# FORM 20-F
# 2016

SANOFI

# 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, 2016**

**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 | New York Stock Exchange |
| Ordinary shares, par value €2 per share | New York Stock Exchange (for listing purposes only) |
| 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, 2016 was:**

Ordinary shares: 1,292,022,324

**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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files).** Yes ☐ No ☐

**Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):**

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐

**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 ☒.

**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, 2016.

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

All references herein to "United States" or "US" are to the United States of America, references to "dollars" or "$" are to the currency of the United States, references to "France" are to the Republic of France, and references to "euro" and "€" are to the 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; Afrezza®, a trademark of Mannkind Corporation; Aldurazyme®, a trademark of the Joint Venture Biomarin/Genzyme LLC; Avilomics®, a trademark of Avila Therapeutics, Inc.; Cialis® OTC, a trademark of Eli Lilly; Copaxone®, a trademark of Teva Pharmaceuticals Industries; Cortizone-10®, a trademark of Johnson & Johnson (except in the United States where it is a Sanofi trademark); Fludara® and Leukine®, trademarks of Alcafleu; Flutiform®, a trademark of Jagotec AG; Gardasil® and Zostavax®, trademarks of Merck & Co.; Hexyon® and Repevax®, trademarks of Sanofi Pasteur MSD; RetinoStat® and UshStat®, trademarks of Oxford Biomedica; Spedra® and Stendra®, trademarks of Vivus Inc.; 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.; Liberty®, Liberty® Herbicide, LibertyLink® Rice 601, LibertyLink® Rice 604 and StarLink®, trademarks of Bayer; Maalox®, a trademark of Novartis in the United States, Canada and Puerto Rico; and Sculptra® a trademark of Valeant; and
- other third party trademarks such as Advantage® and Advantix®, trademarks of Bayer; Atelvia®, a trademark of Actavis in the United States; DDAVP®, a trademark of Ferring (except in the United States where it is a Sanofi trademark); Enbrel®, a trademark of Immunex in the United States and of Wyeth in other geographical areas; GLAAS®, a trademark of Immune Design; Humalog®, Humulin™, Miriopen®, Basaglar® and Kwikpen®, trademarks of Eli Lilly; iPhone® and iPod Touch®, trademarks of Apple Inc.; Lactacyd®, a trademark of Omega Pharma NV in the EU and several other European countries; Rituxan®, a trademark of Biogen Idec, Inc. in the United States and Canada, and Genentech in Japan; Squarekids®, a trademark of Kitasato Daiichi Sankyo Vaccine Co., Ltd.; Unisom® a trademark of Johnson & Johnson in certain geographical areas (except in the United States and Israel where it is a Sanofi trademark and Canada where it is a trademark of Paladin Labs, Inc.); and Yosprala®, a trademark of Pozen, Inc.

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 from QuintilesIMS (MIDAS) on Moving Annual Total September 2016, in constant euros (unless otherwise indicated), supplemented by country-specific sources.

While we believe that the IMS sales data we present below are generally useful comparative indicators for our industry, they may not precisely match the sales figures published by the companies that sell the products (including our company and other pharmaceutical companies). In particular, the rules used by IMS to attribute the sales of a product covered by an alliance or license agreement do not always exactly match the rules of the agreement.

In order to allow a reconciliation with our basis of consolidation as defined in "Item 5. Operating and Financial Review and Prospects – Presentation of Net Sales," IMS data shown in the present document have been adjusted and include:

(i) sales as published by IMS excluding Sanofi sales generated by the vaccines business, equating to the scope of our pharmaceutical operations;

(ii) IMS sales of products sold under alliance or license agreements which we recognize in our consolidated net sales but which are not attributed to us in the reports published by IMS; and

(iii) adjustments related to the exclusion of IMS sales for products which we do not recognize in our consolidated net sales but which are attributed to us by IMS.

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 forward-looking statements. 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," "forecast," "guideline," "should" 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.

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.

# 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 |
| **EMA** | European Medicines Agency |
| **EU** | European Union |
| **FDA** | US Food and Drug Administration |
| **GAVI** | Global Alliance for Vaccines and Immunisation |
| **GBU** | Global Business Unit |
| **GLP-1** | Glucagon-like peptide-1 |
| **GMP** | Good manufacturing practice |
| **HIb** | Haemophilus influenzae type b |
| **HSE** | Health, Safety and Environment |
| **IASB** | International Accounting Standards Board |
| **ICH** | International Council for Harmonization |
| **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 |
| **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 Fund |
| **US** | United States of America |
| **WHO** | World Health Organization |

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## Part I



## Part II



## Part III

# Table of contents

## Part I



## Part II



## Part III

# 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, 2016, 2015 and 2014 are included in Item 18 of this annual report.

The consolidated financial statements of Sanofi for the years ended December 31, 2016, 2015 and 2014 have been prepared in compliance with IFRS issued by the International Accounting Standards Board (IASB) and with IFRS adopted by the European Union as of December 31, 2016. 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, 2016. Sanofi reports its financial results in euros.

# SELECTED CONDENSED FINANCIAL INFORMATION

| | As of and for the year ended December 31, | | | | |
|---|---|---|---|---|---|
| *(€ million, except per share data)* | **2016** | **2015** | **2014** | **2013** | **2012[a]** |
| **IFRS Income statement data** | | | | | |
| Net sales[b] | 33,821 | 34,060 | 31,380 | 30,693 | 34,743 |
| Gross profit | 24,006 | 23,942 | 21,769 | 20,989 | 24,859 |
| Operating income | 6,534 | 5,624 | 6,064 | 4,982 | 6,430 |
| Net income excluding the held-for-exchange Animal Health business | 4,486 | 4,512 | 4,392 | 3,797 | - |
| Net income attributable to equity holders of Sanofi | 4,709 | 4,287 | 4,390 | 3,716 | 4,888 |
| **Basic earnings per share (€)[c] :** | | | | | |
| Net income excluding the held-for-exchange Animal Health business | 3.42 | 3.38 | 3.25 | 2.75 | -[a] |
| Net income attributable to equity holders of Sanofi | 3.66 | 3.28 | 3.34 | 2.81 | 3.70 |
| **Diluted earnings per share (€)[d] :** | | | | | |
| Net income attributable to equity holders of Sanofi | 3.63 | 3.25 | 3.30 | 2.77 | 3.68 |
| **IFRS Balance sheet data** | | | | | |
| Goodwill and other intangible assets | 51,166[e] | 51,583[e] | 53,740 | 52,529 | 58,265 |
| Total assets | 104,672 | 102,321 | 97,392 | 96,055 | 100,399 |
| Outstanding share capital | 2,544 | 2,603 | 2,620 | 2,641 | 2,646 |
| Equity attributable to equity holders of Sanofi | 57,554 | 58,049 | 56,120 | 56,904 | 57,352 |
| Long term debt | 16,815[e] | 13,118[e] | 13,276 | 10,414 | 10,719 |
| Cash dividend paid per share (€)[f] | 2.96[g] | 2.93 | 2.85 | 2.80 | 2.77 |
| Cash dividend paid per share ($)[f][h] | 3.12[g] | 3.19 | 3.46 | 3.86 | 3.65 |

