drugs with high medical needs, clinical trials in Japanese patients are generally required.

To promote the development of innovative drugs and bring them into early practical use in Japan ahead of the world, the Sakigake (a Japanese term meaning forerunner ) review designation program was introduced in April 2015. The Pharmaceuticals and Medical Devices Agency (PMDA) reviews designated products on a priority basis with the aim of reducing their review time from the normal 12 months to six months. Based on the NHI price system, the Premium classification is restricted to new products from companies which conduct R&D on pharmaceuticals truly conducive to the improvement of healthcare quality, i.e. (i) pediatric/orphan drugs and (ii) drugs to treat diseases that cannot be adequately controlled with existing drugs. From 2021, all prescription product prices will be reviewed annually instead of once every two years, but price cuts will actually be conducted only for a limited number of products with big gaps between their official reimbursement prices and market prices (e.g. generic drugs and long-listed original products). On the other hand, prices of products that are rapidly adopted after approvals for new indications may from 2017 be reviewed four times a year.

The PMDA has set a target for 80% (as opposed to the current 50%) of all applications to be reviewed in 12 months for products with standard review status, and in nine months for products with priority review status, by the end of 2018.

The PMDA also plans to eliminate the review lag between the filing and approval of drugs and medical devices relative to the FDA by the end of 2020.

The Pharmaceuticals and Medical Devices Act (PMDA) was implemented on November 25, 2014. There are three major objectives. The first objective is to strengthen safety measures for drugs and medical devices. In particular, MAHs must prepare a package insert based on the latest knowledge and notify the J-MHLW before placing products on the market or when revisions are made. The second objective is to accelerate the development of medical devices. The third-party accreditation system will be expanded to specially controlled generic medical devices (i.e. Class III devices). Consequently, the PMDA can accelerate the review of innovative medical devices. The third objective is accelerated commercialization of regenerative medicinal products.

The term Regenerative Medicinal Products used in the law includes cellular and tissue-based products and gene therapies. This concept is similar to Advanced Therapy Medicinal Products (ATMPs) in the EU. The law allows for conditional regulatory approval based on confirmation of probable efficacy and safety in small-scale clinical trials, followed up by comprehensive studies to confirm safety and efficacy in a wider population that would then lead to a regular (full) approval.

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For new drugs and biosimilar products with approval applications submitted in or after April 2013, Japan has implemented an RMP (Risk Management Plan), similar to the EU Pharmacogivilance system.

For generic products, the data necessary for filing are similar to EU and US requirements. Companies only need to submit quality data, and data demonstrating bioequivalence to the originator product, unless the drug is administered intravenously. Clinical Trial Data (CTD) submission for generics has been mandatory since March 2017.

**B.6.3.2. Biosimilars**

Products can be referred to as biologics when they are derived from natural sources, including blood products or products manufactured within living cells (such as antibodies). Most biologics are complex molecules or mixtures of molecules which are difficult to characterize and require physico-chemical-biological testing, and an understanding of and control over the manufacturing process.

The concept of generics is not scientifically appropriate for biologics due to their high level of complexity. Consequently the concept of biosimilar products is more appropriate. A full comparison of the purity, safety and efficacy of the biosimilar product against the reference biological product should be undertaken, including assessment of physical-chemical-biological, non-clinical and clinical similarity.

**In the EU**, the regulatory framework for developing and evaluating biosimilar products has been in place since 2005. The CHMP has issued several product/disease specific guidelines for biosimilar products including guidance on preclinical and clinical development of biosimilars of Low Molecular Weight Heparin (LMWH) and of insulins. Starting in 2011 and continuing through 2018, the CHMP has been engaged in revising most of the existing biosimilar guidelines (general overarching guidelines, quality, and non-clinical and clinical product-specific guidelines).

While the CHMP has adopted a balanced approach for all biosimilars, allowing evaluation on a case-by-case basis in accordance with relevant biosimilar guidelines, it has also indicated that in specific circumstances, a confirmatory clinical trial may not be necessary. This applies if similar efficacy and safety can clearly be deduced from the similarity of physicochemical characteristics, biological activity/potency, and pharmacokinetic and/or pharmacodynamic profiles of the biosimilar and the reference product. With respect to vaccines, the CHMP currently takes the view that it is at present unlikely that these products can be characterized at the molecular level, and that each vaccine product must be evaluated on a case-by-case basis.

In February 2017, the EMA launched a tailored scientific advice pilot project to support step-by-step development of new biosimilars, based on a review of the quality, analytical and functional data already available. This pilot will encompass six scientific advice requests. The EMA will analyze the outcome after completing the pilot.

In 2017, the EMA and the European Commission published an information guide for healthcare professionals to provide them with reference information on the science and regulation underpinning the use of biosimilar medicines.

In 2018, the EMA gave positive opinions to 19 biosimilars.

**In the US**, the Patient Protection and Affordable Care Act (Affordable Care Act), signed into law in March 2010, amended the Public Health Service Act to create an abbreviated licensure pathway (351k) for biological products that are demonstrated to be biosimilar to or interchangeable with an FDA-licensed biological product.

In 2018, the FDA finalized the biosimilar guidance *Labeling for Biosimilar Products* (first issued in draft in 2016), issued the draft guidance *Formal Meetings Between the FDA and Sponsors or Applicants of BsUFA Products* and withdrew the 2017 draft guidance *Statistical Approaches to Evaluate Analytical Similarity.* Another draft guidance published in 2017, *Considerations in Demonstrating Interchangeability with a Reference Product*, still remains in draft. In December 2018, the FDA also finalized the guidance *Questions and Answers on Biosimilar Development and the BPCi Act Guidance for Industry* and released the draft guidance *New and Revised Draft Q&As on Biosimilar Development and the BPCi Act (Revision2).*

The FDA also published a *Biosimilars Action Plan: Balancing Innovation and Competition* in July 2018, and held a hearing on the Plan in September. The 11-part Action Plan is intended to spur uptake and acceptance of biosimilars in the marketplace by streamlining regulatory review and attempting to address anticompetitive business practices around biosimilar sales. As of the date of this annual report 17 biosimilar products have been approved by the FDA, seven of which were approved in 2018. To date no biosimilar products have been deemed interchangeable.

**In Japan**, guidelines defining the regulatory approval pathway for follow-on biologics were finalized in March 2009. These guidelines set out the requirements on preclinical, clinical and Chemistry, Manufacturing and Control (CMC) data to be considered for the development of the new application category of biosimilars. Unlike the CHMP guidelines, the main scope of the Japanese guidelines includes recombinant proteins and polypeptides, but not polysaccharides such as LMWH.

Many regulatory authorities worldwide have in place, or are in the process of developing, a regulatory framework for biosimilar development and approval. It should be noted that although many emerging markets are basing their regulations and guidance on WHO or EMA documentation, some markets have approved biosimilars under an existing regulatory framework that is not specific to biosimilars.

**B.6.3.3 Regenerative medicine**

The US Center for Biologics Evaluation and Research (CBER) released a suite of 6 draft gene therapy guidances in 2018, addressing three general topics (*Chemistry Manufacturing and Controls*, *Long Term Follow-Up After Administration of Human Gene Therapy Products*, *Testing of Retroviral Vector-Based Human Gene Therapies*) and three more disease-specific topics

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(*Human Gene Therapy for Hemophilia*, *Human Gene Therapy for Rare Diseases*, *Human Gene Therapy for Retinal Disorders*). These guidance documents compliment an existing comprehensive policy framework to address how the agency plans to support and expedite the development of regenerative medicine products, including human cells, tissues, and cellular and tissue-based products (HCT/Ps), which already included guidance on determining whether HCT/Ps are subject to the FDA s premarket review requirements (*Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use*) and whether an establishment may qualify for an exception from the requirements under Part 1271 of the Code of Federal Regulations (CFR) Title 21 by meeting the exception in 21 CFR 1271.15(b) (*Same Surgical Procedure Exception: Questions and Answers Regarding the Scope of the Exception*).

The FDA has continued to move forward with the Regenerative Medicine Advanced Therapy (RMAT) designation program, first established in section 3033 of the 21st Century Cures Act. This program aims to facilitate an efficient development program, expedite review of innovative regenerative medicine therapies, and provide more timely access to potentially life-saving products. Products granted the RMAT designation are eligible for increased early interactions with the FDA, including all the benefits available to breakthrough therapies. As of December 28, 2018, the FDA had granted 24 RMAT designations, as compared with 10 in 2017. Two guidances issued in late 2017 related to the RMAT pathway were finalized in February 2019: *Expedited programs for Regenerative Medicine Therapies for Serious Conditions* and *Evaluation of Devices Used with Regenerative Medicine Advanced Therapies*.

Novel regenerative medicine therapies approved by the CBER in 2017 included the first three gene therapies: Novartis AG s chimeric antigen receptor T-cell (CAR-T) therapy Kymriah (tisagenlecleucel) followed by Kite Pharma Inc. s CAR-T therapy Yescarta (axicabtagene ciloleucel), both for oncology indications, and Spark Therapeutics Inc. s Luxturna (voretigene neparvovec-rzyl) for inherited vision loss.

**B.6.3.4. Generics**

**In the EU** only 11 positive opinions were issued under the centralized procedure for generics in 2017 (versus 20 in 2017 and 16 in 2016). Most of the generics applications for chemical entities use the mutual recognition and decentralized procedures. Pricing systems for generics remain at national level in the EU.

**In the US**, to help the FDA ensure that participants in the US generic drug system comply with US quality standards and to increase the likelihood that American consumers get timely access to low cost, high quality generic drugs, the FDA and the industry have jointly agreed to a comprehensive program (Generic Drug User Fee Amendments) to supplement traditional appropriated funding, focused on safety, access, and transparency. The FDA has made review and approval of generics a priority for the Agency, releasing 23 (mostly product-specific) guidance documents between November 1, 2018 and December 28, 2018, and promising to release an umbrella guidance to help address common challenging regulatory and

scientific issues encountered while developing generic drugs. In the period October 1, 2017 through September 30, 2018 (the FDA s fiscal year), the FDA planned to review and act on 90% of original ANDA submissions within

10 months from the date of submission. During that period, a record number of 781 ANDAs were approved (as compared to 763 in 2017), 190 received tentative approval (174 in 2017), and 2,648 complete responses were issued (1,603 in 2017).

**In Japan**, the 2018 reforms to the NHI price system included a new special price reduction rule for long-listed drugs. Prices for long-listed drugs (10 years after generic entry) will be gradually brought closer to the generic price (starting at 2.5x generic price 10 years after generic entry). Prices will be reduced based on the generic substitution rate. Reductions are 2.0% if the substitution rate is less than 40%, 1.75% if the rate is 40% or higher but less than 60%, and 1.5% if it is 60% or higher but less than 80%.

NHI prices of first generics (previously set at 60%) were set at 50% of the price of the originator product. A 40% rule is applied to oral first generics once more than ten products with the same ingredients have obtained listing.

In addition, Sakigake premium of 10% was introduced in April 2016 for Sakigake-designated products, which have new mechanisms of action and obtain approval in Japan ahead of the rest of the world.

**B.6.3.5. Medical devices**

**In the EU**, there is no pre-market authorization by a regulatory authority. Instead there is a Conformity Assessment Procedure (for medium and high risk devices), possibly involving an independent third party Notified Body (NB) depending on the classification of the device. Once certified, medical devices have to bear the CE-mark, allowing them to circulate freely in the EU/EFTA (European Free Trade Association) countries and Turkey.

To align legal requirements across the EU Member States and to strengthen the protection of public health, two new Regulations came into force in 2017 replacing older EU Directives.

Regulation (EU) 2017/745 of the European Parliament and of the Council of April 5, 2017 on medical devices came into force on May 26, 2017 with a transition period of three years.

Regulation (EU) 2017/746 of the European Parliament and of the Council of April 5, 2017 on in vitro diagnostic medical devices came into force on May 26, 2017 with a transition period of five years.

**In the US**, the FDA Center for Devices and Radiological Health (CDRH) is responsible for regulating firms that manufacture, repackage, relabel and/or import medical devices sold in the US. The CDRH also regulates radiation-emitting electronic products (medical and non-medical) such as lasers, x-ray systems, ultrasound equipment, microwave ovens and color televisions.

Medical devices are classified into Class I, II and III based on their risks and the regulatory controls necessary to provide reasonable assurance of safety and effectiveness. Regulatory control increases from Class I to Class III. The device classification regulation defines the regulatory requirements for a

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general device type. Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval. Low and moderate risk devices (Classes I and II) can also be classified through the de novo pathway if certain conditions are met.

The basic regulatory requirements that manufacturers of medical devices distributed in the US must comply with are: Establishment Registration; Medical Device Listing; Premarket Notification 510(k) (unless exempt) or Premarket Approval; Investigational Device Exemption; Quality System Regulation; Labeling Requirements and Medical Device Reporting. In 2017 the FDA initiated a Software Precertification Program and Pilot. The purpose of the pilot is to test the initial program and model, and for the FDA to learn how companies of varying sizes develop software. As part of the process the FDA hosted a public workshop in January 2018 to gather feedback. The Precertification Program consists of four components: Excellence Appraisal; Review Determination; Streamlined Review; and Real World Performance.

**B.6.3.6. OTC drugs**

**In the EU**, four European centralized prescription to OTC (Rx-to-OTC) switches have occurred since 2009. For nationally authorized products, switches follow national rules for OTC classification. In 2017, a European platform for non-prescription medicines was launched to harmonize non-prescription status and to facilitate the switching environment.

**In the US**, the FDA approved no prescription to OTC switches in 2018 and only one in 2017: Sanofi Consumer Healthcare s Xyzal® Allergy 24HR (levocetirizine dihydrochloride).

**In Japan**, the J-MHLW drug safety committee set new rules in 2013 on the details of safety evaluations for drugs newly switched from prescription to OTC, following the passage of a bill to revise the Pharmaceutical Affairs Law (PAL). The J-MHLW gives the green light for online sales of such OTC drugs if no safety concerns arise during an initial three-year safety evaluation period. During this three-year evaluation period, drugs that moved from prescription to OTC are categorized as products that require pharmacist consultations when purchased. Under the new rules, the J-MHLW requires marketing authorization holders to submit interim reports upon completion of their post marketing surveillance (PMS).

The PMS needs to cover 3,000 patients for oral drugs and 1,000 patients for topical drugs. Based on these interim reports and other reports on adverse events, the J-MHLW performs the first evaluation on whether there are any safety concerns three years after the launch. If no safety concerns are identified during this three-year safety evaluation period, the classification of these Rx-to-OTC switches will be downgraded to Category 1 OTC drugs, i.e. drugs which do not require pharmacist consultation and can be sold online. The J-MHLW performs the second safety evaluation one year after the transfer to Category 1 OTC drugs. If

no safety concerns are identified, the classification of the Category 1 OTC drugs will be downgraded to Category 2 OTC drugs, i.e. drugs that can be handled by pharmacists but also by registered salespersons.

Generic OTC drugs can be filed after completion of the three-year PMS period and will be approved in seven months.

The J-MHLW launched a new panel in April 2016 to pick up Rx-to-OTC switch candidates. Under the new scheme, the MHLW accepts requests for Rx-to-OTC switch candidates from various stakeholders such as medical societies, consumers, and pharmaceutical companies, and then these requests are publicly reviewed by the new panel in order to minimize pressures from medical societies. Based on its deliberations, the panel refers shortlisted requests to the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) committee on nonprescription drugs, which effectively makes decisions on marketing approval for OTCs.

**B.6.3.7. Transparency and public access to documents**

Transparency regarding regulatory information, clinical trials and associated regulatory decision-making

Over the last several years the pharmaceutical industry has been subject to growing pressure for greater transparency about clinical trials (conduct and results). Regulatory authorities are also being pressed for more openness and transparency, for example by making more comprehensive disclosures about the rationale and basis for regulatory decisions on medicinal products, so as to enhance the credibility of the regulatory process. This is a significant driver of the transparency initiatives undertaken in several countries.

Pharmaceutical manufacturers have committed to publishing protocols, study information and results of clinical studies conducted with their products in publicly accessible registries. In addition, both ICH and non-ICH countries often impose mandatory disclosure of clinical trials information.

From a regulatory perspective, ambitious initiatives have been undertaken by the major regulatory authorities and Sanofi has processes in place to address these initiatives.

EU pharmaceutical legislation for medicinal products requires national regulatory authorities and the EMA to actively publish information concerning authorization and supervision of medicinal products. The EMA has introduced a series of initiatives aimed at improving the transparency of its activities, such as improving the format of the European Public Assessment Report and web-published product approvals, withdrawals and rejections. In addition, there is an increased focus on comparative efficacy and effectiveness. EU pharmacovigilance legislation aims at giving greater transparency, especially with regard to communication of safety issues (e.g. public hearings, specific European web portals with information on medicinal products). Finally, patients and consumers are increasingly involved in the work of the EMA s scientific committees.

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The EMA has committed to continuously extend its approach to transparency. A key goal in this process is the proactive publication of clinical trial data for medicines once the decision-making process on an application for an EU-wide marketing authorization is complete.

In 2014, the EMA adopted Policy 70 for publication of clinical trial reports. The policy came into force on January 1, 2015. It applies to clinical reports contained in any new marketing authorization applications for centralized marketing authorizations; to post-authorization procedures for existing centrally authorized medicinal products; and to article 58 applications (medicines that are intended exclusively for markets outside the EU).

For post-authorization procedures for existing centrally authorized medicinal products, the effective date was July 1, 2015 for extension of indication and line extension applications submitted as of that date.

The policy is being implemented in two phases:

- The first phase came into force on January 1, 2015; it applies solely to the publication of clinical reports, the data from which are accessible on the EMA website.

- In the second phase, the EMA will endeavor to find the most appropriate way to make Individual Patient Data (IPD) available, in compliance with privacy and data protection laws. The EMA will implement this phase at a later stage.

In 2016, the EMA Policy 70 process was fully transitioned to the business operational teams within Sanofi.

As of August 1, 2018 the EMA suspended all new activities related to clinical data publication. This is a result of the implementation of the third phase of the EMA s business continuity plan ahead of its relocation to the Netherlands in response to Brexit (see B.6.3.8. Other new legislation proposed or pending implementation Brexit below). The EMA is continuing to publish clinical data submitted on or before July 31, 2018, but no new data packages will be processed until further notice.

**In the US**, the FDA launched a Transparency Initiative in June 2009, with the aim of making the FDA more transparent and open to the American public by providing the public with useful, user-friendly information about agency activities and decision making.

The FDA Transparency Initiative has three phases: Phase I Improving the understanding of the FDA basics (completed, with ongoing updates); Phase II Improving the FDA s disclosure of information to the public (ongoing); and Phase III Improving the FDA s transparency to regulated industry (ongoing). Proposals to improve transparency and access to information have been released for consultation for both Phase II and Phase III. Some of the less controversial proposals have been implemented; others, such as proactive release of information that the Agency has

in its possession, may require revisions to US federal regulations.

In September 2016, the US Department of Health and Human Services, National Institute of Health (NIH) published Final

Rule under Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) on the Dissemination of Clinical Trial Information. The Final Rule requires registration and results submission for applicable clinical trials (ACTs); clarifies and expands registration data elements; expands the scope of results reporting requirements to include trials of unapproved products; clarifies and expands elements of results data; and revises the Quality Control (QC) and posting process. This information is published on a government-run database of clinical trial information (ClinicalTrials.gov) intended to increase the transparency of ongoing clinical trials in humans. In September 2018, the FDA published a draft guidance, *Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank*, delineating consequences for sponsors that fail to comply with the requirements on clinical trial registration, results posting, and certification.

Separately, in January 2018, the FDA launched a new pilot program to evaluate whether disclosing certain information included within clinical study reports (CSRs) of approved drugs is beneficial to the public. CSRs are scientific reports prepared by the sponsor to summarily address a drug s efficacy and safety, and include information related to the methods and results of clinical trials supporting the drug. Traditionally, this information has only been released following submission of a Freedom of Information Act (FOIA) request. Under the pilot program, the Agency will continue to protect trade secrets and confidential commercial information from disclosure, as required by law.

**In Japan**, the J-MHLW/PMDA actively publishes information concerning approvals of medicinal products (ethical drugs, non-prescription drugs, and quasi-drugs) and medical devices. For ethical drugs discussed at the J-MHLW s Pharmaceutical Affairs and Food Sanitation Council, redacted clinical trials data modules 1 and 2 (excluding commercially confidential information and personal data) have been made publicly available on the PMDA website.

Other transparency initiatives also exist in some other countries.

Transparency regarding Health Care Professionals

**In the EU**, there is no harmonized approach regarding transparency for Health Care Professionals (HCPs). For transparency purposes, there is increased external scrutiny of interactions between pharmaceutical companies and HCPs at national level, with legal provisions or healthcare industry voluntary undertakings in some countries (such as the UK, Denmark, France and Portugal).

In mid-2013, the European Federation of Pharmaceutical Industries Association (EFPIA) released a Code on Disclosure of Transfers of Value from Pharmaceutical Companies to HCPs and Healthcare Organizations (HCOs), the EFPIA HCP/HCO Disclosure Code . EFPIA members are required to comply with this Code and transpose it into their national codes.

The Code includes stricter rules on hospitality and gifts, with the requirement for member associations to include a threshold on hospitality and the prohibition of gifts in their national codes.

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**In the US**, the Physician Payments Sunshine Act, or Sunshine Act , was passed as part of the Affordable Care Act. The law is designed to bring transparency to financial relationships between physicians, teaching hospitals, and the pharmaceutical industry. Manufacturers and group purchasing organizations (GPOs) must report certain payments or transfers of value including payments for research, publication support, travel, honoraria and speaking fees, meals, educational items like textbooks and journal reprints whether made directly to a physician or teaching hospital or indirectly through a third party. The law also requires manufacturers and GPOs to report physicians or members of their immediate family who have an ownership interest in the company. Reports are made to the Centers for Medicare and Medicaid Services, a government agency.

**In Japan**, the Japan Pharmaceutical Manufacturers Association (JPMA) member companies started releasing information on their funding of healthcare professionals in 2013 and patient groups in 2014 under the trade group s voluntary guidelines to boost financial transparency. Under the JPMA s transparency guidelines for the relations between companies and medical institutions, its members currently report their payments in five categories: R&D, academic research support, manuscript/writing fees, provision of information, and other expenses.

**B.6.3.8. Other new legislation proposed or pending implementation**

In the **US**, in August 2017 the Food and Drug Reauthorization Act (FDARA) was signed into law. The law reauthorized user fee collection for the next five years for drugs (PDUFA VI), devices (MDUFA IV), generics (GDUFA II) and biosimilars (BsUFA II) and reflects a move to a more stable funded program. In addition to user fees, FDARA focuses on modifications and improvements of the regulation of drugs, devices and generics.

**In China**, since the initial programmatic regulatory reform initiative started in 2015, most of the country s regulatory processes have been adapted to bring them into line with other major regulatory agencies. These include establishing predictable pathways and timelines (including conditional approvals); a Marketing Application Holder system (pilot); risk-based inspections; and clinical trial processes (including 60 working days IND approval) that allow companies developing innovative drugs to conduct clinical trials simultaneously with other countries (International Multicenter Clinical Trials). The National Medical Products Administration (NMPA), formerly the China Food and Drug Administration (CFDA), also has plans to establish a system for intellectual property protection. China became an ICH management committee member in June 2018, and this is driving the need for full ICH implementation in China. The Changchun Changsheng vaccine incident in August caused the Chinese government to focus attention on the quality of vaccines and forced the NMPA to pivot to regulatory enforcement-related reforms, as well as inviting comments on the draft amendment to the Drug Administration Law (DAL) and a new draft Vaccine Administration Law. Vaccines in China are registered in accordance with the relevant provisions for

Preventive Biological Products in the Drug Registration Regulations. The release of vaccines is managed in phase with batch releases by the National Institute; there is a system for compulsory inspection and audit of each batch of products. Any products that fail the test cannot be approved or imported. Under NMPA reforms implemented to encourage approval of innovative drugs, imported vaccines also benefited from accelerated registration.

## Clinical trial regulation in the EU

The Clinical Trial Regulation ((EU) 536/2014) of the European Parliament and of the Council of April 16, 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, was published in the Official Journal of the EU on May 28, 2014.

As a result, pharmaceutical companies and academic researchers will be required to post the results of all their European clinical trials in a publicly-accessible database.

The legislation streamlines the rules on clinical trials across Europe, facilitating cross-border cooperation to enable larger and more reliable trials, as well as trials of products for rare diseases. It simplifies reporting procedures, and gives the European Commission the authority to perform audits. Once a clinical trial sponsor has submitted an application dossier to a Member State, the Member State will have to respond to it within fixed deadlines.

One of the main objectives of the European Commission in introducing the clinical trial regulation was to simplify the clinical trial approval process. The new legislation was drafted in the more stringent form of a regulation rather than as a directive, so as to achieve better harmonization between countries without interfering with Member States competencies in terms of ethical issues.

The major points are:

- The timeline for approving a clinical trial proposal is set at 60 days without questions (and a maximum of 99 with questions and clock stops). In the case of advanced therapy medicinal products, the timeline can be extended by another 50 days, making 110 days in total.

- To make both the reference state and the relevant Member States comply with the timelines, the legislation includes the concept of tacit approval. Selection of reference Member State by the sponsor was maintained.

- As regards transparency requirements for clinical trial data submitted through a single EU submission portal and stored in a Union-level database, the new clinical trial regulation allows for protection of personal data of patients and commercially confidential information, which is in line with the industry data sharing laid out in Policy 70 (see previous section). Although the Regulation was adopted and entered into force in 2014, the timing of its application depends on confirmation of full functionality of the EU portal and database through an

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independent audit. The Regulation becomes applicable six months after the European Commission publishes notice of this confirmation.

In October 2018, the EMA Management Board heard that the development of the auditable release of the portal and database is complete. The release is now in an intensive phase of pre-testing before formal user acceptance testing can start in early 2019.

Taking into account the rate of progress with testing and bug fixing, and the EMA s relocation to Amsterdam, the audit field work will take place once the Agency has settled in Amsterdam, after March 2019. Dependent on successful completion of the audit and review by the Management Board around the end of 2019, the system could be ready to go live later in 2020.

Other transparency initiatives also exist in some other countries.

### Falsified medicines

The EU has reformed the rules for importing active substances for medicinal products for human use into the EU (Directive 2011/62/EU). Since January 2013, all imported active substances must have been manufactured in compliance with GMP standards or standards at least equivalent to GMP. The manufacturing standards in the EU for active substances are those specified in Q7 as issued by the International Council for Harmonization (ICH). With effect from July 2, 2013, such compliance must be confirmed in writing by the competent authority of the exporting country, except for countries with waivers. Written confirmation must also confirm that the plant where the active substance was manufactured is subject to control and enforcement of GMP at least equivalent to that in the EU.

Several implementing measures for the Falsified Medicines Directive have been adopted. A common EU logo for online pharmacies was adopted in June 2014, giving Member States until July 2015 to prepare for its application. Detailed rules for the safety features appearing on the outer packaging of medicinal products for human use have been adopted, meaning that all prescription drugs or reimbursed drugs commercialized on the European market will have to be serialized by February 2019. Within the scope of this directive, a European system is in place to ensure that the product delivered to the patient is genuine by reading the unique serialized number per medicinal box unit at the point of dispensation (pharmacist or hospital).

In the USA, the Drug Supply Chain Security Act was implemented since November 2018 for some prescription products; it will also help guarantee the traceability of drug products and to address falsified medicines.

### Nagoya Protocol

The Nagoya Protocol came into force in October 2014 and was intended to create greater legal certainty and transparency for both providers and users of genetic resources by:

establishing more predictable conditions for access to genetic resources; and

helping to ensure benefit-sharing when genetic resources leave the contracting party providing the genetic resources.

In the EU, the European Commission published the implementation Act in 2015 (Regulation 2015/1866).

It states that the pharmaceutical industry has to implement compliance procedures for non-human biological materials used in the discovery, development, manufacturing and packaging of medicinal products.

The Sanofi Nagoya Ready Project was launched in 2015 to ensure compliance with international treaties on the sustainable use of biodiversity. The Nagoya Ready Project Team has ensured that Sanofi is prepared for compliance with the Nagoya Protocol and ready for full implementation. A Nagoya Expert Group reporting to the Bioethics Committee will continue to monitor the international implementation of the protocol and provide appropriate support and advice to the relevant Sanofi teams.

**In Japan**, the government submitted the instrument of ratification on May 22, 2017; it became effective on August 20, 2017. Currently the discussion on benefit-sharing of genetic resources is ongoing.

NDA electronic clinical trial data submission (eCTD)

**In the EU**, electronic submission for marketing authorization and variation applications has already been in place for many years.

To allow secure submission over the Internet for all types of eCTD applications for human medicines, the EMA launched the eSubmission Gateway, which is now mandatory for all eCTD submissions through the centralized procedure, in order to improve efficiency and decrease costs for applicants.

As of July 1, 2015, companies are obliged to use electronic application forms provided by the EMA for all centralized marketing authorization applications for human and veterinary medicines. From January 2016, the use of electronic application forms became mandatory for all other EU marketing authorization procedures (i.e. mutual recognition and decentralized procedures, and national submissions).

**In Japan**, electronic submission of CDISC-based clinical data will become mandatory after the transition period that runs from October 2016 to March 2020, allowing the authority to efficiently store and analyze the data to improve its efficacy and safety predictions.

Such mandatory electronic submissions are expected to be limited to clinical trial data for new drugs newly filed for regulatory approval. The necessity for electronic submission for Phase I trial data will likely be decided on a case-by-case basis, while pharmaceutical companies will be required to file non-clinical toxicity study data in one of the Standard for the Exchange of Non-clinical Data (SEND) formats in due course.

Brexit

The decision by the UK to withdraw from the EU (Brexit) has triggered a need to adapt regulatory activities in the region. Early in 2017, the EMA established a working group to explore options to redistribute across the remaining network the workload related to human and veterinary medicines and inspections currently managed by the UK.

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The redistribution takes account of the diverse expertise in the network and the workload associated with the regulation of medicines. In April 2018, the remaining Member States (EU27) and the EMA completed the distribution of the UK s portfolio of over 370 centrally authorized products in preparation for Brexit. The new rapporteurs and co-rapporteurs in the EU27, Iceland and Norway will take full responsibility for these products as of March 30, 2019.

To safeguard continuity of operations and secure the timely execution of its core tasks, the EMA has launched a Business Continuity Plan (BCP). The BCP defines priority levels for EMA activities according to their impact on public health and the ability of the EMA to manage its tasks in light of the resources available. The plan entered its third phase on October 1, 2018, with the temporary suspension or reduction of activities; guideline development and revision were scaled back, and non-product-related working parties temporarily put on hold. These changes are currently scheduled to last until June 30, 2019, but will be subject to a review in April 2019 once the EMA has moved to its temporary premises in Amsterdam.

Following the 2017 procedure, the EU has published a regulation officially naming Amsterdam as the new seat of the EMA.

On November 25, 2018, the EU officially endorsed the terms of the UK s withdrawal, bringing to an end negotiations which began in March 2017. The EU leaders have approved the final text of the draft EU Withdrawal Agreement. The Withdrawal Agreement includes provisions for a transition, or implementation , period lasting until December 31, 2020, during which EU law will continue to apply in the UK. During this time, the UK Medicines and Healthcare Regulatory Authority (MHRA) will continue to operate under the jurisdiction of the EMA. However, the MHRA will no longer be able to participate in EMA activities unless expressly invited to do so.

The UK Parliament voted against the Withdrawal Agreement on January 15, 2019 by a large majority. Since then there have been two votes in the UK Parliament on various amendments, and the UK Prime Minister has been tasked to go back to Brussels to ask for change to the Withdrawal agreement. There will be a further vote not later than 27 February 2019, and the UK Parliament will be asked to vote in favour of the Withdrawal deal or on further options. If the agreement is not approved by Parliament then this will be a no deal or hard Brexit scenario in which EU law will cease to apply in the UK as of 11 pm on March 29, 2019. However much could still happen before this date, including a general election, a second referendum or even rescinding Article 50.

Sanofi has set up an internal Brexit Task Force to proactively address issues triggered by Brexit. A Brexit readiness analysis was conducted by a third party. The primary objectives were to provide an external perspective on the level of comprehensiveness and rigor of Sanofi s Brexit planning activities, surface any potential concerns or risks, and suggest targeted mitigation measures where applicable. The stress test concluded that Sanofi is well prepared for Brexit across most

impact categories, with implementation of strategies generally on track. A plan was put into place to address remaining gaps with the goal of achieving full readiness before 29 March 2019. Sanofi has set up contingency plans, such as stockpiling certain medicines or shifting operations from the UK to the EU in the event of a hard Brexit , as

there are no guarantees for effective transitional solutions being in place by March 30, 2019 and because the model for the future UK-EU relationship is still unclear.

### *B.6.4. Pricing & Reimbursement*

Increasingly, efforts to control drug expenditures in most markets in which Sanofi operates result in pricing and market-access controls for pharmaceuticals. The nature and impact of these controls vary from country to country, but some common themes are: reference pricing, systematic price reductions, formularies, volume limitations, patient co-pay requirements, and generic substitution. In addition, governments and third-party payers are increasingly demanding comparative and/or relative effectiveness data and budget impact modelling to support their decision-making process. They are also increasing their use of emerging healthcare information technologies such as electronic prescribing and health records to increase oversight on efficacy and safety and to improve compliance with prescribing guidelines. As a result, the environment in which pharmaceutical companies must operate in order to make their products available to patients and providers who need them becomes more complex each year.

While a drive to expand healthcare coverage has become a noticeable feature in many regions, providing opportunities for the industry, it has also put pressure on these new budgets, bringing with it a wave of price and volume control measures. Many countries and regions have increased pressure on pricing through joint procurement and negotiation. National production, whether through a policy of industrialization, technology transfer agreements or preferential conditions for local production, is also a growing issue.

Significant trends in the US:

Private health insurance is offered widely as part of employee benefit packages, and is the main source of access to subsidized healthcare provision. Some individuals purchase private health plans directly, while publicly-subsidized programs provide cover for retirees, the poor, the disabled, uninsured children, and serving or retired military personnel. Double-coverage can occur. Public health insurances include:

- Medicare, which provides health insurance for retirees and for people with permanent disabilities. The basic Medicare scheme (Part A) provides hospital insurance only and the vast majority of retirees purchase additional cover through some or all of three other plans named Part B, Part C and Part D. Part D enables Medicare beneficiaries to obtain outpatient drug subsidies. Almost two-thirds of all Medicare beneficiaries have enrolled in Part D plans.

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Medicaid, which provides health insurance for low-income families, certain qualified pregnant woman and children, individuals receiving supplemental security income, and other eligible persons determined on a state-by-state basis.

Managed Care Organizations (MCOs) combine the functions of health insurance, delivery of care, and administration. MCOs use

specific provider networks and specific services and products. There are three types of managed care plans: Health Maintenance Organizations (HMOs), Preferred Provider Organizations (PPOs), and Point of Service (POS) plans.

Pharmacy benefit managers (PBMs) serve as intermediaries between insurance companies, pharmacies and manufacturers to secure lower drug costs for commercial health plans, self-insured employer plans, Medicare Part D plans, and federal and state government employee plans.

The US market has seen increased consolidation of key payer organizations. Most notably, the CVS-Aetna and Cigna-ESI mergers point to a strong role for integrated payers and PBMs in terms of product access and affordability. This trend may also impact market pricing for pharmaceuticals going forward. With the largest three PBMs now covering over 75% of the market, consolidation has led to significant negotiating power for commercial plans. Commercial payers continue to employ tools designed to lower plan-level net costs; these include formulary management tools and exclusions, benefit design changes and generic conversions, and the adoption of biosimilars (which are now beginning to transform the US biologics landscape).

The current Administration has increasingly focused on the cost of prescription drugs in order to align policy with the President s campaign promise to address the disparity between drug prices paid by Americans and the rest of the world (referred to as the American Patients First plan). Since the publication of the American Patients First Blueprint in 2018, there has been proposed legislation, rulemaking, and guidance that indicates the Administration s priorities are to cut list prices, increase competition for Medicare part B drugs, and reduce out of pocket costs for patients. These proposals include action like a proposed International Price Index Model to tether domestic prices to the international markets, and suggested reforms to the rebate system to eliminate incentives that lead to higher list prices. These proposals are not settled and there is ongoing uncertainty regarding if, when, and how the costs of federally funded programs would be lowered. Other major changes at the federal level in line with these trends include (i) the early closure of the Medicare Part D donut hole gap in coverage, which saw manufacturer s share of costs increase from 50% to 70%; and (ii) the increasing use of co-pay accumulator adjustment programs. Additionally, these trends are not limited to the federal level as states are also increasingly concerned with prescription drug prices and are continuing to consider legislation that may further impact the regulatory landscape.

Through all of these changes, we remain committed to responsible business practices. In February 2019, we updated our public commitment to the pricing principles we first published

in 2017, impacting our practices both in the US and in other markets (for more information, see https://www.sanofi.com/en/our-responsibility/documents-center/).

Significant trends in China:

China has a quarter of the cancer deaths in the world, a diabetes prevalence of 10.9% and ongoing supply problems for basic medicines. Compounded with public pressure over a range of scandals (such as fake vaccines and the quality of generics) and the affordability of oncology products, there has been continuing pressure on the Chinese government to modernize the national pharmaceutical landscape. Several policy reforms over the past few years are finally beginning to have their effect. There is now a considerable acceleration in updates of the National Reimbursement Drug List (NRDL) and Essential Drugs List, especially for oncology products. The first major update of the NRDL in February 2017 has been followed by further additions, including 17 oncology products that were added in October 2018. However, there is still no clarity on pricing methods. National negotiations and a recent collective negotiation on 47 oncology products run jointly by 14 provinces show a tendency to push for lower prices to reflect these increased volumes. This is not limited to oncology: following the introduction in 2015 of the Generic Quality Consistency Evaluation, a measure designed to ensure bioequivalency of Chinese generics, it was announced in September 2018 that generics demonstrating bioequivalence would be allowed to participate in a pilot tender involving 4 municipalities and 7 major cities. The tender took place in December 2018, and resulted in significant price decreases. In many other pilots, formal and informal international price referencing has again played a part. It remains to be seen how the Chinese authorities will implement health technology assessment (HTA) following the creation of a new HTA body, or how their orphan drug policy will lead to real market access. While access to the market is increasingly being facilitated, especially following the waiver for local clinical trial data, it remains to be seen how the cost of this potentially massive increase in volume will be managed.

Significant trends in other markets:

In Canada, the international price benchmarking basket is set to grow, a change which will be accompanied by a string of cost-cutting measures applied according to the cost-effectiveness level of a drug s indications. In Japan, negotiations are still ongoing for the long-awaited implementation of HTA, which is expected in 2019. Already, 2018 saw a number of new measures implemented: cost-containment mechanisms for market expansion and high sales, new international reference pricing rules, and changes to the price maintenance premium system.

In Europe, the UK s imminent exit from the EU is still uncertain with several possible implications for the pharmaceutical industry. Much remains to be decided on how the two parties, the EC and the UK government, will align and accept the regulations of each other. In the short term, Sanofi has mitigated risk by planning for a no-deal Brexit, stockpiling medicines and vaccines where global supply allows and establishing new supply routes into the

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UK. For the most part, prices of medicines and vaccines to the NHS are fixed in sterling, which gives some risk of sterling-to-euro fluctuations in the event of a no-deal. In the longer term, small increased costs could occur with the application of border checks if customs arrangements have not been resolved at the time of the UK s exit, and as a result of the UK s exit from the EMA and subsequent need to file submissions with the UK Medicines and Healthcare Products Regulatory Agency (MHRA).

We believe that third-party payers will continue to act to curb the cost of pharmaceutical products. While the impact of those measures cannot be predicted with certainty, we are taking the necessary steps to defend the accessibility and price of our products in order to reflect the value of our innovative product offerings, and we continue to develop and pilot innovative contracting platforms with commercial payers to better align our price and value across multiple therapeutic areas including diabetes, rheumatoid arthritis, multiple sclerosis and asthma.

**B.7. Patents, intellectual property and other rights**

*B.7.1. Patents*

**Patent protection**

We own a broad portfolio of patents, patent applications and patent licenses worldwide. These patents are of various types and may cover:

- active ingredients;
- pharmaceutical formulations;
- product manufacturing processes;
- intermediate chemical compounds;
- therapeutic indications/methods of use;
- delivery systems; and

enabling technologies, such as assays.

Patent protection for individual products typically extends for 20 years from the patent filing date in countries where we seek patent protection. A substantial part of the 20-year life span of a patent on a new molecule (small molecule or biologic) has generally already passed by the time the related product obtains marketing authorization. As a result, the effective period of patent protection for an approved product s active ingredient is significantly shorter than 20 years. In some cases, the period of effective protection may be extended by procedures established to compensate regulatory delay in Europe (via Supplementary Protection Certificate or SPC), in the US (via Patent Term Extension or PTE) and in Japan (also via PTE).

Additionally, the product may benefit from the protection of patents obtained during development or after the product s initial marketing authorization. The protection a patent provides to the related product depends upon the type of patent and its scope of coverage, and may also vary from country to country. In Europe for instance, applications for new patents may be submitted to

the European Patent Office (EPO), an intergovernmental organization which centralizes filing and prosecution. As of December 2017, an EPO patent application may cover the 38 European Patent Convention Member States, including all 28 Member States of the EU. The granted European Patent establishes corresponding national patents with uniform patent claims among the Member States. However, some older patents were not approved through this centralized process, resulting in patents having claim terms for the same invention that differ between the countries. Additionally, a number of patents prosecuted through the EPO may pre-date the European Patent Convention accession of some current European Patent Convention Member States, resulting in different treatment in those countries.

In 2013, EU legislation was adopted to create a European Unitary Patent and a Unified Patent Court. However, it will only enter into force once the agreement on the Unified Patent Court is ratified by at least 13 Member States including France, Germany, and the United Kingdom. As of the date of this document, 14 countries including France have ratified the agreement, but ratification by the United Kingdom and Germany is still outstanding, and the process is impacted by Brexit.

The Unitary Patent will provide unitary protection within the participating states of the EU (when ratified by the Member States with the exception of Croatia, Spain, and Poland, not currently signatories of the agreement). The Unified Patent Court will be a specialized patent court with exclusive jurisdiction for litigation relating to European patents and Unitary Patents. The Court will be composed of a central division (headquartered in Paris) and several local and regional divisions in the contracting Member States to the agreement. The Court of Appeal will be located in Luxembourg.

We monitor our competitors and vigorously seek to challenge patent infringements when such infringements would negatively impact our business objectives. See Item 8 A. Consolidated Financial Statements and Other Financial Information Information on Legal or Arbitration Proceedings Patents of this annual report.

The expiration or loss of a patent covering a new molecule, typically referred to as a compound patent, may result in significant competition from generic products and can result in a dramatic reduction in sales of the original branded product (see Item 3. Key Information D. Risk Factors ). In some cases, it is possible to continue to benefit from a commercial advantage through product manufacturing trade secrets or other types of patents, such as patents on processes, intermediates, compound structure, formulations, methods of treatment, indications or delivery systems. Certain categories of products, such as traditional vaccines and insulin, were historically relatively less reliant on patent protection and may in many cases have no patent coverage. It is nowadays increasingly frequent for novel vaccines and insulins also to be patent protected. Finally, patent protection is of comparatively lesser importance to our Consumer Healthcare and generics businesses, which rely principally on trademark protection.

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**Regulatory exclusivity**

In some markets, including the EU and the US, many of our pharmaceutical products may also benefit from multi-year regulatory exclusivity periods, during which a generic competitor may not rely on our clinical trial and safety data in its drug application. Exclusivity is meant to encourage investment in research and development by providing innovators with exclusive use, for a limited time, of the innovation represented by a newly approved drug product. This exclusivity operates independently of patent protection and may protect the product from generic competition even if there is no patent covering the product.

In the US, the FDA will not grant final marketing authorization to a generic competitor for a New Chemical Entity (NCE) until the expiration of the regulatory exclusivity period (five years) that commences upon the first marketing authorization of the reference product. The FDA will accept the filing of an Abbreviated New Drug Application (ANDA) containing a patent challenge one year before the end of this regulatory exclusivity period (see the descriptions of ANDAs in Product Overview Challenges to Patented Products below). In addition to the regulatory exclusivity granted to NCEs, significant line extensions of existing NCEs may qualify for an additional three years of regulatory exclusivity if certain conditions are met. Also, under certain limited conditions, it is possible to extend unexpired US regulatory and patent-related exclusivities by a pediatric extension. See Pediatric Extension , below.

In the US, a different regulatory exclusivity period applies to biological drugs. The Biologics Price Competition and Innovation Act of 2009 ( BPCIA ) was enacted on March 23, 2010 as part of the Affordable Care Act. The BPCIA introduced an approval pathway for biosimilar products. A biosimilar product is a biologic product that is highly similar to the reference (or innovator) product, and which has no clinically meaningful differences from the reference product in terms of the safety, purity, and potency of the product. The BPCIA provides that an application for a biosimilar product that relies on a reference product may not be submitted to the FDA until four years after the date on which the reference product was first licensed, and that the FDA may not approve a biosimilar application until 12 years after the date on which the reference product was first licensed. US Federal and state officials, including the current Administration, are continuing to focus on the cost of health coverage and health care although the future policy, including the nature and timing of any changes to the Affordable Care Act, remains unclear.

In the EU, regulatory exclusivity is available in two forms: data exclusivity and marketing exclusivity. Generic drug applications will not be accepted for review until eight years after the first marketing authorization (data exclusivity). This eight-year period is followed by a two-year period during which generics cannot be marketed (marketing exclusivity). The marketing exclusivity period can be extended to three years if, during the first eight-year period, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which are deemed to provide a significant clinical benefit over existing therapies. This is known as the 8+2+1 rule.

In Japan, the regulatory exclusivity period varies from four years for medicinal products with new indications, formulations, dosages, or compositions with related prescriptions, to six years for new drugs containing a medicinal composition or requiring a new route of administration; eight years for drugs containing a new chemical entity; and ten years for orphan drugs or new drugs requiring pharmaco-epidemiological study.

**Emerging markets**

One of the main limitations on our operations in emerging market countries is the lack of effective intellectual property protection or enforcement for our products. The World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIP) required developing countries to amend their intellectual property laws to provide patent protection for pharmaceutical products since January 1, 2005. However, it also provided a limited number of developing countries with an extended period in which to achieve compliance with TRIP. Additionally, these same countries frequently do not provide non-patent exclusivity for innovative products. While the situation has gradually improved, the lack of protection for intellectual property rights or the lack of robust enforcement of intellectual property rights poses difficulties in certain countries. Additionally, in recent years a number of countries facing health crises have waived or threatened to waive intellectual property protection for specific products, for example through compulsory licensing of generics. See Item 3. Key Information D. Risk Factors Risks Relating to Sanofi s Structure and Strategy The globalization of our business exposes us to increased risks in specific areas .

**Pediatric extension**

In the US and the EU, under certain conditions, it is possible to extend a product s regulatory exclusivity for an additional period of time by providing data on pediatric studies.

In the US, the FDA may ask a company for pediatric studies if it has determined that information related to the use of the drugs in the pediatric population may produce health benefits. The FDA has invited us by written request to provide additional pediatric data on several of our main products. Under the Hatch-Waxman Act, timely provision of data meeting the FDA s requirements (regardless of whether the data supports a pediatric indication) may result in the FDA extending regulatory exclusivity and patent life by six months, to the extent these protections have not already expired (the so-called pediatric exclusivity ).

In Europe, a regulation on pediatric medicines provides for pediatric research obligations with potential associated rewards including extension of patent protection (for patented medicinal products) and six month regulatory exclusivity for pediatric marketing authorization (for off-patent medicinal products).

In Japan, there is no pediatric research extension of patent protection (for patented medicinal products). However, regulatory exclusivity may be extended from eight to ten years.

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**Orphan drug exclusivity**

Orphan drug exclusivity may be granted in the US to drugs intended to treat rare diseases or conditions (affecting fewer than 200,000 patients in the US, or in some cases more than 200,000 with no expectation of recovering costs).

Obtaining orphan drug exclusivity is a two step process. An applicant must first seek and obtain orphan drug designation from the FDA for its drug for one or more indications. If the FDA approves a drug for the designated indication, the drug will generally receive orphan drug exclusivity for such designated indication.

Orphan drug exclusivity runs from the time of approval and bars approval of another application (ANDA, 505(b)(2), New Drug Application (NDA) or Biologic License Application (BLA)) from a different sponsor for the same drug in the same indication for a seven year period. Whether a subsequent application is for the same drug depends upon the chemical and clinical characteristics. The FDA may approve applications for the same drug for indications not protected by orphan exclusivity.

Orphan drug exclusivities also exist in the EU and Japan.

**Product overview**

We summarize below the intellectual property coverage (in some cases through licences) in our major markets of the marketed products described above at B.2. Main Pharmaceutical Products . In the discussion of patents below, we focus on active

ingredient patents (compound patents) and for NCEs on any later filed patents listed, as applicable, in the FDA s list of Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book ) or in their foreign equivalents. For Biologics the Orange Book listing does not apply. These patents or their foreign equivalents tend to be the most relevant in the event of an application by a competitor to produce a generic or a biosimilar version of one of our products (see Challenges to Patented Products below). In some cases, products may also benefit from pending patent applications or from patents not eligible for Orange Book listing (for NCEs) (e.g. patents claiming industrial processes). In each case below, we specify whether the active ingredient is claimed by an unexpired patent. Where patent terms have been extended to compensate for US Patent and Trademark Office (USPTO) delays in patent prosecution (Patent Term Adjustment PTA) or for other regulatory delays, the extended dates are indicated below. The US patent expirations presented below reflect USPTO dates, and also reflect six month pediatric extensions when applicable. Where patent terms have expired we indicate such information and mention whether generics are on the market.

We do not provide later filed patent information relating to formulations already available as an unlicensed generic. References below to patent protection in Europe indicate the existence of relevant patents in most major markets in the EU. Specific situations may vary by country, most notably with respect to older patents and to countries that have only recently joined the EU.

We additionally set out any regulatory exclusivity from which these products continue to benefit in the US, EU or Japan. Regulatory exclusivities presented below incorporate any pediatric extensions obtained. While EU regulatory exclusivity is intended to be applied throughout the EU, in some cases Member States have taken positions prejudicial to our exclusivity rights.

| | United States | European Union | Japan |
|---|---|---|---|
| Aldurazyme® (laronidase) | Compound: November 2019<br><br>Later filed patents: ranging through July 2020 with PTA** | Compound: November 2020 in some EU countries only<br>Later filed patent: November 2020 in some EU countries only | Compound: November 2020 |
| Allegra®/Telfast® (fexofenadine hydrochloride) | Compound: expired<br><br>Generics on the market<br>Converted to over-the-counter | Compound: expired<br><br>Generics on the market<br>Converted to over-the-counter | Compound: expired<br><br>Generics on the market<br>Converted to over-the counter |
| Alprolix®(eftrenonacog alfa) | Compound: March 2028 with PTA** and PTE**<br><br>Later filed patents: coverage ranging through December 2037 (pending)<br>Biologics regulatory exclusivity: March 2026 | Compound: May 2024 (May 2029 with SPC** in most EU countries, if granted)<br><br>Later filed patents: coverage ranging through December 2037 (pending)<br>Regulatory exclusivity: May 2026 | Compound: February 2026 with PTE**<br><br>Later filed patents: coverage ranging through December 2037 (pending)<br>Regulatory exclusivity:<br><br>July 2022 |
| Amaryl®/Amarel® (glimepiride) | Compound: expired<br><br>Generics on the market | Compound: expired<br><br>Generics on the market | Compound: expired<br><br>Generics on the market |

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| | United States | European Union | Japan |
|---|---|---|---|
| Apidra® (insulin glulisine) | Compound: expired | Compound: September 2019 with SPC** in most of the EU countries | Compound: May 2022 with PTE** |
| | Later filed patents: ranging through September 2027 | Later filed patent: March 2022 | Later filed patent: July 2022 |
| Aprovel®/Avapro® (irbesartan) | Compound: expired | Compound: expired | Compound: expired |
| | | | Later filed patent: June 2021 with PTE** |
| | Generics on the market | Generics on the market | Generics on the market |
| **Aubagio® (teriflunomide)*** | **Compound: expired** | **Compound: expired** | **Compound: expired** |
| | **Later filed patents: coverage ranging through February 2034** | **Later filed patent: coverage ranging through September 2030** | **Later filed patent: coverage ranging through March 2024** |
| | | **Regulatory exclusivity: August 2023** | |
| Cablivi® (caplacizumabt) | Compound: August, 2027 (January 2032 with PTE** if granted) | Compound: May 2026 (May 2031 with SPC** if granted) | Compound: May 2026 (with PTE** if granted) |
| | Later filed patents: coverage ranging through June 2035 (pending) | Later filed patents: coverage ranging through June 2035 | Later filed patents: coverage ranging through June 2035 |
| | Biologics regulatory exclusivity: August 2031 (with PED) | Regulatory exclusivity: August 31, 2030 (with orphan PED) | Regulatory exclusivity: to be determined |
| Cerdelga® (eliglustat) | Compound: 2026 with PTE** | Compound: July 2022 (July 2027 with SPC** if granted) | Compound: March 2025 with PTE** |
| | Later filed patent: November 2030 (pending) | Later filed patent: November 2030 | Later filed patent: November 2030 (pending) |
| | Regulatory exclusivity: August 2019 | Orphan drug exclusivity: January 2025 | Regulatory exclusivity: March 2023 |
| | Orphan drug exclusivity: August 2021 | | |
| **Cerezyme® (imiglucerase)*** | **Compound: expired** | **Compound: N/A** | **Compound: N/A** |
| Depakine® (sodium valproate) | Compound: N/A[1] | Compound: N/A | Compound: N/A |
| | | Later filed patent: Expired | Later filed patent: Expired |

| | | | |
|---|---|---|---|
| **Dupixent® (dupilumab)*** | **Compound: October 2027 (Mar 2031 with PTE** if granted)<br>Later filed patents: coverage ranging through January 2036 with PTA**<br>Regulatory exclusivity: March 2029** | **Compound: October 2029 (September 2032 with SPC** if granted)<br>Later filed patents: coverage ranging through November 2035 (pending)<br>Regulatory exclusivity: September 2027** | **Compound: October 2029 (June 2034 with PTE** if granted)<br>Later filed patents: coverage ranging through November 2035 (pending)<br>Regulatory exclusivity: January 2026** |

*(1) No rights to compounds in the US, EU and Japan.*

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| | United States | European Union | Japan |
|---|---|---|---|
| Eloctate® (efmoroctocog alfa) | Compound: June 2028 with PTA** and PTE** | Compound: May 2024 (May 2029 with SPC** in most EU countries, if granted) | Compound: August 2026 with PTE** |
| | Later filed patents: coverage ranging through December 2037 (pending) | Later filed patents: coverage ranging through December 2037 (pending) | Later filed patents: coverage ranging through December 2037 (pending) |
| | Biologics regulatory exclusivity: June 2026 | Regulatory exclusivity: November 2025 | Regulatory exclusivity: December 2022 |
| **Fabrazyme® (agalsidase beta)*** | **Compound: N/A** | **Compound: N/A** | **Compound: N/A** |
| | **Later filed patents: expired** | **Later filed patents: expired** | **Later filed patents: expired** |
| Insuman® (human insulin) | Compound: N/A | Compound: N/A<br>Later filed patents: expired | Compound: N/A |
| Jevtana® (cabazitaxel) | Compound: September 2021 with PTE** and pediatric exclusivity | Compound: expired | Compound: March 2021 with PTE** |
| | Later filed patents: coverage ranging through April 2031 with pediatric exclusivity | Later filed patents: coverage ranging through October 2030 (pending) | Later filed patents: coverage ranging through November 2030 with PTE** |
| | | Regulatory exclusivity: March 2021 | Regulatory exclusivity: July 2022 |
| Kevzara® (sarilumab) | Compound: January 2028 with PTA** | Compound: June 2027 | Compound: June 2027 |
| | Later filed patents: coverage ranging through March 2037 (pending) | Later filed patents: coverage ranging through March 2037 (pending) | Later filed patents: coverage ranging through March 2037 (pending) |
| | Regulatory exclusivity: May 2029 | Regulatory exclusivity: June 2027 | Regulatory exclusivity: September 2025 |
| **Lantus® (insulin glargine)*** | **Compound: expired**<br>**Later filed patents ranging through March 2028**<br>**Generics / biosimilars on the market** | **Compound: Expired**<br>**Later filed patent: June 2023**<br>**Generics / biosimilars on the market** | **Compound: expired**<br>**Later filed patent: June 2023**<br>**Generics / biosimilars on the market** |
| Lemtrada® (alemtuzumab) | Compound: expired | Compound: expired | Compound: expired |

| | | | |
|---|---|---|---|
| | Later filed patent: August 2029 with PTA** | Later filed patent: September 2027(1) | Later filed patent: September 2027 |
| **Lovenox® (enoxaparin sodium)*** | **Compound: N/A** | **Compound: expired** | **Compound: expired** |
| | **Generics / biosimilars on the market** | **Generics / biosimilars on the market** | |
| **Lumizyme® / Myozyme® (alglucosidase alpha)*** | **Compound: N/A** | **Compound: N/A** | **Compound: N/A** |
| | **Later filed patents: coverage ranging through February 2023 with PTA**** | **Later filed patents: coverage ranging through July 2021** | **Later filed patents: coverage ranging through July 2021** |

*(1) Patent revoked, appeal pending.*

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| | United States | European Union | Japan |
|---|---|---|---|
| Lyxumia®/Adlyxin® (lixisenatide) | Compound: July 2020 (July 2025 with PTE** if granted)<br>Later filed patents: coverage ranging through August 2032<br>Regulatory exclusivity: July 2021 | Compound: July 2020 (2025 with SPC** in most EU countries if granted)<br>Later filed patents: November 2030 (pending)<br>Regulatory exclusivity: February 2023 | Compound: July 2024 with PTE**<br>Later filed patents: November 2030<br>Regulatory exclusivity: June 2021 |
| Mozobil® (plerixafor) | Compound: N/A<br>Later filed patents: coverage ranging through July 2023 | Compound: N/A<br>Later filed patent: July 2022 (2024 with SPC** in some EU countries)<br>Orphan drug exclusivity: August 2019 | Compound: N/A<br>Later filed patent: August 2026 with PTE**<br>Orphan drug exclusivity: December 2026 |
| Multaq® (dronedarone hydrochloride) | Compound: expired<br>Later filed patents: coverage ranging through June 2031 | Compound: expired<br>Later filed patent: June 2023 with SPC**<br>Regulatory exclusivity: December 2019 | Compound: expired |
| **Plavix® (clopidogrel bisulfate)*** | **Compound: expired** | **Compound: expired** | **Compound: expired** |
| | **Generics on the market** | **Generics on the market** | **Generics on the market** |
| Praluent® (alirocumab) | Compound: December 2029<br>Later filed patents: coverage ranging through September 2032 (pending)<br>Biologics regulatory exclusivity: July 2027 | Compound: December 2029 (September 2030 if SPC** granted)<br>Later filed patents: coverage ranging through September 2032 (pending)<br>Regulatory exclusivity: September 2025 | Compound: November 2032 with PTE**<br>Later filed patents: coverage ranging through September 2032<br>Regulatory exclusivity: July 2024 |
| | Compound: N/A | Compound: N/A | Compound: N/A |

| | | | |
|---|---|---|---|
| Renagel® (sevelamer hydrochloride) | | | |
| | Later filed patent: October 2020 | Later filed patent: October 2020 | Later filed patent: October 2020 |
| Renvela® (sevelamer carbonate) | Compound: N/A | Compound: N/A | Compound: N/A |
| | Later filed patents: October 2025 (tablet) and December 2030 (sachet) | Later filed patent: November 2025 (tablet) and September 2026 (sachet) | Later filed patents: November 2025 (tablet) and September 2026 (sachet) |
| | Generics on the market | Generics on the market | |
| Soliqua®100/33 / Suliqua® (lixisenatide + insulin glargine) | Compound: July 2020 (July 2025 with PTE** if granted) | Compound: July 2020 (July 2025 with SPC** in most EU countries if granted) | Compound: July 2024 with PTE** |
| | Later filed patents: coverage ranging through November 2035 | Later filed patents: coverage ranging through January 2032 with SPC** | Later filed patents: coverage ranging through November 2030 |
| | Regulatory exclusivity: July 2021 | Regulatory exclusivity: January 2027 | Regulatory exclusivity: to be determined |
| Stilnox®/Ambien® (zolpidem tartrate) | Compound: expired | Compound: expired | Compound: expired |
| | Generics on the market | Generics on the market | Generics on the market |

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| | United States | European Union | Japan |
|---|---|---|---|
| Synvisc® (Hylan G-F 20) | Compound: expired | Compound: N/A | Compound: expired |
| Synvisc-One® (Hylan G-F 20) | Compound: expired | Compound: N/A<br><br>Later filed patent: December 2025 | Compound: expired<br><br>Later filed patent: December 2025 |
| **Toujeo® (insulin glargine)*** | **Compound: expired<br>Later filed patents: coverage ranging through May 2031** | **Compound: expired<br>Later filed patents: coverage ranging through May 2031 (pending)** | **Compound: expired<br>Later filed patents: coverage ranging through July 2033 with PTE**<br>Regulatory exclusivity: July 2019** |
| Zaltrap® (aflibercept) | Compound: May 2020 (July 2022 with PTE** if granted)<br><br>Later filed patents: coverage ranging through April 2032 (pending)<br>Biologics regulatory exclusivity: November 2023 | Compound: May 2020 (May 2025 with SPC** in most EU countries, if granted)<br>Later filed patents: coverage ranging through April 2032<br><br>Regulatory exclusivity: February 2023 | Compound: May 2020 (May 2025 with PTE** if granted)<br><br>Later filed patents: coverage ranging through April 2032<br>Regulatory exclusivity:<br><br>March 2023 |

* *The products shown in bold are the most significant in terms of sales (2% or more of Sanofi s sales in 2018).*

***PTE: Patent Term Extension. SPC: Supplementary Protection Certificate. PTA: Patent Term Adjustment.*

Patents held or licensed by Sanofi do not in all cases provide effective protection against a competitor s generic version of our products. For example, notwithstanding the presence of unexpired patents, competitors launched generic versions of Allegra® in the US (prior to the product being switched to over-the-counter status) and Plavix® in the EU.

We caution the reader that there can be no assurance that we will prevail when we assert a patent in litigation and that there may be instances in which Sanofi determines that it does not have a sufficient basis to assert one or more of the patents mentioned in this report, for example in cases where a competitor proposes a formulation not appearing to fall within the claims of our formulation patent, a salt or crystalline form not claimed by our composition of matter patent, or an indication not covered by our method of use patent. See Item 3. Key Information D. Risk Factors Risks Relating to Legal and Regulatory Matters We rely on our patents and other proprietary rights to provide exclusive

rights to market certain of our products, and if such patents and other rights were limited or circumvented, our financial results could be materially and adversely affected .

As disclosed in Item 8 of this annual report, we are involved in significant litigation concerning the patent protection of a number of our products.

**Challenges to patented products**

Abbreviated New Drug Applications (ANDAs)

In the US, companies have filed Abbreviated New Drug Applications (ANDAs), containing challenges to patents related to a number of our products. An ANDA is an application by a drug manufacturer to receive authority to market a generic version of another company s approved product, by demonstrating that the

purportedly generic version has the same properties as the original approved product. ANDAs may not be filed with respect to drugs licensed as a biological. See B.6.3. Regulatory Framework B.6.3.2. Biosimilars above. An ANDA relies on the safety and other technical data of the original approved product, and does not generally require the generic manufacturer to conduct clinical trials (thus the name abbreviated new drug application), presenting a significant benefit in terms of time and cost. As a result of regulatory protection of our safety and other technical data, the ANDA may generally be filed only five years after the initial US original product marketing authorization. See Regulatory Exclusivity above. This period can be reduced to four years if the ANDA includes a challenge to a patent listed in the FDA s Orange Book. However, in such a case if the patent holder or licensee brings suit in response to the patent challenge within the statutory window, then the FDA is barred from granting final approval to an ANDA during the 30 months following the patent challenge (this bar is referred to in our industry as a 30-month stay ), unless, before the end of the 30 months, a court decision or settlement has determined either that the ANDA does not infringe the listed patent or that the listed patent is invalid and/or unenforceable.

FDA approval of an ANDA after this 30-month period does not resolve outstanding patent disputes, but it does remove the regulatory impediments to a product launch by a generic manufacturer willing to take the risk of later being ordered to pay damages to the patent holder.

The accelerated ANDA-type procedures are potentially applicable to many, but not all, of the products we manufacture. See B.6.3. Regulatory Framework 6.3.2. Biosimilars and Regulation above. We seek to defend o patent rights vigorously in these cases. Success or failure in the assertion of a

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given patent against a competing product is not necessarily predictive of the future success or failure in the assertion of the same patent or *a fortiori* the corresponding foreign patent against another competing product due to factors such as possible differences in the formulations of the competing products, intervening developments in law or jurisprudence, local variations in the patents and differences in national patent law and legal systems. See Item 3. Key Information D. Risk Factors Risks Relating to Legal and Regulatory Matters We rely on our patents and other proprietary rights to provide exclusive rights to market certain of our products, and if such patents and other rights were limited or circumvented, our financial results could be materially and adversely affected .

Section 505(b)(2) New Drug Applications in the US

Our products and patents are also subject to challenge by competitors via another abbreviated approval pathway, under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act. This provision expressly permits an applicant to rely, at least in part, on the FDA s prior findings of safety and effectiveness of a drug that has obtained FDA approval. The FDA may still require applicants to provide additional preclinical or clinical data to ensure that differences from the reference drug do not compromise safety and effectiveness. This pathway allows for approval for a wide range of products, especially for those products that represent only a limited change from an existing approved drug. The 505(b)(2) pathway is distinct from the ANDA pathway, which allows for approval of a generic product based on a showing that it is equivalent to a previously approved product.

A 505(b)(2) applicant is required to identify the reference drug on which it relies, as well as to certify to the FDA concerning any patents listed for the referenced product in the Orange Book. Specifically, the applicant must certify in the application that, for each patent that claims the drug or a use of the drug for which the applicant is seeking approval:

- there is no patent information listed for the reference drug (paragraph I certification);
- the listed patent has expired for the reference drug (paragraph II certification);
- the listed patent for the reference drug has not expired, but will expire on a particular date and approval is sought after patent expiration (paragraph III certification); or
- the listed patent for the reference drug is invalid, unenforceable, or will not be infringed by the manufacture, use or sale of the product for which the 505(b)(2) NDA is submitted (paragraph IV certification).

A paragraph III certification may delay the approval of an application until the expiration of the patent. A paragraph IV certification generally requires notification of the patent owner and the holder of the NDA for the

referenced product. If the patent owner or NDA holder brings patent litigation against the applicant within the statutory window, a 30-month stay is entered on the FDA s ability to grant final approval to the 505(b)(2) applicant

unless, before the end of the stay, a court decision or settlement determines the listed patent is invalid, not enforceable, and/or not infringed. A 505(b)(2) application may also be subject to non-patent exclusivity, and the FDA may be prohibited from giving final approval to a 505(b)(2) application until the expiration of all applicable non-patent exclusivity periods.

In the EU, a generic drug manufacturer may only reference the data of the regulatory file for the original approved product after data exclusivity has expired. However, there is no patent listing system in Europe comparable to the Orange Book, which would allow the patent holder to prevent the competent authorities from granting marketing authorization by bringing patent infringement litigation prior to approval. As a result, generic products may be approved for marketing following the expiration of marketing exclusivity without regard to the patent holder s rights. Nevertheless, in most of these jurisdictions once the competing product is launched, and in some jurisdictions even prior to launch (once launch is imminent), the patent holder may seek an injunction against such marketing if it believes its patents are infringed. See Item 8 of this annual report.

*B.7.2. Trademarks*

Our products are sold around the world under trademarks that we consider to be of material importance in the aggregate. Our trademarks help to identify our products and to protect the sustainability of our growth. Trademarks are particularly important to the commercial success of CHC and generics.

It is our policy to protect and register our trademarks with a strategy adapted to each product or service depending on the countries where they are commercialized: on a worldwide basis for worldwide products or services, or on a regional or local basis for regional or local products or services.

The process and degree of trademark protection vary country by country, as each country applies its own trademark laws and regulations. In most countries, trademark rights may only be obtained through formal trademark application and registration. In some countries, trademark protection can be based primarily on use. Registrations are granted for a fixed term (in most cases ten years) and are renewable indefinitely, except in some countries where maintenance of the trademarks is subject to their effective use.

When trademark protection is based on use, it covers the products and services for which the trademark is used. When trademark protection is based on registration, it covers only the products and services designated in the registration certificate. Additionally, in certain cases, we may enter into a coexistence agreement with a third party that owns potentially conflicting rights in order to avoid any risk of confusion and better protect and defend our trademarks.

Our trademarks are monitored and defended based on this policy and in order to prevent counterfeit, infringement and/or unfair competition.

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**B.8. Production and raw materials**

We have opted to manufacture the majority of our products in-house. There are three principal stages in our production process: the manufacture of active ingredients, the transformation of those ingredients into drug products or vaccines, and packaging those products.

Our general policy is to produce the majority of our active ingredients and principal drug products at our own plants in order to reduce our dependence on external suppliers. We also rely on third parties for the manufacture and supply of certain active ingredients, drug products and medical devices. Active ingredients are manufactured using raw materials sourced from suppliers who have been subject to rigorous selection and approval procedures, in accordance with international standards and our own internal directives. We have outsourced some of our production under supply contracts associated with acquisitions of products or businesses or with plant divestitures, or to establish a local presence to capitalize on growth in emerging markets. Our pharmaceutical subcontractors follow our general quality and logistics policies, as well as meeting other criteria. See Item 3. Key Information D. Risk Factors Risks Relating to Our Business .

At the start of 2017 we launched our Global External Manufacturing team, to enhance the way we manage relations with our third-party suppliers of finished products.

We also obtain active ingredients from third parties under collaboration agreements. This applies in particular to the monoclonal antibodies developed with Regeneron.

Our pharmaceutical production sites are divided into three categories:

- global sites, which serve all markets: located mainly in Europe, these facilities are dedicated to the manufacture of our active ingredients, injectable products, and a number of our main solid-form products;
- regional sites, which serve markets at regional level, in Europe and particularly the BRIC-M countries (Brazil, Russia, India, China and Mexico), giving us a strong industrial presence in emerging markets; and
- local sites, which serve their domestic market only.

Sanofi Pasteur produces vaccines at sites located in the United States, Canada, France, Mexico, China and India. The pharmaceutical site at Le Trait (France) also contributes to Sanofi Pasteur s industrial operations by making available its sterile filling facilities.

All of our production facilities are good manufacturing practice (GMP) compliant, in line with international regulations.

Our principal sites approved by the FDA are:

- the Biologics facilities in the United States (Allston, Framingham and Northborough), France (Lyon Gerland, Vitry-sur-Seine), Germany (Frankfurt) and Belgium (Geel);
- the Injectables facilities in France (Le Trait), Italy (Anagni), Ireland (Waterford), Germany (Frankfurt) and the United States (Ridgefield);
- the Pharmaceuticals facilities in France (Ambarès and Tours) and the United Kingdom (Haverhill);
- the Consumer Healthcare facilities in France (Compiègne) and the United States (Chattanooga); and
- the Vaccines facilities in France (Marcy l Étoile and Le Trait, which handle filling and packaging of Fluzone® ID for the US market), the United States (Swiftwater) and Canada (Toronto).

Wherever possible, we seek to have multiple plants approved for the production of key active ingredients and our strategic finished products (this is the case with Lovenox®, for example).

In May 2010, Genzyme s Allston facility in the United States entered into a consent decree with the US government following FDA inspections at the facility that resulted in observations and a warning letter raising Current Good Manufacturing Practices (CGMP) deficiencies.

The workplan was completed on March 31, 2016. The next step was a third-party certification process. In August 2017, the FDA conducted an inspection of the facility and delivered a favorable conclusion, following which certification was received on October 4, 2017.

The Allston facility is required to engage a third-party expert to audit its manufacturing operations for an additional period of at least five years.

More details about our manufacturing sites are given below at section D. Property, Plant and Equipment .

**B.9. Insurance and risk coverage**

We are protected by four key insurance programs, relying not only on the traditional corporate insurance and reinsurance market but also on our direct insurance company, Carraig Insurance DAC (Carraig).

These four key programs cover Property & Business Interruption, General & Product Liability, Stock and Transit, and Directors & Officers Liability.

Carraig participates in our coverage for various lines of insurance including Property & Business Interruption, Stock and Transit, and General & Product Liability. Carraig is run under the supervision of the Irish regulatory authorities, is wholly owned by Sanofi, and has sufficient resources to meet those portions of our risks that it has agreed to cover.

It sets premiums for our entities at market rates. Claims are assessed using the traditional models applied by insurance and reinsurance companies, and the company s reserves are regularly verified and confirmed by independent actuaries.

Our Property & Business Interruption program covers all our entities worldwide, wherever it is possible to use a centralized

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program operated by Carraig. Through risk mutualization between our entities, this approach enabling us to set tailored deductibles and covers to match local entities needs before market intervention. It also incorporates a prevention program, including a comprehensive site visit schedule covering our production, storage, research and distribution facilities and standardized repair and maintenance procedures across all sites.

The Stock and Transit program protects all goods owned by Sanofi while they are in transit nationally or internationally whatever the means of transport, and all our inventories wherever they are located. Sharing risk between our entities through Carraig means that we can set deductibles at appropriate levels, for instance differentiating between goods that require temperature controlled distribution and those that do not. We have developed a prevention program with assistance from experts, implementing best practices in this area at our distribution sites.

Our General & Product Liability program was renewed in 2018 for all our subsidiaries worldwide wherever it was possible to do so, despite reluctance in the insurance and reinsurance market to cover product liability risks for large pharmaceutical groups. For several years, insurers have been reducing product liability cover because of the difficulty of transferring risk for some products that have been subject to numerous claims. This applies to a few of our products and has led us to increase, year by year, the extent to which we self-insure.

The principal risk exposure for our pharmaceutical products is covered with low deductibles at country level, the greatest level of risk being retained. The level of risk self-insured by Sanofi (including via Carraig) before the market attachment point, enables us to retain control over the management and prevention of risk. Our negotiations with third-party insurers and reinsurers are tailored to our specific risks. In particular, they allow for differential treatment of products in the development phase, for the discrepancies in risk exposure between European countries and the United States, and for specific issues arising in certain jurisdictions such as generics coverage in the United States. Coverage is adjusted every year in order to take into account the relative weight of new product liability risks, such as those relating to rare diseases or to healthcare products which do not require marketing approval.

Our cover for risks that are not specific to the pharmaceutical industry (general liability) is designed to address the potential impacts of our operations.

For all the insurance programs handled by Carraig, outstanding claims are covered by provisions for the estimated cost of settling all claims incurred but not paid at the balance sheet date, whether reported or not, together with all related claims handling expenses. Where there is sufficient data history from Sanofi or from the market for claims made and settled, management with assistance from independent actuaries prepares an actuarial estimate of our exposure to unreported claims for the risks covered. The actuaries perform an actuarial valuation of the

company s IBNR (Incurred But Not Reported) and ALAE (Allocated Loss Adjustment Expense) liabilities at year end. Two ultimate loss projections (based upon reported losses and paid losses, respectively) are computed each year using various actuarial methods including the Bornhuetter-Ferguson method; those projections form the basis for the provisions set.

The Directors & Officers Liability program protects all legal entities under our control, and their directors and officers. Carraig is not involved in this program.

We also operate other insurance programs, but these are of much lesser importance than those described above.

All our insurance programs are backed by best in class insurers and reinsurers and are designed in such a way that we can integrate most newly acquired businesses without interruption of cover. Our cover has been designed to reflect our risk profile and the capacity available in the insurance market. By centralizing our major programs, we are able to provide world-class protection while reducing costs.

**B.10. Health, Safety and Environment**

Our manufacturing and research operations are subject to increasingly stringent health, safety and environmental (HSE) laws and regulations. These laws and regulations are complex and rapidly changing, and Sanofi invests the necessary sums in order to comply with them. This investment, which aims to respect health, safety and the environment, varies from year to year.

Applicable environmental laws and regulations may require us to eliminate or reduce the effects of chemical substance discharge at our various sites. The sites in question may belong to Sanofi, and may be currently operational, or may have been owned or operational in the past. In this regard, Sanofi may be held liable for the costs of removal or remediation of hazardous substances on, under or in the sites concerned, or on sites where waste from activities has been stored, without regard to whether the owner or operator knew of or under certain circumstances caused the presence of the contaminants, or at the time site operations occurred the discharge of those substances was authorized.

As is the case for a number of companies in the pharmaceutical, chemical and intense agrochemical industries, soil and groundwater contamination has occurred at some of our sites in the past, and may still occur or be discovered at others. In Sanofi s case, such sites are mainly located in the United States, Germany, France, Hungary, Italy and the United Kingdom. As part of a program of environmental surveys conducted over the last few years, detailed assessments of the risk of soil and groundwater contamination have been carried out at current and former Sanofi sites. In cooperation with national and local authorities, Sanofi regularly assesses the rehabilitation work required and carries out such work when appropriate. Long-term rehabilitation work is in progress or planned in Mount Pleasant, East Palo Alto and Portland in the United States; Barceloneta in

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Puerto Rico; Frankfurt in Germany; Brindisi in Italy; Dagenham in the United Kingdom; Ujpest in Hungary; Beaucaire, Valernes, Limay, Romainville, Neuville and Vitry in France; and on a number of sites divested to third parties and covered by contractual environmental guarantees granted by Sanofi.

We may also have potential liability for investigation and cleanup at several other sites. We have established provisions for the sites already identified and to cover contractual guarantees for environmental liabilities for sites that have been divested. In France specifically, we have provided the financial guarantees for environmental protection required under French regulations.

Potential environmental contingencies arising from certain business divestitures are described in Note D.22.d to the consolidated financial statements. In 2018, Sanofi spent 62 million on rehabilitating sites previously contaminated by soil or groundwater pollution.

Due to changes in environmental regulations governing site remediation, our provisions for remediation obligations may not be adequate due to the multiple factors involved, such as the complexity of operational or previously operational sites, the nature of claims received, the rehabilitation techniques involved, the planned timetable for rehabilitation, and the outcome of discussions with national regulatory authorities or other potentially responsible parties, as in the case of multiparty sites. Given the long industrial history of some of our sites and the legacy obligations arising from the past involvement of Aventis in the chemical and agrochemical industries, it is impossible to quantify the future impact of these laws and regulations with precision. See Item 3.D. Risk Factors Environmental Risks of Our Industrial Activities .

We have established, in accordance with our current knowledge and projections, provisions for cases already identified and to cover contractual guarantees for environmental liabilities relating to sites that have been divested. In accordance with Sanofi standards, a comprehensive review is carried out once a year on the legacy of environmental pollution. In light of data collected during this review, we adjusted our provisions to approximately 680 million as of December 31, 2018 versus 685 million as of December 31, 2017. The terms of certain business divestitures, and the environmental obligations and retained environmental liabilities relating thereto are described in Note D.22. to our consolidated financial statements.

To our knowledge, Sanofi did not incur any liability in 2018 for non-compliance with current HSE laws and regulations that could be expected to significantly jeopardize its activities, financial situation or operating income. We also believe that we are in substantial compliance with current HSE laws and regulations and that all the environmental permits required to operate our facilities have been obtained.

Regular HSE audits are carried out by Sanofi in order to assess compliance with standards (which implies compliance with regulations) and to initiate corrective measures (50 internal audits

performed by 87 auditors in 2018). Moreover, around 200 specific visits were performed jointly with experts representing our insurers.

Sanofi has implemented a worldwide master policy on health, safety and environment to promote the health and well-being of the employees and contractors working on its sites and respect for the environment. We consider this master policy to be an integral part of our commitment to social responsibility. In order to implement this master policy, Sanofi key requirements have been drawn up in the key fields of HSE management, HSE leadership, safety in the workplace, process safety, occupational hygiene, health in the workplace and protection of the environment.

*Health*

From the development of compounds to the commercial launch of new drugs, Sanofi research scientists continuously assess the effect of products on human health. This expertise is made available to employees through two committees responsible for chemical and biological risk assessment. Sanofi s COVALIS Committee is responsible for the hazard determination and classification of all active pharmaceutical ingredients and synthesis intermediates handled at Sanofi facilities. This covers all active ingredients handled in production at company sites or in processes sub-contracted for manufacture. Any important issues involving raw materials or other substances that lack established occupational exposure limits may also be reviewed. The COVALIS Committee determines the occupational exposure limits required within Sanofi. Our TRIBIO Committee is responsible for classifying all biological agents according to their degree of pathogenicity, and applies rules for their containment and the preventive measures to be respected throughout Sanofi. See Item 3. Key Information D. Risk Factors Environmental Risks of Our Industrial Activities Risks from the handling of hazardous materials could adversely affect our results of operations .

Appropriate occupational hygiene practices and programs are defined and implemented in each site. These practices consist essentially of containment measures for collective and individual protection against exposure in all workplaces where chemical substances or biological agents are handled. All personnel are monitored with an appropriate medical surveillance program, based on the results of professional risk evaluations linked to their duties.

In addition, dedicated resources have been created to implement the EU Regulation on Registration, Evaluation, Authorization and Restriction of Chemicals (REACH). To fully comply with the new European Regulation on Classification, Labeling and Packaging of chemicals, Sanofi has registered the relevant hazardous chemical substances with the European Chemicals Agency (ECHA).

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*Safety*

Sanofi has rigorous policies to identify and evaluate safety risks and to develop preventive safety measures, and methods for checking their efficacy. Additionally, Sanofi invests in training that is designed to instill in all employees a sense of concern for safety, regardless of their duties. These policies are implemented on a worldwide scale to ensure the safety of all employees and to protect their health. Each project, whether in research, development or manufacturing, is subject to evaluation procedures, incorporating the chemical substance and process data communicated by the COVALIS and TRIBIO Committees described above. The preventive measures are designed primarily to reduce the number and seriousness of work accidents and to minimize exposures involving permanent and temporary Sanofi employees as well as our sub-contractors.

The French chemical manufacturing sites in Aramon, Sisteron and Vertolaye, as well as the plants located in the Hoechst Industry Park in Frankfurt, Germany, and the chemical production site in Budapest, Hungary, are listed Seveso III (from the name of the European directive that deals with potentially dangerous sites through a list of activities and substances associated with classification thresholds). In accordance with French law on technological risk prevention, the French sites are also subject to heightened security inspections due to the toxic or flammable materials stored on the sites and used in the operating processes.

Risk assessments of processes and installations are drawn up according to standards and internal guidelines incorporating the best state of the art benchmarks for the industry. These assessments are used to fulfill regulatory requirements and are regularly updated. Particular attention is paid to any risk-generating changes such as process or installation changes, as well as changes in production scale and transfers between industrial or research units.

We have specialized process safety-testing laboratories that are fully integrated into our chemical development activities, apply methods to obtain the physico-chemical parameters of manufactured chemical substances (intermediate chemical compounds and active ingredients) and apply models to measure the effect of potentially leachable substances in the event of a major accident. In these laboratories the parameters for qualifying hazardous reactions are also determined, in order to define scale-up process conditions while transferring from development stage to industrial scale. All these data ensure that our risk assessments are relevant.

We believe that the safety management systems implemented at each site, the hazard studies carried out and the risk management methods implemented, as well as our third-party property insurance policies covering any third-party physical damage, are consistent with legal requirements and the best practices in the industry.

*Environment*

We have committed to an ambitious policy aimed at limiting the direct and indirect impacts of our activities on the environment, throughout the life cycle of our products. We have identified five major environmental challenges

relating to our businesses: greenhouse gas emissions and climate disruption; water; pharmaceuticals in the environment; waste; and biodiversity.

The initiatives already implemented since 2010 are continuing, and we have been keen to give them fresh impetus through the Planet Mobilization program. Reflecting our environment strategy out to 2025, the program sets more ambitious targets for reducing environmental impacts across the entire value chain. Planet Mobilization is a global project that involves all of the Company s resources in defining objectives and engaging with external partners.

Compared with 2015 figures, we are undertaking to halve our carbon emissions by the end of 2025 and reach carbon-neutral status by 2050 on our scope 1 & 2 (industrial, R&D and tertiary sites, including the medical rep fleet). We have also set ourselves the target of achieving sustainable water resource management, especially at sites which are under hydric stress. On this new scope, by the end of 2018, we had reduced $CO_2$ emissions by 9% and water consumption by 14%.

Overall waste recycling at sites is already above 72% and is expected to be more than 90% by the end of 2025. The discharge rate had dropped to 8% at the end of 2017 and we have committed to move towards a maximum of 1% by 2025. Biodiversity management at sites is also a priority, with the aim of making all employees aware of this challenge and implementing risk assessment and management plans at priority sites.

Finally, we are pursuing the policy we began in 2010 of managing pharmaceutical products in the environment throughout their life cycles. At the end of 2018, all priority chemical sites had been evaluated and were shown to present no risk to the environment. The assessment program was extended to other sites, starting with the pharmaceutical production sites. In 2018, eight sites implemented the program.

In line with this approach, we have committed to the Roadmap AMR 2020 initiative, which aims to combat microbial resistance to antibiotics. The initiative brings together thirteen of the major players in the pharmaceutical industry, and will involve co-producing reference guides and methodologies for sustainable management of antibiotics in the pharmaceutical sector. The initiative includes a specific commitment with respect to antibiotic production sites that are operated by signatories or their suppliers, involving firstly the definition and deployment of a shared framework for managing potential waste, and secondly the establishment of environmental thresholds. (See Cautionary statement regarding forward-looking statements ).

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C/ **Organizational Structure**

**C.1. Significant Subsidiaries**

Sanofi is the holding company of a consolidated group consisting of over 300 companies. The table below sets forth our significant

subsidiaries as of December 31, 2018. For a fuller list of the principal companies in our consolidated group, see Note F. to our consolidated financial statements, included in this annual report at Item 18.

| Significant subsidiary | Date of incorporation | Country of incorporation | Principal activity | Financial and voting interest |
|---|---|---|---|---|
| Aventis Inc. | 07/01/1968 | United States | Pharmaceuticals | 100% |
| Aventis Pharma SA | 09/24/1974 | France | Pharmaceuticals | 100% |
| Genzyme Corporation | 11/21/1991 | United States | Pharmaceuticals | 100% |
| Hoechst GmbH | 07/08/1974 | Germany | Pharmaceuticals | 100% |
| Sanofi-Aventis Deutschland GmbH | 06/30/1997 | Germany | Pharmaceuticals | 100% |
| Sanofi-Aventis US LLC | 06/28/2000 | United States | Pharmaceuticals | 100% |
| Sanofi-Aventis Participations SAS | 02/25/2002 | France | Pharmaceuticals | 100% |
| Sanofi Pasteur SA | 02/08/1989 | France | Vaccines | 100% |
| Sanofi Pasteur Inc. | 01/18/1977 | United States | Vaccines | 100% |
| Sanofi Winthrop Industrie | 12/11/1972 | France | Pharmaceuticals | 100% |
| Chattem, Inc. | 11/11/1909 | United States | Pharmaceuticals | 100% |

Since 2009, we have transformed Sanofi through numerous acquisitions (see A. History and Development of the Company above), in particular those of Genzyme in April 2011, Merial in September 2009 and Bioverativ and Ablynx in January 2018. The financial effects of the Genzyme acquisition are presented in Note D.1.3. to our consolidated financial statements for the year ended December 31, 2013, included in our annual report on Form 20-F for that year. The financial effects of the Merial acquisition are presented in Note D.1.3. to our consolidated financial statements for the year ended December 31, 2010, included in our annual report on Form 20-F for that year. At the end of December 2016, Sanofi Pasteur and MSD (known as Merck in the United States and Canada) ended their Sanofi Pasteur MSD joint venture. The financial effects of the resulting divestment/acquisition are presented in Note D.1.2. to our consolidated financial statements for the year ended December 31, 2016, included in our annual report on Form 20-F

for that year. On January 1, 2017, Sanofi and Boehringer Ingelheim (BI) finalized the strategic transaction agreed in June 2016, involving the exchange of Sanofi s Animal Health business (Merial) for BI s Consumer Healthcare business. The financial effects of this transaction are presented in Note D.1. to our consolidated financial statements for the year ended December 31, 2017, included in our annual report on Form 20-F for that year. The financial effects of the Bioverativ and Ablynx acquisitions are presented in Note D.1.1. to our consolidated financial statements, included at Item 18 of this annual report on Form 20 F.

In certain countries, we carry on some of our business operations through joint ventures with local partners. In addition, we have entered into worldwide collaboration agreements (i) with

Regeneron, relating to Zaltrap®, human therapeutic antibodies such as Praluent® and antibodies in immunology such as Dupixent® and Kevzara®; and (ii) with BMS, relating to Plavix®. For further information, refer to Note C. Principal Alliances to our consolidated financial statements.

**C.2. Internal organization of activities**

Sanofi and its subsidiaries collectively form a group organized around three activities: Pharmaceuticals, Consumer Healthcare and Vaccines.

Within Sanofi, responsibility for research and development (R&D) in their respective fields rests with Sanofi SA and Genzyme Corporation in Pharmaceuticals, and with Sanofi Pasteur and Sanofi Pasteur, Inc. in Vaccines. However, within our integrated R&D organization, strategic priorities are set and R&D efforts coordinated on a worldwide scale. In fulfilling their role in R&D, the aforementioned companies subcontract R&D to those of their subsidiaries that have the necessary resources. They also license patents, manufacturing know-how and trademarks to certain of their French and foreign subsidiaries. Those licensee subsidiaries manufacture, commercialize and distribute the majority of our products, either directly or via local distribution entities.

Our industrial property rights, patents and trademarks are mainly held by the following companies:

Pharmaceuticals: Sanofi, Sanofi Mature IP, Sanofi Biotechnology SAS (France), Sanofi-Aventis Deutschland GmbH (Germany), Ablynx (Belgium), and Genzyme Corporation and Bioverativ Inc. (US);

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ITEM 4. INFORMATION ON THE COMPANY

Vaccines: Sanofi Pasteur (France) and Sanofi Pasteur, Inc. (US).

For a description of our principal items of property, plant and equipment, see D. Property, Plant and Equipment below. Our property, plant and equipment is held mainly by the following companies:

in France: Sanofi Pasteur SA, Sanofi Chimie, Sanofi Winthrop Industrie, and Sanofi-Aventis Recherche & Développement;

in the United States: Sanofi Pasteur, Inc., Genzyme Corporation, and Genzyme Therapeutics Products LP;

in Canada: Sanofi Pasteur Limited;

in Germany: Sanofi-Aventis Deutschland GmbH;

in Belgium: Genzyme Flanders BVBA Holding Co; and

in Ireland: Genzyme Ireland Limited.

**C.3. Financing and financial relationships between group companies**

The Sanofi parent company raises the bulk of the Company s external financing and uses the funds raised to meet, directly or indirectly, the financing needs of its subsidiaries. The parent company operates a cash pooling arrangement under which any surplus cash held by subsidiaries is managed centrally. There is also a centralized foreign exchange risk management system in place, whereby the parent company contracts hedges to meet the needs of its principal subsidiaries.

Consequently, at December 31, 2018, the Sanofi parent company held 96% of our external financing and 81% of our surplus cash.

Sanofi European Treasury Center SA (SETC), a 100%-owned Sanofi subsidiary incorporated in 2012 under the laws of Belgium, is dedicated to providing financing and various financial services to our subsidiaries.

**D/ Property, plant and equipment**

**D.1. Overview**

Our headquarters are located in Paris, France. See D.4 Office Space below.

We operate our business through office premises and research, production and logistics facilities in approximately 100 countries around the world. Our office premises house all of our support functions, plus operational representatives from our subsidiaries and the Company.