*(a) For 2012, the lines **Net sales**, **Gross profit**, and **Operating income** include the Animal Health business. For the other periods (2013 to 2016), the net results of the Animal Health business are presented in a separate line item, **Net income/(loss) of the held-for-exchange Animal Health business**, in the consolidated income statements.*

*(b) Due to a change in accounting presentation, VaxServe sales of non-Sanofi products are included in **Other revenues** from 2016 onwards (see Notes A.5. and B.14.). The presentation of prior period **Net sales** and **Other revenues** has been amended accordingly (see Note A.5.).*

*(c) Based on the weighted average number of shares outstanding in each period used to compute basic earnings per share, equal to 1,286.6 million shares in 2016, 1,306.2 million shares in 2015, 1,315.8 million shares in 2014, 1,323.1 million shares in 2013 and 1,319.5 million shares in 2012.*

*(d) 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; i.e., 1,296.0 million shares in 2016, 1,320.7 million shares in 2015, 1,331.1 million shares in 2014, 1,339.1 million shares in 2013 and 1,329.6 million shares in 2012.*

*(e) As reported, excluding the Animal Health business clarified in the line item, **Assets held for sale or exchange and liabilities related to assets held for sale or exchange** as of December 31, 2015 and December 31, 2016.*

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

*(g) Dividends for 2016 will be proposed for approval at the annual general meeting scheduled for May 10, 2017.*

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

# 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 2011 through March 2017 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 |
|---|---|---|---|---|
| 2011 | 1.30 | 1.40 | 1.49 | 1.29 |
| 2012 | 1.32 | 1.29 | 1.35 | 1.21 |
| 2013 | 1.38 | 1.33 | 1.38 | 1.28 |
| 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 |
| Last 6 months | | | | |
| 2016 | | | | |
| September | 1.12 | 1.12 | 1.13 | 1.12 |
| October | 1.10 | 1.10 | 1.12 | 1.09 |
| November | 1.06 | 1.08 | 1.11 | 1.09 |
| December | 1.06 | 1.05 | 1.08 | 1.04 |
| 2017 | | | | |
| January | 1.08 | 1.06 | 1.08 | 1.04 |
| February | 1.06 | 1.07 | 1.08 | 1.06 |
| March[b] | 1.05 | 1.05 | 1.05 | 1.05 |

*(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 February 24, 2017, we have used European Central Bank Rates for the period from February 27, 2017 through March 2, 2017.*

*(b) In each case, measured through March 2, 2017.*

On March 2, 2017 the European Central Bank Rate was 1.05 per euro.

## *B. Capitalization and Indebtedness*

N/A

## *C. Reasons for Offer and Use of Proceeds*

N/A

## 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 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 to country. This protection may not be sufficient to maintain effective product exclusivity because of local differences in the patents, in national laws or 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.

In addition, if we lose patent protection in patent litigation 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 payed 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 obtained against the sale of generic clopidogrel during the course of the litigation.

In certain cases, to terminate or avoid patent litigation, we or our partners may be required to obtain licenses from the holders of third-party intellectual property rights that 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. We have increased the proportion of biological therapeutics in our pipeline relative to traditional small molecule pharmaceutical products. Typically, biological therapeutics face third party intellectual property rights, otherwise known as freedom to operate (FTO) issues, more than small molecule therapeutics because of the types of patents allowed 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. 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 and Item 8 B. of this annual report for more information). If third parties obtain a preliminary or permanent injunction from a court of law or if we fail to obtain a required license for a country where the valid third-party intellectual property right, as confirmed by a court of law, exists 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 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.

We have increased the proportion of biological therapeutics in our pipeline relative to traditional small molecule pharmaceutical products. 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 approved, it could reduce our sales and/or profitability of that product.

However, with our presence as a manufacturer of generics and biosimilars, we will utilize patent challenge strategies against other innovators' patents, similar to those of long-established generic companies, but 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 regards to their nature, scope and level, from the types of product liability claims that we have handled in the past. Substantial damage awards and/or settlements have been handed down – 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 pharmaceutical 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 the Company has 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 from one 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. For example, in August 2016, Sanofi submitted at the FDA's request updated information on the pen delivery device of Soliqua™ 100/33, based on feedback received from the FDA during its review of the New Drug Application for this product. This resulted in a three-month delay of the approval date.

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 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, health 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, impose marketing restrictions, or suspend or withdraw 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 FDA Warning Letters in the past following the inspection of some of our facilities and may receive such letters in the future. In 2016, manufacturing deficiencies were observed by the FDA at our "fill and finish" facility specialized in biologics in Le Trait, France, during a routine CGMP inspection, and the FDA issued a form 483 ("Inspectional Observations") listing manufacturing deficiencies. These CGMP deficiencies led the FDA to issue a Complete Response Letter in October 2016, delaying the approval of sarilumab (Kevzara™). More generally, if we fail to adequately respond to warning letters identifying a deficiency following 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, the EMA or other regulatory authorities. In addition, in order to comply with our duty to report adverse 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, 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. Approximately 60% 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 and/or 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, competition law, marketing practices, pricing and other legal matters could adversely affect our business, results of operations and financial condition.**

The marketing of our products is heavily regulated. Sanofi's business covers an extremely wide range of activities worldwide and involves numerous partners. We have adopted a Code of Ethics that calls for employees to comply with applicable legislation and regulations, as well as with the specific principles and rules of conduct set forth in that 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 and other anti-bribery laws and regulations).