A breakdown of our sites by use and by ownership status (owned versus leasehold) is provided below. This breakdown is based on surface area. All surface area figures are unaudited.

| **Breakdown of sites by use** | |
|---|---|
| Industrial | 60% |
| Research | 13% |
| Offices | 15% |
| Logistics | 9% |
| Other | 4% |

| **Breakdown of sites by ownership status** | |
|---|---|
| Leasehold | 23% |
| Owned | 77% |

We own most of our research & development and production facilities, either freehold or under finance leases with a purchase option exercisable on expiration of the lease.

**D.2. Description of our sites**

*Sanofi industrial sites*

As part of the process of transforming Sanofi and creating Global Business Units, we are continuing to adapt the organization of the Industrial Affairs department in support of our new business model. Since June 2013, the Industrial Affairs department has been responsible for all production and quality operations within Sanofi. The department focuses on customer needs and service quality, the sharing of Sanofi Manufacturing System manufacturing practices, the development of a common culture committed to quality and the pooling of expertise within technology platforms, particularly in biological, injectable and pharmaceutical products.

Since January 2016, the Industrial Affairs department has also been responsible for Sanofi Global HSE and Global Supply Chain.

At the end of 2018, we were carrying out industrial production at 75 sites in 33 countries:

- 8 sites for our Biologics operations;

9 sites for our Injectables operations;

33 sites for our Pharmaceuticals operations;

14 sites for our Consumer Healthcare operations;

11 sites for the industrial operations of Sanofi Pasteur in vaccines.

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## ITEM 4. INFORMATION ON THE COMPANY

In 2018, we produced the following quantities:

Pharmaceuticals: 4,700 million units, comprising:

units manufactured and packaged: 2,939 million;

units packaged only: 375 million;

bulk products in unit equivalents: 454 million;

outsourced units: 932 million; and

Vaccines: 441 million containers (syringes, vials and lyophilized products) filled, including outsourced production. We believe that our production facilities are in compliance with all regulatory requirements, are properly maintained and are generally suitable for future needs. Nonetheless, we regularly inspect and evaluate those facilities with regard to environmental, health, safety and security matters, quality compliance and capacity utilization. For more information about our property, plant and equipment, see Note D.3 to our consolidated financial statements, included at Item 18 of this annual report, and section B.8 Production and Raw Materials above. Production et matières premières ».

Production of biological, chemical and pharmaceutical products, and of vaccines, is the responsibility of our Industrial Affairs department, which is also in charge of most of our logistics facilities (distribution and storage centers).

Our principal production sites by volume are:

Frankfurt (Germany), Framingham (United States) and Geel (Belgium) for biologics;

Le Trait (France), Frankfurt (Germany), Csanyikvölgy (Hungary) and Waterford (Ireland) for injectables;

Ambarès (France), Lüleburgaz (Turkey), Campinas (Brazil) and Hangzhou (China) for pharmaceutical products;

Aramon and Sisteron (France), Frankfurt (Germany) and Jurong (Singapore) for active pharmaceutical ingredients;

Compiègne and Lisieux (France), Cologne (Germany), Suzano (Brazil) and Ocoyoacac (Mexico) for Consumer Healthcare products; and

Marcy-l Étoile and Val-de-Reuil (France), Toronto (Canada) and Swiftwater (United States) for vaccines.

*Research & Development sites*

In Pharmaceuticals, research and development activities are conducted at the following sites:

four operational sites in France: Chilly-Mazarin/Longjumeau, Montpellier, Strasbourg and Vitry-sur-Seine/Alfortville;

three sites in the rest of Europe (Germany, Belgium and the Netherlands), the largest of which is in Frankfurt (Germany);

four sites in the United States: Bridgewater, Cambridge, Framingham/Waltham and Great Valley; and
in Asia, three sites in China (Beijing, Shanghai and Chengdu) and a clinical research unit in Japan.

Vaccines research and development sites are:

Swiftwater, Cambridge and Orlando (United States);

Marcy-l Étoile/Lyon (France); and

Toronto (Canada).

**D.3. Acquisitions, capital expenditures and divestitures**

The carrying amount of our property, plant and equipment at December 31, 2018 was 9,651 million. During 2018, we invested 1,459 million (see Note D.3. to our consolidated financial statements, included at Item 18 of this annual report), mainly in increasing capacity and improving productivity at our various production and R&D sites.

Our principal acquisitions, capital expenditures and divestitures in 2016, 2017 and 2018 are described in Notes D.1. ( Impact of changes in the scope of consolidation ), D.3. ( Property, plant and equipment ) and D.4. ( Goodwill and other intangible assets ) to our consolidated financial statements, included at Item 18 of this annual report.

As of December 31, 2018, our firm commitments in respect of future capital expenditures amounted to 535 million. The principal locations involved were: for the Pharmaceuticals segment, the industrial facilities at Frankfurt (Germany), Framingham (United States), Geel (Belgium), Le Trait and Sisteron (France); and for the Vaccines

segment, the facilities at Toronto (Canada), Marcy-l Étoile and Val de Reuil (France).

In the medium term and assuming no changes in the scope of consolidation, we expect to invest on average some 1.7 billion a year in property, plant and equipment. We believe that our own cash resources and the undrawn portion of our existing credit facilities will be sufficient to fund these expenditures.

Our principal ongoing investments are described below.

*Biologics*

In 2014, a dedicated Biologics platform was launched to develop synergies between Pharmaceuticals, Sanofi Pasteur, Sanofi Genzyme and our Biotherapeutics operations. This platform is helping us extend our footprint in biotechnologies by adopting a multi-disciplinary approach and improving capacity utilization. It also enables us to leverage our expertise in the production of biologics, from active ingredient to integrated manufacturing, including both the medicine itself and associated medical devices.

Three dedicated biotechnology hubs have been developed: Paris/Lyon (France), Frankfurt (Germany) and Boston (United States). Piloting this technology, which relies on cell or microbiological culture or the development of viral vectors, calls for highly specific knowledge and expertise backed by dedicated production platforms to support global product launches.

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*Injectables*

The Frankfurt facility, our principal site for the manufacture of diabetes treatments, is now equipped with an additional sterile filling unit that uses isolator technology. This new filling unit handles Toujeo® and other diabetes products. Our prefilled syringes network mainly delivers Lovenox®/Clexane® from Le Trait (France) to global markets, and from Csanyikvölgy (Hungary) to non-FDA/EMA regulated markets.

*Pharmaceuticals*

The development of our General Medicines & Emerging Markets platform is built on a network of over 30 regional and local industrial sites in 22 countries, supporting growth in those markets.

At Sidi Abdellah in Algeria we are starting up a new facility that will become our largest industrial complex in Africa, mainly producing dry and liquid formulations.

Our Industrial Affairs Department has an ongoing policy of adapting industrial facilities to market needs. As part of this process, during 2018 we sold various facilities, including those at Holmes Chapel (United Kingdom), Guarenas (Venezuela), as well as those at Prague (Czech Republic) and Bucharest (Romania) as part of the sale of our European Generics business.

*Consumer Healthcare*

The pharmaceutical industrial operations of our Consumer Healthcare (CHC) business are spread across a dedicated network. Global markets are supplied from our facilities at Compiègne (France) and Cologne (Germany). We have recently invested heavily in major projects intended to build a specialist CHC industrial network. This has included switching some CHC products from non-CHC facilities to the dedicated CHC network, transferring some liquid and effervescent formulations of CHC products to the Cologne site.

*Vaccines (Sanofi Pasteur)*

Sanofi Pasteur s industrial operations are in a major investment phase, preparing for the upcoming growth of our influenza and Polio/Pertussis/Hib franchises. Major investments were launched during 2018 in France (including construction of a new influenza

vaccine building at Val-de-Reuil), Canada (a new pertussis vaccine building), the US and Mexico.

*Innovation and culture of industrial excellence*

In 2018, we highlighted industrial innovation in our various facilities by organizing our tenth annual round of Industrial Trophies, in five categories: Patient Needs, Technological Innovation, Operational Performance, Energy &

Environment, and Young Industrial Innovation Talent.

The ambition of our Industrial Affairs department is to continue to raise quality standards in Sanofi s production activities, and to remain a world leader and a benchmark in the global pharmaceutical industry. To achieve this goal, all our activities share a common culture of industrial excellence, enshrined in the Sanofi Manufacturing System. This sets out a series of priorities (such as customer service, constant improvement, site network optimization and transverse optimization) that constitute our industrial vision and will be crucial to our mutual success.

Industrial Affairs has its own digital strategy, built on five pillars: Integrated Industrialization, Intelligent Quality, Connected Teams and Operations, Connected Factory, and Real-Time Supply Chain.

**D.4. Office space**

As part of the transformation of Sanofi and the implementation of the ONE SANOFI program, we are undertaking major real estate programs with two core objectives: to bring our teams together on single sites in new workspaces that favor agility, cross-fertilization and communication; and to rationalize office space while achieving a responsible environmental footprint.

Many such projects were completed in 2018, including the rationalization of sites in the United States (Cambridge and Bridgewater), China (Shanghai and Chengdu), Panama, Kenya, Denmark and the Netherlands. In the case of the Netherlands, this involved a masterplan to bring together teams previously located in Gouda and Naarden on a single site in Amsterdam.

This transformation of workspaces to flexible mode has already reached over 16,000 of our people around the globe, and provides strong support for our various operations to attain their objectives. The rollout is due to extend to all regions, with projects including a masterplan for the United Kingdom plus others in Peru, Dubai and China (Beijing).

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ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

## Item 5. **Operating and Financial Review and Prospects**

You should read the following discussion in conjunction with our consolidated financial statements and the notes thereto included in this annual report at Item 18.

Our consolidated financial statements have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB) and with IFRS adopted by the European Union as of December 31, 2018.

The following discussion contains forward-looking statements that involve inherent risks and uncertainties. Actual results may differ materially from those contained in such forward-looking statements. See Cautionary Statement Regarding Forward-Looking Statements at the beginning of this document.

Unless otherwise stated, all financial variations in this item are given on a reported basis.

### A. Operating results

### A.1. Significant operating information

#### *A.1.1. 2018 overview*

During 2018, we continued to progress towards our key strategic objectives: reshape the portfolio, deliver outstanding launches, sustain innovation in R&D and simplify the organization.

We began the year by creating a new global Rare Blood Disorder franchise, with three strategic deals announced within the space of a month. The acquisition of **Bioverativ**, a biotechnology company focused on therapies for hemophilia and other rare blood disorders, was completed in early March 2018 at a price of $11.6 billion. This acquisition brought us a portfolio of products that are delivering growth including the flagship hemophilia treatments Eloctate® and Alprolix®. The acquisition of **Ablynx**, a company engaged in the discovery and development of nanobodies, was completed in June 2018 at a price of 3.9 billion, and enhances our portfolio with the addition of Cablivi® (caplacizumab), which received marketing approval from the European Commission in September 2018. Finally, the reshaping of our alliance with **Alnylam** enabled us to obtain global development and commercialization rights to fitusiran, an investigational RNAi therapeutic currently in development for the treatment of hemophilia A and B.

To streamline and refocus our operations, we completed the sale of our **European Generics** business to **Advent International** for 1.9 billion on September 30, 2018. We also sold most of our infectious disease research and early-stage development portfolio, and our infectious disease research unit, to **Evotec**.

At the start of 2018, Sanofi and **Regeneron** decided to accelerate their investment in the clinical development of three innovative products: cemiplimab (Libtayo®) in oncology, dupilumab (Dupixent®) in the treatment of Type 2 allergies, and REGN3500/SAR440340 (an anti-IL33 monoclonal antibody) in atopic dermatitis, asthma and chronic obstructive pulmonary disease. Our Immuno-Oncology Discovery and Development Agreement with Regeneron has also been restructured, giving us greater flexibility to pursue our own early stage immuno-oncology development projects independently while allowing Regeneron to retain all rights to its other discovery and development programs in that field. The renegotiation of that agreement, effective from December 31, 2018, was signed on January 2, 2019.

We also continued our efforts to secure research and development alliances during 2018, entering into a collaboration agreement with **Denali Therapeutics, Inc.** to develop several molecules with a view to the potential treatment of various neuro-degenerative conditions and systemic inflammatory diseases.

Our research and development efforts led to a number of products entering Phase III in 2018: fitusiran in the treatment of hemophilia type A and B; Dupixent® in the treatment of eosinophilic esophagitis; Kevzara® in the treatment of giant-cell arteritis and polymyalgia rheumatica; isatuximab in the treatment of recently diagnosed multiple myeloma; sotagliflozin in the treatment of worsening heart failure; and Libtayo® as a first line treatment for patients with advanced or metastatic non small cell lung cancer.

A number of product launches took place in 2018 following approvals from regulatory bodies. These included **Dupixent®**, which was launched as a treatment for adults with moderate-to-severe atopic dermatitis in Japan, and in a new indication in the United States for adults with moderate-to-severe asthma. **Cablivi®** was launched in Germany in the treatment of acquired thrombotic thrombocytopenic purpura (aTTP). **Admelog®** was launched in the United States and some European countries as a biosimilar, under the name **Insulin lispro Sanofi®**. **Libtayo®** was launched in the United States in the treatment of advanced cutaneous squamous cell carcinoma (CSCC).

Also in 2018, we invested 350 million (CAD 500 million) in the construction of a newstate-of-the-art vaccine manufacturing facility at the Sanofi Pasteur Canadian headquarters in Toronto (Ontario), to meet the growing demand for vaccines.

Net sales for the year ended December 31, 2018 amounted to 34,463 million, 1.7% lower than in 2017. At constant exchange rates (CER)(1), net sales rose by 2.5%, reflecting the acquisition of Bioverativ s rare blood disorder products. At constant exchange rates and on a constant structure basis (CER/CS)(1),

*(1) Non-GAAP financial measure: see definition in A.1.6. Presentation of Net Sales below.*

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net sales grew by 0.6%. Lower sales in Diabetes in the United States and for Established Prescription Products in mature markets were offset by the performance of Dupixent® and the Rare Diseases franchise, and more generally by increased sales in Emerging Markets.

***Net income attributable to equity holders of Sanofi*** amounted to 4,306 million, 48.8% lower than in 2017, mainly due to the recognition of the gain on the divestment of our Animal Health business in 2017. Earnings per share was 48.5% lower than in 2017, at 3.45. Business net income[1] was 6,819 million, 1.8%

less than in 2017, while business earnings per share (business EPS)[1] was 0.9% lower at 5.47.

As of December 31, 2018, our net debt[2] had increased to 17,628 million (versus 5,161 million as of December 31, 2017). This was largely due to the impact of acquiring Bioverativ and Ablynx, which was partly offset by the divestment of our European Generics business. At the Annual General Meeting of April 30, 2019, we will ask our shareholders to approve a dividend of 3.07 per share, representing a payout of 56.1% of our business net income.

### *A.1.2. Impacts of competition from generics and biosimilars*

Some of our flagship products continued to suffer sales erosion in 2018 due to competition from generics and biosimilars. We do not believe it is possible to state with certainty what level of net sales would have been achieved in the absence of generic competition.

A comparison of our consolidated net sales for the years ended December 31, 2018 and 2017 (see A.2. Results of Operations Year Ended December 31, 2018 Compared with Year Ended December 31, 2017 below) for products affected by generic and biosimilar competition shows a loss of 1,749 million of net sales on a reported basis. Other parameters may have contributed to the loss of sales, such as a fall in the average price of certain products (e.g. Lantus®).

The table below sets forth the impact by product.

| ( *million)* | 2018 | 2017[a] | Change on a reported basis | Change on a reported basis (%) |
|---|---|---|---|---|
| Aprovel® Europe | 108 | 115 | (7) | -6.1% |
| Lantus® Europe | 684 | 760 | (76) | -10.0% |
| Lovenox® Europe | 870 | 951 | (81) | -8.5% |

| | | | | |
|---|---|---|---|---|
| Plavix® Europe | 147 | 150 | (3) | -2.0% |
| Renagel® / Renvela® Europe | 60 | 71 | (11) | -15.5% |
| Ambien® United States | 45 | 55 | (10) | -18.2% |
| Lantus® United States | 1,614 | 2,542 | (928) | -36.5% |
| Lovenox® United States | 38 | 58 | (20) | -34.5% |
| Renagel® / Renvela® United States | 253 | 645 | (392) | -60.8% |
| Taxotere® United States | 1 | | 1 | |
| Allegra® Japan | 112 | 146 | (34) | -23.3% |
| Amaryl® Japan | 18 | 27 | (9) | -33.3% |
| Aprovel® Japan | 28 | 89 | (61) | -68.5% |
| Lantus® Japan | 29 | 43 | (14) | -32.6% |
| Myslee® Japan | 76 | 95 | (19) | -20.0% |
| Plavix® Japan | 156 | 235 | (79) | -33.6% |
| Taxotere® Japan | 9 | 15 | (6) | -40.0% |
| **Total** | **4,248** | **5,997** | **(1,749)** | **-29.2%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements, included at Item 18 of this Annual Report on Form 20-F).*

*(1) Non-GAAP financial measure: see definition in A.1.5. Segment Information 3. Business Net Income below.*

*(2) Non-GAAP financial measure: see definition in B. Liquidity and Capital Resources below.*

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ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

We expect the erosion caused by generic competition to continue in 2019, with a negative impact on our net income. The products likely to be impacted include those that already faced generic competition in 2018, but whose sales can reasonably be expected to be subject to further sales erosion in 2019: Aprovel®, Lantus®, Lovenox®, Plavix® and Renagel®/Renvela® in Europe; Ambien®, Lantus®, Lovenox®, Renagel® / Renvela® and Taxotere® in the United States; and Allegra®, Amaryl®, Aprovel®, Lantus®, Myslee®, Plavix® and Taxotere® in Japan.

In 2018, the aggregate consolidated net sales of those products in countries where generic competition currently exists or is expected in 2019 amounted to 4,248 million; this comprises 1,951 million in the United States (including 1,614 million in net sales of Lantus® and 253 million in net sales of Renagel®/Renvela®); 1,869 million in Europe; and 428 million in Japan. The negative impact on our 2019 net sales is likely to represent a substantial portion of those sales, but the actual impact will depend on a number of factors such as the prices at which the products are sold and potential litigation outcomes.

*A.1.3. Purchase accounting effects*

Our results of operations and financial condition for the years ended December 31, 2018, 2017 and 2016 have been significantly affected by our August 2004 acquisition of Aventis, our April 2011 acquisition of Genzyme, our 2018 acquisition of Bioverativ and certain other transactions. See A.1.11. Critical accounting and reporting policies Business combinations below for an explanation of the impact of business combinations on our results of operations.

The Bioverativ business combination has generated significant amortization of intangible assets ( 430 million in 2018). The Genzyme business combination has generated significant amortization of intangible assets ( 760 million in 2018, 857 million in 2017 and 866 million in 2016) and impairment of intangible assets (expenses of 183 million in 2018, expenses of 16 million in 2017 and net reversal of 6 million in 2016). The Aventis business combination has also generated significant amortization expenses ( 256 million in 2018, 365 million in 2017, and 482 million in 2016).

In order to isolate the purchase accounting effects of all acquisitions and certain other items, we use a non-GAAP financial measure that we refer to as business net income[1].

*A.1.4. Sources of revenues and expenses*

***Revenues.*** Revenue arising from the sale of goods is presented in the income statement within ***Net sales***. Net sales comprise revenue from sales of pharmaceutical products, consumer health care products, active ingredients and vaccines, net of sales returns, of customer incentives and discounts, and of certain sales-based payments paid or payable to the healthcare authorities. Returns, discounts, incentives and rebates are

recognized in the period in which the underlying sales are recognized, as a reduction of sales revenue. See Note B.13.1. to our consolidated financial statements included at Item 18 of this annual report. We sell pharmaceutical products and vaccines directly, through alliances, and by licensing arrangements throughout the world. When we sell products directly, we record sales revenues as part of our consolidated net sales. When we sell products through

alliances, the revenues reflected in our consolidated financial statements are based on the contractual arrangements governing those alliances. For more information about our alliances, see Financial Presentation of Alliances below. When our products are sold by licensing arrangements, we receive royalty income that we record in ***Other revenues***. The sales of non-Sanofi products of our US based entity VaxServe are also presented in ***Other revenues***; see Note B.13.2. to the consolidated financial statements included at Item 18 of this annual report.

***Cost of Sales.*** Our cost of sales consists primarily of the cost of purchasing raw materials and active ingredients, labor and other costs relating to our manufacturing activities, packaging materials, payments made under licensing agreements and distribution costs. We have license agreements under which we manufacture, sell and distribute products that are patented by other companies and license agreements under which other companies distribute products that we have patented. When we pay royalties, we record them in ***Cost of sales***.

***Operating Income.*** Our operating income reflects our revenues, our cost of sales and the remainder of our operating expenses, the most significant of which are research and development expenses and selling and general expenses. For our operating segments, we also measure our results of operations through an indicator referred to as Business Operating Income, which we describe below under A.1.5. Segment Information 2/Business Operating Income of Segments.

*A.1.5. Segment information*

**1/ Operating segments**

In accordance with IFRS 8 (Operating Segments), the segment information reported by Sanofi is prepared on the basis of internal management data provided to the Chief Executive Officer, who is the chief operating decision maker. The performance of those segments is monitored individually using internal reports and common indicators. The operating segment disclosures required under IFRS 8 are provided in Notes B.26. and D.35 ( Segment Information ) to our consolidated financial statements, included at Item 18 of this annual report.

Sanofi has three operating segments: Pharmaceuticals, Consumer Healthcare and Vaccines.

The Pharmaceuticals segment comprises the commercial operations of the following global franchises: Specialty Care (Rare Diseases, Multiple Sclerosis, Oncology, Immunology and Rare Blood Disorder), Diabetes & Cardiovascular, Established

*(1) Non-GAAP financial measure: see definition under A.1.5. Segment information 3/ Business Net Income below.*

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Prescription Products and Generics, together with research, development and production activities dedicated to our Pharmaceuticals segment. This segment also includes associates whose activities are related to pharmaceuticals, in particular our share of Regeneron.

The Consumer Healthcare segment comprises, for all geographical territories, the commercial operations for our Consumer Healthcare products, together with research, development and production activities dedicated to those products.

The Vaccines segment comprises, for all geographical territories (including from January 1, 2017 certain territories previously included in the Sanofi Pasteur MSD joint venture) the commercial operations of Sanofi Pasteur, together with research, development and production activities dedicated to vaccines.

Inter-segment transactions are not material.

The costs of our global functions (Medical Affairs, External Affairs, Finance, Human Resources, Legal Affairs, Information Solutions & Technologies, Sanofi Business Services, etc.) are managed centrally at group-wide level. The costs of those functions are presented within the Other category. That category also includes other reconciling items such as retained commitments in respect of divested activities.

**2/ Business operating income**

We report segment results on the basis of business operating income . This indicator is used internally by Sanofi s chief

operating decision maker to measure the performance of each operating segment and to allocate resources. For a definition of business operating income , and a reconciliation between that indicator and ***Income before tax and investments accounted for using the equity method***, refer to Note D.35. to our consolidated financial statements.

**3/ Business net income**

We believe that understanding of our operational performance by our management and our investors is enhanced by reporting business net income . This non-GAAP financial measure represents business operating income, less net financial expenses and the relevant income tax effects.

Business net income for 2018 was 6,819 million, 1.8% lower than in 2017 ( 6,943 million). Business net income was unchanged year-on-year as a percentage of net sales, at 19.8%.

We also report business earnings per share (business EPS), a non-GAAP financial measure which we define as business net income divided by the weighted average number of shares outstanding.

Business EPS was 5.47 for 2018, 0.9% lower than the 2017 figure of 5.52, based on an average number of shares outstanding of 1,247.1 million for 2018 and 1,256.9 million for 2017.

Our business net income for 2016 was 7,308 million, including 476 million of business net income from Animal Health. Business EPS for 2016 was 5.68, based on an average number of shares outstanding of 1,286.6 million.

The table below reconciles our business operating income to our business net income:

| *( million)* | December 31, 2018 | December 31, 2017[a] | December 31, 2016[a] |
|---|---|---|---|
| **Business operating income** | **8,884** | **9,323** | **9,284** |
| Financial income and expenses | (271) | (273) | (399)[b] |
| Income tax expense | (1,794) | (2,107) | (2,053) |
| **Business net income excluding Animal Health** | **6,819** | **6,943** | **6,832** |
| Animal Health business net income | | | 476 |
| **Business net income** | **6,819** | **6,943** | **7,308** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) This amount does not include the 457 million impairment loss charged against our equity investment in Alnylam.*

We define business net income as ***Net income attributable to equity holders of Sanofi*** determined under IFRS, excluding the following items:

amortization and impairment losses charged against intangible assets (other than software and other rights of an industrial or operational nature);

fair value remeasurements of contingent consideration relating to business combinations or divestments;
other impacts associated with acquisitions (including impacts of acquisitions on investments accounted for using the equity method);

restructuring costs and similar items[1];

other gains and losses (including gains and losses on major disposals of non-current assets[2]);

other costs and provisions related to litigation[2];

*(1) Presented in the line item **Restructuring costs and similar items** in the consolidated income statement.*
*(2) Presented in the line item **Other gains and losses, and litigation** in the consolidated income statement.*

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the tax effects of the items listed above;

the effects of major tax disputes;

the 3% tax levied on the distribution of dividends to equity holders of Sanofi, up to and including 2017;

the direct and indirect effects of the US tax reform in 2017 and the adjustments to our estimates of those effects, recognized in 2018, and the consequences of the French Constitutional Council ruling of October 6, 2017 on the additional 3% tax levied on dividends paid out in cash;

those Animal Health items that are not included in business net income[1]; and

the portion attributable to non-controlling interests of the items listed above.

The table below reconciles our business net income to ***Net income attributable to equity holders of Sanofi*:**

| *( million)* | **2018** | **2017[a]** | **2016[a]** |
|---|---|---|---|
| **Net income attributable to equity holders of Sanofi** | **4,306** | **8,416** | **4,709** |
| Amortization of intangible assets[b] | 2,170 | 1,866 | 1,692 |
| Impairment of intangible assets | 718 | 293 | 192 |
| Fair value remeasurement of contingent consideration | (117) | 159 | 135 |
| Expenses arising from the impact of acquisitions on inventories | 114 | 166 | |
| Other expenses related to business combinations | 28 | | |
| Restructuring costs and similar items | 1,480 | 731 | 879 |
| Impairment loss charged against equity investment in Alnylam | | | 457 |
| Other gains and losses, and litigation[c] | (502) | 215 | (211) |
| Tax effects of the items listed above: | (1,125) | (1,126) | (841) |
| *amortization and impairment of intangible assets* | *(692)* | *(719)* | *(694)* |

| | | | |
|---|---|---|---|
| *fair value remeasurement of contingent consideration* | *38* | *4* | *(24)* |
| *expenses arising from the impact of acquisitions on inventories* | *(27)* | *(52)* | |
| *other expenses related to business combinations* | *(6)* | | |
| *restructuring costs and similar items* | *(435)* | *(134)* | *(95)* |
| *other tax effects* | *(3)* | *(225)* | *(28)* |
| Other tax items[(d)] | (188) | 741 | 113 |
| Share of items listed above attributable to non-controlling interests | (2) | (4) | (22) |
| Investments accounted for using the equity method: restructuring costs and expenses arising from the impact of acquisitions | (76) | 129 | (9) |
| Items relating to the Animal Health business[(e)] | 13 | (4,643) | 162 |
| Other Sanofi Pasteur MSD items[(f)] | | | 52 |
| **Business net income** | **6,819** | **6,943** | **7,308** |
| Average number of shares outstanding (million) | 1,247.1 | 1,256.9 | 1,286.6 |
| Basic earnings per share (in euros) | 3.45 | 6.70 | 3.66 |
| Reconciling items per share (in euros) | 2.02 | (1.18) | 2.02 |
| Business earnings per share (in euros) | 5.47 | 5.52 | 5.68 |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) Includes amortization expense generated by the remeasurement of intangible assets in connection with business combinations: 1,957 million in 2018, 1,726 million in 2017, and 1,550 million in 2016.*

*(c) For 2018, this line consists mainly of the gain on the divestment of our European Generics business, net of separation costs and before any tax effects. For 2017, it mainly comprises a provision for a vendor s liability guarantee on a past divestment; and for 2016, the gain on the divestment of Sanofi s interest in the Sanofi Pasteur MSD joint venture, before any tax effects.*

*(d) For 2018, this line comprises adjustments to our preliminary analysis of the direct and indirect impacts of US tax reform. For 2017, it comprises the estimated initial impact of US tax reform (- 1,193 million) and of the 3% tax levied on dividends in France ( 451 million).*

*(e) For 2017, this line comprises the gain on the divestment of our Animal Health business. For 2016, it comprises (i) the impact of the discontinuation of depreciation and impairment of property, plant & equipment with effect from the start date of application of IFRS 5 included in business net income; (ii) the impact of the amortization and impairment of intangible assets until the start date of IFRS 5 application; (iii) costs directly incurred as a result of the divestment; and (iv) tax effects of those items.*

*(f) For 2016, this line comprises the elimination of our share of the business net income of Sanofi Pasteur MSD from the date when Sanofi and Merck announced their intention to end their joint venture.*

*(1) Comprises (i) impact of the discontinuation of depreciation and impairment of property, plant & equipment with effect from the start date of application of IFRS 5 (Discontinued and Held-for-Sale Operations), included in business net income; (ii) impact of the amortization and impairment of intangible assets until the start date of IFRS 5 application; (iii) costs directly incurred as a result of the divestment; and (iv) tax effects of those items.*

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The most significant reconciling items between our business net income and ***Net income attributable to equity holders of Sanofi*** relate to (i) the purchase accounting effects of our acquisitions and business combinations, particularly the amortization and impairment of intangible assets (other than software and other rights of an industrial or operational nature) and (ii)) the impacts of events regarded as non-recurring, where the amounts involved are particularly significant. We believe that excluding those non-cash or non-recurring charges enhances an investor s understanding of our underlying economic performance, because we do not consider that the excluded charges reflect the combined entity s ongoing operating performance. Rather, we believe that each of the excluded charges reflects the decision to acquire the businesses concerned.

The principal purchase accounting effects of acquisitions and business combinations on net income are:

- amortization and net impairment losses charged against intangible assets (other than software and other rights of an industrial or operational nature), net of taxes and non-controlling interests; and

- the incremental cost of sales incurred on the workdown of acquired inventories remeasured at fair value, net of taxes.

We believe (subject to the limitations described below) that disclosing our business net income enhances the comparability of our operating performance, for the following reasons:

- the elimination of charges related to the purchase accounting effects of our acquisitions and business combinations (particularly amortization and impairment of finite-lived intangible assets, other than software and other rights of an industrial or operational nature) enhances the comparability of our ongoing operating performance relative to our peers in the pharmaceutical industry that carry those intangible assets (principally patents and trademarks) at low book values either because they are the result of in-house research and development that has already been expensed in prior periods or because they were acquired through business combinations that were accounted for as poolings-of-interest;

- the elimination of selected items such as the incremental cost of sales arising from the workdown of acquired inventories remeasured at fair value in business combinations, major gains and losses on disposals, and costs and provisions associated with major litigation and any other major non-recurring items improves comparability from one period to the next; and

the elimination of restructuring costs and similar items enhances comparability because those costs are incurred in connection with reorganization and transformation processes intended to optimize our operations.

We remind investors, however, that business net income should not be considered in isolation from, or as a substitute for, ***Net income attributable to equity holders of Sanofi*** reported in accordance with IFRS. In addition, we strongly encourage

investors and potential investors not to rely on any single financial measure but to review our financial statements, including the notes thereto, carefully and in their entirety.

We compensate for the material limitations described above by using business net income only to supplement our IFRS financial reporting and by ensuring that our disclosures provide sufficient information for a full understanding of all adjustments included in business net income.

Because our business net income is not a standardized measure, it may not be directly comparable with the non-GAAP financial measures of other companies using the same or a similar non-GAAP financial measure.

### *A.1.6. Presentation of net sales*

In the discussion below, we present our consolidated net sales for 2018, 2017, and 2016. We analyze our net sales among various categories, including by business, product and geographical region. In addition to reported net sales, we analyze non-GAAP financial measures designed to isolate the impact on our net sales of currency exchange rates and changes in the structure of our group.

When we refer to changes in our net sales at constant exchange rates (CER), that means that we have excluded the effect of exchange rates by recalculating net sales for the relevant period using the exchange rates that were used for the previous period.

When we refer to changes in our net sales on a constant structure basis, that means that we eliminate the effect of changes in structure by restating the net sales for the previous period as follows:

- by including sales generated by entities or product rights acquired in the current period for a portion of the previous period equal to the portion of the current period during which we owned them, based on sales information we receive from the party from whom we make the acquisition;

- similarly, by excluding sales for a portion of the previous period when we have sold an entity or rights to a product in the current period; and

- for a change in consolidation method, by recalculating the previous period on the basis of the method used for the current period.

In section A.2. below, comparatives for 2017 have been restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impact of these restatements is described in detail in Note A.2.1.1. to the consolidated financial statements.

We believe that the impact of the application of IFRS 15 on net sales for the year ended December 31, 2016 is not material ( 12 million). Given the significant resources required to restate such information by business, segment and geographical region, we concluded that it would be unduly burdensome to restate such amounts. Therefore, we have chosen to present our

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detailed analysis of net sales for 2016 and comparable information for 2017 before the impact of IFRS 15 as set forth in section A.3.1.1.

*A.1.7. Financial presentation of alliances*

We have entered into a number of alliances for the development, co-promotion and/or co-marketing of our products. We believe that a presentation of our two principal alliances is useful to an understanding of our financial statements.

The financial impact of the alliances on our income statement is described in Results of Operations Year Ended December 31, 2018 Compared with Year Ended December 31, 2017 and Year Ended December 31, 2017 Compared with Year Ended December 31, 2016 , in particular in Net Sales , Other Revenues , Share of Profit/Loss Investments Accounted for using the Equity Method and Net Income Attributable to Non-Controlling Interests .

**1/ Alliance arrangements with Regeneron Pharmaceuticals Inc. (Regeneron)**

Collaboration agreement on the discovery, development and commercialization of human therapeutic antibodies

In November 2007, Sanofi and Regeneron signed new agreements (amended in November 2009) for the discovery, development and commercialization of fully human therapeutic antibodies. Under the 2009 amended agreements Sanofi committed to funding the discovery and pre-clinical development of fully human therapeutic antibodies by a maximum of $160 million per year through 2017, with an option to develop and commercialize antibodies discovered by Regeneron pursuant to the collaboration. Sanofi decided not to extend the discovery agreement, which expired on December 31, 2017.

Following the signature in July 2015 of the immuno-oncology collaboration agreements described below, $75 million of the discovery and pre-clinical development funding was reallocated to the new agreements (spread over three years).

If an option is exercised under the 2009 amended agreements, Sanofi co-develops the antibody with Regeneron and is responsible for funding. Sanofi and Regeneron share co-promotion rights and profits on sales of the co-developed antibodies. On receipt of the first positive Phase III trial results for any such antibody, the subsequent Phase III costs for that antibody are split 80% Sanofi, 20% Regeneron. Amounts received from Regeneron under those arrangements are recognized by Sanofi as a reduction in the line item Research and development expenses . Once a product begins to be commercialized, and provided that the share of quarterly results under the agreement represents a profit, Sanofi is entitled to an additional portion of Regeneron s profit-share (capped at 10% of Regeneron s share of quarterly profits) until Regeneron has paid 50% of the cumulative development costs incurred by the parties in the collaboration.

As of December 31, 2018 the cumulative development costs incurred by the two parties were 6.0 billion (comprising

3.2 billion funded 100% by Sanofi, and 2.8 billion funded 80% by Sanofi and 20% by Regeneron, amounts translated into euros at the closing US dollar exchange rate). On the earlier of (i) 24 months before the scheduled launch date or (ii) the first positive Phase III trial results, Sanofi and Regeneron share the commercial expenses of the antibodies co-developed under the license agreement. Sanofi recognizes all the sales of those antibodies. Profits and losses arising from commercial operations in the United States are split 50/50. Outside the United States, Sanofi is entitled to between 55% and 65% of profits depending on sales of the antibodies, and bears 55% of any losses. The share of profits and losses attributable to Regeneron under the agreement is recognized within the line items ***Other operating income*** or ***Other operating expenses***, which are components of operating income. In addition, Regeneron is entitled to receive payments of up to $250 million contingent on the attainment of specified levels of sales outside the United States.

Praluent®, Dupixent®, Kevzara® and REGN3500 (SAR440340) continue to be developed, and commercialized as applicable, with Regeneron under the Antibody License and Collaboration Agreement (LCA) following the expiry of the discovery agreement.

In January 2018, Sanofi and Regeneron signed a set of amendments including an amendment to the collaboration agreement on the development and commercialization of human therapeutic antibodies that allowed for the funding of additional programs on Dupixent® and REGN3500 (SAR440340) which will focus on extending the current range of indications, finding new indications, and improving co-morbidity between multiple pathologies.

Immuno-Oncology (IO) Discovery and Development Agreement and IO License and Collaboration Agreement (IO LCA)

On July 1, 2015, Sanofi and Regeneron entered into a new global collaboration to discover, develop and commercialize new antibody cancer treatments in the emerging field of immuno-oncology. As part of the agreements, Sanofi made an upfront payment of $640 million to Regeneron. The two companies also agreed to reallocate $75 million (spread over three years) to immuno-oncology antibody research and development from Sanofi s $160 million annual contribution to their existing antibody discovery collaboration.

Under the terms of the IO Discovery and Development Agreement, the two companies agreed to invest approximately $1 billion from discovery through proof of concept (POC) development (usually a Phase IIa study) of monotherapy and novel combinations of immuno-oncology antibody candidates to be funded 25% by Regeneron ($250 million) and 75% by Sanofi ($750 million). Beyond the committed funding, additional funding will be allocated as programs enter post-POC development under the IO LCA.

Upon establishment of POC, Sanofi can exercise its opt-in rights to further development and commercialization under the IO LCA for candidates derived from the IO discovery program. Once

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Sanofi has exercised its opt-in rights for a candidate, future development of that candidate will be conducted under the IO LCA either by Sanofi or Regeneron.

Under the terms of the IO Discovery and Development Agreement, Sanofi is entitled to an additional share of profits of up to 50% of the clinical development costs initially funded by Sanofi. That additional profit-share is capped at 10% of the share of Regeneron s quarterly profits arising under the IO LCA.

The Amended and restated Immuno-oncology Discovery and Development Agreement ( Amended IO Discovery Agreement ), effective from December 31, 2018, was signed on January 2, 2019. Through this amendment, Sanofi and Regeneron restructured their global Immuno-oncology Discovery and Development Agreement, effective December 31, 2018. The 2015 agreement was due to end in mid-2020, and the revision provides for ongoing collaborative development of two clinical-stage bispecific antibody programs targeting respectively (i) BCMA and CD3 and (ii) MUC16 and CD3. This gives Sanofi increased flexibility to advance its early-stage immuno-oncology pipeline independently, while Regeneron retains all rights to its other immuno-oncology discovery and development programs.

Under the terms of the Amended IO Discovery Agreement Sanofi paid Regeneron $462 million representing the balance of payments due under the original Immuno-oncology Agreement, which covers the Sanofi share of (i) the immuno-oncology discovery program costs for the last quarter of 2018 and up to $120 million in development costs for the two selected clinical-stage bispecific antibodies, plus (ii) the termination fee for the other programs under the original immuno-oncology agreement. Sanofi secured the right to opt-in to the BCMAxCD3 and MUC16xCD3 bispecific programs when proof of concept is achieved or when the allocated funding is expended.

Post opt-in of the BCMAxCD3 bispecific, Sanofi will lead development and commercialization. Post opt-in of the MUC16xCD3 bispecific, Regeneron will lead development, and also lead commercialization in the United States. Sanofi will lead commercialization outside the United States.

The companies ongoing collaboration for the development and commercialization of Libtayo® (cemiplimab) is unaffected by the Amended IO Discovery Agreement. As of December 31, 2018, the additional share of profits corresponding to 50% of the clinical development costs initially funded by Sanofi amounts to 53 million. This additional profit-share is capped at 10% of the share of Regeneron s quarterly profits arising under the IO LCA.

Under the 2015 IO LCA, the two companies have agreed to jointly develop a programmed cell death protein 1 (PD-1) inhibitor antibody (REGN2810) and committed to provide additional funding of no more than $650 million on a 50/50 basis ($325 million per company) for the development of REGN2810, a PD-1 inhibitor antibody. While they share profits on a 50/50 basis, Sanofi will make a one-time milestone payment of $375 million to Regeneron in the event that sales of a PD-1 product and any other collaboration antibody sold for use in

combination with a PD-1 product were to exceed, in the aggregate, $2 billion in any consecutive 12-month period.

In January 2018, Sanofi and Regeneron announced a set of amendments including an amendment to their IO LCA on the development of cemiplimab (REGN 2810) in the field of immuno-oncology, pursuant to which the $650 million development budget for the PD-1 inhibitor antibody was increased to $1.64 billion through 2022, funded equally by the two companies (i.e. from $325 million to $820 million for each partner).

On September 21, 2018, the US Food and Drug Administration (FDA) approved Libtayo® (cemiplimab) for the treatment of patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. Libtayo® is a fully-human monoclonal antibody targeting the immune checkpoint receptor PD-1 (programmed cell death protein-1) and is the first and only treatment specifically approved and available for advanced CSCC in the U.S. A regulatory application for Libtayo® has also been submitted in the EU.

An ongoing joint clinical program is investigating Libtayo® in multiple other cancers, and includes potentially pivotal trials in lung, cervical and skin cancers. The safety and efficacy of Libtayo® have not been fully evaluated by any regulatory authority for indications beyond advanced CSCC.

Investor agreement

In January 2014, Sanofi and Regeneron amended the investor agreement that has existed between the two companies since 2007 (the Amended Investor Agreement ). Under the terms of the amendment, Sanofi accepted various restrictions. Sanofi is bound by certain standstill provisions, which contractually prohibit Sanofi from seeking to directly or indirectly exert control of Regeneron or acquiring more than 30% of Regeneron s capital stock (consisting of the outstanding shares of common stock and the shares of Class A stock). This prohibition will remain in place until the earlier of (i) the later of the fifth anniversaries of the expiration or earlier termination of the Zaltrap® collaboration agreement with Regeneron (related to the development and commercialization of Zaltrap®) or the collaboration agreement with Regeneron on monoclonal antibodies (see Collaboration agreement on the discovery, development and commercialization of human therapeutics antibodies above), each as amended and (ii) other specified events.

Sanofi has also agreed to vote as recommended by Regeneron s Board of Directors, except that it may elect to vote proportionally with the votes cast by all of Regeneron s other shareholders with respect to certain change-of-control transactions, and to vote in its sole discretion with respect to liquidation or dissolution, stock issuances equal to or exceeding 20% of the outstanding shares or voting rights of Regeneron s Class A Stock and Common Stock (taken together), and new equity compensation plans or amendments if not materially consistent with Regeneron s historical equity compensation practices.

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As soon as it had passed the threshold of 20% ownership of the capital stock, Sanofi exercised its right under the Amended Investor Agreement to designate an independent director, who was appointed to the Board of Directors of Regeneron. The interest held by Sanofi in Regeneron has been consolidated by the equity method since April 2014.

On the conditions set out in the Amended Investor Agreement entered into in January 2014, Sanofi s right to designate a Regeneron board member was contingent on Sanofi maintaining its percentage share of Regeneron s outstanding capital stock (measured on a quarterly basis) at a level no lower than the highest percentage level previously achieved, with the maximum requirement capped at 25%. In addition, Sanofi s interest in Regeneron was subject to a lock-up clause. Those limitations have been amended by the letter agreement of January 2018 (see below).

In November 2015, the Independent Designee (as defined in the Amended Investor Agreement) designated by Sanofi as an independent director resigned from the Regeneron Board of Directors. At Sanofi s request, pursuant to the Amended Investor Agreement, Regeneron appointed N. Anthony Tony Coles, M.D. to its Board of Directors in January 2017 as a successor Sanofi designee.

The Amended Investor Agreement also gives Sanofi the right to receive certain reasonable information as may be agreed upon by the parties and which will facilitate Sanofi s ability to account for its investment in Regeneron using the equity method of accounting under IFRS.

In January 2018, Sanofi and Regeneron announced a set of amendments (i) to their collaboration agreement on the development and commercialization of human therapeutic antibodies; (ii) to their IO License and Collaboration Agreement on the development of cemiplimab (REGN 2810) in the field of immuno-oncology; and (iii) a limited waiver and amendment of the Amended Investor Agreement pursuant to a letter agreement (the 2018 Letter Agreement ).

Pursuant to the 2018 Letter Agreement, Regeneron has agreed to grant a limited waiver of the lock-up clause and the obligation to maintain the Highest Percentage Threshold in the Amended and Restated Investor Agreement between the companies, so that Sanofi may elect to sell a small percentage of the Regeneron common stock it owns to fund a portion of the cemiplimab and dupilumab development expansion. This waiver will allow Sanofi to sell up to an aggregate of 1.4 million shares of Regeneron common stock to Regeneron in private transactions through the end of 2020. If Regeneron decides not to purchase the shares, Sanofi will be allowed to sell those shares on the open market, subject to certain volume and timing limitations. Upon expiration of the limited waiver under the 2018 Letter Agreement, the Amended Investor Agreement will be amended to define Highest Percentage Threshold as the lower of (i) 25% of Regeneron outstanding shares of Class A Stock and Common Stock (taken together) and (ii) the higher of (a) Sanofi s percentage ownership of Class A Stock and Common Stock (taken together) on such

termination date and (b) the highest percentage ownership of Regeneron outstanding shares of Class A Stock and Common Stock (taken together) Sanofi attains following such termination date. As of December 31, 2018 Sanofi has sold 226,153 shares of Regeneron Stock to Regeneron pursuant to the 2018 Letter Agreement.