Notwithstanding these efforts, deviations may occur and there can be no assurance that we, our officers and/or our

directors will not face liability under laws and regulations 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 lead to substantial liabilities 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, and data privacy legislation. Sanofi and certain of its subsidiaries are under investigation or could become the subject of additional investigations by various government entities and the Company is defending a number of lawsuits relating to pricing and marketing practices (including, for example, "whistleblower" litigation in the United States). The Company also faces 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 distracts management's attention from our business.

Unfavorable outcomes in any of these matters, or in similar matters to be faced in the future, could preclude the commercialization of 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 this could have a material adverse effect on our business, results of operations or financial condition.

These risks may encourage us to enter into settlement agreements and those 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. For example in 2015 we entered into such an agreement as part of settlements relating to the Seprafilm® and Hyalgan® products.

**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, or in their application, 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 or circumvented, our financial results could be materially and adversely affected" above).

This new competitive environment and the potential regulatory changes may further limit the exclusivity enjoyed by 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".

In addition to international tax law and regulatory changes such as the OECD BEPS initiatives and EU directives still to be adopted, 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. These changes may cover matters such as taxable income, tax rates, indirect taxation, transfer pricing, 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 the decreasing sales of our products facing expiry of patents and regulatory data exclusivity or competition from new products of

competitors that are perceived as being superior or equivalent. In 2016, we spent €5,172 million on research and development (excluding Animal Health), amounting to 15.3% 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 to build a robust pipeline and fulfill unmet medical needs. 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 take up 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 2016, four of those six key products have already been approved or launched: Toujeo®, Praluent®, Dengvaxia® and Soliqua™ 100/33 / Suliqua™. However, there can be no assurance that all (or any) of the other products will be approved, or with the targeted indications, and/or within the expected timeline, or that all the products approved will achieve commercial success.

Following each product marketing approval, 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, 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 and it may take time for Sanofi to address the 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; and
- aggressive pricing strategies by some of our competitors.

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 payer market exposes us to greater pricing pressure" below).

In the United States, the federal Affordable Care Act has increased the government's role with respect to price, reimbursement, and coverage levels for healthcare services and products within the large government healthcare sector. This law also imposed rebates and fees on pharmaceutical companies. Some US states are also considering legislation that could affect transparency practices, the marketing and prices of, and access to, drugs. US federal and state officials will continue to focus on healthcare reform in the future, creating multiple risks for the sector.

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 encounter similar 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".

We are also unable to predict the availability or level of reimbursement and related restrictions for our product candidates.

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 pricing and usage negotiations, and competition among pharmaceutical companies to have their products included in the care providers' formulary 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 example, since 2014, we have increased the level of rebates granted for Lantus® in order to maintain favorable formulary positions with key payers in the US. Despite these efforts, in 2016, CVS and UnitedHealthcare (a PBM and MCO, respectively) decided that effective January 1, 2017 and April 1, 2017, respectively, Lantus®/Toujeo® will be excluded from the formulary across the commercial and MMC (Medicaid Managed Care) template formularies covering several million people, thus reducing the potential patient populations to whom Lantus® may be prescribed.

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 Medicare patients.

In addition, distributors have increased their capacity to negotiate price and other terms as a consequence of the growing number of mergers of retail chains and distributors, resulting in consolidation of the distribution channel.

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 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. 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. With respect to biosimilars, in the United States only biosimilars that refer to an innovator drug that was approved under a Biologics License Application may be designated as interchangeable with the original biologic and only in circumstances where specific criteria are met. In many European countries, automatic substitution of biologics is officially prohibited or not recommended. Nevertheless, 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.

**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, 2016 compared with year ended December 31, 2015 – Net Sales – Pharmaceuticals segment"). Lantus® is particularly important; it was Sanofi's leading product with revenues of €5,714 million in 2016, representing 16.9% of Sanofi's net sales for the year. Lantus® is a flagship product of the Diabetes franchise. Accounting for market trends, we announced in October 2015 that we project global diabetes sales over the period from 2015 to 2018 to decline at an average annualized rate of between 4% and 8% at constant exchange rate (CER). Nevertheless our actual sales may differ from these expectations given the numerous underlying assumptions (for example the outlook for insulin glargine sales, the introduction of one or several biosimilar glargines and their penetration of the market or the market uptake of our new products).

Furthermore, 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 Lantus® to our overall performance.

Our flagship products benefit from certain intellectual property protections such as patents and exclusivity periods but patent and proprietary rights, even if they are not challenged, are subject to expiration dates. 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).

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, changes in labeling, or if a new, more effective treatment were introduced, or if there were a reduction in sales of one or more of our flagship products or in their growth, the adverse impact on our business, results of operations and financial condition could be significant.

**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. Third parties supply us with a substantial 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 to Sanofi 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 in October 2015, we voluntary recalled all Auvi-Q® (epinephrine injection, USP) marketed in the US and Canada as the product was found to potentially have inaccurate dosage delivery, which may include failure to deliver the drug. Sanofi ultimately decided to return all US and Canadian rights to the developer of Auvi-Q®. One of our newly launched products, Praluent®, is administered with an auto-injector manufactured by a third party. The success of this product will depend partially on the performance of this device.

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. 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. Effective insurance coverage for biological products in the event of contaminated batches may also be difficult to obtain 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 the Company's results of operations and financial results." below)

For example, in the US we have encountered production issues for several years which caused delays in the supply of Pentacel® vaccine starting from 2013. While the supply conditions have been improving since the end of 2016, there can be no guarantee that we will not face similar issues in the future or that we will successfully manage such issues when they arise.

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 for certain vaccines and insulin-based products is required. Failure to adhere to these requirements may result in lost product inventory.

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, which 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").

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. 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 require significant time.

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 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 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. In addition, negative publicity regarding our use, or the industry's use, of animal subjects could harm our reputation.

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

Our industry is highly collaborative, 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.

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 for the discovery, development, commercialization and manufacturing of therapies based on monoclonal antibodies. With Alnylam, we have an agreement to develop and commercialize treatments for rare genetic diseases (See "Item 4. Information on the Company – B. Business Overview – B.2. Main pharmaceutical products"). In addition we may also rely on partners to design and manufacture medical devices, notably for the administration of our products.