**2/ Alliance arrangements with Bristol-Myers Squibb (BMS)**

Two of Sanofi s leading products were jointly developed with BMS: the anti-hypertensive agent irbesartan (Aprovel®/Avapro®/Karvea®) and the anti-atherothrombosis treatment clopidogrel bisulfate (Plavix®/Iscover®).

On September 27, 2012, Sanofi and BMS signed an agreement relating to their alliance following the loss of exclusivity of Plavix® and Avapro®/Avalide® in many major markets.

Under the terms of this agreement, effective January 1, 2013, BMS returned to Sanofi its rights to Plavix® and Avapro®/Avalide® in all markets worldwide with the exception of Plavix® in the United States and Puerto Rico, giving Sanofi sole control and freedom to operate commercially in respect of those products. In exchange, BMS received royalty payments on Sanofi s sales of branded and unbranded Plavix® and Avapro®/Avalide® worldwide (except for Plavix® in the United States and Puerto Rico) until 2018, and also received a payment of $200 million from Sanofi in December 2018, part of which is for buying out the non-controlling interests (see Note D.18. to our consolidated financial statements). Rights to Plavix® in the United States and Puerto Rico remain unchanged and continue to be governed by the terms of the original agreement until December 2019.

In all of the territories managed by Sanofi (including the United States and Puerto Rico for Avapro®/Avalide®) as defined in the new agreement, Sanofi recognizes in its consolidated financial statements the revenue and expenses generated by its own operations. The share of profits reverting to BMS subsidiaries is presented within ***Net income attributable to non-controlling interests*** in the income statement.

In the territory managed by BMS (United States and Puerto Rico for Plavix®), Sanofi recognizes its share of profits and losses within the line item ***Share of profit/(loss) from investments accounted for using the equity method***.

*A.1.8. Impact of Exchange Rates*

We report our consolidated financial statements in euros. Because we earn a significant portion of our revenues in countries where the euro is not the local currency, our results of operations can be significantly affected by exchange rate movements between the euro and other currencies, primarily the US dollar and, to a lesser extent, the Japanese yen, and currencies in emerging countries. We experience these effects even though certain of these countries do not account for a large portion of our net sales. In 2018, we earned 33.5% of our net sales in the United States. An increase in the value of the US dollar against the euro has a positive impact on both our

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revenues and our operating income. A decrease in the value of the US dollar against the euro has a negative impact on our revenues, which is not offset by an equal reduction in our costs and therefore negatively affects our operating income. A variation in the value of the US dollar has a particularly significant impact on our operating income, which is higher in the United States than elsewhere, and on the contribution to net income of our collaborations with Regeneron and BMS in the United States (see A.1.7. Financial Presentation of Alliances above).

For a description of arrangements entered into to manage operating foreign exchange risks as well as our hedging policy, see Item 11. Quantitative and Qualitative Disclosures about Market Risk , and Item 3. Key Information D. Risk Factors Risks Related to Financial Markets Fluctuations in currency exchange rates could adversely affect our results of operations and financial condition .

### *A.1.9. Divestments*

On September 30, 2018, Sanofi finalized the divestment of Zentiva, its European Generics business, generating a pre-tax gain of 510 million euros in 2018.

On January 1, 2017, Sanofi and Boehringer Ingelheim (BI) finalized the strategic transaction agreed in June 2016, involving the exchange of our Animal Health business (Merial) for BI s Consumer Healthcare business. After final enterprise value adjustments, the exchange values of the two businesses effectively transferred during 2017 were determined to be 10,557 million for Sanofi s Animal Health business and 6,239 million for BI s Consumer Healthcare business. The divestment of the Animal Health business generated an after-tax gain of 4,643 million in 2017.

At the end of December 2016, Sanofi Pasteur and MSD ended their European joint venture Sanofi Pasteur MSD (SPMSD). This transaction involved the divestment of Sanofi s share in the joint venture and the acquisition of the vaccines portfolio that reverts to Sanofi. The consideration for the transfer was (i) a fixed sum of 127 million received on January 4, 2017 and (ii) contingent consideration based on a percentage of MSD sales during the 2017-2024 period of specified products previously distributed by SPMSD, and receivable in annual installments over the same period. As of December 31, 2016, the fair value of the contingent consideration was measured at 458 million and recognized in the available-for-sale financial assets category.

For further details about the divestments mentioned above, see Note D.1. and D.2. to our consolidated financial statements included at Item 18 of this annual report.

### *A.1.10. Acquisitions*

Sanofi acquired Bioverativ Inc. ( Bioverativ ) on March 8, 2018 for $11.6 billion ( 9.4 billion). The provisional purchase price allocation resulted in the recognition of goodwill amounting to 2,676 million. The contributions from Bioverativ to net sales and business operating income of the Pharmaceuticals segment in

2018 amount to 892 million and 389 million, respectively. Over the same period, Bioverativ made a negative contribution of 325 million to net profit, including expenses charged during the period relating to the fair value remeasurement of assets recognized at the acquisition date. During the year ended December 31, 2018, Bioverativ generated net sales of 1,068 million. The net cash outflow on this acquisition amounted to 8,932 million, and is recorded within ***Acquisitions of consolidated undertakings and investments accounted for using the equity method*** in the consolidated statements of cash flows.

Sanofi acquired Ablynx on May 14, 2018 for 3,897 million. The provisional purchase price allocation resulted in the recognition of goodwill amounting to 1,372 million. The impacts of this acquisition on Sanofi s business operating income and consolidated net income for the year ended December 31, 2018 are not material. The net cash outflow on this acquisition amounted to 3,639 million, and is recorded within ***Acquisitions of consolidated undertakings and investments accounted for using the equity method*** in the consolidated statements of cash flows.

In 2018, Sanofi sold shares in the biopharmaceutical company Regeneron with a carrying amount of 24 million. Sanofi had acquired shares in Regeneron in 2017 (at a cost of 184 million) and in 2016 (at a cost of 115 million in 2016). Our investment in Regeneron had a carrying amount of 3,055 million as of December 31, 2018, compared with 2,496 million as of December 31, 2017 and 2,550 million as of December 31, 2016 (see Note D.1. to our consolidated financial statements). This represents an equity interest of 21.7% as of December 31, 2018, compared with 22.2% as of December 31, 2017 and 22.1% as of December 31, 2016.

In 2017, as part of the strategic transaction between Sanofi and Boehringer Ingelheim (BI), we acquired BI s Consumer Healthcare business. The goodwill arising on that acquisition represents (i) the capacity to draw on a specialized structure to refresh the existing product portfolio; (ii) the competencies of the staff transferred to Sanofi; (iii) the benefits derived from the creation of new growth platforms; and (iv) the expected future synergies and other benefits from combining the CHC operations of BI and Sanofi. The tax-deductible portion of goodwill amounted to 1,876 million out of total goodwill of 2,222 million. This business generated sales of 1,407 million in the year ended December 31, 2017.

On August 25, 2017, Sanofi acquired 100% of Protein Sciences, a biotechnology company headquartered in Meriden, Connecticut (United States). The principal product of Protein Sciences is Flublok®, the only recombinant protein-based influenza vaccine approved by the FDA in the United States. The acquisition price included two contingent purchase consideration elements of 42 million each. The impacts of this acquisition on Sanofi s business operating income and consolidated net income for the year ended December 31, 2017 were not material.

In 2016, as part of the dissolution of the Sanofi Pasteur MSD joint venture, we acquired the vaccines portfolio that reverts to us. The

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purchase price essentially comprised (i) a fixed sum of 154 million paid on January 4, 2017 and (ii) contingent consideration of 354 million based on a percentage of future sales made by Sanofi Pasteur during the 2017-2024 period of specified former SPMSD products, to be paid in installments over that period.

For further information about the acquisitions mentioned above, see Notes D.1. and D.2. to our consolidated financial statements included at Item 18 of this annual report.

*A.1.11. Critical accounting and reporting policies*

Our consolidated financial statements are affected by the accounting and reporting policies that we use. Certain of our accounting and reporting policies are critical to an understanding of our results of operations and financial condition, and in some cases the application of these critical policies can be significantly affected by the estimates, judgments and assumptions made by management during the preparation of our consolidated financial statements. The accounting and reporting policies that we have identified as fundamental to a full understanding of our results of operations and financial condition are the following:

**1/ Revenue recognition**

Our policies with respect to revenue recognition are discussed in Note B.13. to our consolidated financial statements included at Item 18 of this annual report. Revenue arising from the sale of goods is presented in the income statement within ***Net sales***. ***Net sales*** comprise revenue from sales of pharmaceutical products, consumer healthcare products, active ingredients and vaccines, net of sales returns, of customer incentives and discounts, and of certain sales-based payments paid or payable to the healthcare authorities. In accordance with IFRS 15 (Revenue from Contracts with Customers), such revenue is recognized when Sanofi transfers control over the product to the customer. Control refers to the ability to direct the use of, and obtain substantially all of the remaining benefits from the products. For the vast majority of contracts, revenue is recognized when the product is physically transferred, in accordance with the delivery and acceptance terms agreed with the customer.

For contracts entered into by Sanofi Pasteur, transfer of control is usually determined by reference to the terms of release (immediate or deferred) and acceptance of batches of vaccine.

As regards contracts with distributors, Sanofi does not recognize revenue when the product is physically transferred to the distributor in case of products sold on consignment, or if the distributor acts as an agent. In such cases, revenue is recognized when control is transferred to the end customer and the distributor s commission is presented within the line item *Selling and general expenses* in the income statement.

We offer various types of price reductions on our products. In particular, products sold in the United States are covered by various programs (such as Medicare and Medicaid) under which

products are sold at a discount. Rebates are granted to healthcare authorities, and under contractual arrangements with certain customers. Some wholesalers are entitled to chargeback incentives based on the selling price to the end customer, under specific contractual arrangements. Cash discounts may also be granted for prompt payment. The discounts, incentives and rebates described above are estimated on the basis of specific contractual arrangements with our customers or of specific terms of the relevant regulations and/or agreements applicable for transactions with healthcare authorities, and of assumptions about the attainment of sales targets. We also estimate the amount of sales returns, on the basis of contractual sales terms and reliable historical data. Discounts, incentives, rebates and sales returns are recognized in the period in which the underlying sales are recognized within ***Net Sales***, as a reduction of gross sales. For additional details regarding the financial impact of discounts, incentives, rebates and sales returns, see Note D.23. to our consolidated financial statements included at Item 18 of this annual report.

Revenues from non-Sanofi products, mainly comprising royalty income from license arrangements and sales of non-Sanofi products by our US-based entity VaxServe, are presented within ***Other revenues***.

**2/ Business combinations**

As discussed in Note B.3. Business combinations and transactions with non-controlling interests to our consolidated financial statements included at Item 18 of this annual report, business combinations are accounted for by the acquisition method. The acquiree s identifiable assets and liabilities that satisfy the recognition criteria of IFRS 3 (Business Combinations) are measured initially at their fair values as at the acquisition date, except for (i) non-current assets classified as held for sale, which are measured at fair value less costs to sell and (ii) assets and liabilities that fall within the scope of IAS 12 (Income Taxes) and IAS 19 (Employee Benefits). Business combinations completed on or after January 1, 2010 are accounted for in accordance with the revised IFRS 3 and the revised IAS 27, (Consolidated and Individual Financial Statements), now superseded by IFRS 10 (Consolidated Financial Statements). In particular, contingent consideration payable to former owners agreed in a business combination, e.g. in the form of payments upon the achievement of certain R&D milestones, is recognized as a liability at fair value as of the acquisition date irrespective of the probability of payment. If the contingent consideration was originally recognized as a liability, subsequent adjustments to the liability are recognized in profit or loss (see Note D.18. Liabilities related to business combinations and non-controlling interests to our consolidated financial statements included at Item 18 of this annual report).

**3/ Goodwill impairment and intangible assets**

As discussed in Note B.6. Impairment of property, plant and equipment, intangible assets, and investments accounted for using the equity method and in Note D.5. Impairment of

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intangible assets and property, plant and equipment to our consolidated financial statements included at Item 18 of this annual report, we test our intangible assets for impairment periodically or when there is any internal or external indication of impairment. We test for impairment on the basis of the same objective criteria that were used for the initial valuation. Our initial valuation and ongoing tests are based on the relationship of the value of our projected future cash flows associated with the asset to either the purchase price of the asset (for its initial valuation) or the carrying amount of the asset (for ongoing tests). The determination of the underlying assumptions relating to the recoverability of intangible assets is subjective and requires the exercise of considerable judgment. Key assumptions relating to goodwill impairment and intangible assets are the perpetual growth rate and the post-tax discount rate. Any changes in key assumptions could result in an impairment charge. A sensitivity analysis to the key assumptions is disclosed in Note D.5. Impairment of intangible assets and property, plant and equipment to our consolidated financial statements included at Item 18 of this annual report.

**4/ Contingent consideration receivable**

As described in Note B.8.1 and D.7.2 to our consolidated financial statements included at Item 18 of this annual report, contingent consideration receivable such as earn-outs on disposals, for example in the form of a percentage of future sales of the acquirer, are recognized as an asset at fair value as of the date of divestment. Subsequent remeasurements of the fair value of the asset are recognized in profit or loss.

**5/ Pensions and post-retirement benefits**

As described in Note B.23. Employee benefit obligations to our consolidated financial statements included at Item 18 of this annual report, we recognize our pension and retirement benefit commitments as liabilities on the basis of an actuarial estimate of the rights vested in employees and retirees at the end of the reporting period, net of the fair value of plan assets held to meet these obligations. We prepare this estimate at least on an annual basis taking into account financial assumptions (such as discount rates) and demographic assumptions (such as life expectancy, retirement age, employee turnover, and the rate of salary increases).

We recognize all actuarial gains and losses (including the impact of a change in discount rate) immediately through equity. A sensitivity analysis to the discount rate is set forth in Note D.19.1. Provisions for pensions and other benefits to our consolidated financial statements included at Item 18 of this annual report.

Depending on the key assumptions used, the pension and post-retirement benefit expense could vary within a range of outcomes and have a material effect on reported earnings. A sensitivity analysis to these key assumptions is set forth in Note D.19.1. Provisions for pensions and other benefits to our consolidated financial statements included at Item 18 of this annual report.

**6/ Deferred taxes**

As discussed in Note B.22. Income tax expense to our consolidated financial statements included at Item 18 of this annual report, we recognize deferred income taxes on tax loss carry-forwards and on temporary differences between the tax base and carrying amount of assets and liabilities. We calculate our deferred tax assets and liabilities using enacted tax rates applicable for the years during which we estimate that the temporary differences are expected to reverse. We do not recognize deferred tax assets when it is more likely than not that the deferred tax assets will not be realized. The recognition of deferred tax assets is determined on the basis of profit forecasts for each tax group, and of the tax consequences of the strategic opportunities available to Sanofi.

**7/ Provisions for risks**

Sanofi and its subsidiaries and affiliates may be involved in litigation, arbitration or other legal proceedings. These proceedings typically are related to product liability claims, intellectual property rights, compliance and trade practices, commercial claims, employment and wrongful discharge claims, tax assessment claims, waste disposal and pollution claims, and claims under warranties or indemnification arrangements relating to business divestitures. As discussed in Note B.12. Provisions for risks at Item 18 of this annual report, we record a provision where we have a present obligation, whether legal or constructive, as a result of a past event; it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation; and a reliable estimate can be made of the amount of the outflow of resources. For additional details regarding the financial impact of provisions for risks see Notes D.19.3. Other provisions and D.22. Legal and Arbitral Proceedings to our consolidated financial statements included at Item 18 of this annual report.

**8/ Provisions for restructuring costs**

Provisions for restructuring costs include early retirement benefits, compensation for early termination of contracts, and rationalization costs relating to restructured sites. Refer to Note D.19.2 to our consolidated financial statements included in Item 18 of this annual report.

Provisions are estimated on the basis of events and circumstances related to present obligations at the end of the reporting period and of past experience, and to the best of management s knowledge at the date of preparation of the financial statements. The assessment of provisions can involve a series of complex judgments about future events and can rely heavily on estimates and assumptions. Given the inherent uncertainties related to these estimates and assumptions, the actual outflows resulting from the realization of those risks could differ from our estimates.

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**A.2. Results of operations year ended December 31, 2018 compared with year ended December 31, 2017**

Consolidated income statements

The consolidated income statements for the years ended December 31, 2018 and December 31, 2017 are presented below, with information for the year ended December 31, 2017 restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impacts of these restatements are described in detail in Note A.2.1.1. to our consolidated financial statements.

| ( *million*) | 2018 | as % of net sales | 2017[a] | as % of net sales |
|---|---|---|---|---|
| **Net sales** | **34,463** | **100.0%** | **35,072** | **100.0%** |
| Other revenues | 1,214 | 3.5% | 1,149 | 3.3% |
| Cost of sales | (11,435) | (33.2%) | (11,613) | (33.1%) |
| **Gross profit** | **24,242** | **70.3%** | **24,608** | **70.2%** |
| Research and development expenses | (5,894) | (17.1%) | (5,472) | (15.6%) |
| Selling and general expenses | (9,859) | (28.6%) | (10,072) | (28.7%) |
| Other operating income | 484 | | 237 | |
| Other operating expenses | (548) | | (233) | |
| Amortization of intangible assets | (2,170) | | (1,866) | |
| Impairment of intangible assets | (718) | | (293) | |
| Fair value remeasurement of contingent consideration | 117 | | (159) | |
| Restructuring costs and similar items | (1,480) | | (731) | |
| Other gains and losses, and litigation | 502 | | (215) | |
| **Operating income** | **4,676** | **13.6%** | **5,804** | **16.5%** |
| Financial expenses | (435) | | (420) | |
| Financial income | 164 | | 147 | |
| **Income before tax and investments accounted for using the equity method** | **4,405** | **12.8%** | **5,531** | **15.8%** |
| Income tax expense | (481) | | (1,722) | |
| Share of profit/(loss) from investments accounted for using the equity method | 499 | | 85 | |
| **Net income excluding the exchanged/held-** | **4,423** | **12.8%** | **3,894** | **11.1%** |

| | | | | |
|---|---|---|---|---|
| **for-exchange Animal Health business** | | | | |
| Net income/(loss) of the exchanged/held-for-exchange Animal Health business[(b)] | (13) | | 4,643 | |
| **Net income** | **4,410** | **12.8%** | **8,537** | **24.3%** |
| Net income attributable to non-controlling interests | 104 | | 121 | |
| **Net income attributable to equity holders of Sanofi** | **4,306** | **12.5%** | **8,416** | **24.0%** |
| Average number of shares outstanding (million) | 1,247.1 | | 1,256.9 | |
| Average number of shares after dilution (million) | 1,255.2 | | 1,266.8 | |
| Basic earnings per share (in euros) | 3.45 | | 6.70 | |
| Basic earnings per share (in euros) excluding the exchanged/held-for-exchange Animal Health business | 3.46 | | 3.00 | |
| Diluted earnings per share (in euros) | 3.43 | | 6.64 | |
| Diluted earnings per share (in euros) excluding the exchanged/held-for-exchange Animal Health business | 3.44 | | 2.98 | |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) For 2017, the gain on the divestment of the Animal Health business is presented separately in accordance with IFRS 5 (Non-Current Assets Held for Sale and Discontinued Operations); see Note D.36 to our consolidated financial statements.*

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*A.2.1. Net Sales*

Information regarding net sales for the year ended December 31, 2017 as presented in this section has been restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impacts of these restatements are described in detail in Note A.2.1.1. to our consolidated financial statements.

Consolidated net sales for the year ended December 31, 2018 amounted to 34,463 million, 1.7% lower than in 2017. Exchange rate fluctuations had a negative effect of 4.2 percentage points overall, due mainly to unfavorable trends in the exchange rate for the euro against the US dollar, Argentinean peso, Brazilian real and Turkish lira. The unfavorable impact of

the Argentinean peso was 196 million, including the effects of applying hyperinflation accounting from July 1, 2018 onwards (see Note A.4. to our consolidated financial statements) and the effects of devaluation on our Argentinean subsidiaries relative to 2017.

At constant exchange rates (CER), net sales rose by 2.5%, reflecting the acquisition of Bioverativ s rare blood disorder products. At constant exchange rates and on a constant structure basis (CER/CS), net sales grew by 0.6%. Lower sales in Diabetes in the United States and for Established Prescription Products in mature markets were offset by the performance of Dupixent® and the Rare Diseases franchise, and more generally by increased sales in Emerging Markets.

**Reconciliation of net sales to net sales at constant exchange rates and on a constant structure basis**

| *( million)* | **2018** | **2017[(a)]** | **Change** |
|---|---|---|---|
| **Net sales** | **34,463** | **35,072** | **-1.7%** |
| Effect of exchange rates | 1,492 | | |
| **Net sales at constant exchange rates** | **35,955** | **35,072** | **+2.5%** |
| Impact of changes in structure (Bioverativ and Zentiva) | | 664 | |
| **Net sales at constant exchange rates and on a constant structure basis** | **35,955** | **35,736** | **+0.6%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

When we refer to changes in our net sales at constant exchange rates (CER), that means that we have excluded the effect of exchange rates by recalculating net sales for the relevant period using the exchange rates that were used for the previous period.

When we refer to changes in our net sales on a constant structure (CS) basis, that means that we eliminate the effect of changes in structure by restating the net sales for the previous period as follows:

- by including sales generated by entities or product rights acquired in the current period for a portion of the previous period equal to the portion of the current period during which we owned them, based on sales information we receive from the party from whom we make the acquisition;
- similarly, by excluding sales for a portion of the previous period when we have sold an entity or rights to a product in the current period; and
- for a change in consolidation method, by recalculating the previous period on the basis of the method used for the current period.

To facilitate analysis and comparisons with prior periods, some figures are given at constant exchange rates and on a constant structure basis (CER/CS).

**Analysis of impact on net sales of changes in structure**

| *( million)* | **2017** |
|---|---|
| Net sales of Bioverativ[(a)] | 828 |
| Net sales of Zentiva (European Generics business)[(b)] | (164) |
| **Total impact on net sales of changes in structure** | **664** |

*(a) Net sales of Bioverativ products (consolidated from March 8, 2018) for the period from March 9, 2017 through December 31, 2017.*

*(b) Net sales of Zentiva (European Generics business), divested on September 30, 2018, for the period from October 1, 2017 through December 31, 2017.*

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**1/ Net Sales by Operating Segment**

Our net sales comprise the net sales generated by our Pharmaceuticals, Consumer Healthcare and Vaccines segments.

| *( million)* | 2018 | 2017[a] | Change |
|---|---|---|---|
| Pharmaceuticals | 24,685 | 25,173 | -1.9% |
| Consumer Healthcare | 4,660 | 4,798 | -2.9% |
| Vaccines | 5,118 | 5,101 | +0.3% |
| **Net sales** | **34,463** | **35,072** | **-1.7%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

**2/ Net Sales by Global Business Unit (GBU)**

The table below presents net sales for our Global Business Units (GBUs). Note that Emerging Markets sales of Diabetes & Cardiovascular and Specialty Care products are included in the General Medicines & Emerging Markets GBU.

| *( million)* | 2018 | 2017[a] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| Sanofi Genzyme (Specialty Care) GBU[b][c] | 7,226 | 5,674 | +27.4% | +30.8% |
| Diabetes & Cardiovascular GBU[b] | 4,511 | 5,399 | -16.4% | -13.8% |
| General Medicines & Emerging Markets GBU[d][e] | 12,948 | 14,100 | -8.2% | -2.8% |
| **Total Pharmaceuticals** | **24,685** | **25,173** | **-1.9%** | **+2.4%** |
| Consumer Healthcare GBU | 4,660 | 4,798 | -2.9% | +3.0% |
| Sanofi Pasteur (Vaccines) GBU | 5,118 | 5,101 | +0.3% | +2.4% |
| **Total net sales** | **34,463** | **35,072** | **-1.7%** | **+2.5%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) Does not include Emerging Markets net sales.*

*(c) Rare Diseases, Multiple Sclerosis, Oncology and Immunology, and Rare Blood Disorder.*

*(d) Includes net sales in Emerging Markets of Specialty Care and Diabetes & Cardiovascular products.*

*(e) Emerging Markets: World excluding United States, Canada, Europe (apart from Eurasia: Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**New GBUs**

We have announced our intention to adjust the structure of two of our GBUs with effect from January 1, 2019, so as to refocus our operations in mature and emerging markets. This involves creating a new Primary Care GBU that combines the product portfolio of the former Diabetes & Cardiovascular GBU with the

Established Products portfolio previously contained in the former General Medicines & Emerging Markets GBU. The new Primary Care GBU will focus exclusively on mature markets. We have also created a second GBU: China and Emerging Markets. This new GBU will focus on the specific characteristics and growth potential of emerging markets and especially China, which is our second-largest market after the United States.

To give investors a better understanding of the presentation of our net sales from 2019 onwards, the table below provides a breakdown of our 2018 net sales based on this new structure:

| *( million)* | **2018** |
|---|---|
| Sanofi Genzyme (Specialty Care) GBU | 7,226 |
| Primary Care GBU | 10,406 |
| China & Emerging Markets GBU | 7,053 |
| **Total Pharmaceuticals** | **24,685** |
| Consumer Healthcare GBU | 4,660 |
| Sanofi Pasteur (Vaccines) GBU | 5,118 |
| **Total net sales** | **34,463** |

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**3/ Net sales by franchise**

The table below sets forth our 2018 and 2017 net sales by franchise in order to facilitate direct comparisons with our peers. For a detailed reconciliation of net sales by franchise and net sales by GBU for our Pharmaceuticals segment, refer to the table in section 4 below, entitled 2018 Pharmaceuticals net sales by geographical region .

| *( million)* | **2018** | **2017[a]** | **Change on a reported basis** | **Change at constant exchange rates** |
|---|---|---|---|---|
| Rare Diseases | 2,958 | 2,890 | +2.4% | +8.3% |
| Multiple Sclerosis | 2,049 | 2,041 | +0.4% | +4.4% |
| Oncology | 1,494 | 1,517 | -1.5% | +2.1% |
| Immunology | 871 | 230 | +278.7% | +287.0% |
| Rare Blood Disorder | 897 | | | |
| **Total Specialty Care** | **8,269** | **6,678** | ***+23.8%*** | ***+29.0%*** |
| *of which Developed Markets (Sanofi Genzyme GBU)* | *7,226* | *5,674* | *+27.4%* | *+30.8%* |
| *of which Emerging Markets[b][c]* | *1,043* | *1,004* | *+3.9%* | *+18.7%* |
| Diabetes | 5,472 | 6,398 | -14.5% | -10.4% |
| Cardiovascular | 611 | 510 | +19.8% | +23.5% |
| **Total Diabetes & Cardiovascular** | **6,083** | **6,908** | **-11.9%** | **-7.9%** |
| *of which Developed Markets (Diabetes & Cardiovascular GBU)* | *4,511* | *5,399* | *-16.4%* | *-13.8%* |
| *of which Emerging Markets[b][c]* | *1,572* | *1,509* | *+4.2%* | *+13.1%* |
| **Established Prescription Products[b]** | **8,843** | **9,818** | **-9.9%** | **-6.1%** |
| **Generics[b]** | **1,490** | **1,769** | **-15.8%** | **-9.8%** |
| **Total Pharmaceuticals** | **24,685** | **25,173** | **-1.9%** | **+2.4%** |
| **Consumer Healthcare (Consumer Healthcare GBU)** | **4,660** | **4,798** | **-2.9%** | **+3.0%** |
| **Vaccines (Sanofi Pasteur GBU)** | **5,118** | **5,101** | **+0.3%** | **+2.4%** |
| **Total net sales** | **34,463** | **35,072** | **-1.7%** | **+2.5%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) These lines are aggregated to form the net sales of the General Medicines and Emerging Markets GBU.*

*(c) Emerging Markets: World excluding United States, Canada, Europe (apart from Eurasia: Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**4/ Net Sales Pharmaceuticals Segment**

In 2018, net sales for the Pharmaceuticals segment were 24,685 million, down 1.9% on a reported basis but up 2.4% at constant exchange rates (CER). At constant exchange rates and on a constant structure basis, net sales of the Pharmaceuticals segment were virtually unchanged, down just 0.2% in 2018 versus 2017. The year-on-year decline of 488 million on a reported basis reflects (i) an unfavorable effect of 1,104 million from exchange rates; (ii) the positive net effect of 664 million from the acquisition of Bioverativ products and the divestment of the European Generics business; and (iii) the following effects at constant exchange rates:

- positive performances from the Immunology franchise (up 660 million), the Rare Diseases franchise (up 239 million),
- the Cardiovascular franchise (up 120 million), the Multiple Sclerosis franchise (up 90 million), the Rare Blood Disorder franchise on a constant structure basis (up 89 million), and the Oncology franchise (up 32 million); and

- offset by lower net sales for the Diabetes franchise (down 666 million), the Established Prescription Products franchise (down 603 million), and the Generics franchise on a constant structure basis (down 9 million).

Comments on the performances of our major Pharmaceuticals segment products are provided below.

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**Pharmaceuticals segment net sales, 2018 and 2017**

| *( million)* | Indication | 2018 | 2017[(a)] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|---|
| Cerezyme® | Gaucher disease | 711 | 731 | -2.7% | +6.4% |
| Cerdelga® | Gaucher disease | 159 | 126 | +26.2% | +31.0% |
| Myozyme® / Lumizyme® | Pompe disease | 840 | 789 | +6.5% | +10.8% |
| Fabrazyme® | Fabry disease | 755 | 722 | +4.6% | +9.8% |
| Aldurazyme® | Mucopolysaccharidosis | 206 | 208 | -1.0% | +6.7% |
| Other | | 287 | 314 | -8.6% | -5.4% |
| **Total Rare Diseases** | | **2,958** | **2,890** | **+2.4%** | **+8.3%** |
| Aubagio® | Multiple Sclerosis | 1,647 | 1,567 | +5.1% | +9.3% |
| Lemtrada® | Multiple Sclerosis | 402 | 474 | -15.2% | -11.6% |
| **Total Multiple Sclerosis** | | **2,049** | **2,041** | **+0.4%** | **+4.4%** |
| Jevtana® | Prostate cancer | 422 | 386 | +9.3% | +13.0% |
| Thymoglobulin® | Organ rejection | 297 | 290 | +2.4% | +7.2% |
| Eloxatin® | Colorectal cancer | 182 | 179 | +1.7% | +5.0% |
| Taxotere® | Breast, lung, prostate, stomach, and head & neck cancers | 166 | 173 | -4.0% | -0.6% |
| Mozobil® | Hematological malignancies | 171 | 163 | +4.9% | +8.6% |
| Other | | 256 | 326 | -21.5% | -18.7% |
| **Total Oncology** | | **1,494** | **1,517** | **-1.5%** | **+2.1%** |
| Eloctate® | Hemophilia A | 608 | | | |
| Alprolix® | Hemophilia B | 285 | | | |
| Cablivi® | Acquired thrombotic thrombocytopenic purpura (aTTP) | 4 | | | |
| **Total Rare Blood Disorder** | | **897** | | | |

| | | | | | |
|---|---|---|---|---|---|
| Dupixent® | Atopic dermatitis and asthma | 788 | 219 | +259.8% | +268.0% |
| Kevzara® | Rheumatoid arthritis | 83 | 11 | +654.5% | +663.6% |
| **Total Immunology** | | **871** | **230** | **+278.7%** | **+287.0%** |
| **Total Specialty Care** | | **8,269** | **6,678** | **+23.8%** | **+29.0%** |
| Lantus® | Diabetes | 3,565 | 4,625 | -22.9% | -19.0% |
| Toujeo® | Diabetes | 840 | 816 | +2.9% | +7.2% |
| Apidra® | Diabetes | 357 | 377 | -5.3% | +0.3% |
| Amaryl® | Diabetes | 335 | 336 | -0.3% | +4.8% |
| Admelog®/Insulin lispro Sanofi® | Diabetes | 93 | 1 | | |
| Soliqua®/ Suliqua® | Diabetes | 73 | 26 | +180.8% | +188.5% |
| Other | Diabetes | 209 | 217 | -3.7% | -0.9% |
| **Total Diabetes** | | **5,472** | **6,398** | **-14.5%** | **-10.4%** |
| Multaq® | Atrial fibrillation | 350 | 339 | +3.2% | +7.1% |
| Praluent® | Hypercholesterolemia | 261 | 171 | +52.6% | +56.1% |
| **Total Cardiovascular** | | **611** | **510** | **+19.8%** | **+23.5%** |
| **Total Diabetes & Cardiovascular** | | **6,083** | **6,908** | **-11.9%** | **-7.9%** |

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| ( *million*) | Indication | 2018 | 2017[(a)] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|---|
| Lovenox® | Thrombosis | 1,465 | 1,574 | -6.9% | -3.0% |
| Plavix® | Atherothrombosis | 1,440 | 1,470 | -2.0% | +1.2% |
| Aprovel® / Avapro® | Hypertension | 652 | 690 | -5.5% | -1.7% |
| Depakine® | Epilepsy | 452 | 447 | +1.1% | +4.7% |
| Renagel® / Renvela® | Hyperphosphatemia | 411 | 801 | -48.7% | -46.7% |
| Synvisc® / Synvisc-One® | Arthritis | 313 | 387 | -19.1% | -15.0% |
| Stilnox® / Ambien® / Myslee® | Sleep disorders | 231 | 259 | -10.8% | -6.9% |
| Tritace® | Hypertension | 221 | 240 | -7.9% | -3.8% |
| Allegra® | Allergic rhinitis, urticaria | 124 | 158 | -21.5% | -17.7% |
| Other | | 3,534 | 3,792 | -6.8% | -2.5% |
| **Total Established Prescription Products** | | **8,843** | **9,818** | **-9.9%** | **-6.1%** |
| **Generics** | | **1,490** | **1,769** | **-15.8%** | **-9.8%** |
| **Total Pharmaceuticals** | | **24,685** | **25,173** | **-1.9%** | **+2.4%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

## Rare Diseases franchise

Net sales for the **Rare Diseases** franchise amounted to 2,958 million in 2018, up 2.4% on a reported basis and 8.3% at constant exchange rates (CER). Growth is being driven by medicines indicated for the treatment of Gaucher disease, Pompe disease and Fabry disease, especially in Emerging Markets[(1)]. In the United States and Europe[(2)], net sales for the franchise rose year-on-year by 5.8% CER (to 1,072 million) and 5.3% CER (to 1,008 million), respectively. Sales in Emerging Markets were up 21.5% CER at 542 million.

Net sales of **Myozyme® / Lumizyme®** in Pompe disease rose by 10.8% CER to 840 million, driven by sales growth in the United States (+13.0% CER at 284 million) and in Emerging Markets (+22.4% CER at 124 million). Sales also grew in Europe (+6.5% CER at 374 million) and in the Rest of the World region[(3)] (+3.4% CER at 58 million). This

growth reflects the rising number of patients diagnosed with, and treated for, Pompe disease.

In 2018, net sales for the Gaucher disease franchise (**Cerezyme**® and **Cerdelga**®) reached 870 million, up 10.0% CER, on strong sales of Cerezyme® in Emerging Markets (+24.3% CER at 230 million) and growth for Cerdelga® in Europe (+96.2% CER at 51 million). During 2018, Cerezyme® posted net sales of 711 million (+6.4% CER), while net sales of Cerdelga® reached 159 million (+31.0% CER).

**Fabrazyme**® recorded net sales growth of 9.8% CER to 755 million. Sales are advancing in all regions due to the rising number of patients diagnosed with, and treated for, Fabry

disease. Growth was particularly strong in Emerging Markets (+25.6% CER at 82 million) and the United States (+8.1% CER at 383 million).

### Multiple Sclerosis franchise

The Multiple Sclerosis franchise generated 2018 net sales of 2,049 million, up 0.4% on a reported basis and up 4.4% CER. Strong growth in sales of **Aubagio**® offset lower sales of **Lemtrada**® in mature markets.

**Aubagio**® generated net sales of 1,647 million (+9.3% CER), driven mainly by the United States (+11.4% CER at 1,157 million), but also by growth in Emerging Markets (+59.5% CER at 48 million).

Net sales of **Lemtrada**® in 2018 were 402 million, down 11.6% CER on lower sales in the United States (-19.1% CER at 189 million), Europe(2) (-3.4% CER at 167 million) and the Rest of the World region(3) (-33.3% CER at 19 million), mainly due to increased competition.

### Oncology franchise

Net sales for the Oncology franchise in 2018 totaled 1,494 million, down 1.5% on a reported basis but up 2.1% CER. We divested Leukine® on January 31, 2018, as part of our portfolio refocusing strategy. Excluding Leukine®, Oncology franchise net sales were up 6.3% CER in 2018, reflecting good performances by Jevtana® in the United States and Thymoglobulin® in China.

*(1) World excluding United States, Canada, Europe (other than Eurasia: Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

*(2) Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(3) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

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**Jevtana**® reported 2018 net sales of 422 million, up 13.0% CER, mainly on sales growth in the United States (+17.6% CER at 179 million), though sales were also stronger in Europe (+7.4% CER at 158 million) and Japan (+19.6% CER at 54 million).

Net sales of **Thymoglobulin**® advanced by 7.2% CER to 297 million, largely on a good performance in Emerging Markets (+22.7% CER at 75 million), especially China (+33.% CER at 39 million). **Eloxatin**® experienced similar trends, with net sales up 5.0% CER at 182 million, generated mainly in Emerging Markets (+6.8% CER at 150 million), particularly China (+17.5% CER at 118 million).

In September 2018, **Libtayo**® (cemiplimab, developed in collaboration with Regeneron) was approved in the United States for patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. Libtayo® is the only treatment for advanced CSCC to have been approved by the FDA. Sales of this product in the United States are consolidated by Regeneron under the terms of our alliance with Regeneron; see Note C.1, Alliance Arrangements with Regeneron Pharmaceuticals, Inc. to our consolidated financial statements.

Rare Blood Disorder franchise

Our Rare Blood Disorder franchise was created in 2018 following two acquisitions. The first was the acquisition of Bioverativ, which added two products to our portfolio: the flagship hemophilia treatments Eloctate® and Alprolix®. This was followed by the acquisition of Ablynx, enhancing our portfolio with the addition of Cablivi® (caplacizumab), which received marketing approval from the European Commission in September 2018 in the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

Net sales for the Rare Blood Disorder franchise have been consolidated by Sanofi since March 9, 2018, and in the period from that date to December 31, 2018 amounted to 897 million, including 175 million of non-US sales (mainly in Japan). At constant exchange rates and on a constant structure basis, the sales of the franchise grew by 10.7%.

Consolidated sales of **Eloctate**®, indicated in the treatment of hemophilia A, reached 608 million. At constant exchange rates and on a constant structure basis, that represents growth of 12.5%. This was mainly a result of sales growth in the United States, Japan and Australia, more than offsetting lower sales in Canada due to a failed tender bid.

Consolidated sales of the hemophilia B treatment **Alprolix**® reached 285 million. At constant exchange rates and on a constant structure basis, that represents growth of 5.8%.

**Cablivi**® was launched in Germany, its first-ever market, in the last quarter of 2018. The product is also on sale in France under a temporary license for use issued by the healthcare authorities. A temporary license for use allows specialty pharmaceutical products to be used in exceptional circumstances without marketing approval, and may be issued for a product that treats a

serious or rare condition for which there is no appropriate treatment available in the market. In those two countries, the product generated net sales of 4 million.

### Immunology franchise

**Dupixent**® (developed in collaboration with Regeneron) was launched in the United States in April 2017 for moderate-to-severe atopic dermatitis in adults, and in Germany in December 2017. Further launches followed in 2018 in many European countries, Emerging Markets countries, and Japan. Net sales of Dupixent® reached 788 million in 2018, of which 660 million was generated in the United States, where sales were 213.9% higher CER than in 2017. In October 2018, Dupixent® was approved in the United States for moderate-to-severe asthma in adults.

**Kevzara**® (developed in collaboration with Regeneron) was launched as a rheumatoid arthritis treatment in the United States in June 2017; in Germany, the United Kingdom and the Netherlands in the second half of 2017; and in Japan and many European Union countries in 2018. Net sales of Kevzara® in 2018 amounted to 83 million, of which 64 million was generated in the United States.

### Diabetes franchise

Net sales for the Diabetes franchise totaled 5,472 million in 2018, down 14.5% on a reported basis and 10.4% at constant exchange rates. This reflects a decline in sales for the franchise in the United States (-26.9% CER at 2,185 million), especially of insulin glargines (Lantus® and Toujeo®) as a result of changes to Medicare Part D welfare program cover and the ongoing decline in average net prices for insulin glargines in the United States. Elsewhere in the world, net sales for the Diabetes franchise rose in Emerging Markets (+12.7% CER at 1,554 million) and fell slightly in Europe (-0.9% CER at 1,272 million) and in the Rest of the World region (-0.8% CER at 461 million), where good performances from Toujeo® nearly offset lower sales of Lantus®.

Over 2018, net sales of our **insulin glargines** (Lantus® and Toujeo®) were down 19.0% on a reported basis and 15.1% CER at 4,405 million.

Net sales of **Lantus**® in 2018 were down 19.0% CER at 3,565 million. In the United States, sales were down 33.3% CER at 1,614 million, for the reasons explained above. Net sales in Europe decreased by 9.7% CER to 684 million, due largely to the launch of a biosimilar of Lantus® and the switching of patients to Toujeo®. In Emerging Markets, sales of Lantus® advanced by 5.3% CER to 977 million. Following Merck s decision not to commercialize its insulin glargine in the United States and the filing by Merck of motions to dismiss the insulin glargine pen and vial pending legal actions, on October 26, 2018 Sanofi and Merck filed joint requests with the District Courts for the districts of Delaware and New Jersey to discontinue the pending litigation. The courts accepted those requests in October 2018 (Delaware) and

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November 2018 (New Jersey), and the cases are now closed (for further information, refer to Item 8.A. Consolidated Financial Statements and Other Financial Information Information on Legal or Arbitration Proceedings ).

In 2018, **Toujeo**® posted net sales of 840 million, up 7.2% CER, driven by strong performances in Europe (+34.6% at 290 million) and Emerging Markets (+83.5% at 130 million). However sales fell in the United States (-20.7% CER at 344 million), mainly as a result of a decrease in the average net selling price.

We expect a further decline in net selling prices for our insulin glargines in 2019, as we offer further rebates in the United States in order to maintain broad coverage by commercial insurers and Medicare. From 2015 to 2018 net sales for the Diabetes franchise have decreased at an annualized average rate of 7.4% CER, in line with our previously-announced guidance of a 6%-8% annualized average decrease over that period.

Net sales of **Apidra**® were stable year-on-year in 2018 at 357 million (+0.3% CER). Lower sales in the United States (-23.5% CER at 74 million) were compensated for by sales growth in Emerging Markets (+26.5% CER at 109 million).

**Amaryl**® posted net sales growth of 4.8% CER to 335 million in 2018. Higher sales in Emerging Markets (+9.4% CER at 288 million) offset a decrease in the Rest of the World region (-16.7% CER at 28 million) and Europe (-19.0% CER at 17 million).

**Admelog**® (injectable insulin lispro 100 units/ml, in vials or the pre-filled SoloStar® pen) was launched in 2018 in the United States, and also as a biosimilar in some European countries under the name **Insulin lispro Sanofi**®. The product generated net sales of 93 million in 2018, including 86 million in the United States as a result of its being accepted onto the Managed Medicaid program.

**Soliqua® 100/33 and Suliqua®** (insulin glargine 100 units/ml and lixisenatide 33 mcg/ml injectable) were launched (respectively) in the United States in January 2017, and in various European and Emerging Markets countries during the rest of 2017. The product generated net sales of 73 million, including 62 million in the United States.

### Cardiovascular franchise

Net sales of **Praluent**® (developed in collaboration with Regeneron) increased by 56.1% CER to 261 million in 2018, including 154 million in the United States (+37.1% CER) and 86 million in Europe (+87.0% CER). During 2018, Sanofi and Regeneron negotiated with US payers to streamline the reimbursement criteria in order to improve patient access to the product, in exchange for a significant price reduction.

Net sales of **Multaq**® in 2018 were 350 million, up 7.1% CER on 2017. Sales were generated primarily in the United States (net sales of 296 million, +8.0% CER) and in Europe ( 43 million, +2.4% CER).

### Established Prescription Products

Net sales of Established Prescription Products in 2018 amounted to 8,843 million, down 9.9% on a reported basis and 6.1%

CER. Stronger sales in Emerging Markets (+6.6% CER at 3,753 million) failed to offset lower net sales in mature markets (-14.1% CER at 5,090 million). In the United States for example, the franchise saw net sales fall by 38.2% CER to 751 million, mainly due to generic competition for Renvela®/Renagel® (sevelamer). In the Rest of the World region, net sales were down 16.9% CER at 1,009 million, largely as a result of competition from generics of Plavix® and Aprovel® in Japan. In Europe, the franchise posted net sales of 3,330 million, down 4.4% CER, impacted by generic competition for Lovenox®.

Net sales of **Lovenox®** totaled 1,465 million, down 3.0% CER; this reflects tougher competition in Europe (-8.3% CER at 870 million) with the arrival of biosimilars in various countries including Germany, France, Italy, Poland and the United Kingdom. The impact of generic competition is also being felt in the United States, where the product saw net sales decrease by 29.3% CER to 38 million. A strong performance in Emerging Markets (+11.4% CER at 476 million) failed to fully offset the decline in mature markets.

**Plavix®** posted 2018 net sales of 1,440 million (+1.2% CER). This reflects a solid performance in Emerging Markets (+8.8% at 1,075 million), especially in China (+10.6% CER at 817 million), more than offsetting the effect of lower sales in the Rest of the World region (-23.5% at 218 million), especially in Japan (-31.5% CER at 156 million) due to competition from generics. Sales of Plavix® in the United States and Puerto Rico are handled by BMS under the terms of the Sanofi-BMS alliance; see Note C.2. ( Alliance Arrangements with Bristol-Myers Squibb (BMS) ) to our consolidated financial statements.

In 2018, net sales of **Aprovel® /Avapro®** amounted to 652 million, down 1.7% CER, reflecting competition from generics in Japan (-66.3% CER at 28 million) and Europe (-6.1% CER at 108 million). The effect was partly offset by stronger sales in Emerging Markets (+12.7% CER at 465 million), especially China (+15.5% CER at 297 million).

Net sales of **Renvela®/Renagel®** in 2018 were 411 million, down 46.7% CER, mainly due to competition from generics in the United States (-59.1% CER at 253 million).

### Generics

Net sales of Generics were 1,490 million, down 15.8% on a reported basis and 9.8% CER. The main reason for the decrease was the sale of our European Generics business (Zentiva) to Advent International on September 30, 2018. This divestment was in line with our strategy of streamlining and refocusing our operations.

At constant exchange rates and on a constant structure basis, Generics net sales were relatively stable, falling by just 0.6%. Higher sales in Emerging Markets (+3.0% CER at 685 million) and the Rest of the World region (+9.1% CER at 113 million), especially in Japan, failed to fully offset lower sales in Europe (-15.3% CER at 124 million) and the United States (-3.2% at constant exchange rates and on a constant structure basis at 568 million).

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**2018 Pharmaceuticals net sales by geographical region**

| *( million)* | Total GBU | Europe[a] | Change at CER | United States | Change at CER | Rest of the World[b] | Change at CER | Emerging Markets[c] | Change at CER | Total Franchise | Change at CER |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cerezyme® | 481 | 270 | -3.6% | 174 | +2.8% | 37 | -9.3% | 230 | +24.3% | 711 | +6.4% |
| Cerdelga® | 156 | 51 | +96.2% | 98 | +7.4% | 7 | +100.0% | 3 | +300.0% | 159 | +31.0% |
| Myozyme® /Lumizyme® | 716 | 374 | +6.5% | 284 | +13.0% | 58 | +3.4% | 124 | +22.4% | 840 | +10.8% |
| Fabrazyme® | 673 | 175 | +7.4% | 383 | +8.1% | 115 | +8.0% | 82 | +25.6% | 755 | +9.8% |
| Aldurazyme® | 144 | 76 | +1.3% | 44 | +9.5% | 24 | +4.0% | 62 | +12.1% | 206 | +6.7% |
| Other | 246 | 62 | 0.0% | 89 | -16.8% | 95 | 0.0% | 41 | +4.4% | 287 | -5.4% |
| **Total Rare Diseases** | **2,416** | **1,008** | **+5.3%** | **1,072** | **+5.8%** | **336** | **+3.6%** | **542** | **+21.5%** | **2,958** | **+8.3%** |
| Aubagio® | 1,599 | 385 | -0.3% | 1,157 | +11.4% | 57 | +0.0% | 48 | +59.5% | 1,647 | +9.3% |
| Lemtrada® | 375 | 167 | -3.4% | 189 | -19.1% | 19 | -33.3% | 27 | +33.3% | 402 | -11.6% |
| **Total Multiple Sclerosis** | **1,974** | **552** | **-1.2%** | **1,346** | **+5.8%** | **76** | **-11.2%** | **75** | **+49.2%** | **2,049** | **+4.4%** |
| Jevtana® | 399 | 158 | +7.4% | 179 | +17.6% | 62 | +20.8% | 23 | +0.0% | 422 | +13.0% |
| Thymoglobulin® | 222 | 37 | -5.1% | 162 | +4.9% | 23 | +0.0% | 75 | +22.7% | 297 | +7.2% |
| Eloxatin® | 32 | 2 | -50.0% | | -100.0% | 30 | +7.1% | 150 | +6.8% | 182 | +5.0% |
| Taxotere® | 32 | 3 | +0.0% | 1 | | 28 | -17.6% | 134 | +2.9% | 166 | -0.6% |
| Mozobil® | 161 | 47 | +9.1% | 96 | +5.2% | 18 | +21.4% | 10 | +22.2% | 171 | +8.6% |
| Other | 229 | 104 | +2.9% | 85 | -47.4% | 40 | +41.4% | 27 | +20.8% | 256 | -18.7% |
| **Total Oncology** | **1,075** | **351** | **+4.1%** | **523** | **-6.8%** | **201** | **+12.2%** | **419** | **+8.8%** | **1,494** | **+2.1%** |
| Eloctate® | 606 | | | 500 | | 106 | | 2 | | 608 | |
| Alprolix® | 285 | | | 222 | | 63 | | | | 285 | |
| Cablivi® | 4 | 4 | | | | | | | | 4 | |
| **Total Rare Blood Disorder** | **895** | **4** | | **722** | | **169** | | **2** | | **897** | |
| Dupixent® | 783 | 75 | +3,650.0% | 660 | +213.9% | 48 | +4,700.0% | 5 | | 788 | **+268.0%** |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Kevzara® | 83 | 14 | +1,300.0% | 64 | +550.0% | 5 | | | | 83 | +663.6% |
| **Total Immunology** | **866** | **89** | **+2,866.7%** | **724** | **+228.8%** | **53** | **+5,200.0%** | **5** | | **871** | **+287.0%** |
| **Sanofi Genzyme (Specialty Care)** | **7,226** | **2,004** | **+7.9%** | **4,387** | **+42.3%** | **835** | **+40.9%** | **1,043** | **+18.7%** | **8,269** | **+29.0%** |
| Lantus® | 2,588 | 684 | -9.7% | 1,614 | -33.3% | 290 | -3.8% | 977 | +5.3% | 3,565 | **-19.0%** |
| Toujeo® | 710 | 290 | +34.6% | 344 | -20.7% | 76 | +18.5% | 130 | +83.5% | 840 | +7.2% |
| Apidra® | 248 | 136 | +0.0% | 74 | -23.5% | 38 | -2.4% | 109 | +26.5% | 357 | +0.3% |
| Amaryl® | 47 | 17 | -19.0% | 2 | +0.0% | 28 | **-16.7%** | 288 | +9.4% | 335 | **+4.8%** |
| Admelog®/Insulin lispro Sanofi® | 93 | 7 | +600.0% | 86 | | 0 | | 0 | | 93 | |
| Soliqua®/Suliqua® | 70 | 5 | | 62 | +142.3% | 3 | | 3 | | 73 | +188.5% |
| Other | 162 | 133 | -12.5% | 3 | +200% | 26 | -3.6% | 47 | +44.4% | 209 | -0.9% |
| **Total Diabetes** | **3,918** | **1,272** | **-0.9%** | **2,185** | **-26.9%** | **461** | **-0.8%** | **1,554** | **+12.7%** | **5,472** | **-10.4%** |
| Multaq® | 343 | 43 | +2.4% | 296 | +8.0% | 4 | +0.0% | 7 | +0.0% | 350 | +7.1% |
| Praluent® | 250 | 86 | +87.0% | 154 | +37.1% | 10 | +120.0% | 11 | +175.0% | 261 | +56.1% |
| **Total Cardiovascular** | **593** | **129** | **+46.6%** | **450** | **+16.4%** | **14** | **+66.7%** | **18** | **+63.6%** | **611** | **+23.5%** |
| **Diabetes & Cardiovascular** | **4,511** | **1,401** | **+2.2%** | **2,635** | **-22.0%** | **475** | **+0.4%** | **1,572** | **+13.1%** | **6,083** | **-7.9%** |

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| *( million)* | Total GBU | Europe[a] | Change at CER | United States | Change at CER | Rest of the World[b] | Change at CER | Emerging Markets[c] | Change at CER | Total Franchise | Change at CER |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Lovenox® | 1,465 | 870 | -8.3% | 38 | -29.3% | 81 | -6.6% | 476 | +11.4% | 1,465 | -3.0% |
| Plavix® | 1,440 | 147 | -2.0% | 0 | -100.0% | 218 | -23.5% | 1,075 | +8.8% | 1,440 | +1.2% |
| Aprovel®/Avapro® | 652 | 108 | -6.1% | 10 | +0.0% | 69 | -45.5% | 465 | +12.7% | 652 | -1.7% |
| Depakine® | 452 | 163 | -1.2% | 0 | | 14 | -6.7% | 275 | +9.0% | 452 | +4.7% |
| Renagel®/Renvela® | 411 | 60 | -15.5% | 253 | -59.1% | 31 | -8.6% | 67 | +42.0% | 411 | -46.7% |
| Synvisc®/Synvisc-One® | 313 | 25 | -16.7% | 217 | -22.3% | 13 | +0.0% | 58 | +23.5% | 313 | -15.0% |
| Stilnox®/Ambien®/Myslee® | 231 | 39 | -2.5% | 45 | -14.5% | 86 | -16.0% | 61 | +13.8% | 231 | -6.9% |
| Tritace® | 221 | 142 | -5.9% | 0 | | 5 | +0.0% | 74 | +0.0% | 221 | -3.8% |
| Allegra® | 124 | 8 | -11.1% | 0 | | 116 | -18.1% | 0 | | 124 | -17.7% |
| Other | 3,534 | 1,768 | -2.0% | 188 | -6.3% | 376 | -7.1% | 1,202 | -1.1% | 3,534 | -2.5% |
| **Total Established Prescription Products** | **8,843** | **3,330** | **-4.4%** | **751** | **-38.2%** | **1,009** | **-16.9%** | **3,753** | **+6.6%** | **8,843** | **-6.1%** |
| **Generics** | **1,490** | **568** | **-24.4%** | **124** | **-15.3%** | **113** | **+9.1%** | **685** | **+3.0%** | **1,490** | **-9.8%** |
| **Total Emerging Markets Specialty Care** | **1,043** | | | | | | | **1,043** | **+18.7%** | | |
| **Total Emerging Markets Diabetes & Cardiovascular** | **1,572** | | | | | | | **1,572** | **+13.1%** | | |
| **General Medicines & Emerging Markets** | **12,948** | **3,898** | **-7.9%** | **875** | **-35.8%** | **1,122** | **-14.8%** | **7,053** | **+9.3%** | | |
| **Total Pharmaceuticals** | **24,685** | **7,303** | **-2.1%** | **7,897** | **+0.9%** | **2,432** | **+1.9%** | **7,053** | **+9.3%** | **24,685** | **+2.4%** |

*(a) Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

*(c) World excluding United States, Canada, Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

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**5/ Net sales Consumer Healthcare Segment**

Net sales of **Consumer Healthcare** products for 2018 were 4,660 million, down 2.9% on a reported basis but up 3.0% at constant exchange rates, driven by Emerging Markets (+8.9% CER at 1,588 million) especially Latin America and by the Pain (+6.7% CER at 1,254 million) and Digestive (+8.7% CER at 986 million) categories. Sales of Consumer Health products were stable in Europe at 1,403 million, but decreased slightly in the United States (-1.1% CER at 1,066 million).

| ( *million*) | 2018 | 2017[(a)] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| Allegra® | 396 | 422 | -6.2% | +1.2% |
| Mucosolvan® | 110 | 112 | -1.8% | +1.8% |
| Other | 618 | 671 | -7.9% | -4.0% |
| **Allergy, Cough & Cold** | **1,124** | **1,205** | **-6.7%** | **-1.7%** |
| Doliprane® | 333 | 323 | +3.1% | +4.0% |
| Buscopan® | 194 | 194 | +0.0% | +16.0% |
| Other | 727 | 744 | -2.3% | +5.4% |
| **Pain** | **1,254** | **1,261** | **-0.6%** | **+6.7%** |
| Dulcolax® | 216 | 210 | +2.9% | +7.1% |
| Enterogermina® | 183 | 168 | +8.9% | +16.1% |
| Essentiale® | 177 | 172 | +2.9% | +8.7% |
| Zantac® | 127 | 117 | +8.5% | +13.7% |
| Other | 283 | 287 | -1.4% | +3.5% |
| **Digestive** | **986** | **954** | **+3.4%** | **+8.7%** |
| Pharmaton® | 90 | 99 | -9.1% | -1.0% |
| Other | 585 | 586 | -0.2% | +5.6% |
| **Nutritionals** | **675** | **685** | **-1.5%** | **+4.7%** |
| Gold Bond® | 211 | 201 | +5.0% | +9.5% |
| Other | 410 | 492 | -16.7% | -11.2% |
| **Other products** | **621** | **693** | **-10.4%** | **-5.2%** |
| **Total Consumer Healthcare** | **4,660** | **4,798** | **-2.9%** | **+3.0%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

In Emerging Markets, Consumer Healthcare net sales reached 1,588 million, up 8.9% CER, boosted by Pain (+14.0% CER at 449 million) and Digestive (+14.4% CER at 423 million), especially in Brazil.

In Europe, Consumer Healthcare net sales remained stable in 2018 at 1,403 million. Sales growth in the Pain (+1.8% CER at 521 million) and Digestive (+2.6% CER at 314 million) categories offset a decrease in sales for Allergy, Cough & Cold (-0.9% CER at 347 million, reflecting a strong comparative base in 2017) and Other Products (-19.7% CER at 96 million, linked to the June 2018 sale of a portfolio of 12 brands to

Cooper-Vemedia, the European subsidiary of Charterhouse Capital Partners.

Sales of Consumer Healthcare products in the United States totaled 1,066 million in 2018, down slightly (-1.1% CER) on 2017. The main category affected was Allergy, Cough & Cold (-12.3% CER at 303 million), reflecting inventory build-ups ahead of the Xyzal® launch during 2017 and competition from retailer own brands, especially in anti-allergy nasal sprays.

In the Rest of the World region, Consumer Healthcare net sales reached 603 million in 2018, up 2.1% CER, driven largely by Japan (+4.7% CER at 302 million).

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**2018 Consumer Healthcare net sales by geographical region**

| *( million)* | Total | Europe[a] | Change at CER | United States | Change at CER | Rest of the World[b] | Change at CER | Emerging Markets[c] | Change at CER |
|---|---|---|---|---|---|---|---|---|---|
| Allegra® | 396 | 17 | +50.0% | 207 | -5.2% | 44 | | 128 | +8.5% |
| Mucosolvan® | 110 | 57 | -1.7% | | | 3 | | 50 | +5.8% |
| Other | 618 | 273 | -2.9% | 96 | -24.6% | 88 | +4.4% | 161 | +6.0% |
| **Allergy, Cough & Cold** | **1,124** | **347** | **-0.9%** | **303** | **-12.3%** | **135** | **+2.9%** | **339** | **+6.9%** |
| Doliprane® | 333 | 281 | +1.4% | | | | | 52 | +19.6% |
| Buscopan® | 194 | 79 | +5.3% | | | 10 | -23.1% | 105 | +28.6% |
| Other | 727 | 161 | +0.6% | 165 | +3.6% | 109 | +6.7% | 292 | +8.3% |
| **Pain** | **1,254** | **521** | **+1.8%** | **165** | **+3.6%** | **119** | **+3.4%** | **449** | **+14.0%** |
| Dulcolax® | 216 | 99 | +6.5% | 62 | +6.6% | 19 | -4.8% | 36 | +17.1% |
| Enterogermina® | 183 | 67 | +4.7% | | | (1) | | 117 | +23.1% |
| Essentiale® | 177 | 36 | +5.9% | | | | | 141 | +9.4% |
| Zantac® | 127 | | | 113 | +13.3% | 14 | +16.7% | | |
| Other | 283 | 112 | -2.6% | 20 | -9.1% | 22 | | 129 | +12.0% |
| **Digestive** | **986** | **314** | **+2.6%** | **195** | **+8.5%** | **54** | **+1.8%** | **423** | **+14.4%** |
| Pharmaton® | 90 | 19 | | | | 1 | | 70 | -1.3% |
| Other | 585 | 106 | +7.1% | 37 | -5.0% | 255 | +5.9% | 187 | +6.7% |
| **Nutritionals** | **675** | **125** | **+5.9%** | **37** | **-5.0%** | **256** | **+5.9%** | **257** | **+4.4%** |
| Gold Bond® | 211 | | | 207 | +9.1% | 4 | +33.3% | | |
| Other | 410 | 96 | -19.7% | 159 | -2.9% | 35 | -26.7% | 120 | -9.2% |
| **Other products** | **621** | **96** | **-19.7%** | **366** | **+3.5%** | **39** | **-22.9%** | **120** | **-9.2%** |
| **Total Consumer Healthcare** | **4,660** | **1,403** | **-0.2%** | **1,066** | **-1.1%** | **603** | **+2.1%** | **1,588** | **+8.9%** |

*(a) Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

(c) *World excluding United States, Canada, Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**6/ Net sales Vaccines segment**

The Vaccines segment posted 2018 net sales of 5,118 million, up 0.3% on a reported basis and 2.4% CER, driven by influenza vaccines in mature markets. US vaccine sales advanced by 1.1% CER to 2,577 million, with higher influenza vaccine sales more than offsetting lower sales for other vaccine categories. Sales

growth was robust in the Rest of the World region and Europe, at 16.0% CER (to 728 million) and 9.5% CER (to 342 million), respectively. However, net sales fell by 2.3% in Emerging Markets to 1,471 million, mainly due to weaker influenza vaccines sales.

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**Vaccines net sales 2018 and 2017**

| ( million) | 2018 | 2017[a] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| Polio/Pertussis/Hib Vaccines (including Pentacel®, Pentaxim®, Imovax® and Hexaxim®) | 1,749 | 1,827 | -4.3% | -0.7% |
| Influenza Vaccines (including Vaxigrip®, Fluzone® and Flublok®) | 1,708 | 1,589 | +7.5% | +7.2% |
| Meningitis/Pneumonia Vaccines (including Menactra®) | 609 | 623 | -2.2% | +0.6% |
| Travel and Other Endemics Vaccines | 488 | 493 | -1.0% | +1.8% |
| Adult Booster Vaccines (including Adacel®) | 470 | 474 | -0.8% | +1.3% |
| Other vaccines | 94 | 95 | -1.1% | +3.2% |
| **Total Vaccines** | **5,118** | **5,101** | **+0.3%** | **+2.4%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

Net sales of **Polio/Pertussis/Hib vaccines** were 1,749 million in 2018, down 0.7% CER. In Emerging Markets, sales for the franchise remained stable at 900 million. Lower net sales linked to supply constraints on Pentaxim® in China during the first half were offset by ongoing expansion of pediatric combination vaccines in other emerging markets countries. Net sales of Polio/Pertussis/Hib vaccines decreased in the United States (-4.8% CER at 397 million), reflecting fluctuations in inventory levels at our principal customers. In Europe, net sales fell slightly (-1.0% CER at 296 million) due to the arrival of a new competitor in the pediatric combination vaccines market.

Net sales of **Influenza vaccines** rose by 7.2% CER to 1,708 million. This performance was driven by stronger sales in the United States (+7.5% CER at 1,233 million), boosted by a successful launch for Flublok®. Influenza vaccine sales also rose sharply in Europe (+57.5% CER at 177 million), largely on the

successful launch of Vaxigrip® QIV. These performances more than offset lower sales for the franchise in Emerging Markets (-22.9% CER at 217 million, due to the loss of a public tender in Latin America.

Net sales of **Meningitis/Pneumonia** vaccines were stable at 609 million. Menactra® reported net sales of 608 million (+4.5% CER), of which 466 million was generated in the United States.

**Travel and Other Endemics vaccines** posted a 1.8% CER rise in net sales to 488 million in 2018, driven by increased demand for yellow fever and hepatitis A vaccines.

Net sales of **Adult Booster vaccines** reached 470 million in 2018 (+1.3% CER), driven by growth in Europe (+9.2% CER at 129 million) as limitations on supplies of Repevax® ended in the first half of 2018.

**2018 Vaccines net sales by geographical region**

| *( million)* | Total | Europe[(a)] | Change at CER | United States | Change at CER | Rest of the World[(b)] | Change at CER | Emerging Markets[(c)] | Change at CER |
|---|---|---|---|---|---|---|---|---|---|
| Polio/Pertussis/Hib Vaccines (including Pentacel®, Pentaxim®, Imovax® and Hexaxim®) | 1,749 | 296 | -1.0% | 397 | -4.8% | 156 | +5.9% | 900 | +0.3% |
| Influenza Vaccines (including Vaxigrip®, Fluzone® and Flublok®) | 1,708 | 177 | +57.5% | 1,233 | +7.5% | 81 | +62.7% | 217 | -22.9% |
| Meningitis/Pneumonia Vaccines (including Menactra®) | 609 | 0 | -100.0% | 466 | -1.6% | 16 | -50.0% | 127 | +29.1% |
| Travel and Other Endemics Vaccines | 488 | 117 | +31.1% | 134 | -10.3% | 56 | +7.4% | 181 | -3.6% |
| Adult Booster Vaccines (including Adacel®) | 470 | 129 | +9.2% | 273 | -4.1% | 26 | 0.0% | 42 | +18.9% |
| Other vaccines | 94 | 9 | +14.3% | 74 | 0.0% | 7 | +33.3% | 4 | -25% |
| **Total Vaccines** | **5,118** | **728** | **+16.0%** | **2,577** | **+1.1%** | **342** | **+9.5%** | **1,471** | **-2.3%** |

*(a) Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

*(c)*

*World excluding United States, Canada, Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

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**7/ Net sales by geographical region**

The table below sets forth our net sales for 2018 and 2017 by geographical region:

| *( million)* | 2018 | 2017[a] | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| United States | 11,540 | 11,855 | -2.7% | +0.7% |
| Emerging Markets[b] | 10,112 | 10,275 | -1.6% | +7.5% |
| *of which Asia (including South Asia[c])* | 3,962 | *3,755* | +5.5% | +9.3% |
| *of which Latin America* | 2,612 | *2,837* | -7.9% | +8.1% |
| *of which Africa and Middle East* | 2,232 | *2,311* | -3.4% | +1.1% |
| *of which Eurasia[d]* | 1,152 | *1,251* | -7.9% | +10.1% |
| Europe[e] | 9,434 | 9,525 | -1.0% | -0.6% |
| Rest of the World[f] | 3,377 | 3,417 | -1.2% | +2.7% |
| *of which Japan* | 1,710 | *1,803* | -5.2% | -2.0% |
| *of which South Korea* | 432 | *426* | +1.4% | +3.3% |
| **Total net sales** | **34,463** | **35,072** | **-1.7%** | **+2.5%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

*(b) World excluding United States, Canada, Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

*(c) India, Bangladesh and Sri Lanka.*

*(d) Russia, Ukraine, Georgia, Belarus, Armenia and Turkey.*

*(e) Europe excluding Eurasia.*

*(f) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

Net sales in the **United States** were 11,540 million in 2018, down 2.7% on a reported basis but up 0.7% at constant exchange rates. Good performances from Dupixent® and Aubagio® and the first-time consolidation of sales of Eloctate® and Alprolix® offset lower sales for the Diabetes franchise (-26.9% CER at 2,185 million) and Renvela®/Renagel® (-59.1% CER at 253 million).

Net sales in **Emerging Markets** reached 10,112 million, down 1.6% on a reported basis but up 7.5% CER. All Pharmaceuticals segment franchises saw net sales growth in Emerging Markets, as did Consumer Healthcare; the only exception was vaccines, with net sales down 2.3% CER at 1,471 million. The biggest contributors to growth in Emerging Markets were Established Prescription Products (+6.6% CER at 3,753 million), Diabetes (+12.7% CER at 1,554 million) and Consumer Healthcare (+8.9% CER at 1,588 million). In **Asia**, net sales rose by 9.3% CER to 3,962 million on a solid performance in China (+12.7% CER at 2,464 million), despite local supply constraints on Pentaxim® in the first half. In **Latin America**, net sales reached 2,612 million, up 8.1% CER, fueled by Brazil (+7.0% CER at 1,023 million). The best performers in this zone were Consumer Healthcare (+15.4% CER at 641 million) and Rare Diseases (+32.8% CER at 231 million). In **Africa and the Middle East**, net sales were up 1.1% CER at 2,232 million, boosted by the Diabetes franchise (+10.3% CER at 426 million) and Consumer Healthcare (+7.1% CER at 274 million), which offset lower Vaccines sales. In **Eurasia**, net sales were 10.1% higher CER at 1,152 million, reflecting strong sales growth in Turkey (+17.6% CER at 426 million) and Russia (+4.6% CER at 605 million).

In **Europe**, net sales remained stable in 2018 at 9,434 million. Robust performances by Vaccines (+16.0% CER at 728 million) and from Dupixent® and Praluent® offset lower sales of Established Prescription Products (-4.4% CER at 3,330 million), and of Generics following the divestment of Zentiva on September 30, 2018. At constant exchange rates and on a constant structure basis, sales in Europe rose by 1.1%.

In the **Rest of the World** region, net sales advanced by 2.7% CER to 3,377 million. Net sales in Japan totaled 1,710 million, down 2.0% CER. Good performances from Dupixent® and the first-time consolidation of sales of Eloctate® and Alprolix® failed to fully offset a sharp decline in net sales of Established Prescription Products (-16.9% CER at 1,009 million), attributable in part to generic competition for Plavix® and Aprovel®.

*A.2.2. Other income statement items*

Comparable information for the year ended December 31, 2017 has been restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impact of these restatements is described in detail in Note A.2.1.1. to our consolidated financial statements, and affects not only ***Net sales*** but also some of the line items discussed below.

**1/ Other revenues**

Other revenues increased by 5.7% to 1,214 million in 2018 (versus 1,149 million in 2017). This line item mainly comprises

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VaxServe sales of non-Sanofi products ( 959 million, versus 859 million in 2017, recorded within the Vaccines segment), and revenues associated with the distribution of Eloctate® and Alprolix® (primarily in Europe) under our agreements with Swedish Orphan Biovitrum AB.

**2/ Gross profit**

Gross profit for 2018 amounted to 24,242 million, versus 24,608 million in 2017, a decrease of 1.5%. As a percentage of net sales, that represents an improvement on 2017 (70.3% of net sales, versus 70.2% in 2017). The year-on-year change includes the impacts of the remeasurement of inventories acquired in the transaction with Boehringer Ingelheim ( 166 million in 2017) and the acquisition of Bioverativ ( 114 million in 2018).

For the Pharmaceuticals segment, gross margin was 0.6 of a percentage point lower at 73.7%. Good performances from the Immunology, Rare Diseases and Multiple Sclerosis franchises, plus the inclusion of Bioverativ products in the consolidation, failed to offset lower average net prices for insulin glargines in the United States, competition from generics of Renagel®/Renvela®, and unfavorable foreign exchange effects.

Gross margin for the Consumer Healthcare segment rose by 0.6 of a percentage point in 2018 to 67.0%, thanks largely to a good performance in Emerging Markets and a favorable product mix in Europe.

Gross margin for the Vaccines segment rose by one percentage point to 63.0%, reflecting a reduction in the value of Dengvaxia® inventories in 2017 following the product label update announced at the end of that year.

**3/ Research and development expenses**

Research and development (R&D) expenses amounted to 5,894 million in 2018 (versus 5,472 million in 2017) and represented 17.1% of net sales (versus 15.6% in 2017). Overall, R&D expenses increased by 7.7%, mainly due to the acquisitions of Bioverativ and Ablynx and to spending on immuno-oncology and diabetes programs in the Pharmaceuticals segment.

**4/ Selling and general expenses**

Selling and general expenses were 9,859 million in 2018 (28.6% of net sales), compared with 10,072 million in 2017 (28.7% of net sales); this represented a year-on-year decrease of 2.1%, attributable mainly to the effect of exchange rates. At constant exchange rates, selling and general expenses increased year-on-year, reflecting the first-time consolidation of Bioverativ and Ablynx and investments in immunology, partly offset by lower spending on Diabetes in the United States, within the Pharmaceuticals segment.

For the Consumer Healthcare segment, selling and general expenses were 1.4 percentage points lower at 32.9% of net sales, versus 34.3% in 2017. This was mainly due to synergies realized following the integration of Boehringer Ingelheim s Consumer Healthcare business, as well as the reduction in

marketing expenses linked to the launch of Xyzal® in the US in March 2017.

**5/ Other operating income and expenses**

Other operating income amounted to 484 million in 2018 (versus 237 million in 2017), and other operating expenses to 548 million (versus 233 million in 2017).

Overall, this represented a net expense of 64 million in 2018, compared with net income of 4 million in 2017.

| ( *million)* | 2018 | 2017 | Change |
|---|---|---|---|
| Other operating income | 484 | 237 | +247 |
| Other operating expenses | (548) | (233) | -315 |
| **Other operating income/(expenses), net** | **(64)** | **4** | **-68** |

The net negative movement of 68 million is largely due to (i) an increase in the net expense relating to our pharmaceutical alliance partners ( 243 million in 2018, versus 29 million in 2017), the main factor being an increase in the share of profits reverting to Regeneron under our collaboration agreement (see Note C.1. to our consolidated financial statements) due primarily to higher sales of Dupixent®; and (ii) costs relating to our acquisitions of Bioverativ and Ablynx ( 56 million). Other factors include (i) an increase in operating foreign exchange losses to 91 million in 2018 from 80 million in 2017 (presented in Other for segment reporting purposes) and (ii) the recognition of 122 million in provisions, mainly to cover litigation and environmental risks. Those effects were partly offset by (i) gains on disposals, which amounted to 326 million in 2018 (versus 90 million in 2017), mainly on the sale of some mature products in Latin America and some Consumer Healthcare products in Europe (reported in the results of the Consumer Healthcare segment) and (ii) a gain of 112 million related to a data transfer agreement.

**6/ Amortization of intangible assets**

Amortization charged against intangible assets amounted to 2,170 million in 2018, compared with 1,866 million in 2017.

This 304 million rise was due to an increase in amortization expense generated by the intangible assets recognized in connection with the acquisition of Bioverativ ( 430 million), partly offset by reductions in amortization expense on assets recognized on the acquisitions of Aventis ( 256 million in 2018, versus 365 million in 2017) and Genzyme ( 760 million in 2018, versus 857 million in 2017) as some products reached the end of their life cycles.

**7/ Impairment of intangible assets**

This line item showed net impairment losses of 718 million in 2018, versus 293 million in 2017. In 2018, it included impairment losses of (i) 183 million, taken against rights to Lemtrada® and (ii) 454 million, taken against assets associated

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with internal or collaborative development projects (including 92 million relating to the agreement with MyoKardia, and 129 million relating to certain projects arising from the acquisition of Ablynx.

In 2017, this line item included (i) a 190 million impairment loss taken against intangible assets associated with the dengue vaccine; (ii) a 54 million impairment loss relating to *Clostridium difficile* vaccine development projects following our decision to discontinue the related programs; and (iii) impairment losses of 23 million taken against rights relating to a number of marketed products in the Pharmaceuticals segment.

**8/ Fair value remeasurement of contingent consideration**

Fair value remeasurements of contingent consideration relating to acquisitions (in accordance with the revised IFRS 3) represented a net gain of 117 million in 2018, versus a net expense of 159 million in 2017.

The net gain in 2018 corresponds mainly to a remeasurement of contingent consideration payable to Bayer as a result of an acquisition made by Genzyme prior to the latter s acquisition by Sanofi (gain of 109 million in 2018, versus a gain of 28 million in 2017; see Note D.18. to our consolidated financial statements).

**9/ Restructuring costs and similar items**

Restructuring costs and similar items amounted to a charge of 1,480 million in 2018, compared with a charge of 731 million in 2017. In 2018, restructuring costs include (i) termination benefit payments of 517 million in 2018, including provisions associated with the headcount adjustments in Europe announced in December 2018; (ii) a provision of 283 million booked as of December 31, 2018 for penalties arising from the restructuring of the immuno-oncology discovery and development agreement with Regeneron, and in particular on termination of the collaboration on research programs included in the initial July 2015 agreement (see Note C.1) which gives Sanofi the option of pursuing its own immuno-oncology development projects independently; (iii) losses on property, plant and equipment due to site closures or divestments under transformation or reorganization programs ( 162 million); and (iv) the costs of transferring the infectious diseases early stage R&D pipeline and research unit. Those transfer costs amounted to 252 million and primarily consist of payments to Evotec over a five-year period, including an upfront payment of 60 million on finalization of the agreement in early July 2018.

**10/ Other gains and losses, and litigation**

***Other gains and losses, and litigation*** showed a gain of 502 million in 2018, compared with a loss of 215 million in 2017. In 2018, this line item consisted of the pre-tax gain arising on the divestment of our European Generics business (completed September 30, 2018), net of separation costs.

**11/ Operating income**

Operating income totaled 4,676 million for 2018, compared with 5,804 million for 2017. The year-on-year decrease of 19.4%

was attributable mainly to increases in R&D expenses, amortization of intangible assets, impairment losses against intangible assets, and restructuring costs and similar items.

**12/ Financial income and expenses**

Net financial expenses were 271 million in 2018, 2 million lower than the 2017 figure of 273 million.

The cost of our net debt (see the definition in B. Liquidity and Capital Resources below) increased to 273 million, versus 237 million in 2017.

Other factors underlying the year-on-year change in net financial expenses were:

- a lower level of gains on disposals of non-current financial assets ( 63 million, versus 96 million in 2017);
- fair value remeasurements of certain financial assets taken through profit or loss in accordance with IFRS 9 which became applicable on January 1, 2018 (+ 7 million in 2018); and
- a reduction in the net interest cost on pension plans ( 75 million, versus 92 million in 2017).

**13/ Income before tax and investments accounted for using the equity method**

Income before tax and investments accounted for using the equity method for 2018 was 4,405 million, compared with 5,531 million for 2017, a decrease of 20.4%.

**14/ Income tax expense**

Income tax expense represented 481 million in 2018, versus 1,722 million in 2017, giving an effective tax rate based on consolidated net income of 10.9% in 2018, compared with 31.1% in 2017. The decrease in the effective tax rate can be attributed to the reduced US Federal income tax rate and a favorable impact from revised estimates in 2018 of the direct and indirect impacts of the US tax reform (the Tax Cuts and Jobs Act of 2017). In 2017, there was a significant adverse impact of 1,193 million as a result of the deemed repatriation cost that was attributable to the accumulated earnings of non-US operations. The effects of the US tax reform were based on a preliminary analysis of the Tax Cuts and Jobs Act of 2017. As more detailed information has become available adjustments have been made accordingly to reflect the progress of our analysis.

Changes in the level of income tax expense are also significantly impacted by the tax effects of the amortization and impairment of intangible assets ( 692 million in 2018, versus 719 million in 2017) and of restructuring costs ( 435 million in 2018, versus 134 million in 2017).

The effective tax rate on our business net income[(1)] is a non-GAAP financial measure. It is calculated on the basis of

*(1) Non-GAAP financial measure: see definition under A.1.5. Segment information 3. Business Net Income above.*

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business operating income, minus net financial expenses and before (i) the share of profit/loss from investments accounted for using the equity method and (ii) net income attributable to non-controlling interests. We believe the presentation of this measure, used by our management, is also useful for investors as it provides a means to analyze the effective tax cost of our current business activities. It should not be seen as a substitute for the effective tax rate based on consolidated net income.

When calculated on business net income, our effective tax rate was 21.6% in 2018, compared with 23.5% in 2017. The main impacts on this tax rate are the geographical mix of the profits of Sanofi entities, reflecting the reduced US Federal income tax rate and the tax effects of the elimination of intragroup margin on inventory.

The table below reconciles our effective tax rate based on consolidated net income to **our effective tax rate based on business net income:**

| *(as a percentage)* | 2018 | 2017 |
|---|---|---|
| **Effective tax rate based on consolidated net income** | **10.9** | **31.1** |
| Tax effects: | | |
| Amortization and impairment of intangible assets | 1.3 | 3.2 |
| Restructuring costs and similar items | 3.4 | (0.2) |
| Other tax effects[(a)] | 6.0 | (10.6) |
| **Effective tax rate based on business net income** | **21.6** | **23.5** |

*(a) This line includes the direct and indirect effects of the US tax reform (positive impact of 188 million in 2018 versus a negative impact of 1,193 million in 2017). In 2017 this line also includes the consequences of the French Constitutional Council ruling of October 6, 2017 with respect to the additional 3% levy on dividends paid out in cash (positive impact of 451 million).*

**15/ Share of profit/(loss) from investments accounted for using the equity method**

Investments accounted for using the equity method contributed net income of 499 million in 2018, compared with 85 million in 2017. This line item mainly comprises our share of profits from Regeneron ( 484 million in 2018, versus 82 million in 2017); the increase was attributable mainly to a rise in Regeneron s profits after adjustment to align on our accounting policies.

**16/ Net income excluding the exchanged/held-for-exchange animal health business**

Net income excluding the exchanged/held-for-exchange Animal Health business amounted to 4,423 million in 2018, versus 3,894 million in 2017.

**17/ Net income/(loss) of the exchanged/held-for-exchange animal health business**

In accordance with IFRS 5, the line item ***Net income/(loss) of the exchanged/held-for-exchange Animal Health business*** includes, in 2017, the net after-tax gain of 4,643 million on the sale of that business to Boehringer Ingelheim. For 2018, this line item shows an expense of 13 million, associated with the contingent consideration paid to Boehringer Ingelheim.

**18/ Net income**

Net income amounted to 4,410 million in 2018, compared with 8,537 million in 2017.

**19/ Net income attributable to non-controlling interests**

Net income attributable to non-controlling interests was 104 million in 2018, versus 121 million in 2017. This line item mainly comprises the share of pre-tax profits paid to BMS from territories managed by Sanofi ( 83 million, versus 84 million in 2017); the year-on-year decrease was directly related to competition from generics of clopidogrel (the active ingredient of Plavix®) and of irbesartan (the active ingredient of Aprovel®) in Europe.

**20/ Net income attributable to equity holders of Sanofi**

Net income attributable to equity holders of Sanofi amounted to 4,306 million in 2018, compared with 8,416 million in 2017.

Basic earnings per share for 2018 was 3.45, 48.5% lower than the 2017 figure of 6.70 (which included the net gain on the sale of the Animal Health business), based on an average number of shares outstanding of 1,247.1 million in 2018 and 1,256.9 million in 2017. Diluted earnings per share for 2018 was 3.43, 48.3% lower than the 2017 figure of 6.64, based on an average number of shares after dilution of 1,255.2 million in 2018 and 1,266.8 million in 2017.

*A.2.3. Segment results*

Our business operating income, as defined in Note D.35 ( Segment information ) to our consolidated financial statements, amounted to 8,884 million in 2018, compared with 9,323 million in 2017, a decrease of 4.7%. That represents 25.8% of net sales, compared with 26.6% in 2017.

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As indicated in Notes B.26. and D.35. ( Segment information ) to our consolidated financial statements, Sanofi has three operating segments: Pharmaceuticals, Consumer Healthcare and Vaccines.

The comparable information for the year ended December 31, 2017 presented below reflects the impact of IFRS 15, the new standard on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).

The table below sets forth our business net income for the **years ended December 31, 2018 and 2017**:

| *( million)* | December 31, 2018 | December 31, 2017[(a)] | Change |
|---|---|---|---|
| Pharmaceuticals | 8,488 | 9,125 | -7.0% |
| Consumer Healthcare | 1,536 | 1,498 | +2.5% |
| Vaccines | 1,954 | 1,774 | +10.1% |
| Other | (3,094) | (3,074) | +0.7% |
| **Business operating income** | **8,884** | **9,323** | **-4.7%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

The table below sets forth our segment results for the **year ended December 31, 2018**:

| | December 31, 2018 | | | | |
|---|---|---|---|---|---|
| *( million)* | Pharmaceuticals | Consumer Healthcare | Vaccines | Other | Total Sanofi |
| **Net sales** | **24,685** | **4,660** | **5,118** | | **34,463** |
| Other revenues | 252 | | 962 | | 1,214 |
| Cost of sales | (6,738) | (1,539) | (2,854) | (190) | (11,321) |
| Research and development expenses | (4,572) | (143) | (555) | (624) | (5,894) |
| Selling and general expenses | (5,431) | (1,534) | (710) | (2,156) | (9,831) |
| Other operating income and expenses | (37) | 101 | (4) | (124) | (64) |
| Share of profit/(loss) from investments accounted for using the equity method | 425 | 1 | (3) | | 423 |
| Net income attributable to non-controlling interests | (96) | (10) | | | (106) |

| | | | | | |
|---|---|---|---|---|---|
| **Business operating income** | **8,488** | **1,536** | **1,954** | **(3,094)** | **8,884** |

The table below sets forth our segment results for the **year ended December 31, 2017**:

| | December 31, 2017[(a)] | | | | |
|---|---|---|---|---|---|
| *( million)* | **Pharmaceuticals** | **Consumer Healthcare** | **Vaccines** | **Other** | **Total Sanofi** |
| **Net sales** | **25,173** | **4,798** | **5,101** | | **35,072** |
| Other revenues | 287 | | 862 | | 1,149 |
| Cost of sales | (6,766) | (1,612) | (2,798) | (271) | (11,447) |
| Research and development expenses | (4,056) | (123) | (557) | (736) | (5,472) |
| Selling and general expenses | (5,649) | (1,645) | (728) | (2,050) | (10,072) |
| Other operating income and expenses | 34 | 94 | (107) | (17) | 4 |
| Share of profit/(loss) from investments accounted for using the equity method | 212 | 1 | 1 | | 214 |
| Net income attributable to non-controlling interests | (110) | (15) | | | (125) |
| **Business operating income** | **9,125** | **1,498** | **1,774** | **(3,074)** | **9,323** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

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**Business operating income: Pharmaceuticals segment**

| ( million) | December 31, 2018 | as % of net sales | December 31, 2017[a] | as % of net sales | Change |
|---|---|---|---|---|---|
| **Net sales** | **24,685** | **100.0%** | **25,173** | **100.0%** | **-1.9%** |
| Other revenues | 252 | 1.0% | 287 | 1.1% | -12.2% |
| Cost of sales | (6,738) | (27.3)% | (6,766) | (26.9)% | -0.4% |
| **Gross profit** | **18,199** | **73.7%** | **18,694** | **74.3%** | **-2.6%** |
| Research and development expenses | (4,572) | (18.5)% | (4,056) | (16.1)% | +12.7% |
| Selling and general expenses | (5,431) | (22.0)% | (5,649) | (22.4)% | -3.9% |
| Other operating income and expenses | (37) | | 34 | | |
| Share of profit/(loss) from investments accounted for using the equity method | 425 | | 212 | | |
| Net income attributable to non-controlling interests | (96) | | (110) | | |
| **Business operating income** | **8,488** | **34.4%** | **9,125** | **36.2%** | **-7.0%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

**Business operating income: Consumer Healthcare segment**

| ( million) | December 31, 2018 | as % of net sales | December 31, 2017[a] | as % of net sales | Change |
|---|---|---|---|---|---|
| **Net sales** | **4,660** | **100%** | **4,798** | **100.0%** | **-2.9%** |
| Other revenues | | | | | |
| Cost of sales | (1,539) | (33.0)% | (1,612) | (33.6)% | -4.5% |
| **Gross profit** | **3,121** | **67.0%** | **3,186** | **66.4%** | **-2.0%** |
| Research and development expenses | (143) | (3.1)% | (123) | (2.6)% | +16.3% |
| Selling and general expenses | (1,534) | (32.9)% | (1,645) | (34.3)% | -6.7% |
| Other operating income and expenses | 101 | | 94 | | |

| | | | | | |
|---|---|---|---|---|---|
| Share of profit/(loss) from investments accounted for using the equity method | 1 | | 1 | | |
| Net income attributable to non-controlling interests | (10) | | (15) | | |
| **Business operating income** | **1,536** | **33.0%** | **1,498** | **31.2%** | **+2.5%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

**Business operating income: Vaccines segment**

| *( million)* | December 31, 2018 | as % of net sales | December 31, 2017[(a)] | as % of net sales | Change |
|---|---|---|---|---|---|
| **Net sales** | **5,118** | **100%** | **5,101** | **100.0%** | **+0.3%** |
| Other revenues | 962 | 18.8% | 862 | 16.9% | +11.6% |
| Cost of sales | (2,854) | (55.8)% | (2,798) | (54.9)% | +2.0% |
| **Gross profit** | **3,226** | **63.0%** | **3,165** | **62.0%** | **+1.9%** |
| Research and development expenses | (555) | (10.8)% | (557) | (10.9)% | -0.4% |
| Selling and general expenses | (710) | (13.9)% | (728) | (14.3)% | -2.5% |
| Other operating income and expenses | (4) | | (107) | | |
| Share of profit/(loss) from investments accounted for using the equity method | (3) | | 1 | | |
| Net income attributable to non-controlling interests | | | | | |
| **Business operating income** | **1,954** | **38.2%** | **1,774** | **34.8%** | **+10.1%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

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**A.3. Results of operations year ended December 31, 2017 compared with year ended December 31, 2016**

The consolidated income statements for the years ended December 31, 2017 and December 31, 2016 are presented below: The figures below have been restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impacts of those restatements are described in detail in Note A.2.1.1. to the consolidated financial statements.

| *( million)* | 2017[a] | as % of net sales | 2016[a] | as % of net sales |
|---|---|---|---|---|
| **Net sales** | **35,072** | **100.0%** | **33,809** | **100.0%** |
| Other revenues | 1,149 | 3.3% | 887 | 2.6% |
| Cost of sales | (11,613) | (33.1%) | (10,701) | (31.7%) |
| **Gross profit** | **24,608** | **70.2%** | **23 995** | **71.0%** |
| Research and development expenses | (5,472) | (15.6%) | (5,172) | (15.3%) |
| Selling and general expenses | (10,072) | (28.7%) | (9,478) | (28.0%) |
| Other operating income | 237 | | 355 | |
| Other operating expenses | (233) | | (482) | |
| Amortization of intangible assets | (1,866) | | (1,692) | |
| Impairment of intangible assets | (293) | | (192) | |
| Fair value remeasurement of contingent consideration | (159) | | (135) | |
| Restructuring costs and similar items | (731) | | (879) | |
| Other gains and losses, and litigation | (215) | | 211 | |
| **Operating income** | **5,804** | **16.5%** | **6,531** | **19.3%** |
| Financial expenses | (420) | | (924) | |
| Financial income | 147 | | 68 | |
| **Income before tax and investments accounted for using the equity method** | **5,531** | **15.8%** | **5,675** | **16.8%** |
| Income tax expense | (1,722) | | (1,325) | |
| Share of profit/(loss) from investments accounted for using the equity method | 85 | | 136 | |
| **Net income excluding the exchanged/held-for-exchange Animal Health business** | **3,894** | **11.1%** | **4,486** | **13.3%** |
| Net income/(loss) of the exchanged/held-for-exchange Animal Health business[b] | 4,643 | | 314 | |
| **Net income** | **8,537** | **24.3%** | **4,800** | **14.2%** |

| | | | | |
|---|---|---|---|---|
| Net income attributable to non-controlling interests | 121 | | 91 | |
| **Net income attributable to equity holders of Sanofi** | **8,416** | **24.0%** | **4,709** | **13.9%** |
| Average number of shares outstanding (million) | 1,256.9 | | 1,286.6 | |
| Average number of shares outstanding after dilution (million) | 1,266.8 | | 1,296.0 | |
| Basic earnings per share (in euros) | 6.70 | | 3.66 | |
| Basic earnings per share excluding the exchanged/held-for-exchange Animal Health business (in euros) | 3.00 | | 3.42 | |
| Diluted earnings per share (in euros) | 6.64 | | 3.63 | |
| Diluted earnings per share excluding the exchanged/held-for-exchange Animal Health business (in euros) | 2.98 | | 3.39 | |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

*(b) The results of the Animal Health business (in 2016), and the gain on the divestment of that business (in 2017), are presented separately in accordance with IFRS 5 (Non-Current Assets Held for Sale and Discontinued Operations); see Notes D.2. and D.36 to the consolidated financial statements).*

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## ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

### *A.3.1. Net sales*

After the application of IFRS 15, net sales for the year ended December 31, 2017 were 35,072 million, 3.7% higher than in 2016. Exchange rate fluctuations had a negative effect of two percentage points overall, mainly as a result of unfavorable trends in the euro against the US dollar, the Egyptian pound, the

Turkish lira, the Japanese yen and the Chinese yuan renminbi. At constant exchange rates (CER), net sales were up 5.7%, reflecting the acquisition of BI s Consumer Healthcare business and the first-time consolidation of Sanofi s European vaccines business. At constant exchange rates and on a constant structure basis (CER/CS), net sales rose by 0.5%.