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 arrangements, the performance of certain key tasks or functions are the responsibility of our collaboration partners. We are therefore subject to the risk that they do not perform effectively. We are also subject to the risk that decisions may be under the control of or subject to the approval of our collaboration partners, and we may have differing views. 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 and negatively affect our results of operations.

### 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 12%, 7% and 6% of our consolidated net sales in 2016. We are also exposed to large wholesalers in other markets, particularly in Europe. An inability of one or more of these wholesalers to honor their debts to us would 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 the coming 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, 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 less effective treatments to reduce their costs. In the United States there has been an 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, as a result of the insurance coverage mandate that came into effect in the United States in 2015, some employers may seek to reduce costs by reducing or eliminating employer group healthcare plans or transferring a greater portion of healthcare costs to their employees.

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*(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.*

In certain emerging markets countries where the economy is highly dependent on oil, a decline in oil prices may impact the ability of those countries to sustain healthcare spending, which could adversely affect our sales in those countries.

Our Consumer HealthCare (CHC) 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 of non-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."

**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."

**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 information technologies. Certain key areas such as research and development, production and sales are to a large extent dependent on our information systems, including cloud-based computing, or those of third party providers, including for the storage and transfer of critical, confidential or sensitive information. We and our third-party service providers are implementing secure information technology systems for the protection of data and threat detection. However, 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.

We commercialize a number of devices using new information technologies which, if they malfunction or are compromised could lead to a risk of harm to patients (see "– Product liability claims could adversely affect our business, results of operations and financial condition" above), including the unavailability of our products.

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

We increasingly rely on social media and new technologies 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 the Company, 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. Such uses of social media and mobile technologies could have a material adverse effect on our reputation, business, financial condition and results of operations.

**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. (22.1% of its share capital as of December 31, 2016), which is listed on the 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 in particular the economic difficulties affecting Russia, Venezuela, Brazil, China and the Middle East 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 long term 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 will look 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 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" 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 towards 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. As of the end of 2016, four of those six key products have already been approved or launched: Toujeo®, Praluent®, Dengvaxia® and Soliqua™ 100/33 / Suliqua™. However there can be no assurance that all of these products will be approved, or with the targeted indications, and/or within the expected timeline or that, if approved, they will achieve commercial success. For example, we announced in July 2016 that the overall uptake of Dengvaxia® had been delayed by recent political changes and economic volatility in Latin America. Also, the level of Praluent® sales reflects the implementation of management restrictions by payers in the United States and limited market access in Europe. 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 the expected 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 ongoing simplification of our global organization through the implementation, starting from January 2016, of five global business units (GBUs) to meet significant growth objectives requires substantial attention from our management. There is no guarantee that this new 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.

Failure to successfully implement and meet our strategic objectives 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.**

We pursue a strategy of selective acquisitions, in-licensing and collaborations in order to reinforce our pipeline and portfolio. The implementation of this strategy depends on our ability to identify business development opportunities and execute them at reasonable cost and 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.

In January 2017, we completed the acquisition of Boehringer Ingelheim's consumer healthcare (CHC) business in exchange for our animal health business (Merial), but we cannot guarantee that Boehringer Ingelheim's CHC business will be successfully integrated with ours and that we will be able to retain key personnel. Also, the expected benefits of the transaction 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 regards 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, 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, competition law, marketing practices, pricing 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.

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 generics and consumer healthcare, whose business models and trade channels are different from our traditional pharmaceutical business, in particular regarding promotional efforts and trade terms.

**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. 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 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 wastes, 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.e) 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 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. 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, and to currencies in emerging markets. In 2016, 36.6% of our net sales were realized in the United States, 28.4% in Emerging Markets (including countries that are, or may in future become, subject to exchange controls or hyper-inflation), and 5% 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 New York Stock Exchange (NYSE), 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 portion of them, the depositary is allowed, at its own discretion, to sell for their benefit that right to subscribe for new shares instead of making it available to ADS holders. Also, holders of ADSs must instruct the depositary how to vote their shares. Because of this extra 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, 2016, L'Oréal held approximately 9.15% of our issued share capital, accounting for approximately 16.7% 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.*

**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 trends to date, product sales milestone #1 has not been met. There can be no assurance that the other product sales milestones will be achieved. Failure to achieve the sales milestones would have an adverse effect on the value, if any, of the CVRs (see also Note D.22.d) to the consolidated financial statements included at Item 18 of the annual report regarding the ongoing CVR Trustee Claim).

# 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 2016, our net sales were €33,821 million. This figure excludes the net sales of our Animal Health business.

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), in constant euros, on a September 2016 MAT (Moving Annual Total) basis. The data are mainly from Quintiles IMS (MIDAS), supplemented by country-specific sources: Knobloch (Mexico), GERS (France hospital channel), and HMR (Portugal). Market share data for the Consumer Healthcare business are from Nicholas Hall, June 2016 MAT.
- For our Human Vaccines (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 two principal activities: pharmaceuticals, 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 in Item 18 of this annual report). We exited the Animal Health business on January 1, 2017 when we closed a transaction with Boehringer Ingelheim (BI) in most markets to swap our Animal Health business for BI's Consumer Healthcare (CHC) business.

We invest in the following activities (see "B. Business Overview – B.1. Strategy" below): Rare Diseases, Multiple Sclerosis, Oncology, Diabetes, Cardiovascular, Established Prescription Products[1], Consumer Healthcare, Generics, and Vaccines. Unlike our Vaccines activity, which is an operating segment within the meaning of IFRS 8, our Rare Diseases, Multiple Sclerosis, Oncology, Diabetes, Cardiovascular, Established Prescription Products, Consumer Healthcare 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 both our activities (pharmaceuticals and vaccines); 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, 2016, refer to "Item 5 – Results of Operations – Year Ended December 31, 2016 Compared with Year Ended December 31, 2015".

Our pharmaceuticals activity generated net sales of €29,244 million in 2016. The most important pharmaceutical products marketed by us are described below.