The following table sets forth a reconciliation of **our reported net sales for the years ended December 31, 2017 and December 31, 2016 to our net sales at constant exchange rates and on a constant structure basis:**

| *( million)* | 2017 | 2016 | Change |
|---|---|---|---|
| **Net sales** | **35,072** | **33 809** | **+3.7%** |
| Effect of exchange rates | 670 | | |
| **Net sales at constant exchange rates** | **35,742** | **33 809** | **+5.7%** |
| Impact of changes in structure | | 1,741 | |
| **Net sales at constant exchange rates and on a constant structure basis** | **35,742** | **35,550** | **+0.5%** |

When we refer to changes in our net sales at constant exchange rates (CER), that means that we have excluded the effect of exchange rates by recalculating net sales for the relevant period using the exchange rates that were used for the previous period.

When we refer to changes in our net sales on a constant structure basis (CS), that means that we eliminate the effect of changes in structure by restating the net sales for the previous period as follows:

- by including sales generated by entities or product rights acquired in the current period for a portion of the previous period equal to the portion of the current period during which we owned them, based on sales information we receive from the party from whom we make the acquisition;

similarly, by excluding sales for a portion of the previous period when we have sold an entity or rights to a product in the current period; and

for a change in consolidation method, by recalculating the previous period on the basis of the method used for the current period.

To facilitate analysis and comparisons with prior periods, some figures are given at constant exchange rates and on a constant structure basis (CER/CS).

**Analysis of impact on net sales of changes in structure**

| ( *million)* | **2016** |
|---|---|
| BI Consumer Healthcare net sales[(a)] | 1,484 |
| Net sales effect of first-time consolidation of the European vaccines activity (SPMSD transaction)[(a)] | 261 |
| **Total impact of BI and SPMSD** | **1,745** |
| Other | (4) |
| **Total impact on net sales of changes in structure** | **1,741** |

*(a) Based on an unaudited sales estimate.*

### *A.3.1.1. Net sales before the impact of IFRS 15*

We believe that the impact of the application of IFRS 15 on net sales for the year ended December 31, 2016 is not material ( 12 million). Given the significant resources required to restate such information by business, segment and geographical region, we concluded that it would be unduly burdensome to restate such amounts. Therefore, we have chosen to present our detailed analysis of net sales for 2017 and comparable information for 2016 before the impact of IFRS 15 as set forth below. These effects for the years ended December 31, 2017 and 2016 are presented in our consolidated financial statements (Note A.2.1.1. Impacts of the first-time application of IFRS 15 to our consolidated financial statements). Details of our 2017 net sales as restated for IFRS 15 are presented in the previous

section ( A.2. ) in order to facilitate comparisons with our 2018 net sales for the year ended December 31, 2018.

Before the impact of IFRS 15, net sales for the year ended December 31, 2017 were 35,055 million, 3.6% higher than in 2016. Exchange rate fluctuations had a negative effect of two percentage points overall, mainly as a result of unfavorable trends in the euro against the US dollar, the Egyptian pound, the Turkish lira, the Japanese yen and the Chinese yuan renminbi. At constant exchange rates (CER), net sales were up 5.6%, reflecting the acquisition of BI s Consumer Healthcare business and the first-time consolidation of Sanofi s European vaccines business. At constant exchange rates and on a constant structure basis (CER/CS), net sales rose by 0.5%.

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The following table sets forth a reconciliation of **our reported net sales for the years ended December 31, 2017 and December 31, 2016 to our net sales at constant exchange rates and on a constant structure basis:**

| *( million)* | 2017 | 2016 | Change |
|---|---|---|---|
| **Net sales** | **35,055** | **33,821** | **+3.6%** |
| Effect of exchange rates | 672 | | |
| **Net sales at constant exchange rates** | **35,727** | **33,821** | **+5.6%** |
| Impact of changes in structure | | 1,741 | |
| **Net sales at constant exchange rates and on a constant structure basis** | **35,727** | **35,562** | **+0.5%** |

**1/ Net sales by operating segment**

**Our net sales comprise the net sales generated by our Pharmaceuticals, Consumer Healthcare and Vaccines segments.**

| *( million)* | 2017 | 2016 | Change |
|---|---|---|---|
| Pharmaceuticals | 25,122 | 25,914 | -3.1% |
| Consumer Healthcare | 4,832 | 3,330 | +45.1% |
| Vaccines | 5,101 | 4,577 | +11.4% |
| **Net sales** | **35,055** | **33,821** | **+3.6%** |

**2/ Net sales by Global Business Unit (GBU)**

The table below presents **net sales for our Global Business Units (GBUs)**, reflecting our internal organizational structure that aims to streamline our organization, sharpen our focus and concentrate our efforts on growth drivers. Note that Emerging Markets sales of Diabetes & Cardiovascular and Specialty Care products are included in the General Medicines & Emerging Markets GBU.

| *( million)* | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Sanofi Genzyme GBU[(a)] (Specialty Care)[(b)] | 5,674 | 5,019 | +13.1% | +15.1% |
| Diabetes & Cardiovascular GBU[(a)] | 5,400 | 6,397 | -15.6% | -14.3% |
| General Medicines & Emerging Markets GBU[(c)(d)] | 14,048 | 14,498 | -3.1% | -1.0% |
| **Total Pharmaceuticals[(e)]** | **25,122** | **25,914** | **-3.1%** | **-1.2%** |
| **Consumer Healthcare GBU[(e)]** | **4,832** | **3,330** | **+45.1%** | **+46.3%** |
| **Sanofi Pasteur (Vaccines) GBU** | **5,101** | **4,577** | **+11.4%** | **+14.5%** |
| **Total** | **35,055** | **33,821** | **+3.6%** | **+5.6%** |

*(a) Does not include Emerging Markets net sales.*

*(b) Rare Diseases, Multiple Sclerosis, Oncology and Immunology.*

*(c) Includes net sales in Emerging Markets of Specialty Care and Diabetes & Cardiovascular products.*

*(d) Emerging Markets: World excluding United States, Canada, Western and Eastern Europe (apart from Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

*(e) Following the integration of BI s Consumer Healthcare business, acquired on January 1, 2017, our Consumer Healthcare business represents a separate operating segment of Sanofi in accordance with IFRS 8. Consequently, we present our Consumer Healthcare net sales separately for the year ended December 31, 2017. Comparatives for the year ended December 31, 2016 have been restated accordingly (Consumer Healthcare was previously included within the Pharmaceuticals segment).*

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**3/ Net sales by franchise**

The table below sets forth our 2017 net sales by franchise in order to facilitate comparisons with our peers. For a detailed reconciliation of net sales by franchise and net sales by GBU for our Pharmaceuticals segment, refer to the table later in this section showing Pharmaceuticals segment net sales by geographical region.

| *( million)* | **2017** | **2016** | **Change on a reported basis** | **Change at constant exchange rates** |
|---|---|---|---|---|
| Rare Diseases | 2,888 | 2,777 | +4.0% | +6.0% |
| Multiple sclerosis | 2,041 | 1,720 | +18.7% | +20.8% |
| Oncology | 1,519 | 1,453 | +4.5% | +6.4% |
| Immunology | 230 | | | |
| Total Specialty Care | 6,678 | 5,950 | +12.2% | +14.5% |
| *of which Developed Markets (Sanofi Genzyme GBU)* | *5,674* | *5,019* | *+13.1%* | *+15.1%* |
| *of which Emerging Markets[(a)(b)]* | *1,004* | *931* | *+7.8%* | *+11.3%* |
| Diabetes | 6,395 | 7,341 | -12.9% | -11.1% |
| Cardiovascular | 510 | 458 | +11.4% | +13.3% |
| Total Diabetes & Cardiovascular | 6,905 | 7,799 | -11.5% | -9.6% |
| *of which Developed Markets (Diabetes & Cardiovascular GBU)* | *5,400* | *6,397* | *-15.6%* | *-14.3%* |
| *of which Emerging Markets[(a)(b)]* | *1,505* | *1,402* | *+7.3%* | *+11.6%* |
| Established Prescription Products[(a)] | 9,761 | 10,311 | -5.3% | -3.4% |
| Generics[(a)] | 1,778 | 1,854 | -4.1% | -3.3% |
| **Total Pharmaceuticals** | **25,122** | **25,914** | **-3.1%** | **-1.2%** |
| **Consumer Healthcare (Consumer Healthcare GBU)** | **4,832** | **3,330** | **+45.1%** | **+46.3%** |
| **Vaccines (Sanofi Pasteur GBU)** | **5,101** | **4,577** | **+11.4%** | **+14.5%** |
| **Total** | **35,055** | **33,821** | **+3.6%** | **+5.6%** |

*(a) These lines are aggregated to form the net sales of the General Medicines and Emerging Markets GBU.*

*(b) Emerging Markets: World excluding United States, Canada, Western and Eastern Europe (apart from Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**4/ Net sales Pharmaceuticals segment**

In 2017, net sales for the Pharmaceuticals segment were 25,122 million, down 3.1% on a reported basis and 1.2% at constant exchange rates (CER). The year-on-year decrease of 792 million includes a reduction of 492 million due to unfavorable exchange rate effects, and the following impacts at constant exchange rates:

- growth in net sales for the Multiple Sclerosis franchise (up 358 million), the launch of the Immunology franchise (positive effect of 246 million), and positive performances for the Rare Diseases franchise (up 167 million), the Oncology franchise (up 93 million and the Cardiovascular franchise (up 61 million);

- offset by lower net sales for the Diabetes franchise (down 813 million), Established Prescription Products (down 351 million), and Generics (down 61 million).

Comments on the performances of major Pharmaceuticals segment products are provided below.

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**Pharmaceuticals segment net sales, 2017 and 2016**

| *( million)* | Indication | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|---|
| Cerezyme® | Gaucher disease | 730 | 748 | -2.4% | +0.4% |
| Cerdelga® | Gaucher disease | 126 | 106 | +18.9% | +20.8% |
| Myozyme®/Lumizyme® | Pompe disease | 789 | 725 | +8.8% | +10.1% |
| Fabrazyme® | Fabry disease | 722 | 674 | +7.1% | +9.2% |
| Aldurazyme® | Mucopolysaccharidosis | 207 | 201 | +3.0% | +5.5% |
| Other | | 314 | 323 | -2.8% | -1.2% |
| **Total Rare Diseases** | | **2,888** | **2,777** | **+4.0%** | **+6.0%** |
| Aubagio® | Multiple sclerosis | 1,567 | 1,295 | +21.0% | +23.2% |
| Lemtrada® | Multiple sclerosis | 474 | 425 | +11.5% | +13.6% |
| **Total Multiple Sclerosis** | | **2,041** | **1,720** | **+18.7%** | **+20.8%** |
| Jevtana® | Prostate cancer | 386 | 358 | +7.8% | +9.8% |
| Thymoglobulin® | Organ rejection | 291 | 281 | +3.6% | +5.3% |
| Taxotere® | Breast, lung, prostate, stomach, and head & neck cancers | 173 | 179 | -3.4% | -0.6% |
| Eloxatin® | Colorectal cancer | 179 | 170 | +5.3% | +8.2% |
| Mozobil® | Hematologic malignancies | 163 | 152 | +7.2% | +9.2% |
| Zaltrap® | Colorectal cancer | 75 | 65 | +15.4% | +16.9% |
| Other | | 252 | 248 | +1.6% | +2.0% |
| **Total Oncology** | | **1,519** | **1,453** | **+4.5%** | **+6.4%** |
| Dupixent® | Atopic dermatitis | 219 | | | |
| Kevzara® | Rheumatoid arthritis | 11 | | | |
| **Total Immunology** | | **230** | | | |
| **Total Specialty Care** | | **6,678** | **5,950** | **+12.2%** | **+14.5%** |

| | | | | | |
|---|---|---|---|---|---|
| Lantus® | Diabetes | 4,622 | 5,714 | -19.1% | -17.5% |
| Toujeo® | Diabetes | 816 | 649 | +25.7% | +27.0% |
| Apidra® | Diabetes | 377 | 367 | +2.7% | +4.9% |
| Amaryl® | Diabetes | 337 | 362 | -6.9% | -1.4% |
| Insuman® | Diabetes | 107 | 129 | -17.1% | -15.5% |
| Lyxumia® | Diabetes | 26 | 33 | -21.2% | -18.2% |
| Soliqua® | Diabetes | 26 | | | |
| Other | Diabetes | 84 | 87 | -3.4% | -2.3% |
| **Total Diabetes** | | **6,395** | **7,341** | **-12.9%** | **-11.1%** |
| Multaq® | Atrial fibrillation | 339 | 353 | -4.0% | -2.5% |
| Praluent® | Hypercholesterolemia | 171 | 105 | +62.9% | +66.7% |
| **Total Cardiovascular** | | **510** | **458** | **+11.4%** | **+13.3%** |
| **Total Diabetes & Cardiovascular** | | **6,905** | **7,799** | **-11.5%** | **-9.6%** |
| Lovenox® | Thrombosis | 1,575 | 1,636 | -3.7% | -2.1% |
| Plavix® | Atherothrombosis | 1,471 | 1,544 | -4.7% | -1.2% |
| Renagel®/Renvela® | Hyperphosphatemia | 802 | 922 | -13.0% | -12.3% |
| Aprovel®/Avapro® | Hypertension | 691 | 681 | +1.5% | +3.7% |
| Depakine® | Epilepsy | 443 | 416 | +6.5% | +9.6% |
| Synvisc®/Synvisc-One® | Arthritis | 387 | 408 | -5.1% | -3.9% |
| Allegra® | Allergic rhinitis, urticaria | 158 | 186 | -15.1% | -12.9% |

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| ( *million*) | Indication | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|---|
| Stilnox®/Ambien®/Myslee® | Sleep disorders | 259 | 304 | -14.8% | -13.5% |
| Tritace® | Hypertension | 241 | 245 | -1.6% | +1.2% |
| Targocid® | Bacterial infections | 130 | 149 | -12.8% | -10.1% |
| Lasix® | Edema, hypertension | 137 | 148 | -7.4% | -4.7% |
| Other | | 3,467 | 3,672 | -5.6% | -4.1% |
| **Total Established Prescription Products** | | **9,761** | **10,311** | **-5.3%** | **-3.4%** |
| **Generics** | | **1,778** | **1,854** | **-4.1%** | **-3.3%** |
| **Total Pharmaceuticals** | | **25,122** | **25,914** | **-3.1%** | **-1.2%** |

Rare diseases franchise

Net sales for the **Rare Diseases** franchise reached 2,888 million in 2017, up 4.0% on a reported basis and 6.0% at constant exchange rates (CER). Sales growth was recorded across all geographies: 8.5% CER in Emerging Markets(1), 6.4% CER in the United States, 5.0% CER in Europe(2) and 3.9% CER in the Rest of the World region(3).

In Gaucher disease, net sales of **Cerezyme®** were stable year-on-year at 730 million. Sales growth in Emerging Markets (+2.1% CER at 229 million) offset a decrease in the Rest of the World region (-8.3% CER at 43 million). **Cerdelga®** reported net sales of 126 million (+20.8% CER), of which 95 million were generated in the United States (+14.1% CER). In Europe, net sales of Cerdelga® rose by 52.9% CER to 26 million.

Net sales of **Myozyme® / Lumizyme®** in Pompe disease rose by 10.1% CER to 789 million, driven by sales in the United States (+11.3% CER, at 262 million) and Europe (+8.6% CER, at 352 million). Net sales also rose in Emerging Markets (+12.7% CER, at 116 million) and in the Rest of the World region (+8.9% CER, at 59 million). This sales growth was fueled by increased diagnosis and treatment of Pompe disease.

**Fabrazyme®** achieved net sales growth of 9.2% CER, to 722 million. Sales are advancing in many countries due to growth in the number of patients diagnosed with, and treated for, Fabry disease. Net sales of the product were up 9.3% CER in the United States (at 369 million); 5.8% CER in Europe (at 163 million) despite the launch of new rival products; 9.5% CER in the Rest of the World region (at 112 million); and 16.2% CER in Emerging Markets (at 78 million).

### Multiple sclerosis franchise

Net sales for the **Multiple Sclerosis** franchise reached  2,041 million in 2017, up 18.7% on a reported basis and 20.8% CER, on strong performances by **Aubagio®** and **Lemtrada®** in the United States and Europe.

**Aubagio®** posted net sales of  1,567 million (+23.2% CER), driven by the United States (+22.0% CER, at 1,084 million) and Europe (+26.0% CER, at  387 million).

Net sales of **Lemtrada®** amounted to  474 million (+13.6% CER), including 246 million in the United States (+7.3% CER) and  174 million in Europe (+18.5% CER).

### Oncology franchise

The **Oncology** franchise generated net sales of  1,519 million, up 4.5% on a reported basis and 6.4% CER, due largely to public-sector orders for Leukine® in the United States, a good performance for the franchise in Emerging Markets, and overall growth in sales of Jevtana® and Thymoglobulin®.

Net sales of **Jevtana®** totaled  386 million in 2017 (+9.8% CER), driven by growth in the United States (+6.6% CER, at  159 million), Europe (+7.2% CER, at 148 million) and Japan (+17.1% CER, at 46 million).

**Thymoglobulin®** net sales rose by 5.3% CER to  291 million, largely on a good performance in Emerging Markets (+13.6% CER, at  66 million).

Net sales of **Taxotere®** were stable year-on-year at  173 million. This reflects stronger sales in Emerging Markets (+7.7% CER, at  136 million), especially in China (+13.6% CER, at 65 million), which more than offset the effect of competition from generics, especially in Japan (-38.5% CER, at  15 million).

Net sales of **Eloxatin®** rose by 8.2% CER to  179 million. This reflects stronger sales in Emerging Markets (+13.4% CER, at  147 million), especially in China (+15.2% CER, at 103 million), which more than offset a fall in Canadian sales due to competition from generics.

*(1) World excluding United States, Canada, Western and Eastern Europe (apart from Russia, Ukraine, Georgia, Belarus, Armenia and Turkey), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

*(2) Western Europe and Eastern Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(3) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

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## Immunology franchise

Dupixent® (dupilumab, developed in collaboration with Regeneron), for adults with moderate to severe atopic dermatitis, was approved by the FDA in March 2017 and made available in the US market. Since then, the product has generated US net sales of 216 million, reflecting substantial unmet medical needs and rapid access to the market. In Europe, Dupixent® was approved at the end of September 2017 for the treatment of adults with moderate to severe atopic dermatitis requiring systemic treatment; the product was made available at the end of the year in Germany, where it generated net sales of 2 million.

**Kevzara®** (sarilumab, developed in collaboration with Regeneron), a treatment for rheumatoid arthritis, was approved by the FDA on May 22, 2017 and made available in June 2017 in the US market, where it achieved net sales of 10 million. The product has also been approved in Europe, and has been launched in a number of countries (Germany, the Netherlands and the United Kingdom).

## Diabetes franchise

Net sales for the Diabetes franchise amounted to 6,395 million in 2017, down 12.9% on a reported basis and 11.1% CER. The main factor was a fall in sales of Lantus® in the United States, where Diabetes franchise net sales were down 22.8% CER at 3,128 million. As previously indicated, the decline in US net sales for the Diabetes franchise accelerated during 2017, following the consecutive exclusion of a number of diabetes treatments from the reimbursement lists of two of the country s leading healthcare insurance providers: UnitedHealth (from April 1, 2017) and CVS. Outside the United States, Diabetes franchise net sales advanced in Emerging Markets (+11.4% CER, at 1,494 million) but fell in Europe (-2.0% CER, at 1,287 million), where a good performance from Toujeo® partially compensated for weaker sales of Lantus®.

In 2017, net sales of **insulin glargines** (Lantus® and Toujeo®) were down 13.0% CER at 5,438 million.

Net sales of **Lantus®** were down 17.5% CER in 2017, at 4,622 million. In the United States, sales were down 26.6% CER at 2,542 million, due mainly to a lower average net price, the switching of patients to Toujeo®, and the effect of the product s exclusion from reimbursement lists as described above. Net sales in Europe fell by 12.8% CER to 760 million, due largely to the launch of a biosimilar of Lantus® and the switching of patients to Toujeo®. Over the same period, sales of Lantus® in Emerging Markets reached 1,005 million, up 9.2% CER, driven largely by Africa and Middle East (+18.8% CER, at 288 million) and Asia (+10.6% CER, at 424 million), especially China (+15.8% CER, at 319 million). During 2017, Sanofi filed two patent infringement suits relating to Lantus® in the United States District Court for the District of New Jersey (United States): one against Merck (in August) and the other against Mylan (in October). For further information, refer to Item 8 Information on Legal or Arbitration Proceedings .

The new-generation basal insulin **Toujeo®** posted net sales growth of 27.0% CER in 2017, to 816 million. Net sales in the United States decreased by 2.1% CER to 455 million essentially as the result of a decrease in the average net price of the product during the fourth quarter of 2017. However, this was more than offset by sales growth in Europe

(+80.8% CER, at 217 million), Emerging Markets (+300.0% CER, at 79 million) and the Rest of the World region (+88.6% CER, at 65 million).

Net sales of **Amaryl®** fell by 1.4% CER in 2017, to 337 million. Sales growth in Emerging Markets (+2.1% CER, at 278 million) did not fully compensate for lower net sales in the Rest of the World region (-10.0% CER, at 36 million) and in Europe (-22.2% CER, at 21 million).

Net sales of **Apidra®** rose by 4.9% CER in 2017, to 377 million. Lower sales in the United States (-10.4% CER, at 102 million) were offset by sales growth in Emerging Markets (+25.9% CER, at 97 million) and in Europe (+7.1% CER, at 136 million).

**Soliqua®** 100/33 / Suliqua® (injectable insulin glargine 100 Units/mL and lixisenatide 33 mcg/mL) were launched at the start of 2017 in the United States, and at the end of 2017 in the Netherlands. Soliqua® 100/33 has generated 26 million of net sales in the United States since launch.

### Cardiovascular franchise

In 2017, net sales of **Praluent®** (alirocumab, developed in collaboration with Regeneron) reached 171 million, of which 116 million was generated in the United States and 46 million in Europe. The relatively limited rise in sales during the period reflects significant restrictions by US payers and limited access to the European market. In October 2017, the US Court of Appeals for the Federal Circuit ordered a new trial and vacated the permanent injunction in the dispute concerning Amgen s asserted patent claims for antibodies targeting PCSK9. This ruling means that Sanofi and Regeneron will continue marketing, selling and manufacturing Praluent® in the US. For further information on litigation relating to Praluent®, refer to Note D.22. to our consolidated financial statements (included as Item 18 of this Annual Report on Form 20-F) and Item 8 Information on Legal or Arbitration Proceedings .

Net sales of **Multaq®** amounted to 339 million in 2017, down 2.5% CER year-on-year. The bulk of the sales were generated in the United States (-2.7% CER, at 286 million) and Europe (-2.3% CER, at 42 million).

### Established prescription products

Net sales of Established Prescription Products in 2017 were 9,761 million, down 5.3% on a reported basis and 3.4% CER. Growth in Emerging Markets net sales (+4.8% CER, at 3,800 million) failed to offset lower net sales in Europe (-4.4% CER, at 3,473 million), the start of generic competition for Renvela®/Renagel® in the United States, and the impact of

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competition from generics of Plavix® in Japan. In the United States and the Rest of the World region, net sales of Established Prescription Products fell by 13.8% CER (to 1,269 million) and 11.7% CER (to 1,219 million), respectively.

Net sales of **Lovenox®** were 1,575 million, down 2.1% CER, due largely to increased competition in Europe (-7.1% CER, at 951 million) with the arrival of biosimilars in the United Kingdom and Germany. This decline canceled out a good performance in Emerging Markets (+7.8% CER, at 475 million).

Net sales of **Plavix®** in 2017 were 1,471 million (-1.2% CER), reflecting generic competition in Japan (-30.7% CER, at 235 million) and Europe (-7.4% CER, at 150 million). The effect was partly offset by growth in sales of Plavix® in Emerging Markets (+10.4% CER, at 1,026 million), especially in China where the product posted net sales of 758 million (+12.1% CER). Sales of Plavix® in the United States and Puerto Rico are handled by BMS under the terms of the Sanofi-BMS alliance (see Note C.2., Alliance Arrangements with Bristol-Myers Squibb (BMS) , to our consolidated financial statements, included at Item 18 of this Annual Report on Form 20-F).

**Renvela®/Renagel®** posted net sales of 802 million in 2017, down 12.3% CER, mainly on generic competition in the United States (-14.8% CER, at 645 million) where the first generic versions in powder and pill form were approved in June and July 2017, respectively. In October 2017, Sanofi launched an approved generic version of Renvela®/Renagel® in the United States. In Europe, sales of Renvela®/Renagel® fell by 13.4% CER to 71 million, also due to competition from generics.

Net sales of **Aprovel®/Avapro®** for 2017 were 691 million (+3.7% CER), largely on sales growth in Emerging Markets (+8.7% CER, at 433 million), especially China (+14.2% CER, at 264 million), and in the Rest of the World region (+3.1% CER, at 132 million). In Europe, net sales of Aprovel®/Avapro® were down 9.4% CER at 115 million, due to competition from generics.

We have no comments on sales of our other Established Prescription Products.

Generics

**Generics** net sales for 2017 were 1,778 million, down 4.1% on a reported basis and 3.3% CER.

Emerging Markets generated net sales of 758 million, down 2.9% CER, due mainly to lower sales in Asia (-68.5% CER, at 22 million) following the divestment of a distribution business in China. The decrease in net sales in Asia more than offset increased Generics sales in Latin America (+1.7% CER, at 428 million), Africa and Middle East (+1.6% CER, at 117 million) and Eurasia (+9.3% CER, at 190 million). Generics sales were also lower in Europe (-4.9% CER, at 760 million) and the United States (-12.0% CER, at 150 million), but increased in the Rest of the World region (+23.9% CER, at 110 million).

We have confirmed our commitment to our Generics business in other parts of the world, and will focus more on Emerging Markets in order to develop the business in those countries.

The following table breaks down 2017 net sales of our **Pharmaceuticals segment products by geographical region:**

| *( million)* | Total GBU | Europe[a] | Change at CER | United States | Change at CER | Rest of the World[b] | Change at CER | Emerging Markets[c] | Change at CER | Total Franchise | Change at CER |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cerezyme® | 501 | 281 | +0.7% | 177 | 0.0% | 43 | -8.3% | 229 | +2.1% | 730 | +0.4% |
| Cerdelga® | 125 | 26 | +52.9% | 95 | +14.1% | 4 | 0.0% | 1 | | 126 | +20.8% |
| Myozyme®/Lumizyme® | 673 | 352 | +8.6% | 262 | +11.3% | 59 | +8.9% | 116 | +12.7% | 789 | +10.1% |
| Fabrazyme® | 644 | 163 | +5.8% | 369 | +9.3% | 112 | +9.5% | 78 | +16.2% | 722 | +9.2% |
| Aldurazyme® | 142 | 75 | +1.3% | 42 | +2.4% | 25 | +8.3% | 65 | +11.7% | 207 | +5.5% |
| Other | 269 | 64 | -4.5% | 113 | -5.8% | 92 | 0.0% | 45 | +15.8% | 314 | -1.2% |
| **Total Rare Diseases** | **2,354** | **961** | **+5.0%** | **1,058** | **+6.4%** | **335** | **+3.9%** | **534** | **+8.5%** | **2,888** | **+6.0%** |
| Aubagio® | 1,530 | 387 | +26.0% | 1,084 | +22.0% | 59 | +31.1% | 37 | +17.6% | 1,567 | +23.2% |
| Lemtrada® | 450 | 174 | +18.5% | 246 | +7.3% | 30 | +26.1% | 24 | +38.9% | 474 | +13.6% |
| **Total Multiple Sclerosis** | **1,980** | **561** | **+23.5%** | **1,330** | **+19.0%** | **89** | **+29.4%** | **61** | **+25.0%** | **2,041** | **+20.8%** |
| Jevtana® | 359 | 148 | +7.2% | 159 | +6.6% | 52 | +25.0% | 27 | +17.4% | 386 | +9.8% |
| Thymoglobulin® | 225 | 39 | +2.6% | 162 | +3.8% | 24 | 0.0% | 66 | +13.6% | 291 | +5.3% |
| Taxotere® | 37 | 3 | -25.0% | | -100.0% | 34 | -14.6% | 136 | +7.7% | 173 | -0.6% |
| Eloxatin® | 32 | 4 | 0.0% | 1 | | 27 | -15.6% | 147 | +13.4% | 179 | +8.2% |
| Mozobil® | 154 | 44 | +4.8% | 96 | +3.2% | 14 | +87.5% | 9 | +28.6% | 163 | +9.2% |
| Zaltrap® | 67 | 51 | +8.5% | 9 | -35.7% | 7 | | 8 | +125.0% | 75 | +16.9% |
| Other | 236 | 51 | +1.9% | 162 | +3.8% | 23 | -16.7% | 16 | +13.3% | 252 | +2.0% |

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| *million)* | Total GBU | Europe[a] | Change at CER | United States | Change at CER | Rest of the world[b] | Change at CER | Emerging Markets[c] | Change at CER | Total Franchise | Chang at CE |
|---|---|---|---|---|---|---|---|---|---|---|---|
| tal Oncology | 1,110 | 340 | +5.2% | 589 | +2.9% | 181 | +5.8% | 409 | +13.2% | 1,519 | +6.4 |
| pixent® | 219 | 2 | | 216 | | 1 | | | | 219 | |
| vzara® | 11 | 1 | | 10 | | | | | | 11 | |
| **tal Immunology** | **230** | **3** | | **226** | | **1** | | | | **230** | |
| **nofi Genzyme (Specialty are)** | **5,674** | **1,865** | **+10.2%** | **3,203** | **+19.8%** | **606** | **+7.7%** | **1,004** | **+11.3%** | **6,678** | **+14.5** |
| ntus® | 3,617 | 760 | -12.8% | 2,542 | -26.6% | 315 | -10.7% | 1,005 | +9.2% | 4,622 | -17.5 |
| ujeo® | 737 | 217 | +80.8% | 455 | -2.1% | 65 | +88.6% | 79 | +300.0% | 816 | +27.0 |
| idra® | 280 | 136 | +7.1% | 102 | -10.4% | 42 | 0.0% | 97 | +25.9% | 377 | +4.9 |
| maryl® | 59 | 21 | -22.2% | 2 | -33.3% | 36 | -10.0% | 278 | +2.1% | 337 | -1.4 |
| suman® | 78 | 76 | -7.3% | 2 | -33.3% | | | 29 | -29.5% | 107 | -15.5 |
| xumia® | 24 | 16 | -23.8% | | | 8 | 0.0% | 2 | -33.3% | 26 | -18.2 |
| liqua® | 26 | | | 26 | | | | | | 26 | |
| her | 80 | 61 | -4.7% | -1 | -133.3% | 20 | +23.5% | 4 | +33.3% | 84 | -2.3 |
| **tal Diabetes** | **4,901** | **1,287** | **-2.0%** | **3,128** | **-22.8%** | **486** | **-1.4%** | **1,494** | **+11.4%** | **6,395** | **-11.1** |
| ultaq® | 332 | 42 | -2.3% | 286 | -2.7% | 4 | -25.0% | 7 | +16.7% | 339 | -2.5 |
| aluent® | 167 | 46 | +155.6% | 116 | +40.0% | 5 | +500.0% | 4 | +300.0% | 171 | +66.7 |
| **tal Cardiovascular** | **499** | **88** | **+43.5%** | **402** | **+6.8%** | **9** | **+80.0%** | **11** | **+57.1%** | **510** | **+13.3** |
| **tal Diabetes & rdiovascular** | **5,400** | **1,375** | **+0.1%** | **3,530** | **-20.2%** | **495** | **-0.6%** | **1,505** | **+11.6%** | **6,905** | **-9.6** |
| venox® | 1,575 | 951 | -7.1% | 58 | +9.3% | 91 | -2.2% | 475 | +7.8% | 1,575 | -2.1 |
| avix® | 1,471 | 150 | -7.4% | 1 | 0.0% | 294 | -26.0% | 1,026 | +10.4% | 1,471 | -1.2 |
| nagel®/Renvela® | 802 | 71 | -13.4% | 645 | -14.8% | 36 | +6.1% | 50 | +20.9% | 802 | -12.3 |
| provel®/CoAprovel® | 691 | 115 | -9.4% | 11 | -20.0% | 132 | +3.1% | 433 | +8.7% | 691 | +3.7 |
| epakine® | 443 | 161 | +1.2% | | | 15 | 0.0% | 267 | +15.8% | 443 | +9.6 |
| nvisc® / Synvisc-One® | 387 | 30 | -9.1% | 292 | -5.1% | 14 | 0.0% | 51 | +6.3% | 387 | -3.9 |
| legra® | 158 | 9 | 0.0% | | | 149 | -13.6% | | | 158 | -12.9 |
| lnox®/Ambien®/Myslee® | 259 | 40 | -9.1% | 55 | -33.3% | 106 | -8.3% | 58 | +1.8% | 259 | -13.5 |
| itace® | 241 | 152 | -1.3% | | | 5 | +25.0% | 84 | +4.6% | 241 | +1.2 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| rgocid® | 130 | 59 | -18.9% | | | 6 | -14.3% | 65 | 0.0% | 130 | -10.1 |
| six® | 137 | 72 | -4.0% | | | 11 | -36.8% | 54 | +5.6% | 137 | -4.7 |
| her | 3,467 | 1,663 | -1.7% | 207 | -19.7% | 360 | -5.5% | 1,237 | -3.8% | 3,467 | -4.1 |
| **tal Established escription Products** | **9,761** | **3,473** | **-4.4%** | **1,269** | **-13.8%** | **1,219** | **-11.7%** | **3,800** | **+4.8%** | **9,761** | **-3.4** |
| **nerics** | **1,778** | **760** | **-4.9%** | **150** | **-12.0%** | **110** | **+23.9%** | **758** | **-2.9%** | **1,778** | **-3.3** |
| **tal Emerging Markets ecialty Care** | **1,004** | | | | | | | **1,004** | **+11.3%** | | |
| **tal Emerging Markets abetes & Cardiovascular** | **1,505** | | | | | | | **1,505** | **+11.6%** | | |
| **neral Medicines & nerging Markets** | **14,048** | **4,233** | **-4.5%** | **1,419** | **-13.6%** | **1,329** | **-9.5%** | **7,067** | **+6.2%** | | |
| **tal Pharmaceuticals** | **25,122** | **7,473** | **-0.3%** | **8,152** | **-6.7%** | **2,430** | **-4.0%** | **7,067** | **+6.2%** | **25,122** | **-1.2** |

*(a) Western Europe and Eastern Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

*(c) World excluding United States, Canada, Western and Eastern Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

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**5/ Net sales Consumer Healthcare segment**

During 2017, we gradually integrated the Consumer Healthcare operations of BI into our Consumer Healthcare GBU. Following completion of the integration process and with effect from

December 31, 2017, we identified our Consumer Healthcare business as an operating segment. Consequently, the net sales of our Consumer Healthcare business are presented separately below, for 2017 and comparative periods.

Net sales of **Consumer Healthcare** products reached 4,832 million in 2017, up 45.1% on a reported basis and 46.3% at constant exchange rates, reflecting the acquisition of BI s Consumer Healthcare business. On a constant structure basis and at constant exchange rates, Consumer Healthcare net sales rose by 2.1%, driven by growth in Emerging Markets and Europe.

| *( million)* | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| Allegra® | 423 | 417 | +1.4% | +2.4% |
| Mucosolvan® | 125 | | | |
| Other | 678 | 374 | +81.3% | +84.0% |
| **Allergy, Cough and Cold** | **1,226** | **791** | **+55.0%** | **+56.6%** |
| Doliprane® | 323 | 309 | +4.5% | +5.5% |
| Buscopan® | 191 | | | |
| Other | 744 | 563 | +32.1% | +32.5% |
| **Pain** | **1,258** | **872** | **+44.3%** | **+45.9%** |
| Dulcolax® | 211 | | | |
| Enterogermina® | 168 | 159 | +5.7% | +6.9% |
| Essentiale® | 150 | 145 | +3.4% | +0.7% |
| Zantac® | 117 | | | |
| Other | 284 | 217 | +30.9% | +31.8% |

| | | | | |
|---|---|---|---|---|
| **Digestive** | **930** | **521** | **+78.5%** | **+79.5%** |
| Pharmaton® | 100 | | | |
| Other | 552 | 450 | +22.7% | +22.2% |
| **Nutritionals** | **652** | **450** | **+44.9%** | **+44.9%** |
| Gold Bond® | 201 | 195 | +3.1% | +5.6% |
| Other | 565 | 501 | +12.8% | +13.4% |
| **Other products** | **766** | **696** | **+10.1%** | **+11.2%** |
| **Total Consumer Healthcare** | **4,832** | **3,330** | **+45.1%** | **+46.3%** |

In Emerging Markets, Consumer Healthcare net sales rose by 31.3% CER in 2017 to 1,616 million. On a constant structure basis and at constant exchange rates (CER/CS), net sales rose by 3.0%, driven by growth for Pain Relief (+43.9% CER and +5.5% CER/CS, at 454 million), Allergy, Cough and Cold (+33.1 CER and +5.0% CER/CS, at 349 million) and Digestive Health (+22.1% CER and +3.3% CER/CS, at 377 million), though the effect was mitigated by lower sales in Food Supplements (+36.5% CER but -3.6% CER/CS, at 273 million).

In Europe, net sales rose by 62.0% CER to 1,422 million. On a constant structure basis and at constant exchange rates, net sales were up 2.0%, propelled by growth in Pain Relief (+34.8% CER and +4.3% CER/CS, at 515 million) and in particular higher sales of Doliprane® in France.

In the United States, net sales advanced by 22.5% CER to 1,133 million. On a constant structure basis and at constant

exchange rates, net sales rose by 1.3%, driven by strong growth in Allergy, Cough and Cold (+10.8% CER and CER/CS, at 367 million), largely as a result of the launch of Xyzal® Allergy 24HR (net sales 65 million) which was authorized for OTC sale in February 2017. However the effect was offset by lower net sales in Digestive Health (-13.1% CER/CS, at 188 million), especially sales of Zantac®.

In the Rest of the World region, Consumer Healthcare net sales for 2017 reached 661 million, up 145.1% CER. On a constant structure basis and at constant exchange rates, net sales rose by 1.5%, driven by Pain Relief (+9.4% CER/CS, at 122 million) and Digestive Health (+13.5% CER/CS, at 58 million). The effect was partly offset by lower sales in Allergy, Cough and Cold (-12.5% CER/CS, at 158 million).

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**The following table breaks down 2017 net sales of our Consumer Healthcare segment by geographical region:**

| *( million)* | Total | Europe[a] | Change at CER | United States | Change at CER | Rest of the world[b] | Change at CER | Emerging Markets[c] | Change at CER |
|---|---|---|---|---|---|---|---|---|---|
| Allegra® | 423 | 12 | +33.3% | 233 | -3.3% | 47 | +17.5% | 131 | +6.4% |
| Mucosolvan® | 125 | 58 | | | | 15 | | 52 | |
| Other | 678 | 282 | +145.2% | 134 | +49.4% | 96 | +284.6% | 166 | +20.1% |
| **Allergy, Cough and Cold** | **1,226** | **352** | **+183.9%** | **367** | **+10.8%** | **158** | **+143.9%** | **349** | **+33.1%** |
| Doliprane® | 323 | 277 | +6.5% | | | | | 46 | |
| Buscopan® | 191 | 76 | | | | 17 | | 98 | |
| Other | 744 | 162 | +32.0% | 167 | +8.3% | 105 | +692.9% | 310 | +12.6% |
| **Pain** | **1,258** | **515** | **+34.8%** | **167** | **+8.3%** | **122** | **+814.3%** | **454** | **+43.9%** |
| Dulcolax® | 211 | 93 | | 61 | | 22 | | 35 | |
| Enterogermina® | 168 | 64 | -3.0% | | | | | 104 | +14.0% |
| Essentiale® | 150 | 34 | +17.2% | | | 1 | | 115 | -3.4% |
| Zantac® | 117 | | | 105 | | 12 | | | |
| Other | 284 | 116 | +34.9% | 22 | -12.0% | 23 | +271.4% | 123 | +23.2% |
| **Digestive** | **930** | **307** | **+70.2%** | **188** | **+668.0%** | **58** | **+742.9%** | **377** | **+22.1%** |
| Pharmaton® | 100 | 20 | | | | | | 80 | |
| Other | 552 | 102 | +7.4% | 2 | -50.0% | 255 | +67.7% | 193 | -5.1% |
| **Nutritionals** | **652** | **122** | **+28.7%** | **2** | **-50.0%** | **255** | **+67.7%** | **273** | **+36.5%** |
| Gold Bond® | 201 | | | 198 | +5.8% | 3 | | | |
| Other | 565 | 126 | +30.6% | 211 | -6.1% | 65 | +113.8% | 163 | +12.4% |
| **Other products** | **766** | **126** | **+30.6%** | **409** | **-0.7%** | **68** | **+100.0%** | **163** | **+12.4%** |
| **Total Consumer Healthcare** | **4,832** | **1,422** | **+62.0%** | **1,133** | **+22.5%** | **661** | **+145.1%** | **1,616** | **+31.3%** |

*(a) Western Europe and Eastern Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

*(c) World excluding United States, Canada, Western and Eastern Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**6/ Net Sales Vaccines segment**

In 2017, net sales for our Vaccines segment were 5,101 million, up 11.4% on a reported basis and 14.5% CER, as a result of the dissolution of the SPMSD joint venture in Europe. On a constant structure basis and at constant exchange rates, Vaccines net sales rose by 8.3%, driven mainly by the performance of the

Polio/Pertussis/Hib franchise across all geographies. In the United States, Vaccines net sales increased by 5.6% CER to 2,570 million. Net sales for the Vaccines segment in Emerging Markets were up 7.8% CER at 1,575 million. In Europe, Vaccines net sales reached 630 million (+137.3% CER and +20.7% CER/CS).

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The table below sets forth 2017 and 2016 net sales for our **Vaccines segment by product range:**

| *( million)* | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| Polio/Pertussis/Hib Vaccines (including Hexaxim®/Hexyon®, Pentacel®, Pentaxim® and Imovax®) | 1,827 | 1,495 | +22.2% | +24.3% |
| Influenza vaccines (including Vaxigrip®, Fluzone HD® and Fluzone®) | 1,589 | 1,521 | +4.5% | +9.5% |
| Meningitis/Pneumonia Vaccines (including Menactra®) | 623 | 633 | -1.6% | +0.2% |
| Travel and Other Endemics Vaccines | 493 | 368 | +34.0% | +35.9% |
| Adult Booster Vaccines (including Adacel®) | 474 | 417 | +13.7% | +16.5% |
| Dengvaxia® | 3 | 55 | -94.5% | -98.2% |
| Other Vaccines | 92 | 88 | +4.5% | +9.1% |
| **Total Vaccines** | **5,101** | **4,577** | **+11.4%** | **+14.5%** |

In 2017, **Polio/Pertussis/Hib vaccines** posted net sales of 1,827 million (+24.3% CER). On a constant structure basis and at constant exchange rates, net sales for the franchise rose by 15.3%. In Emerging Markets, sales for this franchise reached 940 million (+14.5% CER), driven by strong growth in Asia (+44.1% CER, at 360 million) on higher sales of Pentaxim® in China, although we expect more limited shipments there in the first half of 2018. Net sales of Polio/Pertussis/Hib vaccines also advanced in the United States (+10.1% CER, at 435 million) and in Europe (+37.3% CER/CS, at 300 million), reflecting good performances by Pentacel® and Hexaxim®, respectively.

Net sales of **Influenza vaccines** rose by 9.5% CER, to 1,589 million. This performance reflected higher sales for the franchise in the United States (+7.3% CER, at 1,128 million), largely as a result of sales to the Biomedical Advanced Research and Development Authority (BARDA) of the US Department of Health and Human Services. Sales of influenza vaccines also rose in Emerging Markets (+7.4% CER, at 297 million) largely on sales growth in Brazil, and in Europe (+12.9% CER/CS, at 113 million) due in particular to the success of VaxigripTetra®.

Net sales of **Meningitis/Pneumonia vaccines** were stable year-on-year at 623 million. **Menactra®** posted net sales of 600 million (+4.6% CER), of which 484 million was generated in the United States.