- Rare Diseases: a portfolio of enzyme replacement therapies including Cerezyme® and Cerdelga® for Gaucher disease; Myozyme® and Lumizyme® for Pompe disease; Fabrazyme® for Fabry 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.
- Oncology: Jevtana®, a taxane derivative, indicated for patients with prostate cancer; Taxotere®, a taxoid representing a cornerstone therapy for several cancer types; Eloxatin®, a platinum agent, which is a key treatment for colorectal cancer; Thymoglobulin®, a broad immunosuppressive and immunomodulating agent; Mozobil®, a hematopoietic stem cell mobilizer for patients with hematologic malignancies; and Zaltrap®, a recombinant fusion protein, indicated for patients with metastatic colorectal cancer that is resistant to or has progressed following an oxaliplatin-containing regimen.
- 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-

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

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

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; and Soliqua™ 100/33 / Suliqua™, a once-daily combination of insulin glargine and lixisenatide.

- 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 prescription anti-histamine for the treatment of seasonal allergic rhinitis (hay fever) and uncomplicated hives.
- Consumer Healthcare (CHC): our CHC sales are supported by a wide range of products. On January 1, 2017, we acquired BI's CHC business in most markets except China.
- Generics: our pharmaceuticals portfolio also includes a wide range of generics. In October 2016, we announced our intention to initiate a carve-out process in order to divest our European Generics business.

Our Vaccines activity is operated through Sanofi Pasteur, and generated net sales of €4,577 million in 2016. We sell leading vaccines in five areas: pediatric vaccines, influenza vaccines, adult and adolescent booster vaccines, meningitis vaccines, and travel and endemic vaccines. At the end of December 2016, Sanofi Pasteur and MSD ended their vaccines joint venture in Europe and integrated their respective European vaccines business into their own operations.

We obtained regulatory approval for one new product in 2016: Soliqua™ 100/33 in the US. The product was also approved in the EU as Suliqua™ in January 2017.

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, and our main telephone number is +33 1 53 77 40 00. Our principal US subsidiary's office is located at 55 Corporate Drive, Bridgewater, NJ 08807; telephone: +1 (908) 981 5000.

### Main changes since 2011

On April 4, 2011, following a tender offer, we acquired control of Genzyme, a US biotechnology group headquartered in Cambridge, Massachusetts.

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

## 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 has returned to consistently 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, with the promise of genomics being realized, immuno-oncology transforming cancer treatments, big data generating new insights into disease, and digital technologies helping to transform care delivery.

At the same time, the industry faces challenges. Economic growth in emerging markets has slowed. Affordability is a key concern globally. In 2016, patient, payer, and politicians' concerns about drug prices, reimbursement, and access reached new levels, generating headlines particularly in the US and Europe. The pricing of products as varied as insulin, generics, mature products, and new cholesterol-lowering biologics all have come under scrutiny, with patient activism and social media playing a new and distinctive role. Biosimilars are now firmly part of the competitive landscape in both the US and Europe. More focused competitors are building leadership positions in their priority therapy areas.

#### Implementing the strategic roadmap

To compete and win in this market, we are implementing our 2020 strategic roadmap, announced in November 2015. We have made real progress against each of the four pillars of

that strategy in 2016: reshape the portfolio, deliver outstanding launches, sustain innovation in R&D, and simplify the organization.

### Reshape the portfolio

To reshape the portfolio, we segmented our businesses focusing on three targets: to sustain leadership, build competitive positions, and explore strategic options.

#### Sustain leadership

- **Diabetes and Cardiovascular Diseases.** We remain committed to fighting the global epidemic of diabetes and to treating cardiovascular disease, the leading cause of death globally. Our three priorities over the next few years are to develop the insulin franchise with Lantus®, Toujeo®, and Soliqua™ 100/33 / Suliqua™; strengthen our pipeline; and lead the market shift to managing diabetes outcomes. In 2016, notable product achievements included continued global momentum behind Toujeo®, approval of Soliqua™ 100/33 in the US (launched in January 2017); and ongoing early stage development of dual agonist drug candidates.

  Also in 2016, we took a substantial step forward in leading the market shift to managing diabetes outcomes by establishing Onduo, our diabetes solutions joint venture with world-class partner Verily (formerly Google Life Sciences).

  In cardiovascular, we have the opportunity to transform the management of hypercholesterolemia through Praluent®, developed jointly with Regeneron. In a challenging payer environment, we continue to work on securing access for patients to this important medication. We look forward to the results of the ODYSSEY cardiovascular outcomes study of 18,000 patients, which continues as planned after its second interim analysis in November 2016.

- **Vaccines.** Our growth will be driven by leading products in flu, pediatric combinations, and the launch of Dengvaxia®. Demand typically exceeds supply, so a key priority for us is to produce more. We are investing to secure and expand flu and pediatric capacity. To pursue their own distinct growth strategies, Sanofi Pasteur and MSD mutually agreed to end their joint vaccines operations in Europe. The change in operations took effect at the end of December 2016. To secure growth for the longer term, we are working on novel vaccines such as Meningitis combination, Fluzone® QIV HD and Clostridium difficile.

- **Rare Diseases.** We continue to sustain our market share leadership in rare genetic diseases through the patient-centered approach unique to Sanofi Genzyme, product differentiation, and market access. We continue to grow the market through screening and manufacturing expansion. We also expect to advance our strong pipeline, where four of our assets have received breakthrough or fast-track designation from the FDA.

- **Emerging Markets.** We are the pharmaceutical industry leader in emerging markets and a major multinational player in the BRIC-M countries (Brazil, Russia, India, China and Mexico).

#### Build competitive positions

- **Multiple Sclerosis.** We already have a competitive position in multiple sclerosis: since entering the market in 2012, we have built a franchise with sales of €1.7 billion in 2016. We will continue to maximize our support to these products through life cycle management in a competitive market and we intend to strengthen our portfolio.

- **Oncology.** We are rebuilding our oncology portfolio. We intend to maximize our clinical assets, particularly isatuximab, an anti-CD38 monoclonal antibody now in late stage development for multiple myeloma and SAR439684, a PD-1 inhibitor derived from our alliance with Regeneron, in development in the treatment of cutaneous squamous cell carcinoma.

- **Immunology.** We have the cornerstones of an important new franchise in immunology through sarilumab (Kevzara™) for rheumatoid arthritis and Dupixent™ in several indications including atopic dermatitis, asthma and nasal polyposis. Both drugs have been developed in collaboration with Regeneron and both are currently under regulatory review by the FDA. We aim to lead in atopic dermatitis with Dupixent™, which should be the first in class biologic to reach the market.