Net sales of **Travel and Other endemics vaccines** increased by 35.9% CER in 2017, to  493 million. On a constant structure basis and at constant exchange rates, net sales rose by 19.0%, reflecting increased supply of rabies and hepatitis A vaccines.

Net sales of **Adult Booster vaccines** in 2017 were  474 million, up 16.5% CER. On a constant structure basis and at constant exchange rates, net sales were virtually unchanged year-on-year (-0.2%). Increased sales in Europe (+6.2% CER/CS, at  119 million) and the Rest of the World region (+12.5% CER, at 26 million) offset lower sales in Emerging Markets (-22.9% CER, at  37 million).

**Dengvaxia®** posted net sales of  3 million in 2017, reflecting repurchases of inventory following discontinuation of the public vaccination program initiated in the Philippines in early 2016. On November 29, 2017 Sanofi announced results of a new analysis of long-term Dengvaxia® data which found differences in vaccine performance depending on whether or not the vaccinated individual had previously been infected with the dengue virus.

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The following table presents **the 2017 net sales of our Vaccines segment by geographical region:**

| *( million)* | Total | Europe[a] | Change at CER | United States | Change at CER | Rest of the world[b] | Change at CER | Emerging Markets[c] | Change at CER |
|---|---|---|---|---|---|---|---|---|---|
| Polio/Pertussis/Hib Vaccines (including Hexaxim®/Hexyon®, Pentacel®, Pentaxim® and Imovax®) | 1,827 | 300 | +187.6% | 435 | +10.1% | 152 | +2.6% | 940 | +14.5% |
| Influenza Vaccines (including Vaxigrip®, Fluzone HD® and Fluzone®) | 1,589 | 113 | +37.3% | 1,128 | +7.3% | 51 | +28.2% | 297 | +7.4% |
| Meningitis/Pneumonia Vaccines (including Menactra®) | 623 | 1 | -80.0% | 485 | -4.1% | 34 | +106.3% | 103 | +9.6% |
| Travel and Other Endemics Vaccines | 493 | 90 | +253.8% | 155 | +26.2% | 54 | +6.0% | 194 | +18.1% |
| Adult Booster Vaccines (including Adacel®) | 474 | 119 | +172.7% | 292 | | 26 | +17.4% | 37 | -22.9% |
| Dengvaxia® | 3 | | | | | | | 3 | -98.2% |
| Other Vaccines | 92 | 7 | +40.0% | 75 | +8.3% | 9 | | 1 | |
| **Total Vaccines** | **5,101** | **630** | **+137.3%** | **2,570** | **+5.6%** | **326** | **+13.4%** | **1,575** | **+7.8%** |

*(a) Western Europe and Eastern Europe excluding Eurasia (Russia, Ukraine, Georgia, Belarus, Armenia and Turkey).*

*(b) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

*(c) World excluding United States, Canada, Western and Eastern Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

**7/ Net sales by geographical region**

The following table presents our **net sales by geographical region for the years ended December 31, 2017 and 2016:**

| *( million)* | 2017 | 2016 | Change on a reported basis | Change at constant exchange rates |
|---|---|---|---|---|
| United States | 11,855 | 12,391 | -4.3% | -2.0% |
| Emerging Markets[a] | 10,258 | 9,593 | +6.9% | +9.7% |
| *of which Asia (including South Asia[b])* | *3,732* | *3,468* | *+7.6%* | *+10.3%* |
| *of which Latin America* | *2,837* | *2,503* | *+13.3%* | *+12.8%* |
| *of which Africa and Middle East* | *2,326* | *2,405* | *-3.3%* | *+2.5%* |
| *of which Eurasia[c]* | *1,242* | *1,090* | *+13.9%* | *+18.3%* |
| Europe[d] | 9,525 | 8,679 | +9.7% | +10.2% |
| Rest of the world[e] | 3,417 | 3,158 | +8.2% | +10.6% |
| *of which Japan* | *1,803* | *1,688* | *+6.8%* | *+11.6%* |
| *of which South Korea* | *426* | *360* | *+18.3%* | *+17.8%* |
| **Total net sales** | **35,055** | **33,821** | **+3.6%** | **+5.6%** |

*(a) World excluding United States, Canada, Western and Eastern Europe (apart from Eurasia), Japan, South Korea, Australia, New Zealand and Puerto Rico.*

*(b) India, Bangladesh and Sri Lanka. In 2016, South Asia was included in the Africa, Middle East and South Asia region. The presentation of 2016 net sales has been amended accordingly in the interests of comparability.*

*(c) Russia, Ukraine, Georgia, Belarus, Armenia and Turkey.*

*(d) Western Europe and Eastern Europe (excluding Eurasia).*

*(e) Japan, South Korea, Canada, Australia, New Zealand and Puerto Rico.*

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Sales in the **United States** totaled 11,855 million in 2017, down 4.3% on a reported basis and 3.5% on a constant structure basis and at constant exchange rates. The main factor was lower sales for two franchises: Diabetes (-22.8% CER at 3,128 million), and Established Prescription Products (-13.8% CER, at 1,269 million) due to competition from generics of Renvela®/Renagel®. The impact was partly offset by the performance of the Multiple Sclerosis franchise (+19.0% CER, at 1,330 million), the launch of Dupixent®, and growth in Vaccines sales (+5.6% CER at 2,570 million).

In **Emerging Markets**, net sales reached 10,258 million, up 6.9% on a reported basis and up 9.7% CER. On a constant structure basis and at constant exchange rates net sales rose by 6.0%, driven by sales growth for Established Prescription Products (+4.8% CER, at 3,800 million) and the Diabetes franchise (+11.4% CER, at 1,494 million), and a good performance from Vaccines (+7.8% CER, at 1,575 million). In **Asia**, net sales were 3,732 million, up 10.3% CER (+8.7% CER/CS), reflecting a solid performance in China (+15.1% CER/CS, at 2,218 million) on a recovery in Vaccines sales and growth for Established Prescription Products and the Diabetes franchise. In **Latin America**, net sales advanced by 12.8% CER (+5.9% CER/CS) to 2,837 million, boosted by good performances in Brazil (+5.7% CER/CS) and Argentina (+21.0% CER/CS, at 311 million). Net sales in Brazil reached 1,133 million, driven by Established Prescription Products and Consumer Healthcare. In the **Africa and Middle East** region, net sales totaled 2,326 million, up 2.5% CER but down 0.5% on a constant structure basis and at constant exchange rates. Solid performances in Egypt (+28.3% CER/CS) and Algeria (+6.8% CER/CS) were offset by lower sales in Morocco (-27.0% CER/CS) following the divestment of the Maphar site, in Saudi Arabia (-7.5% CER/CS), and in South Africa (-7.1% CER/CS). In the **Eurasia** region net sales reached 1,242 million, up 18.3% CER (+12.6% CER/CS) reflecting strong sales growth in Turkey (+18.1% CER/CS) and in Russia (+8.2% CER/CS). Net sales in Russia were 642 million, driven by Consumer Healthcare and by the Diabetes and Rare Diseases franchises.

In **Europe**, net sales were 9,525 million, up 10.2% CER and stable on a constant structure basis and at constant exchange rates. Lower sales of Established Prescription Products (-5.6% CER/CS, at 3,473 million) were offset by growth in sales of Vaccines (+20.7% CER/CS, at 630 million) and the Multiple Sclerosis franchise (+23.5% CER/CS, at 561 million). Net sales in France amounted to 2,330 million, down 2.3% CER/CS, as lower sales of Established Prescription Products and Generics were only partially offset by sales growth for Vaccines, Consumer Healthcare and the Multiple Sclerosis franchise.

In the **Rest of the World** region, net sales rose by 10.6% CER to 3,417 million. However, on a constant structure basis and at constant exchange rates net sales for the region fell by 1.5%.

This reflects a drop in sales for Established Prescription Products (-11.8% CER/CS, at 1,219 million) and the Diabetes franchise (-1.4% CER/CS, at 486 million), partly offset by stronger sales for Vaccines, the Specialty Care franchise, Generics and Consumer Healthcare. In Japan, net sales were up 11.6% CER at 1,803 million. On a constant structure basis, Japanese net sales fell by 7.3% due to the impact of generic competition for Plavix® and lower sales of Lantus®.

*A.3.2. Other income statement items*

The figures below have been restated in accordance with the new standard on revenue recognition, IFRS 15, which became applicable on January 1, 2018. The impacts of those restatements are described in detail in Note A.2.1.1. to the consolidated financial statements.

**1/ Other revenues**

Other revenues mainly comprise royalties under licensing agreements, and VaxServe sales of non-Sanofi products. Other revenues rose by 29.5% to 1,149 million in 2017, compared with 887 million in 2016. This was mainly due to higher sales at VaxServe ( 859 million, versus 581 million in 2016).

**2/ Gross profit**

Gross profit reached 24,608 million in 2017, versus 23,995 million in 2016, a rise of 2.5%. The gross margin ratio (gross profit as a percentage of net sales) was 70.2% in 2017 compared with 71.0% in 2016. The decrease includes the impact of the fair value remeasurement of inventories acquired in the exchange transaction with BI ( 166 million in 2017).

The gross margin ratio for the Pharmaceuticals segment(1) decreased by 0.2 of a percentage point to 72.2%, mainly reflecting the negative effect of lower US sales for the Diabetes franchise, though the effect was partly offset by Emerging Markets (especially China), and the Multiple Sclerosis and Immunology franchises.

The gross margin ratio for the Vaccines segment(2) was 0.2 of a percentage point lower at 61.7%.

**3/ Research and development expenses**

Research and development (R&D) expenses amounted to 5,472 million in 2017 (versus 5,172 million in 2016) and represented 15.6% of net sales (versus 15.3% in 2016). The overall year-on-year increase of 300 million (+5.8%) included 217 million for the Pharmaceuticals segment(1) (+4.7%) and 83 million for the Vaccines segment(2) (+15.0%).

The year-on-year increase in R&D expenses was due partly to the integration of BI Consumer Healthcare products and of Sanofi products that were previously in the SPMSD portfolio, and partly



*(1) Includes the Consumer Healthcare business and an allocation of global support function costs. For more information see A.3.3. Segment Results below.*

*(2) Includes an allocation of global support function costs. For more information see A.3.3. Segment Results below.*

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to progress on development projects in immuno-oncology (isatixumab, PD-1) and for sotagliflozin.

**4/ Selling and general expenses**

Selling and general expenses totaled 10,072 million (28.7% of net sales), compared with 9,478 million in 2016 (28.0% of net sales). This represents a year-on-year rise of 594 million (+6.3%).

Selling and general expenses for the Pharmaceuticals[1] and Vaccines[2] segments rose by 455 million (+5.2%) and 138 million (+18.6%), respectively. This increase mainly reflected the launch costs of Dupixent®, Kevzara® and Xyzal®, plus investment in marketing and sales efforts in key emerging markets and in the European vaccines business.

**5/ Other operating income and expenses**

Overall, this represented net income of 4 million in 2017, compared with a net expense of 127 million in 2016.

| ( *million*) | 2017 | 2016 | Change 2017/2016 |
|---|---|---|---|
| Other operating income | 237 | 355 | -118 |
| Other operating expenses | (233) | (482) | +249 |
| **Other operating income/(expenses), net** | **4** | **(127)** | **+131** |

The overall year-on-year positive change of 131 million reflected (i) a reduction in operating foreign exchange losses from 146 million (including 102 million on our Venezuelan operations) in 2016 to 80 million in 2017; and (ii) a decrease in income from our pharmaceutical alliance partners from 191 million in 2016 to 7 million in 2017, mainly relating to Regeneron following the launch of Dupixent® and Kevzara®. This was partly offset by (i) gains on disposals relating to ongoing operations ( 90 million in 2017, compared with 40 million in 2016) and (ii) impairment losses of 87 million taken against property, plant and equipment associated with the dengue vaccine (see Notes D.25. and D.26. to our consolidated financial statements).

**6/ Amortization of intangible assets**

Amortization charged against intangible assets amounted to 1,866 million in 2017, versus 1,692 million in 2016.

The 174 million year-on-year increase was mainly due to a 245 million rise in amortization expense following the recognition of intangible assets in connection with the exchange transaction with BI finalized on January 1, 2017. The effect was partly offset by a reduction in amortization charged against intangible assets recognized on the acquisition

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( 365 million in 2017, versus 482 million in 2016) as some products reached the end of their life cycles.

**7/ Impairment of intangible assets**

In 2017, this line item showed impairment losses of 293 million against intangible assets, compared with 192 million in 2016.

In 2017, this line item included (i) a 190 million impairment loss taken against intangible assets associated with the dengue vaccine; (ii) a 54 million impairment loss relating to *Clostridium difficile* vaccine development projects following our decision to discontinue the related programs; and (iii) impairment losses of 23 million taken against rights relating to a number of marketed products in the Pharmaceuticals segment.

In 2016, this line item included (i) a net impairment loss of 58 million on various R&D projects in the Pharmaceuticals and Vaccines segments; and (ii) impairment losses of 134 million taken against rights relating to a number of marketed products in the Pharmaceuticals segment.

**8/ Fair value remeasurement of contingent consideration**

Fair value remeasurements of contingent consideration liabilities recognized on acquisitions in accordance with the revised IFRS 3 represented a net expense of 159 million in 2017, versus a net expense of 135 million in 2016.

The 2017 remeasurements relate to contingent consideration arising from the dissolution of the SPMSD joint venture (expense of 187 million), and to contingent consideration payable to Bayer as a result of an acquisition made by Genzyme prior to the latter s acquisition by Sanofi (gain of 28 million in 2017, versus expense of 78 million in 2016). See Note D.18. to our consolidated financial statements.

**9/ Restructuring costs and similar items**

Restructuring costs and similar items amounted to 731 million in 2017, compared with 879 million in 2016.

In 2017, restructuring costs mainly comprised employee-related expenses arising from headcount adjustment plans in the United States and Europe, and write-downs of industrial assets in France and the United States.

**10/ Other gains and losses, and litigation**

In 2017, the line item ***Other gains and losses, and litigation*** shows an expense of 215 million, including a provision for a vendor s liability guarantee relating to a past divestment.

At the end of December 2016, Sanofi Pasteur and MSD ended their SPMSD joint venture. The derecognition of Sanofi s investment in SPMSD generated a pre-tax gain on disposal of 211 million in 2016.

*(1) Includes the Consumer Healthcare business and an allocation of global support function costs. For more information see A.3.3. Segment Results below.*

*(2) Includes an allocation of global support function costs. For more information see A.3.3. Segment Results below.*

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**11/ Operating income**

Operating income totaled 5,804 million for 2017, compared with 6,531 million for 2016. The year-on-year decrease of 11.1% was attributable mainly to increases in cost of sales, R&D expenses, selling and general expenses, and amortization and impairment of intangible assets.

**12/ Financial income and expenses**

Net financial expenses for 2017 were 273 million, compared with 856 million for 2016, a decrease of 583 million. This decrease mainly reflected the impairment loss of 457 million taken against our equity investment in Alnylam in 2016, in line with a decline in its market value of as of the reporting date relative to historical cost. Most of that decline occurred when Alnylam decided to discontinue the revusiran development program on October 5, 2016.

Net financial expenses directly related to our net debt (see the definition in section B.2. Consolidated balance sheet and debt below) amounted to 221 million in 2017, compared with 218 million in 2016, reflecting an increase in the cost of debt.

The net interest cost relating to employee benefits amounted to 92 million in 2017, compared with 114 million in 2016.

**13/ Income before tax and investments accounted for using the equity method**

Income before tax and investments accounted for using the equity method totaled 5,531 million in 2017, compared with 5,675 million in 2016, a fall of 2.5%.

**14/ Income tax expense**

Income tax expense represented 1,722 million in 2017, versus 1,325 million in 2016, giving an effective tax rate (based on consolidated net income) of 31.1% in 2017, compared with 23.4% in 2016. The increase in the effective tax rate was mainly due to the direct and indirect effects of the US tax reform (the Tax Cuts and Jobs Act of 2017, which came into force on January 1, 2018). The effect was partially offset by the consequences of the French Constitutional Council ruling of October 6, 2017 with respect to the additional 3% levy on dividends paid out in cash. The net effect of those two items was to increase the effective tax rate by 8% (see Note D.30. to our consolidated financial statements).

The effects of the US tax reform were based on a preliminary analysis of the Tax Cuts and Jobs Act of 2017.

Changes in the level of income tax expense are also significantly impacted by the tax effects of the amortization and impairment of intangible assets ( 719 million in 2017, versus 694 million in 2016) and of restructuring costs ( 134 million in 2017, versus 95 million in 2016).

The effective tax rate on our business net income[1] is a non-GAAP financial measure. It is calculated on the basis of business operating income, minus net financial expenses and before (i) the share of profit/loss from investments accounted for using the equity method and (ii) net income attributable to non-controlling interests. We believe the presentation of this measure, used by our management, is also useful for investors as it provides a means to analyze the effective tax cost of our current business activities. It should not be seen as a substitute for the effective tax rate based on consolidated net income.

When calculated on business net income[1], our effective tax rate was 23.5% in 2017, compared with 23.3% in 2016. The main impacts on this tax rate are the geographical mix of the profits of Sanofi entities; the tax effects of the elimination of intragroup margin on inventory; favorable settlements of recent proceedings involving the tax authorities in various countries; and changes in tax rates, particularly in France, the Netherlands and Belgium.

The table below reconciles our effective tax rate based on consolidated net income to our effective tax rate based on business net income:

| *(as a percentage)* | 2017 | 2016[(a)] |
|---|---|---|
| **Effective tax rate based on consolidated net income** | **31.1** | **23.4** |
| Tax effects: | | |
| Amortization and impairment of intangible assets | 3.2 | 3.7 |
| Restructuring costs and similar items | (0.2) | (1.3) |
| Impairment loss charged against the investment in Alnylam | | (1.5) |
| Other tax effects[(b)] | (10.6) | (1.0) |
| **Effective tax rate based on business net income** | **23.5** | **23.3** |

*(a) The results of the Animal Health business are presented separately in accordance with IFRS 5 (Non-Current Assets Held for Sale and Discontinued Operations); see Notes D.1. and D.36. to our consolidated financial statements.*

*(b) For 2017, this line comprises (i) the direct and indirect effects of the US tax reform (negative impact of 1,193 million) and (ii) the consequences of the French Constitutional Council ruling of October 6, 2017 with respect to the additional 3% levy on dividends paid out in cash (positive impact of 451 million).*

**15/ Share of profit/(loss) from investments accounted for using the equity method**

Investments accounted for using the equity method contributed net income of 85 million in 2017, compared with 136 million in 2016.

This line item mainly comprises our share of the profits and losses of Regeneron, which represented net income of 82 million in 2017 and 128 million in 2016.

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**16/ Net income excluding the exchanged/held-for-exchange Animal Health business**

Net income excluding the held-for-exchange Animal Health business amounted to 3,894 million in 2017, versus 4,486 million in 2016.

**17/ Net income/(loss) of the exchanged/held-for-exchange Animal Health business**

In accordance with IFRS 5, the net income or loss of the Animal Health business is presented in a separate line item, ***Net income/(loss) of the held-for-exchange Animal Health business*** (see Notes D.2. and D.36. to our consolidated financial statements). At the start of January 2017, Sanofi and BI confirmed that they had finalized the strategic transaction agreed in June 2016, involving the exchange of Sanofi s Animal Health business (Merial) for BI s Consumer Healthcare business. Consequently, for 2017 this line item shows the net after-tax gain of 4,643 million on the divestment of the Animal Health business.

**18/ Net income**

Net income amounted to 8,537 million in 2017, compared with 4,800 million in 2016.

**19/ Net income attributable to non-controlling interests**

Net income attributable to non-controlling interests was 121 million in 2017, versus 91 million in 2016. This line item mainly comprises the share of pre-tax profits paid to BMS from territories managed by Sanofi ( 84 million, versus 86 million in 2016). The year-on-year decrease was directly related to competition from generics of clopidogrel (active ingredient of Plavix®) and irbesartan (active ingredient of Aprovel®) in Europe.

**20/ Net income attributable to equity holders of Sanofi**

Net income attributable to equity holders of Sanofi amounted to 8,416 million, versus 4,709 million in 2016.

Basic earnings per share for 2017 was 6.70 (including the net gain on the divestment of the Animal Health business), 83.1% higher than the 2016 figure of 3.66, based on an average number of shares outstanding of 1,256.9 million in 2017 (1,286.6 million in 2016). Diluted earnings per share for 2017 was 6.64, 82.9% higher than the 2016 figure of 3.63, based on an average number of shares outstanding after dilution of 1,266.8 million in 2017 and 1,296.0 million in 2016.

*A.3.3. Segment results*

Business operating income (defined in Note D.35. to our consolidated financial statements) amounted to 9,323 million in 2017 (26.6% of net sales), lower than the 2016 figure of 9,284 million (27.5% of net sales).

Sanofi acquired the Consumer Healthcare operations of BI on January 1, 2017, and during 2017 we gradually integrated those operations into our Consumer Healthcare Global Business Unit (GBU). Following completion of the integration process and with effect from December 31, 2017, we identified our Consumer Healthcare business as an operating segment, the financial information for which is reported separately to, and reviewed separately by, our Chief Executive Officer. Up to December 31, 2017, the results of the Consumer Healthcare business were included in the Pharmaceuticals segment. Consequently, as of December 31, 2017 Sanofi has three operating segments: Pharmaceuticals, Consumer Healthcare and Vaccines.

However, due to lack of available data and the unduly complex and significant adjustments that would be required (in particular to our reporting tools), the 2016 comparative information has not been restated to reflect the changes arising from our new segment reporting model. Consequently, we present segment information for 2017 and comparative periods using our previous segment reporting model in the table below:

| *( million)* | December 31, 2017[(a)] | December 31, 2016[(a)] | Change |
|---|---|---|---|
| Pharmaceuticals[(b)] | 7,871 | 7,823 | +0.6% |
| Vaccines[(c)] | 1,521 | 1,573 | -3.3% |
| Other | (69) | (112) | -38.4% |
| **Business operating income** | **9,323** | **9,284** | **+0.4%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

*(b) Includes Consumer Healthcare and an allocation of global support function costs.*

*(c) Includes an allocation of global support function costs.*

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The table below sets forth our segment results for the **year ended December 31, 2017**, based on our **previous segment reporting model**:

| | December 31, 2017[a] | | | |
|---|---|---|---|---|
| *( million)* | Pharma-ceuticals[b] | Vaccines[c] | Other | Total Sanofi |
| **Net sales** | **29,971** | **5,101** | | **35,072** |
| Other revenues | 287 | 862 | | 1,149 |
| Cost of sales | (8,630) | (2,817) | | (11,447) |
| Research and development expenses | (4,835) | (637) | | (5,472) |
| Selling and general expenses | (9,190) | (881) | (1) | (10,072) |
| Other operating income and expenses | 180 | (108) | (68) | 4 |
| Share of profit/(loss) from investments accounted for using the equity method | 213 | 1 | | 214 |
| Net income attributable to non-controlling interests | (125) | | | (125) |
| **Business operating income** | **7,871** | **1,521** | **(69)** | **9,323** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

*(b) Includes Consumer Healthcare and an allocation of global support function costs.*

*(c) Includes an allocation of global support function costs.*

The table below sets forth our segment results for the **year ended December 31, 2016**, based on our **previous segment reporting model**:

| | December 31, 2016[a] | | | |
|---|---|---|---|---|
| *( million)* | Pharma-ceuticals[b] | Vaccines[c] | Other | Total Sanofi |
| **Net sales** | **29,232** | **4,577** | | **33,809** |
| Other revenues | 274 | 613 | | 887 |

| | | | | |
|---|---|---|---|---|
| Cost of sales | (8,348) | (2,353) | | (10,701) |
| Research and development expenses | (4,618) | (554) | | (5,172) |
| Selling and general expenses | (8,735) | (743) | | (9,478) |
| Other operating income and expenses | (1) | (14) | (112) | (127) |
| Share of profit/(loss) from investments accounted for using the equity method | 131 | 48 | | 179 |
| Net income attributable to non-controlling interests | (112) | (1) | | (113) |
| **Business operating income** | **7,823** | **1,573** | **(112)** | **9,284** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

*(b) Includes Consumer Healthcare and an allocation of global support function costs.*

*(c) Includes an allocation of global support function costs.*

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The tables below provide an analysis of business operating income for the Pharmaceuticals and Vaccines segments, based on our **previous segment reporting model**:

**Business operating income: Pharmaceuticals segment[a]**

| *( million)* | December 31, 2017[b] | as % of net sales | December 31, 2016[b] | as % of net sales | Change 2017/2016 |
|---|---|---|---|---|---|
| **Net sales** | **29,971** | **100.0%** | **29,232** | **100.0%** | **+2.5%** |
| Other revenues | 287 | 1,0% | 274 | 0.9% | +4.7% |
| Cost of sales | (8,630) | (28.8)% | (8,348) | (28.6)% | +3.4% |
| **Gross profit** | **21,628** | **72.2%** | **21,158** | **72.4%** | **+2.2%** |
| Research and development expenses | (4,835) | (16.1)% | (4,618) | (15.8)% | +4.7% |
| Selling and general expenses | (9,190) | (30.7)% | (8,735) | (29.9)% | +5.2% |
| Other operating income and expenses | 180 | | (1) | | |
| Share of profit/(loss) from investments accounted for using the equity method | 213 | | 131 | | |
| Net income attributable to non-controlling interests | (125) | | (112) | | |
| **Business operating income** | **7,871** | **26.3%** | **7,823** | **26.8%** | **+0.6%** |

*(a) Includes Consumer Healthcare and an allocation of global support function costs.*

*(b) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

**Business operating income: Vaccines segment[a]**

| *( million)* | December 31, 2017[b] | as % of net sales | December 31, 2016[b] | as % of net sales | Change 2017/2016 |
|---|---|---|---|---|---|
| **Net sales** | **5,101** | **100%** | **4,577** | **100.0%** | **+11.4%** |
| Other revenues | 862 | 16.9% | 613 | 13.4% | +40.6% |
| Cost of sales | (2,817) | (55.2)% | (2,353) | (51.4)% | +19.7% |

| | | | | | |
|---|---|---|---|---|---|
| **Gross profit** | **3,146** | **61.7%** | **2,837** | **62.0%** | **+10.9%** |
| Research and development expenses | (637) | (12.5)% | (554) | (12.1)% | +15.0% |
| Selling and general expenses | (881) | (17.3)% | (743) | (16.2)% | +18.6% |
| Other operating income and expenses | (108) | | (14) | | |
| Share of profit/(loss) from investments accounted for using the equity method | 1 | | 48 | | |
| Net income attributable to non-controlling interests | | | (1) | | |
| **Business operating income** | **1,521** | **29.8%** | **1,573** | **34.4%** | **-3.3%** |

*(a) Includes an allocation of global support function costs.*

*(b) Includes the effects of first-time application of IFRS 15 on revenue recognition (see note A.2.1.1. to our consolidated financial statements).*

**B. Liquidity and capital resources**

Our operations generate significant positive cash flows. We fund our day-to-day investments (with the exception of significant acquisitions) primarily with operating cash flow, and pay regular dividends on our shares.

Net debt is a non-GAAP financial indicator which is reviewed by our management, and which we believe provides useful information to measure our overall liquidity and capital resources. We define net debt as (i) the sum total of short term debt, long term debt, and interest rate derivatives and currency derivatives

used to manage debt, minus (ii) the sum total of cash and cash equivalents and interest rate derivatives and currency derivatives used to manage cash and cash equivalents.

As of December 31, 2018 our net debt had increased to 17,628 million, due mainly to the acquisitions of Bioverativ and Ablynx. As of December 31, 2017, our net debt stood at 5,161 million, due largely to the receipt of a balancing cash payment as part of the transaction with Boehringer Ingelheim. As of December 31, 2016, our net debt was 8,234 million, mainly due to share repurchases made at the end of 2016, carried out in anticipation of the receipt of net proceeds from the transaction

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with BI finalized in most markets in early 2017. See Note D.17. to our consolidated financial statements.

In order to assess our financing risk, we also use the gearing ratio, a non-GAAP financial measure (see table in section B.2. Consolidated Balance Sheet and Debt below). We define the gearing ratio is defined as the ratio of net debt to total equity. As of December 31, 2018, our gearing ratio was 29.9%, compared with 8.9% as of December 31, 2017 and 14.3% as of December 31, 2016.

**B.1. Consolidated statement of cash flows**

Generally, factors that affect our earnings for example, pricing, volume, costs and exchange rates flow through to cash from operations. The most significant source of cash from operations is sales of our branded pharmaceutical products and vaccines. Receipts of royalty payments also contribute to cash from operations.

**Summarized consolidated statements of cash flows**

| *( million)* | **2018** | **2017[(a)]** | **2016[(a)]** |
|---|---|---|---|
| Net cash provided by/(used in) operating activities | 5,547 | 7,379 | 7,838 |
| Net cash provided by/(used in) investing activities | (12,866) | (2,896) | (2,511) |
| Net cash inflow from the exchange of the Animal Health business for BI s Consumer Healthcare business | (6) | 3,535 | |
| Net cash provided by/(used in) financing activities | 3,934 | (7,902) | (4,101) |
| Impact of exchange rates on cash and cash equivalents | 1 | (74) | (101) |
| **Net change in cash and cash equivalents** | **(3,390)** | **42** | **1,125** |

*(a) Includes the effects of first-time application of IFRS 15 (see Note A.2.1.1. to our consolidated financial statements).*

*B.1.1. Year ended December 31, 2018 compared with year ended December 31, 2017*

***Net cash provided by operating activities*** amounted to 5,547 million in 2018, against 7,379 million in 2017.

Operating cash flow before changes in working capital for 2018 was 6,827 million, compared with 7,232 million in 2017. Working capital requirements increased by 1,280 million in 2018, compared with a reduction of 147 million in 2017. The main factors in 2018 were (i) an increase of 701 million in inventories, associated with new products (especially Dupixent®) and (ii) the net change in other current assets and liabilities (negative change of 814 million in 2018, versus positive change of 243 million in 2017), due mainly to a decrease in provisions for discounts, rebates and sales returns (especially in the United States), and to differences between the date of recognition of income taxes and the timing of tax payments during the year.

We run the risk of delayed payments or even non-payment by our customers, who consist principally of wholesalers, distributors, pharmacies, hospitals, clinics and government agencies (see Item 3.D Risk Factors 2. Risks Relating to Our Business We are subject to the risk of non payment by our customers ). Over our business as a whole, the amount of trade receivables overdue by more than 12 months which primarily consists of amounts due from public sector bodies decreased from 93 million as of December 31, 2017 to 61 million as of December 31, 2018 (see Note D.10. to our consolidated financial statements).

***Net cash used in investing activities*** totaled 12,866 million in 2018, compared with 2,896 million in 2017.

Acquisitions of property, plant and equipment and intangible assets amounted to 1,977 million, versus 1,956 million in 2017. There were 1,415 million of acquisitions of property, plant and equipment (versus 1,388 million in 2017), most of which ( 1,046 million) were in the Pharmaceuticals segment, primarily in industrial facilities. The Vaccines segment accounted for 364 million of acquisitions of property, plant and equipment during 2018. Acquisitions of intangible assets ( 562 million, versus 568 million in 2017) mainly comprised contractual payments for intangible rights under license and collaboration agreements.

Acquisitions of investments during 2018 totaled 12,994 million, net of the cash of acquired entities and after including assumed liabilities and commitments; this compares with 1,212 million in 2017. The main acquisitions in 2018 were Bioverativ ( 8,932 million) and Ablynx ( 3,639 million).

After-tax proceeds from disposals amounted to 2,163 million in 2018, and arose mainly from the sale of the European Generics business ( 1,598 million), the sale of some Consumer Healthcare products to Cooper-Vemedia ( 158 million), and the divestment of equity interests in Impact Therapeutics ( 99 million). In 2017, after-tax proceeds from disposals amounted to 535 million, and arose mainly from the sale of mutual fund investments previously held to meet commitments under post-employment plans; divestments of Consumer Healthcare brands in the United States; and the divestment of Consumer Healthcare products to Ipsen (for 83 million).

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***Net cash inflow from the exchange of the Animal Health business for BI s Consumer Healthcare business*** comprised the following items in 2017: (i) the receipt by Sanofi of a balancing cash payment of 4,207 million; (ii) reimbursements of intragroup accounts with Merial entities totaling 967 million; (iii) the 1,784 million payment of the tax due on the gain arising on the divestment; and (iv) the cash held by the BI subsidiaries acquired by Sanofi. After taking account of final enterprise value adjustments, the total consideration for the businesses effectively transferred in 2017 was 10,557 million for the sale of the Animal Health business to BI, and 6,239 million for the acquisition of BI s Consumer Healthcare business (see Note D.1. to our consolidated financial statements for the year ended December 31, 2017).

***Net cash provided by/used in financing activities*** represented a net cash inflow of 3,934 million in 2018, compared with a net outflow of 7,902 million in 2017. The 2018 figure includes net external debt finance obtained of 8,722 million (compared with a net repayment of 2,297 million of debt in 2017), including a debt issue of 8 billion under the Euro Medium Term Note program in March 2018 and a further $2 billion bond issue in June 2018. Other cash outflows in 2018 included the dividend payout to our shareholders of 3,773 million (versus 3,710 million in 2017), and the effect of changes in our share capital (repurchases of our own shares, net of capital increases) amounting to 924 million ( 1,843 million in 2017).

The ***net change in cash and cash equivalents*** during 2018 was a decrease of 3,390 million, compared with an increase of 42 million in 2017.

*B.1.2. Year ended December 31, 2017 compared with year ended December 31, 2016*

***Net cash provided by operating activities*** amounted to 7,379 million in 2017, versus 7,838 million in 2016.

Operating cash flow before changes in working capital for 2017 was 7,232 million, versus 7,008 million in 2016. Working capital requirements fell by 147 million in 2017, compared with a reduction of 830 million in 2016; the main factors in 2017 were an increase in accounts receivable of 529 million and an increase in accounts payable of 577 million.

Over our business as a whole, the amount of trade receivables overdue by more than 12 months which primarily consists of amounts due from public sector bodies decrease to 93 million as of December 31, 2017 from 198 million as of December 31, 2016 (see Note D.10. to our consolidated financial statements).

***Net cash used in investing activities*** amounted to 2,896 million in 2017, compared with 2,511 million in 2016.

Acquisitions of property, plant and equipment and intangible assets totaled 1,956 million, versus 2,083 million in 2016. There were 1,388 million of acquisitions of property, plant and equipment (versus 1,219 million in 2016), most of which were in the Pharmaceuticals segment, primarily in industrial facilities. The Vaccines segment invested 346 million in property, plant and

equipment in 2017 (versus 315 million in 2016). Acquisitions of intangible assets ( 568 million, versus 864 million in 2016) mainly comprised contractual payments for intangible rights under license and collaboration agreements.

Acquisitions of investments during 2017 amounted to 1,212 million, net of cash acquired and after including assumed liabilities and commitments, compared with 534 million in 2016. In 2017, these included the acquisition of Protein Sciences ( 594 million), our contribution to the Onduo joint venture ( 50 million), and purchases of additional shares in Regeneron ( 184 million).

After-tax proceeds from disposals ( 535 million) arose mainly from the sale of mutual fund investments previously held to meet commitments under post-employment plans; divestments of Consumer Healthcare brands in the United States; and the divestment of Consumer Healthcare products to Ipsen (for 83 million)After-tax proceeds from disposals in 2016 amounted to 209 million and arose mainly from the divestment of the equity interest in Nichi-Iko Pharmaceutical Co., Inc. and the divestment of product rights relating to Oenobiol®.

***Net cash inflow from the exchange of the Animal Health business for BI s Consumer Healthcare business*** comprised the following items for 2017: (i) the receipt by Sanofi of a balancing cash payment of 4,207 million; (ii) reimbursements of intragroup accounts with Merial entities totaling 967 million; (iii) a tax payment of 1,784 million on the gain arising on the divestment; and (iv) the cash held by the BI subsidiaries acquired by Sanofi. After final enterprise value adjustments, the exchange values of the two businesses effectively transferred during 2017 were determined to be 10,557 million for Sanofi s Animal Health business and 6,239 million for BI s Consumer Healthcare business (see Note D.2. to the consolidated financial statements for the year ended December 31, 2018).

**Net cash used in financing activities** amounted to 7,902 million in 2017, compared with 4,101 million in 2016. The 2017 figure includes net external debt finance repaid (i.e., net change in short-term and long-term debt) of 2,297 million; this compares with net external debt financing raised of 2,293 million in 2016. It also includes the effect of changes in share capital (repurchases of own shares, net of capital increases), amounting to 1,843 million (versus 2,603 million in 2016), and the dividend payout to our shareholders of 3,710 million (versus 3,759 million in 2016).

The **net change in cash and cash equivalents** during 2017 was an increase of 42 million compared with an increase of 1,125 million in 2016.

**B.2. Consolidated balance sheet and debt**

Total assets were 111,408 million as of December 31, 2018, compared with 99,813 million as of December 31, 2017, an increase of 11,595 million.

**Net debt** was 17,628 million as of December 31, 2018, compared with 5,161 million as of December 31, 2017, due largely to the acquisitions of Bioverativ and Ablynx. Net debt is

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a non-GAAP financial indicator which is reviewed by our management, and which we believe provides useful information to measure our overall liquidity and capital resources. We define net debt as (i) the sum total of short term debt, long term debt,

and interest rate derivatives and currency derivatives used to manage debt, minus (ii) the sum total of cash and cash equivalents and interest rate derivatives and currency derivatives used to manage cash and cash equivalents.

| *( million)* | 2018 | 2017[(a)] | 2016[(a)] |
|---|---|---|---|
| Long-term debt | 22,007 | 14,326 | 16,815 |
| Short-term debt and current portion of long-term debt | 2,633 | 1,275 | 1,764 |
| Interest rate and currency derivatives used to manage debt | (54) | (133) | (70) |
| **Total debt** | **24,586** | **15,468** | **18,509** |
| Cash and cash equivalents | (6,925) | (10,315) | (10,273) |
| Interest rate and currency derivatives used to manage cash and cash equivalents | (33) | 8 | (2) |
| **Net debt** | **17,628** | **5,161** | **8,234** |
| Total equity | 59,035 | 58,239 | 57,722 |
| **Gearing ratio** | **29.9%** | **8.9%** | **14.3%** |

*(a) Includes the effects of first-time application of IFRS 15 on revenue recognition (see Note A.2.1.1. to our consolidated financial statements).*

To assess our financing risk, we use the gearing ratio , another non-GAAP financial measure. This ratio (which we define as the ratio of net debt to total equity) increased from 8.9% as of December 31, 2017 to 29.9% as of December 31, 2018. Analyses of debt as of December 31, 2018 and December 31, 2017, by type, maturity, interest rate and currency, are provided in Note D.17. to our consolidated financial statements.

We expect that the future cash flows generated by our operating activities will be sufficient to repay our debt. The financing arrangements in place as of December 31, 2018 at the Sanofi parent company level are not subject to covenants regarding financial ratios and do not contain any clauses linking credit spreads or fees to Sanofi s credit rating.

Other key movements in the balance sheet are described below.

Total **equity** was 59,035 million as of December 31, 2018, versus 58,239 million as of December 31, 2017. The year-on-year change reflects the following principal factors:

- increases: our net income for 2018 ( 4,410 million) and movements in currency translation differences ( 1,194 million, mainly on the US dollar); and
- decreases: the dividend payout to our shareholders in respect of the 2017 financial year ( 3,773 million), and repurchases of our own shares ( 1,100 million).

As of December 31, 2018 we held 1.9 million of our own shares, recorded as a deduction from equity and representing 0.15% of our share capital.

***Goodwill*** and ***Other intangible assets*** ( 66,124 million in total) rose by 12,780 million year-on-year, the main factors being:

- increases: movements related to the acquisitions of Bioverativ ( 2,676 million of goodwill and 8,113 million of other intangible assets) and Ablynx ( 1,372 million of goodwill and 2,409 million of other intangible assets); and
- decreases: amortization and impairment charged during the period ( 3,033 million), and the effects of the divestment of our European Generics business ( 988 million).

***Investments accounted for using the equity method*** ( 3,402 million) increased by 555 million, mainly due to the recognition of our share of the profits of Regeneron.

***Other non-current assets*** were 393 million lower at 2,971 million. The main movement during the year was a decrease in the market value of our equity investment in Alnylam ( 447 million, including the effect of exchange rates).

**Net deferred tax assets** were 1,199 million as of December 31, 2018, versus 2,686 million as of December 31, 2017, a decrease of 1,487 million. This was largely due to deferred taxes arising on the remeasurement of other intangible assets acquired in business combinations, primarily 1,906 million relating to Bioverativ as of December 31, 2018.

***Non-current provisions and other non-current liabilities*** ( 8,613 million) decreased by 541 million, mainly due to a reduction in provisions for pensions and other post-employment benefits.

***Liabilities related to business combinations and to non-controlling interests*** ( 1,304 million) decreased by 65 million. The main movements in this line item are (i) the effects of buying out non-controlling interests from BMS and (ii) fair value remeasurements of contingent consideration payable to Bayer as a result of an acquisition made by Genzyme prior to the latter s acquisition by Sanofi; those movements were partly offset by the effect of the acquisition of Bioverativ (see Note D.18. to our consolidated financial statements).

**B.3. Liquidity**

We expect that our existing cash resources and cash from operations will be sufficient to finance our foreseeable working

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capital requirements. At year-end 2018, we held cash and cash equivalents amounting to 6,925 million, substantially all of which were held in euros (see Note D.13. to our consolidated financial statements included at Item 18 of this annual report). As at December 31, 2018, 505 million of our cash and cash equivalents were held by our captive insurance and reinsurance companies in accordance with insurance regulations.

We run the risk of delayed payments or even non-payment by our customers, who consist principally of wholesalers, distributors, pharmacies, hospitals, clinics and government agencies (see Item 3.D. Risk Factors 2. Risks Relating to Our Business We are subject to the risk ofion-payment by our customers ). Deteriorating credit and economic conditions and other factors in some countries have resulted in, and may continue to result in an increase in the average length of time taken to collect our accounts receivable in these countries. Should these factors continue, it may require us to re-evaluate the collectability of these receivables in future periods. We carefully monitor sovereign debt issues and economic conditions and evaluate accounts receivable in these countries for potential collection risks. We have been conducting an active recovery policy, adapted to each country and including intense communication with customers, negotiations of payment plans, charging of interest for late payments, and legal action. Over our business as a whole, the amount of trade receivables overdue by more than 12 months (which primarily consists of amounts due

from public sector bodies) decreased from 93 million as of December 31, 2017 to 61 million as of December 31, 2018 (see Note D.10. to our consolidated financial statements).

In November 2011, Sanofi obtained the necessary corporate authorizations to purchase any or all of the outstanding Contingent Value Rights ( CVRs ) and subsequently purchased CVRs in 2011. In 2012 following a tender offer initiated in September 2012 on the basis of the same corporate authorization, Sanofi purchased an additional 40,025,805 CVRs (for a total consideration of approximately $70 million), followed by a further 10,928,075 CVRs (for approximately $9 million) in 2013, 1,879,774 CVRs (for approximately $1 million) in 2014, and none in 2015, 2016, 2017 and 2018. As of December 31, 2018, a total of 236,457,284 CVRs were outstanding out of the 291,313,510 issued at the time of the Genzyme acquisition.

At year-end 2018, we had no commitments for capital expenditures that we consider to be material to our consolidated financial position. Undrawn confirmed credit facilities amounted to a total of 8 billion at December 31, 2018. For a discussion of our treasury policies, see Item 11. Quantitative and Qualitative Disclosures about Market Risk.

We expect that cash from our operations will be sufficient to repay our debt. For a discussion of our liquidity risks, see Item 11. Quantitative and Qualitative Disclosures about Market Risk.

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**C. Off-balance sheet arrangements / contractual obligations and other commercial commitments**

We have various contractual obligations and other commercial commitments arising from our operations. Our contractual obligations and our other commercial commitments as of December 31, 2018 are shown in Notes D.3., D.17., D.18., D.21. and D.36. to our consolidated financial statements included at Item 18 of this annual report. Note D.21. to our consolidated financial statements discloses details of commitments under our principal research and development collaboration agreements. For a description of the principal contingencies arising from certain business divestitures, refer to Note D.22.d) to our 2018 consolidated financial statements.

**Sanofi s contractual obligations and other commercial commitments are set forth in the table below:**

| **December 31, 2018** | | **Payments due by period** | | | |
|---|---|---|---|---|---|
| *( million)* | **Total** | **Less than 1 year** | **1 to 3 years** | **3 to 5 years** | **More than 5 years** |
| Future contractual cash flows relating to debt and debt hedging instruments[a] | 26,831 | 2,810 | 6,810 | 5,948 | 11,263 |
| Operating lease obligations | 2,427 | 289 | 457 | 378 | 1,303 |
| Finance lease obligations[b] | 25 | 5 | 7 | 8 | 5 |
| Irrevocable purchase commitments[c] | | | | | |
| *given* | *6,549* | *3,654* | *1,247* | *489* | *1,159* |
| *received* | *(175)* | *(120)* | *(21)* | *(12)* | *(22)* |
| Research & development license agreements | | | | | |
| *Commitments related to R&D and other commitments* | *954* | *675* | *257* | *14* | *8* |
| *Potential milestone payments[d]* | *3,241* | *249* | *728* | *947* | *1,317* |
| *Obligations related to R&D license agreements reflected in the balance sheet* | *249* | *79* | *34* | *21* | *115* |
| Obligations relating to business combinations[e] | 3,638 | 313 | 2,840 | 331 | 154 |
| Firm commitment related to the BMS agreement[f] | 1,060 | 62 | 115 | 118 | 765 |

| | | | | | |
|---|---|---|---|---|---|
| Estimated benefit payments on unfunded pensions and post employment benefits[g] | | | | | |
| **Total contractual obligations and other commitments** | **44,799** | **8,016** | **12,474** | **8,242** | **16,067** |
| **Undrawn general-purpose credit facilities** | **8,000** | | **8,000** | | |

*(a) See Note D.17. to our consolidated financial statements included at Item 18 of this annual report.*

*(b) See Note D.3. to our consolidated financial statements included at Item 18 of this annual report.*

*(c) These comprise irrevocable commitments to suppliers of (i) property, plant and equipment, net of down payments (see Note D.3. to our consolidated financial statements included at Item 18 of this annual report) and (ii) goods and services.*

*(d) This line includes all potential milestone payments on projects regarded as reasonably possible, i.e., on projects in the development phase.*

*(e) See Note D.18. to our consolidated financial statements included at Item 18 of this annual report.*

*(f) See Note C.2. to our consolidated financial statements included at Item 18 of this annual report.*

*(g) See Note D.19.1. to our consolidated financial statements included at Item 18 of this annual report. The table above does not include the ongoing annual employer s contributions to plan assets, estimated at 136 million in 2018.*

We may have payments due to our current or former research and development partners under collaborative agreements. These agreements typically cover multiple products, and give us the option to participate in development on a product-by-product basis. When we exercise our option with respect to a product, we pay our collaboration partner a fee and receive intellectual property rights to the product in exchange. We are also generally required to fund some or all of the development costs for the products that we select, and to make payments to our partners when those products reach development milestones.