- **Consumer Healthcare.** On January 1, 2017, Sanofi and Boehringer Ingelheim successfully closed in most markets a transaction to swap Sanofi's animal health and BI's CHC businesses. With this transaction, we acquired BI's CHC business in all countries except China and enhanced our position in four of our strategic categories – Vitamins, Minerals and Supplements, Cough & Cold Care, Digestive Health, and Pain Care.

#### Explore strategic options

- **Animal Health.** We have exited the animal health business through the swap with BI.

- **Generics in Europe.** As announced in our 2020 strategic roadmap, we carefully reviewed all options for our European Generics business in 2016. In October 2016, we announced that we would initiate a carve-out process in order to divest this business. We will be looking for a potential acquirer that will leverage the mid and long-term sustainable growth opportunities for this business. We have also confirmed our commitment to our Generics business in other parts of the world, and will further focus on emerging markets in order to develop this business in those countries.

### Deliver outstanding launches

Our second strategic priority is to deliver outstanding launches of new medicines and vaccines. We have focused the organization on six major product launches: Toujeo®, Praluent®, Dengvaxia®, Soliqua™ 100/33, sarilumab, and Dupixent™.

Performance of these products has been mixed, as described in greater detail in "Item 5. Operating and Financial Review and Prospects – Results of Operations". In 2016, we continued the global launch and ramp-up of Toujeo® in diabetes and Praluent® for hypercholesterolemia; we also launched Dengvaxia® , the first vaccine for dengue fever, and Soliqua™ 100/33 (in January 2017), a combination of lixisenatide and insulin glargine treatment for diabetes. We received priority review from the FDA for Dupixent™ in moderate to severe atopic dermatitis.

Sanofi and Regeneron received a Complete Response Letter (CRL) from the FDA regarding the Biologics License Application (BLA) for sarilumab (Kevzara™), an investigational interleukin-6 receptor (IL-6R) antibody for the treatment of adult patients with moderately to severely active rheumatoid arthritis. For further information, see "– B.5. Global Research & Development – Pharmaceuticals" below.

### 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. Having delivered real improvements in development productivity, we are now particularly focused on improving research productivity. In 2016, we 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.

We have a number of anchor collaborations in R&D, most notably with Regeneron for monoclonal antibodies (increasingly focused on immuno-oncology) and with Alnylam for RNAi therapeutics in rare genetic diseases. Fostering these collaborations is an important part of our R&D strategy.

Our R&D investments will follow our business priorities, focusing on those businesses where we aim to sustain leadership and build competitive positions. We expect to increase our R&D investments to €6 billion annually by 2020.

### Simplify the organization

Our final strategic priority is to drive focus and simplification within our organization. In 2016, we implemented a new organizational structure, to enable us to be more closely aligned with our strategy and more effective in our execution across R&D and commercial, from global to country level. Specifically, we have created:

- Global Business Units (GBUs) integrating global franchises and country-level commercial and medical organizations for each of our major businesses: Sanofi Genzyme (specialty care); Diabetes and Cardiovascular; General Medicines and Emerging Markets (established products, generics, and all pharmaceutical sales – including Sanofi Genzyme and Diabetes and Cardiovascular – in emerging markets); Sanofi Pasteur (vaccines and infectious disease); and Consumer Healthcare.
- Centralized global functions (Finance, Human Resources, Information Technology and Solutions, etc.).
- An R&D organization organized by therapy area to align with the GBUs for late stage products.
- A global Industrial Affairs platform aligned with the GBUs.
- A strengthened Medical Affairs function, with our new Chief Medical Officer, Dr. Ameet Nathwani, now a member of the Executive Committee.

Reshaping the plant network is a second element in our program of simplification. We have continued to reshape the network to better match our evolving business by implementing a more focused approach in emerging markets, improving competitiveness and simplifying product lines. At the same time, we have continued to invest in biologics capacity to support our product launches and growth.

One of the outcomes of simplification will be a reduction in costs. To balance the need for increased resources and to partly offset lower diabetes sales expectations, we are committed to deliver at least €1.5 billion in cost savings. The savings, which we are on track to deliver, will largely be reinvested in the business.

The third element of the simplification program is to unite the different parts of the Company behind a single vision, a common set of values, and a shared culture.

## 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.

The table below shows the net sales of our main pharmaceutical products for the year ended December 31, 2016 (for more information on sales performance, see "Item 5. Operating and Financial Review and Prospects – Results of Operations").

| Franchises / Product Name | 2016 Net Sales (€ million) | Drug Category / Main Areas of Use |
|---|---|---|
| **Rare Diseases** | | |
| Cerezyme® (imiglucerase for injection) | 748 | Enzyme replacement therapy<br>• Gaucher disease |
| Myozyme®/Lumizyme® (alglucosidase alpha) | 725 | Enzyme replacement therapy<br>• Pompe disease |
| Fabrazyme® (agalsidase beta) | 674 | Enzyme replacement therapy<br>• Fabry disease |
| Aldurazyme® (laronidase) | 201 | Enzyme replacement therapy<br>• Mucopolysaccharidosis Type 1 |
| Cerdelga® (eliglustat) | 106 | Enzyme replacement therapy<br>• Gaucher disease Type 1 |
| **Multiple Sclerosis** | | |
| Aubagio® (teriflunomide) | 1,295 | Immunomodulating agent<br>• Multiple Sclerosis (MS) |
| Lemtrada® (alemtuzumab) | 425 | Humanized monoclonal antibody<br>• Multiple Sclerosis (MS) |
| **Oncology** | | |
| Jevtana® (cabazitaxel) | 358 | Cytotoxic agent<br>• Prostate cancer |
| Thymoglobulin® (anti-thymocyte globulin) | 281 | Polyclonal anti-human thymocyte antibody preparation<br>• Acute rejection in organ transplantation<br>• Aplastic anemia<br>• Graft-versus-Host Disease |
| Taxotere® (docetaxel) | 179 | Cytotoxic agent<br>• Breast cancer<br>• Non small cell lung cancer<br>• Prostate cancer<br>• Gastric cancer<br>• Head and neck cancer |
| Eloxatin® (oxaliplatin) | 170 | Cytotoxic agent<br>• Colorectal cancer |
| Mozobil® (plerixafor) | 152 | Hematopoietic stem cell mobilizer<br>• Hematologic malignancies |
| Zaltrap® (aflibercept) | 65 | Recombinant fusion protein<br>• Oxaliplatin resistant metastatic colorectal cancer |
| **Diabetes** | | |
| Lantus® (insulin glargine) | 5,714 | Long-acting analog of human insulin<br>• Type 1 and 2 diabetes |
| Toujeo® (insulin glargine 300U/mL) | 649 | Long-acting analog of human insulin<br>• Type 1 and 2 diabetes |

| Franchises / Product Name | 2016 Net Sales (€ million) | Drug Category / Main Areas of Use |
|---|---|---|
| Apidra® (insulin glulisine) | 367 | Rapid-acting analog of human insulin<br>• Type 1 and 2 diabetes |
| Insuman® (insulin) | 129 | Human insulin (rapid and intermediate acting)<br>• Type 1 and 2 diabetes |
| Lyxumia® (lixisenatide) | 33 | GLP-1 receptor agonist<br>• Type 2 diabetes |
| Soliqua™ 100/33 / Suliqua™ (insulin glargine and lixisenatide) | N/A | Type 2 diabetes |
| **Cardiovascular Diseases** | | |
| Praluent® (alirocumab) | 105 | Cholesterol-lowering drug that inhibits PCSK9<br>• Heterozygous familial hypercholesterolemia<br>• Clinical atherosclerotic cardiovascular disease |
| Multaq® (dronedarone) | 353 | Anti-arrhythmic drug<br>• Atrial Fibrillation (AF) |
| **Established Prescription Products** | | |
| Lovenox® (enoxaparin sodium) | 1,636 | Low molecular weight heparin<br>• Treatment and prevention of deep vein thrombosis<br>• Treatment of acute coronary syndromes |
| Plavix® (clopidogrel bisulfate) | 1,544 | Platelet adenosine diphosphate receptor antagonist<br>• Atherothrombosis<br>• Acute coronary syndrome with and without ST segment elevation |
| Renagel® (sevelamer hydrochloride) / Renvela® (sevelamer carbonate) | 922 | Oral phosphate binders<br>• High phosphorus levels in patients with chronic kidney disease (CKD) on dialysis |
| Aprovel® (irbesartan) / CoAprovel® (irbesartan & hydrochlorothiazide) | 681 | Angiotensin II receptor antagonist<br>• Hypertension |
| Depakine (sodium valproate) | 416 | Anti-epileptic |
| Synvisc® / Synvisc-One® (hylan G-F 20) | 408 | Viscosupplements<br>• Pain associated with osteoarthritis of the knee |
| Stilnox® / Ambien® / Myslee® (zolpidem tartrate) | 304 | Hypnotic<br>• Sleep disorders |
| Allegra® (fexofenadine hydrochloride) | 186[a] | Anti-histamine<br>• Allergic rhinitis<br>• Urticaria |
| **Consumer Healthcare** | | |
| Allegra® (range of fexofenadine HCl-based products) | 417 | Anti-histamine<br>• Allergy symptoms including sneezing |
| Doliprane® (range of paracetamol / acetaminophen-based products) | 309 | Analgesic<br>• Pain and fever |
| Enterogermina® | 159 | Probiotic<br>• Maintenance and restoration of intestinal flora |
| Essentiale® | 145 | Natural soybean remedy<br>• To improve liver health |
| **Generics** | | |
| Total | 1,854 | |

*(a) Excluding sales of self-care versions of Allegra®.*

**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 for injection) is an enzyme replacement therapy used to treat Gaucher disease, an inherited, 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® is the only therapy with a 25-year history of reducing, relieving and reversing many of the symptoms and risks of Type 1 and Type 3 (in certain markets) Gaucher disease. Cerezyme® is administered by intravenous infusion over one or two hours.

The principal markets for Cerezyme® are the US, Europe and Latin America.

**Cerdelga®**

Cerdelga® (eliglustat) is the first and only first-line oral therapy for Gaucher disease Type 1. A potent, highly specific ceramide analogue 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 switch from enzyme replacement therapy (ERT).

Cerdelga® was approved by the FDA in August 2014 and by the European Commission in January 2015; the product is now available in several European countries. It was approved in Japan in March 2015 and launched in the same year. Regulatory submissions are ongoing in other countries. The principal market for Cerdelga® is currently the US.

**Myozyme® and Lumizyme®**

Myozyme® and Lumizyme® (alglucosidase alfa) are enzyme replacement therapies used to treat Pompe disease, an inherited, progressive and often fatal LSD. Pompe disease occurs in approximately one in 40,000 newborns worldwide, but the incidence and patient severity vary among regions.

Myozyme® has been marketed since 2006 in the US and the EU and is approved in 76 countries. Outside the US, Myozyme® is marketed for patients with both infantile- and late-onset disease. Lumizyme® has been marketed in the US since June 2010. Initially designed specifically to treat patients with late-onset Pompe disease and patients over eight years of age without evidence of cardiac hypertrophy, on August 1, 2014 it was approved for infantile-onset Pompe disease.

Myozyme® and Lumizyme® are administered by intravenous infusion once every two weeks. Both products are recombinant forms of the same human enzyme.

**Fabrazyme®**

Fabrazyme® (agalsidase beta) 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 the 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 75 countries. Fabrazyme® is administered by intravenous infusion once every two weeks.

**Aldurazyme®**

Aldurazyme® (laronidase) is the first and only approved treatment for mucopolysaccharidosis type 1 (MPS 1). A human recombinant enzyme therapy with over 13 years of clinical post-marketing experience, Aldurazyme® has been shown to be safe and effective in symptomatic MPS 1 patients of all phenotypes. MPS 1 occurs in approximately one per 100,000 live births worldwide, but the incidence and patient severity vary among regions. Aldurazyme® is administered once weekly as an intravenous infusion.

**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 have been developed to treat patients with relapsing forms of MS.