We have entered into collaboration agreements under which we have rights to acquire products or technology from third parties through the acquisition of shares, loans, license agreements, joint development, co-marketing and other contractual arrangements. In addition to upfront payments on signature of the agreement, our contracts frequently require us to make payments contingent upon the completion of development milestones by our alliance partner or upon the granting of approvals or licenses.

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Because of the uncertain nature of development work, it is impossible to predict (i) whether Sanofi will exercise further options for products, or (ii) whether the expected milestones will be achieved, or (iii) the number of compounds that will reach the relevant milestones. It is therefore impossible to estimate the maximum aggregate amount that Sanofi will actually pay in the future under existing collaboration agreements.

Given the nature of its business, it is highly unlikely that Sanofi will exercise all options for all products or that all milestones will be achieved.

The main collaboration agreements relating to development projects are described in Note D.21.1. to our consolidated financial statements included at Item 18 of this annual report. Milestone payments relating to development projects under these agreements included in the table above exclude projects still in the research phase ( 6.8 billion in 2018, 7.2 billion in 2017 and 6.2 billion in 2016) and payments contingent upon the attainment of sales targets once a product is on the market ( 9.9 billion in 2018, 10.1 billion in 2017, 8.2 billion in 2016).

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ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

## Item 6. **Directors, Senior Management and Employees**

### A. Directors and senior management

Since January 1, 2007, Sanofi has separated the offices of Chairman and Chief Executive Officer. Annual evaluations conducted since that date have indicated that this governance structure is appropriate to Sanofi s current configuration. This arrangement was maintained with the appointment of Serge Weinberg to the office of Chairman firstly on May 17, 2010, then on May 6, 2011 and again on May 4, 2015. The Board of Directors regards this governance structure as appropriate to the current context in which Sanofi operates and its share ownership structure, and as protecting the rights of all of its stakeholders.

The **Chairman** organizes and directs the work of the Board, and is responsible for ensuring the proper functioning of the corporate decision-making bodies in compliance with good governance principles. The Chairman coordinates the work of the Board of Directors with that of its Committees. He ensures that the Company s management bodies function properly, and in particular that the directors are able to fulfil their duties. The Chairman is accountable to the Shareholders General Meeting, which he chairs.

In addition to these roles conferred by law, the Chairman:

- in coordination with the Chief Executive Officer, liaises between the Board of Directors and the shareholders of the Company;
- is kept regularly informed by the Chief Executive Officer of significant events and situations affecting the affairs of the Company, and may request from the Chief Executive Officer any information useful to the Board of Directors;
- may, in close collaboration with the Chief Executive Officer, represent the Company in high-level dealings with governmental bodies and with key partners of the Company and/or of its subsidiaries, both nationally and internationally;

seeks to prevent any conflict of interest and manages any situation that might give rise to a conflict of interest. He also gives rulings, in the name of the Board, on requests to take up external directorships of which he may become aware or that may be submitted to him or her by a director;

may interview the statutory auditors in preparation for the work of the Board of Directors and the Audit Committee; and

strives to promote in all circumstances the values and image of the Company.

The Chairman is also required to develop and maintain a proper relationship of trust between the Board and the Chief Executive

Officer, so as to ensure that the latter consistently and continuously implements the orientations determined by the Board.

In fulfilling his remit, the Chairman may meet with any individual, including senior executives of the Company, while avoiding any involvement in directing the Company or managing its operations, which are exclusively the responsibility of the Chief Executive Officer.

Finally, the Chairman reports to the Board on the fulfilment of his remit.

The Chairman carries out his duties during the entire period of his term of office, subject to the caveat that a director who is a natural person may not be appointed or reappointed once he or she has reached the age of 70.

The **Chief Executive Officer** manages the Company, and represents it in dealings with third parties within the limit of the corporate purpose. The Chief Executive Officer has the broadest powers to act in all circumstances in the name of the Company, subject to the powers that are attributed by law to the Board of Directors and to the Shareholders General Meeting and within the limits set by the Board of Directors.

The Chief Executive Officer must be less than 65 years old.

**Limitations on the powers of the Chief Executive Officer set by the Board**

With effect from March 6, 2018, the limitations on the powers of the Chief Executive Officer are specified in the Board Charter. Without prejudice to legal provisions regarding authorizations that must be granted by the Board (regulated agreements, guarantees, divestments of equity holdings or real estate, etc.), prior approval from the Board of Directors is required for transactions or decisions resulting in an investment or divestment, or an expenditure or guarantee commitment, made by the Company and its subsidiaries, in excess of:

a cap of 500 million (per transaction) for transactions, decisions or commitments pertaining to a previously approved strategy; and

a cap of 150 million (per transaction) for transactions, decisions or commitments not pertaining to a previously approved strategy.

When such transactions, decisions or commitments give rise to installment payments to the contracting third party (or parties) that are contingent upon future results or objectives, such as the registration of one or more products, attainment of the caps is calculated by aggregating the various payments due from

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signature of the contract until (and including) filing of the first application for marketing authorization in the United States or in Europe.

Attainment of the above caps is also assessed after taking into account all commitments to make payments on exercise of a firm or conditional option with immediate or deferred effect, and all guarantees or collateral to be provided to third parties over the duration of such commitments.

The prior approval procedure does not apply to transactions and decisions that result in the signature of agreements that solely involve subsidiaries and the Company itself.

**Board of Directors**

Each year, the Board of Directors conducts a review to ensure that there is an appropriate balance in its composition and in the composition of its Committees. In particular, the Board seeks to ensure gender balance and a broad diversity of competencies, experience, nationalities and ages, reflecting our status as a diversified global business. The Board investigates and evaluates not only potential candidates, but also whether existing directors should seek reappointment. Above all, the Board seeks directors who show independence of mind and are competent, dedicated and committed, with compatible and complementary personalities.

As of December 31, 2018 the Board of Directors had 16 members, including two directors representing employees. 43% of the directors were women and 38% were non-French nationals.

The Board works with the Compensation Committee and the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019), to ensure that the Executive Committee operates an inclusion (non-discrimination) and diversity policy, especially as regards gender balance. As of December 31, 2018, 20% of the 15 Executive Committee members were women, and 67% were non-French nationals.

The Board of Directors is also kept informed, in particular on the occasion of its annual discussion on professional and pay equality policy, on how the inclusion and diversity policy is cascaded down to Senior Leaders (the positions in the Company with the highest level of responsibility). In 2018, there were 2,044 Senior Leaders within Sanofi, including Executive Committee members and other executives; of that total, 35.4% were women.

Subject to the powers expressly attributed to the Shareholders General Meeting and within the scope of the Company s corporate purpose, the Board of Directors remit covers all issues relating to the proper management of the Company, and through its decisions the Board determines matters falling within its authority.

The rules and operating procedures of our Board of Directors are defined by law, by our Articles of Association, and by our Board

charter (an English language version of which is reproduced in full as Exhibit 1.2 to this Annual Report on Form 20-F).

**Term of office**

The term of office of directors is four years. Directors are required to seek reappointment by rotation, such that members of the Board are required to seek reappointment on a regular basis in the most equal proportions possible. Exceptionally, the Shareholders Ordinary General Meeting may appoint a director to serve for a term of one, two or three years, in order to ensure adequate rotation of Board members. Each director standing down is eligible for reappointment. Should one or more directorships fall vacant as a result of death or resignation, the Board of Directors may make provisional appointments in the period between two Shareholders General Meetings, in accordance with applicable laws.

Directors may be removed from office at any time by a Shareholders General Meeting.

**Independence of Board members**

Under the terms of the AFEP-MEDEF corporate governance code (the AFEP-MEDEF Code), a director is independent when he or she has no relationship of any kind whatsoever with the Company, its group or its senior management that may color his or her judgment. More specifically, a director can only be regarded as independent if he or she:

is not (and has not been during the past five years):

an employee or executive officer of the Company;

an employee, executive officer or director of an entity consolidated by the Company; or

an employee, executive officer or director of the Company s parent, or of an entity consolidated by that parent (criterion 1);

is not an executive officer of an entity in which (i) the Company directly or indirectly holds a directorship or (ii) an employee of the Company is designated as a director or (iii) an executive officer of the Company (currently, or who has held office within the past five years) holds a directorship (criterion 2);

is not a customer, supplier, investment banker or corporate banker that is material to the Company or its group, or for whom the Company or its group represents a significant proportion of its business (criterion 3);

has no close family ties with a corporate officer of the Company (criterion 4);

has not acted as auditor for the Company over the course of the past five years (criterion 5);

has not been a director of the Company for more than twelve years (criterion 6);

does not receive variable compensation in cash or in the form of shares or any compensation linked to the performance of the Company or its group (criterion 7); or

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does not represent a shareholder that has a significant or controlling interest in the Company (criterion 8).
The influence of other factors such as the ability to understand challenges and risks, and the courage to express ideas and form a judgment, is also evaluated before it is decided whether a director can be regarded as independent.

In compliance with our Board Charter and pursuant to the AFEP-MEDEF Code, the Board of Directors meeting of March 8, 2019 discussed the independence of the current directors. Of the sixteen directors, eleven were deemed to be independent directors by reference to the independence criteria used by the

Board of Directors pursuant to the AFEP-MEDEF Code: Serge Weinberg, Emmanuel Babeau, Bernard Charlès, Claudie Haigneré, Patrick Kron, Fabienne Lecorvaisier, Melanie Lee, Suet-Fern Lee, Carole Piwnica, Diane Souza and Thomas C. Südhof.

Consequently, the proportion of independent directors is 79%. This compares with the AFEP-MEDEF recommendation of 50% in companies with dispersed ownership and no controlling shareholder (which is the case for Sanofi). In accordance with the recommendations of the AFEP-MEDEF Code, directors representing employees are excluded when calculating the proportion of independent directors.

| | Serge Weinberg | Emmanuel Babeau | Bernard Charlès | Claudie Haigneré | Patrick Kron | Fabienne Lecorvaisier | Melanie Lee | Suet-Fern Lee | Carole Piwnica | Diane Souza | T |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1:** not an executive past 5 years | No[(1)] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **2:** No cross-directorships | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **3:** no significant business p[(2)] | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **4:** no close family ties | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **5:** not an auditor | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **6:** not held office for >12 | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **7:** no variable or ce-linked compensation | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| **8:** not a shareholder dependent | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |
| | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | |

Failure to fulfil one of the criteria does not automatically disqualify a director from being independent.

The Board s conclusions on the situation of Serge Weinberg and on the business relationships review are set out below.

(1) Serge Weinberg

When the offices of Chairman of the Board and Chief Executive Officer were temporarily combined on October 29, 2014, the Board of Directors determined that Serge Weinberg given his role as Chief Executive Officer could no longer be regarded as independent. When the two offices were separated again in April 2015, the Board of Directors determined that Serge Weinberg could be regarded as independent and could therefore resume the chairmanship of the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019).

Under Article 8.6 of the AFEP-MEDEF Code, a non-executive officer cannot be regarded as independent if he or she receives variable compensation in cash or shares or any compensation linked to the performance of the Company or group. This is consistent with recommendations made by the AMF in its 2017

report on corporate governance, executive compensation, internal control and risk management. Serge Weinberg complies with this criterion, in that he receives fixed compensation only, with no entitlement to variable compensation in either cash or shares.

(2) Business Relationships Review

In its examination of the independence of each director, the Board of Directors took into account the various relationships between directors and Sanofi and concluded that no relationships were of a kind that might undermine their independence. The Board of Directors noted that the Company and its subsidiaries had, in the normal course of business, over the past three years, sold products and provided services to, and/or purchased products and received services from, companies in which certain of the Company s directors who are classified as independent (or their close family members) were senior executives or employees during 2018. In each case, the amounts paid to or received from such companies over the past three years were determined on an arm s length basis and did not represent amounts that the Board regarded as undermining the independence of the directors in question.

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**Board evaluation**

Under the terms of the Board Charter, a discussion of the Board s operating procedures must be included on the agenda of one Board meeting every year. The Charter also requires a formal evaluation to be performed at least every three years under the direction of the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019), with assistance from an independent consultant if deemed necessary.

In 2017, the evaluation was conducted on the basis of a questionnaire. Each director was allowed a few weeks to

complete the questionnaire using a secure digital platform. The responses were then analyzed by the Secretary to the Board, and supplemented by one-on-one interviews. The results were then presented to, and discussed by, the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019). A detailed report prepared at that meeting was presented at the Board meeting of March 6, 2018. The directors welcomed the progress made in the operation of the Board and its Committees since the previous evaluation. The issues most frequently raised in the evaluation were the diversity and complementarity of the Board following the appointment of the new directors, the role of the Committees, executive sessions, an update on the implementation of the Company s digital strategy, and implementation of the external growth strategy.

The table below shows the areas for progress and vigilance identified in the evaluation, and action taken in response by the Board in 2018:

| Areas for progress and vigilance identified | Actions taken by the Board |
|---|---|
| Continuing to work on succession planning for the Chief Executive Officer, the Chairman, and key executive posts | Work continued on succession planning for the Chief Executive Officer and key executive posts, with both the Board and the Appointments and Governance Committee reaffirming this as a priority for the years ahead;<br><br>An update on succession planning is now included in the agenda for each meeting of the Appointments, Governance and CSR Committee. |

The Committee has retained an external consultant to monitor and implement the succession plan.

See also the section on Succession Planning below.

Closer monitoring of the principal risks facing Sanofi

The principal risks facing Sanofi were discussed at the Board meeting of February 6, 2018 and the Audit Committee meeting of July 26, 2018.

The presentation made to the Board used detailed risk mapping to explain governance issues, active risks, mitigation strategies, and emerging risks. The following issues were addressed during the presentation:

key achievements in 2017;

Risk Committee composition and practices;

segmentation and seriousness of risks assessed in 2017;

risk identification and assessment;

Sanofi s risk profile, with a list of major risks and mitigation plans;

allocation of roles between the Executive Committee and the Risk Committee; and

a presentation of imaginable scenarios and their potential consequences.

Subsequent to that meeting, an update on risk management is now proposed systematically at each Board meeting.

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| Areas for progress and vigilance identified | Actions taken by the Board |
|---|---|
| | The issues on the agenda for the July 2018 Audit Committee meeting were:<br>changes in risk management policy during 2018 (in particular the new methodology for quantifying financial impacts);<br>review of priority risks;<br>analysis of new risks added to the risk mapping;<br>adjustments to the list of operational and financial matters to be reviewed by the Audit Committee; and<br>the two-year plan.<br>A detailed report on this meeting was presented to the Board by the Chairman of the Audit Committee. |
| Deeper understanding of changes in the industry environment (markets and competition), and the potential implications for Sanofi | A three-day Innovation Tour strategy seminar took place in Boston in March 2018, giving directors an opportunity to address various issues including: |

Deeper strategic thinking

the life sciences ecosystem in the state of Massachusetts;

biotechnology innovations, and transformative innovations in healthcare generally;

oncology;

challenges and future prospects for the US healthcare sector;

new ways of delivering therapeutic solutions to patients;

the Sanofi-Alnylam alliance;

drug pricing;

the Sanofi-Regeneron alliance; and

the history and specialties of Bioverativ.

A second strategy seminar was held in Paris in October 2018. The following issues were discussed over two days, in the presence of all Sanofi directors and representatives of the Company:

developments in strategy;

| | |
|---|---|
| | R&D;<br><br>growth accelerators;<br><br>digital trends;<br><br>business transformation; and<br><br>financial outlook. |
| | In addition, the strategic plan and proposals for investments, divestments and alliances are reviewed at meetings of the Strategy Committee. The chairman of the Committee systematically presents a detailed report on the work of the Committee to the Board (after validation by the Committee members), so that the Board is fully informed whenever it takes a decision. |
| Ex post assessment of the impact of strategic decisions, especially acquisitions | An assessment of recent strategic decisions and acquisitions will be conducted during 2019. |
| Preparation of more detailed reports by the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019); | Reports of Committee meetings are now more detailed and issued more quickly. The chairman of the Committee systematically presents those reports to the Board (after validation by the Committee members), so that the Board is fully informed whenever it takes a decision. |
| Increase in the number of executive sessions | The Board Charter was amended on March 6, 2018 to require the Board to hold at least two executive sessions a year. |

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In 2018, a formal evaluation of the Board was conducted under the direction of the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019), with assistance from the same specialist consultancy firm retained for the previous formal evaluation.

The evaluation took place over several weeks:

Appointments and Governance Committee meeting of October 30, 2018: review of the process and methodology, and appointment of consultancy firm (after a tendering process).

Board meeting of October 30, 2018: launch of the evaluation, acting on a proposal from the Appointments and Governance Committee.

November 2018 through January 2019: the evaluation was conducted using the process described below:

Distribution of a questionnaire to all directors, the main issues addressed by the questionnaire being: whether the composition of the Board is in line with Sanofi s needs; quality of background material and presentations; working practices; relevance of the resources made available to the Board and its Committees; compliance of Sanofi s corporate governance with best practice; quality and candor of discussions; composition and remit of the Committees; relations between the Board and the Executive Committee, shareholders and stakeholders; directors expectations; and personal contributions in terms of skill set and effective participation in discussions.

Review of directors responses to the questionnaire.

Appointments and Governance Committee meeting of December 18, 2018: progress report on the evaluation.

Individual interviews conducted by a consultant.

Appointments and Governance Committee meeting of February 26, 2019: presentation of results, and preparation of an executive summary including areas for progress and vigilance identified.

Board meeting of March 8, 2019: review of executive summary, and decisions on actions to be taken.

The results of the 2018 evaluation showed a positive assessment of the way in which the Board and its Committees operate. The directors observed that there had been constant progress since the previous evaluation conducted using a similar process, in 2015.

The main issues on which the directors expressed satisfaction were:

- the diversity and complementarity of the Board, with a balance of skills that generates productive and lively debate;
- the well-prepared and informative off-site strategy seminar, which helped members to gain a better understanding of Sanofi s markets and challenges, and get to know the management team;
- the Board s ability to challenge management on strategy;
- the contribution of the Scientific Committee to the work of the Board;
- the good interaction between the Board and the Committees, and the quality of the Committee s reports;
- the Board s ability to prepare succession issues;
- the dynamic between Directors, enabling the Board to operate effectively as a team.

The Board also welcomed the way in which the composition of the Board had evolved to adapt to changes in the Company s strategy and environment.

Finally, the directors judged the current governance structure (separation of the office of Chairman of the Board from that of Chief Executive Officer) to be appropriate to the Company s needs and to be working effectively.

The areas for progress and vigilance identified in the latest evaluation and formally noted by the Board were:

- deeper long-term strategic thinking in the work of the Board and the Committees;
- better follow-up on the implementation of strategic decisions through the use of a dashboard;
- more interaction with the management team, especially with Executive Committee members;
- regular scheduling of executive sessions, and preparation of more detailed reports on such sessions;

- improved presentations, especially through more concise and relevant materials, to allow more time for debate and discussions during meetings;

- better prioritization of items on the agenda for Board meetings;

- continuing to diversify the Board without increasing its size; and

- further strengthening the links between Directors, and helping new Board members to integrate by allocating them a mentor.

The evaluation also included a review of each director s contribution to the work of the Board and its Committees, which in each case was judged to have met the Company s needs and to have been in line with its expectations. More generally, the Board found that directors had once again demonstrated strong commitment and were working well together. The diversity of their competencies, expertise and profiles contributed significantly to the quality of the work done by the Board and its Committees.

**Succession planning**

The remit of the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019) includes preparing for the future of the Company s executive bodies, in particular through the establishment of a succession plan for executive officers. The Committee has a retained a specialist consultancy firm to evaluate and implement the plan.

The plan, which is systematically reviewed at meetings of the Appointments and Governance Committee (renamed the

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Appointments, Governance and CSR Committee effective March 8, 2019), addresses various scenarios:

- unplanned vacancy due to prohibition, resignation or death;
- forced vacancy due to poor performance, mismanagement or misconduct; and
- planned vacancy due to retirement or expiration of term of office.

Through its work and discussions, the Committee seeks to devise a succession plan that is adaptable to situations arising in the short, medium or long term, but which also builds in diversity in all its facets as a key factor.

Although aware that separating the offices of Chairman and Chief Executive Officer provides continuity of power, the Committee nonetheless assesses the situation of the Chairman as well as that of the executive team.

To fulfill its remit, the Appointments, Governance and CSR Committee:

- provides the Board with progress reports, in particular at executive sessions;
- co-ordinates with the Compensation Committee. In that regard, having directors that sit on both Committees is a great advantage;
- works closely with the Chief Executive Officer to (i) ensure the plan is consistent with the Company s own practices and market practices, (ii) ensure high-potential internal prospects receive appropriate support and training, and (iii) check there is adequate monitoring of key posts likely to fall vacant;
- meets with key executives as needed; and
- involves the Chief Executive Officer insofar as he has a key role in planning for his own successor, though without him directing the process.

In fulfilling their remit, Committee members are acutely conscious of confidentiality issues.

The succession plan was reviewed three times in 2018 (February 26, October 29 and December 18). Alongside the implementation of the succession plan, the situation of the Chairman was examined in detail in light of the expiration

of Serge Weinberg s term of office (the renewal of which the shareholders will be asked to approve at the Annual General Meeting of April 30, 2019). As with the Chief Executive Officer, the Chairman has a key role in planning for his own successor, though without him directing the process.

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*Composition of the Board of Directors as of December 31, 2018*

As of December 31, 2018, our Board of Directors comprised:

| Director | Age | Gender | Nationality | Number of shares held | Number of directorships in listed companies(a) | Independent | First appointed | Term expires | Years of Board service | AC | AGC | CC | SC | SciC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Serge Weinberg, Chairman of the Board | 67 | M | French | 1,636 | 1 | Yes | 2009 | 2019 AGM | 9 | | C | | C | Ö |
| Olivier Brandicourt, Chief Executive Officer | 62 | M | French | 1,000 | 1 | No | 2015 | 2022 AGM | 3 | | | | Ö | |
| Laurent Attal | 60 | M | French | 1,000 | 1 | No | 2012 | 2020 AGM | 6 | | | | Ö | Ö |
| Emmanuel Babeau | 51 | M | French | 500 | 3 | Yes | 2018 | 2022 AGM | 1 | Ö | | | | |
| Bernard Charlès | 61 | M | French | 1,000 | 2 | Yes | 2017 | 2021 AGM | 2 | | | | | |
| Claudie Haigneré | 61 | F | French | 1,000 | 1 | Yes | 2008 | 2020 AGM | 10 | | Ö | Ö | | |
| Patrick Kron | 65 | M | French | 1,000 | 4 | Yes | 2014 | 2022 AGM | 4 | | Ö | C | Ö | |
| Fabienne Lecorvaisier | 56 | F | French | 1,000 | 2 | Yes | 2013 | 2021 AGM | 5 | C | | | | |
| Melanie Lee | 60 | F | British | 1,000 | 1 | Yes | 2017 | 2021 AGM | 2 | | | | | Ö |
| Suet-Fern Lee | 60 | F | Singaporean | 1,000 | 2 | Yes | 2011 | 2019 AGM | 7 | | | | | |
| Christian Mulliez | 58 | M | French | 1,590 | 2 | No | 2004 | 2022 AGM | 14 | Ö | | Ö | | |
| Marion Palme(b) | 36 | F | German | 109 | 1 | No | 2017 | 2021 AGM | 2 | | | | | |
| Carole Piwnica | 60 | F | Belgian | 1,000 | 4 | Yes | 2010 | 2020 AGM | 8 | | | | | |
| Christian Senectaire(b) | 54 | M | French | 251 | 1 | No | 2017 | 2021 AGM | 2 | | | | | |
| Diane Souza | 66 | F | American | 1,066 | 1 | Yes | 2016 | 2020 AGM | 3 | Ö | | Ö | | |
| Thomas C. Südhof | 63 | M | American/ German | 512 | 1 | Yes | 2016 | 2020 AGM | 3 | | | | | C |

| Independent directors | Female directors | Non-French directors |
|---|---|---|
| 79% | 43% | 38% |

*AC: Audit Committee*

*AGC: Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019)*

*CC: Compensation Committee*

*SC: Strategy Committee*

*SciC: Scientific Committee*

*C: Chairman/Chairwoman*

*(a) Includes all non-executive and executive directorships held in listed companies.*

*(b) Director representing employees.*

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**Competencies of Board members**

The Board of Directors, in liaison with the Appointments and Governance Committee (renamed the Appointments, Governance and CSR Committee effective March 8, 2019), must ensure that the composition of the Board is balanced, diverse and fit for purpose.

In assessing its composition, the Board takes account of the corporate strategy and of the new challenges facing the Company, and determines whether the qualities of serving directors are sufficient for the Board to deliver on its remit.

Over the past several years, the Board has adapted its composition in line with its roadmap by:

- bringing additional scientific expertise onto the Board;
- further raising the proportion of non-French directors;
- increasing the proportion of women on the Board;
- developing its competencies in digital; and
- maintaining the level of core competencies, especially in accounting and finance.

The Board has completed an overview of the competencies currently represented. The matrix below shows a comprehensive, balanced spread of the types of competencies required, both in general terms and by reference to our strategic ambitions (the matrix shows the number of directors possessing each of those competencies)[(1)]:

*(1) The information shown excludes directors representing employees.*

The Annual General Meeting of April 30, 2019 will be asked to renew the terms of office of Serge Weinberg and Suet-Fern Lee as directors. The Annual General Meeting will also be asked to ratify the Board s decision of February 6, 2019 to co-opt Christophe Babule as a director following the resignation of Christian Mulliez as a director on the same date.

The following pages provide key information about each director individually:

- directorships and appointments held during 2018 (directorships in listed companies are indicated by an asterisk, and each director s principal position is indicated in bold);
- other directorships held during the last five years; and
- education and professional experience.

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## Serge Weinberg

| | |
|---|---|
| Date of birth: | February 10, 1951 (aged 67) |
| Nationality: | French |
| First elected: | December 2009 |
| Last reappointment: | May 2015 |
| Term expires: | 2019 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Serge Weinberg

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director and Chairman of the Board of Directors of Sanofi*,<br><br>Chairman of the Strategy Committee of Sanofi<br><br>Chairman of the Appointments and Governance Committee of Sanofi (renamed the Appointments, Governance and CSR Committee effective March 8, 2019)<br><br>Member of the Scientific Committee of Sanofi | **Chairman of Weinberg Capital Partners**<br><br>Chairman of Maremma<br><br>Manager of Alret<br><br>Weinberg Capital Partners permanent representative on the Board of ADIT<br><br>Director of Madrigall |
| | **In foreign companies**<br>None | None |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | Director of Alliance Automotive Participations SAS and Schneider Electric*<br><br>Member of the Supervisory Boards of Financière BFSA and Schneider Electric* |

Weinberg Capital Partners permanent representative on the Board of Sasa Industrie

Vice Chairman and Director of Financière Sasa

Chairman of the Supervisory Boards of Financière Climater SAS and Financière Tess SAS

Chairman of Financière Piasa and Piasa Holding

**In foreign companies**

None

Chairman of Corum (Switzerland)

**Education and professional experience**

Graduate in law, degree from the *Institut d Etudes Politiques*
Graduate of ENA (*Ecole Nationale d Administration*)

| | |
|---|---|
| **Since 2005** | **Chairman of Weinberg Capital Partners** |
| 1976-1982 | *Sous-préfet* and then Chief of Staff of the French Budget Minister (1981) |
| 1982-1987 | Deputy General Manager of FR3 (French television channel) and then Chief Executive Officer of Havas Tourisme |
| 1987-1990 | Chief Executive Officer of Pallas Finance |
| 1990-2005 | Various positions at PPR* group including Chairman of the Management Board for 10 years |
| 2006-2009 | Chairman of the Board of Accor* |
| 2005-2010 | Vice Chairman of the Supervisory Board of Schneider Electric* |

**Number of shares held**

1,636 shares

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## ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

### Olivier Brandicourt

| | |
|---|---|
| Date of birth: | February 13, 1956 (aged 62) |
| Nationality: | French |
| First elected: | April 2015 |
| Last reappointment: | May 2018 |
| Term expires: | 2022 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Olivier Brandicourt

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| Current directorships and appointments | **In French companies**<br>**Chief Executive Officer of Sanofi***<br>Chairman of the Executive Committee of Sanofi<br>Director of Sanofi<br>Member of the Strategy Committee of Sanofi<br>Chairman of Sanofi Biotechnology SAS | None |
| | **In foreign companies**<br>None | Member of the Board of Management of the Pharmaceutical Research and Manufacturers of America (PhRMA, United States)<br>Member of the Council of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA, Switzerland)<br>Member and Vice-President of the European Federation of Pharmaceutical Industries and Associations (EFPIA, Brussels)<br>Member of the National Committee on U.S.-China Relations (United States) |

Honorary Member of the Royal College of Physicians (United Kingdom)

**Past directorships expiring within the last five years**

**In French companies**

None

**In foreign companies**

None

None

Bayer Group (Germany):
Chief Executive Officer and Chairman of the Executive Committee of Bayer HealthCare AG
Member of the Executive Council of Bayer AG*
Member and Vice-Chair of the Board of Trustees of the Children s Aid Society of New York (United States)

**Education and professional experience**

Degree in Medical Mycology, Pasteur Institute, France
Masters in Human Biology, Paris XII University, France
Medical Degree with subspecialty in Infectious Diseases and Tropical Medicine, Paris V University, France

| | |
|---|---|
| **Since 2015** | **Chief Executive Officer of Sanofi*** |
| 1979-1981 | National Service with the *Office de la recherche scientifique et technique outre-mer* (ORSTOM) (Republic of Congo) |
| 1981-1987 | Research Fellow and Hospital & University Assistant in the Department of Parasitology, Tropical Medicine and Public Health at the Pitié-Salpêtrière Hospital (France) |
| 1987-2000 | Various operational and commercial positions at Warner-Lambert/Parke-Davis, including Vice-President and General Manager (1998-2000) |
| 2000-2013 | Various operational and managerial positions at Pfizer Inc.*, including member of the Executive Leadership Team (2010-2013) and President & General Manager Emerging Markets & Established Business Unit (2012-2013) |
| 2013-2015 | Chief Executive Officer and Chairman of the Executive Committee of Bayer HealthCare AG and Member of the Executive Council of Bayer AG* |

**Number of shares held**

1,000 shares

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## Laurent Attal

| | |
|---|---|
| Date of birth: | February 11, 1958 (aged 60) |
| Nationality: | French |
| First appointed: | May 2012 |
| Last reappointment: | May 2016 |
| Term expires: | 2020 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Laurent Attal

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Director of Sanofi*<br>Member of the Strategy Committee of Sanofi<br>Member of the Scientific Committee of Sanofi | Director of *Fondation d Entreprise L Oréal* |
| | **In foreign companies**<br>None | None |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | None |
| | **In foreign companies**<br>None | None |

### Education and professional experience

Doctor of medicine, dermatologist
MBA from INSEAD (*Institut Européen d Administration des Affaires*)

| | |
|---|---|
| **Since 2010** | **Vice-President General Manager Research and Innovation at L Oréal*** |
| Since 1986 | Various positions within the L Oréal* Group, including posts within the active cosmetics division and as President and Chief Executive Officer of L Oréal USA (United States) |
| Since 2002 | Member of the Executive Committee of L Oréal* |

### Number of shares held

1,000 shares

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## ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

### Emmanuel Babeau

| | |
|---|---|
| Date of birth: | February 13, 1967 (aged 51) |
| Nationality: | French |
| First elected: | May 2018 |
| Term expires: | 2022 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Emmanuel Babeau

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi*<br>Member of the Audit Committee of Sanofi | Schneider Electric Group (of which Schneider Electric SE* is the parent company)<br>Director of Schneider Electric Industries SAS<br>Member of the Supervisory Boards of Aster Capital Partners SAS and Schneider Electric Energy Access (representing Schneider Electric Industries SAS)<br>Director of Sodexo*<br>Chairman of the Audit Committee of Sodexo<br>Managing Partner of SCI GETIJ |
| | **In foreign companies**<br>None | Schneider Electric Group (of which Schneider Electric SE* is the parent company)<br>Vice Chairman and non-executive director of Aveva Group Plc.*<br>Director of AO Schneider Electric, Schneider Electric (China) Co. Ltd., Samos Acquisition Company Ltd., Schneider Electric USA Inc., Schneider Electric Holdings Inc., Carros Sensors Topco Ltd. (formerly InnoVista Sensors Topco Ltd.) |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | Schneider Electric Group (of which Schneider Electric SE* is the parent company) |

Member of the Management Board of Schneider Electric SA*

Director of Telvent GIT SA

Member of the Strategy Committee of Aster Capital Partners

Member of the Supervisory Board of Innovista Sensors SAS

**In foreign companies**

None

Schneider Electric Group (of which Schneider Electric SE* is the parent company)

Director of Invensys Ltd.

Chairman and member of the Management Board of Schneider Electric Services International Sprl.

**Education and professional experience**

Graduate of ESCP (*École Supérieure de Commerce de Paris*, 1989)

Post-graduate diploma in accounting and finance

| | |
|---|---|
| **Since 2013** | **Deputy Chief Executive Officer in charge of Finance and Legal Affairs of Schneider Electric SE*** |
| 1990-1993 | Arthur Andersen |
| 1996-2009 | Various functions within the Pernod Ricard* Group, including Chief Development Officer and Chief Financial Officer |
| 2009-2013 | Various functions within Schneider Electric SE*, including Deputy Chief Executive Officer in charge of Finance and Legal Affairs |

**Number of shares held**

500 shares(1)

*(1) Under the Board Charter, each director must be a shareholder in a personal capacity and hold at least 1,000 Sanofi shares in their own name. However, directors are allowed a period of two years in which to acquire these shares.*

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ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

## Bernard Charlès

| | |
|---|---|
| Date of birth: | March 30, 1957 (aged 61) |
| Nationality: | French |
| First elected: | May 2017 |
| Term expires: | 2021 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Bernard Charlès

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi* | **Vice-Chairman of the Board of Directors and Chief Executive Officer of Dassault Systèmes*** |
| | **In foreign companies**<br>None | Dassault Systèmes Group:<br>Chairman of the Board of Directors of Dassault Systemes Corp., Dassault Systemes SolidWorks Corp., Dassault Systemes Simulia Corp., and Centric Software Inc. (United States)<br>Chairman of the Advisory Board of Dassault Systemes 3DExcite GmbH (Germany) |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | None |
| | **In foreign companies**<br>None | Dassault Systèmes Group:<br>Chairman of the Board of Directors of Dassault Systemes Biovia Corp. and Dassault Systemes Enovia Corp. (United States), and of Dassault Systemes Canada Software Inc. (Canada)<br>Chairman of the Supervisory Board of RealTime Technology AG (Germany) |

**Education and professional experience**

Graduate of *École Normale Supérieure* engineering school, Cachan (France)

*Agrégé* and Ph.D. in mechanical engineering, majoring in automation engineering and information science

| | |
|---|---|
| **Since 2016** | **Vice-Chairman of the Board of Directors and Chief Executive Officer of Dassault Systèmes* (France)** |
| 1983-1984 | National Service as Scientific Advisor in the ministry of Defense (France) |
| 1986-1988 | Founder of the New Technology, Research and Strategy division at Dassault Systèmes* (France) |
| 1988-1994 | Head of Strategy, Research and Development at Dassault Systèmes* (France) |
| Since 1995 | Chief Executive Officer of Dassault Systèmes* (France) |
| 2005 | Knight of the *Légion d honneur* (France) |
| 2009 | Member of the *Académie des Technologies* (France) |
| 2012 | Officer of the *Légion d honneur* (France) |
| 2017 | Member of the National Academy of Engineering (United States) |

**Number of shares held**

1,000 shares

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## ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

### Claudie Haigneré

| | |
|---|---|
| Date of birth: | May 13, 1957 (aged 61) |
| Nationality: | French |
| First appointed: | May 2008 |
| Last reappointment: | May 2016 |
| Term expires: | 2020 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Claudie Haigneré

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi*<br><br>Member of the Appointments and Governance Committee of Sanofi (renamed the Appointments, Governance and CSR Committee effective March 8, 2019)<br><br>Member of the Compensation Committee of Sanofi | Director of *Fondation de l Université de Lyon*, *Fondation C-Génial*, *Fondation d Entreprise L Oréal* and *Fondation Airbus*<br><br>Member of *Académie des Technologies*, *Académie des Sports*, *Académie Nationale de l Air et de l Espace* and *Académie des Sciences de l Outre-Mer*<br><br>Director of IRIS (French Institute for International and Strategic Affairs) |
| | **In foreign companies**<br>None | None |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | Director and member of the Innovation and Technology Committee of Orange*<br><br>Chairwoman of Universcience (*Cité des Sciences et de l Industrie et Palais de la Découverte*)<br>Director of *Fondation de France*, *École Normale Supérieure*, *Campus Condorcet*, *Pôle de Recherche et d Enseignement Supérieur Hautes-Études-Sorbonne-Arts-et-Métiers* and *Fondation Lacoste* |

Chairwoman of the Board of Directors of *La Géode*

**In foreign companies**

None None

**Education and professional experience**

Rheumatologist, doctorate in sciences majoring in neurosciences

Selected in 1985 by the CNES (French National Space Center) as an astronaut candidate

| | |
|---|---|
| 1984-1992 | Rheumatologist, Cochin Hospital (Paris) |
| 1996 | Scientific space mission to the MIR space station (Cassiopée, Franco-Russian mission) |
| 2001 | Scientific and technical space mission to the International Space Station (Andromède mission) |
| 2002-2004 | Deputy Minister for Research and New Technologies in the French government |
| 2004-2005 | Deputy Minister for European Affairs in the French government |
| 2005-2009 | Adviser to the Director General of the European Space Agency |
| 2007-2011 | Vice-Chairwoman (Finance) of the IAA (International Academy of Astronautics) |
| 2010-2011 | Director of *Aéro Club de France* |
| 2010-2015 | Chairwoman of Universcience (French public-sector body) |
| 2015 | Special Adviser to the Director General of the European Space Agency |

**Number of shares held**

1,000 shares

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ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

## Patrick Kron

| | |
|---|---|
| Date of birth: | September 26, 1953 (aged 65) |
| Nationality: | French |
| First appointed: | May 2014 |
| Last reappointment: | May 2018 |
| Term expires: | 2022 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Patrick Kron

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi*<br><br>Chairman of the Compensation Committee of Sanofi<br><br>Member of the Appointments and Governance Committee of Sanofi (renamed the Appointments, Governance and CSR Committee effective March 8, 2019)<br><br>Member of the Strategy Committee of Sanofi | **Chairman of Truffle Capital SAS**<br>Director of Lafarge-Holcim*<br><br>Director of Halcor Metal Works*<br><br>Director of Bouygues*<br><br>Chairman of PKC&I SAS<br><br>Permanent representative of PKC&I on the Supervisory Board of Segula Technologies<br><br>Vice-President of the *Les Arts Florissants* choral group association |
| | **In foreign companies**<br>None | None |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | Alstom*:<br>Chairman and Chief Executive Officer<br><br>Chairman of Alstom Resources Management<br>Director of *Association Française des Entreprises Privées* (AFEP) |

**In foreign companies**

None

Alstom*:
Director and Managing Director of Alstom Asia Pte. Ltd (Singapore)

**Education and professional experience**

Degree from *École Polytechnique* and *École Nationale Supérieure des Mines de Paris*

| | |
|---|---|
| **Since 2016** | **Chairman of Truffle Capital CAS** |
| 1979-1984 | Various positions at the French Ministry of Industry, including as project officer at the *Direction régionale de l Industrie, de la Recherche et de l Environnement* (DRIRE) and in the Ministry s general directorate |
| 1984-1988 | Operational responsibilities in one of the Pechiney Group s biggest factories in Greece, then manager of the Greek subsidiary |
| 1988-1993 | Various senior operational and financial positions within the Pechiney Group |
| 1993 | Member of the Executive Committee of the Pechiney Group |
| 1993-1997 | Chairman and Chief Executive Officer of Carbone Lorraine |
| 1995-1997 | Manager of the Food and Health Care Packaging Sector at Pechiney, and Chief Operating Officer of American National Can Company in Chicago (United States) |
| 1998-2002 | Chief Executive Officer of Imerys |
| 2003-2016 | Chief Executive Officer, then Chairman and Chief Executive Officer, of Alstom* |
| Since 2016 | Chairman of PKC&I SAS |

**Number of shares held**

1,000 shares

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## ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

### Fabienne Lecorvaisier

| | |
|---|---|
| Date of birth: | August 27, 1962 (aged 56) |
| Nationality: | French |
| First appointed: | May 2013 |
| Last reappointment: | 2017 |
| Term expires: | 2021 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Fabienne Lecorvaisier

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi*<br><br>Chairwoman of the Audit Committee of Sanofi | Air Liquide Group*:<br><br>Director of Air Liquide International<br><br>Chairwoman and Chief Executive Officer of Air Liquide Finance<br><br>Director of Air Liquide Eastern Europe<br><br>Director of The Hydrogen Company |
| | **In foreign companies**<br>None | Air Liquide Group*:<br><br>Executive Vice President of Air Liquide International Corporation<br><br>Director of American Air Liquide Holdings, Inc.<br><br>Chairwoman of Air Liquide US LLC |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | Air Liquide Group*: |

Director of Air Liquide France Industries, Aqualung International, Air Liquide Welding SA and SOAEO

**In foreign companies**

None

Air Liquide Group*:

Director of Air Liquide Japon (Japan)

**Education and professional experience**

Civil engineer, graduate of *Ecole Nationale des Ponts et Chaussées*

| | |
|---|---|
| **Since July 2017** | **Executive Vice President, Chief Financial Officer and Executive Committee member of Air Liquide*** |
| 1985-1989 | Member of the Corporate Finance Department, then Mergers and Acquisitions Department of Société Générale* |
| 1989-1990 | Senior Banking Executive in charge of the LBO Department (Paris)/Corporate Finance Department (Paris and London) at Barclays |
| 1990-1993 | Assistant General Manager of Banque du Louvre, Taittinger Group |
| 1993-2007 | Various positions within Essilor* including Group Chief Financial Officer (2001-2007) and Chief Strategy and Acquisitions Officer (2007-2008) |
| Since 2008 | Chief Financial Officer and Executive Committee member of Air Liquide* |

**Number of shares held**

1,000 shares

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## Melanie Lee

| | |
|---|---|
| Date of birth: | July 29, 1958 (aged 60) |
| Nationality: | British |
| First elected: | May 2017 |
| Term expires: | 2021 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Melanie Lee

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| **Current directorships and appointments** | **In French companies**<br>Independent director of Sanofi*<br>Member of the Scientific Committee of Sanofi | None |
| | **In foreign companies**<br>None | Director of Think10 (United Kingdom) |
| **Past directorships expiring within the last five years** | **In French companies**<br>None | None |
| | **In foreign companies**<br>None | Director of Syntaxin Ltd* (United Kingdom)<br>Director of BTG plc* (United Kingdom)<br>Non-executive director of Lundbeck A/S (Denmark)<br>Director of NightstaRx Ltd. (United Kingdom) |

### Education and professional experience

Degree in Biology, University of York
Ph.D. from the National Institute for Medical Research, London

| | |
|---|---|
| **Since 2018** | **Chief Executive Officer of LifeArc (United Kingdom)** |
| 1988-1998 | Senior Biologist and subsequently Research Unit Head, Receptor Systems at Glaxo/GlaxoWellcome (United Kingdom) |
| 2004-2007 | Chairwoman of the Board of Directors of Cancer Research Technology Ltd. United Kingdom |

| | |
|---|---|
| 1998-2009 | Executive Director of Research at Celltech plc., and subsequently Executive Vice President, Research and President New Medicines at UCB Celltech (United Kingdom) |
| 2003-2011 | Deputy Chairwoman of Cancer Research U.K. United Kingdom |
| 2009-2013 | Chief Executive Officer and Director of Syntaxin Ltd.* (United Kingdom) |
| 2014 | Founder of NightstaRx Ltd. (United Kingdom) |
| 2011-2015 | Non-executive director of Lundbeck A/S (Denmark) |
| 2014-2018 | Chief Scientific Officer of BTG plc* (United Kingdom) |
| Since 2013 | Director and Consultant, Think10 (United Kingdom) |

**Number of shares held**
1,000 shares

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ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

## Suet-Fern Lee

| | |
|---|---|
| Date of birth: | May 16, 1958 (aged 60) |
| Nationality: | Singaporean |
| First appointed: | May 2011 |
| Last reappointment: | May 2015 |
| Term expires: | 2019 |
| Business address: | Sanofi 54, rue La Boétie 75008 Paris France |

### Directorships and appointments of Suet-Fern Lee

| | Within the Sanofi Group | Outside the Sanofi Group |
|---|---|---|
| Current directorships and appointments | In French companies<br>Independent director of Sanofi* | Rothschild & Co*:<br>Independent member of the Supervisory Board<br>Member of the Audit Committee |