**Aubagio®**

Aubagio® (teriflunomide), a small molecule immunomodulatory agent with anti-inflammatory properties, reversibly inhibits dihydroorotate dehydrogenase, a mitochondrial enzyme involved in the de novo pyrimidine synthesis required for activated lymphocytes to multiply. The exact mechanism by which teriflunomide exerts its therapeutic effect in MS is unknown but may involve a reduction in the number of activated lymphocytes in the central nervous system. Aubagio® is a once-daily oral therapy. Aubagio® has shown significant efficacy across key measures of MS disease activity, including slowing the progression of physical disability, reducing relapses, and

reducing the number of brain lesions as detected by magnetic resonance imaging (MRI). Aubagio® is the first and only oral MS therapy to significantly slow the progression of disability in two Phase III trials (TEMSO and TOWER). Consistent with its effect on slowing disability progression, Aubagio® is the only oral therapy shown to prevent or delay a second clinical attack in patients who have experienced initial neurological symptoms suggestive of MS (TOPIC trial).

Ongoing development efforts include the TeriKIDS study to assess the safety and efficacy of teriflunomide in children (10-17 years old) and global post-marketing registries for pregnancy.

Aubagio® was granted marketing authorization by the FDA in September 2012 for the treatment of patients with relapsing forms of MS, and by the European Commission in August 2013 for the treatment of adult patients with relapsing remitting MS. Aubagio® is now approved in more than 70 countries around the world. To date, more than 65,000 people have been treated with Aubagio®.

We have filed lawsuits against Watson Laboratories, Inc., Aurobindo Pharma Ltd. and Alvogen Group, Inc. alleging infringement of two patents for Aubagio®. For further information, see "Item 8. Information on Legal or Arbitration Proceedings – Aubagio® Patent Litigation".

The principal markets for Aubagio® in terms of sales are the US, Germany, France, Canada, the UK, Italy, and Spain.

**Lemtrada®**

Lemtrada® (alemtuzumab) is a humanized monoclonal antibody targeting the CD52 antigen. The exact mechanism by which alemtuzumab exerts its therapeutic effect in MS is unknown. Research suggests immunomodulatory effects through the selective depletion and repopulation of T and B lymphocytes, resulting in a resetting of the immune system. Lemtrada® is administered 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® was able to show statistically significant improvement across many key measurements of MS disease activity including improvement in physical disability, reducing relapses, and reducing the number of brain lesions as detected by MRI. Lemtrada® is the first and only approved DMT to show an improvement in six-month confirmed disability improvement (CDI) against an active comparator (CARE MS II study). Lemtrada® was also able to reduce brain volume loss over six years to levels seen in healthy controls, despite the majority of Lemtrada® patients receiving no treatment after the initial two treatment courses (extension of CARE MS I and II studies).

In September 2013, Lemtrada® was granted marketing authorization by the European Commission for treatment of adult patients with relapsing forms of MS with active disease defined by clinical or imaging features. In November 2014, the FDA approved Lemtrada® for the treatment of patients with relapsing forms of multiple sclerosis. 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. Lemtrada® is only available in the US through a restricted program called the Lemtrada® Risk Evaluation and Mitigation Strategy (REMS) Program. Lemtrada® is currently approved in more than 60 countries with additional marketing applications under review by regulatory authorities globally. To date, more than 11,800 people have been treated with Lemtrada®.

The principal markets for Lemtrada® in terms of sales are the US, the UK, Germany, Australia, Canada and Spain.

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

**c) Oncology**

**Jevtana®**

Jevtana® (cabazitaxel), a cytotoxic agent, is a semi-synthetic taxane promoting tubulin assembly and stabilizing microtubules, approved in combination with prednisone for the treatment of patients with hormone-refractory 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 now approved in over 85 countries.

The main countries contributing to sales of Jevtana® in 2016 were the US, France, Germany, Japan, Italy and Spain.

**Taxotere®**

Taxotere® (docetaxel), a taxoid class derivative, inhibits cancer cell division by essentially "freezing" the cell's internal skeleton, which is comprised of microtubules. Microtubules assemble and disassemble during a cell-division cycle. Taxotere® promotes their assembly and blocks their disassembly, thereby preventing many cancer cells from dividing, which ultimately results in destroying many cancer cells.

Taxotere® is available in more than 90 countries as an injectable solution. It has been approved for use in 11 indications in five different tumor types (breast, prostate, gastric, lung, and head and neck).

Generics of docetaxel have been launched in Europe, the US and Japan.

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

**Eloxatin®**

Eloxatin® (oxaliplatin) is a platinum-based cytotoxic agent. Eloxatin®, in combination with infusional administration of two other chemotherapy drugs, 5-fluorouracil/leucovorin (the FOLFOX regimen), is approved by the FDA for adjuvant treatment of people with stage III colon cancer who have had their primary tumors surgically removed. This approval was based on evidence of an improvement in disease-free survival after four years.

Eloxatin® is in-licensed from Debiopharm and is marketed in more than 70 countries worldwide.

Generics of oxaliplatin have been launched in Europe, the US, Canada and Japan.

**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. Thymoglobulin® is currently marketed in over 65 countries. Depending on the country, Thymoglobulin® is indicated for the treatment and/or 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.

The main countries contributing to Thymoglobulin® sales in 2016 were the US, China, France, Japan and South Korea.

**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).

**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 VEGF from binding to their native receptors. VEGF-A is one of the mediators contributing to angiogenesis. VEGF-B and PIGF, related growth factors in the VEGF family, may contribute to tumor angiogenesis as well.

The FDA approved Zaltrap® in August 2012 for use in combination with FOLFIRI (chemotherapy regimen made 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 71 countries worldwide. Zaltrap® is commercialized in collaboration with Regeneron Pharmaceuticals, Inc. For additional information, see "Item 5 – Financial Presentation of Alliances – Alliance Arrangements with Regeneron".

**d) Diabetes**

The prevalence of diabetes is expected to increase significantly by 2030, reflecting multiple socio-economic factors including sedentary lifestyles, excess weight and obesity, unhealthy diet and an aging population.

Our main diabetes products are Lantus® and Toujeo®, long acting analogs of human insulin; Apidra®, a rapid acting analog of human insulin; Insuman®, a range of human insulin; Lyxumia® (lixisenatide), a once-daily injectable prandial GLP-1 receptor agonist; and Soliqua™ 100/33 / Suliqua™, an injectable once-daily insulin glargine and lixisenatide combination.

**Lantus®**

Lantus® (insulin glargine) is a long-acting analog of human insulin, indicated for once-daily subcutaneous administration in the treatment of adult patients with type 2 diabetes who require basal insulin for the control of hyperglycemia, and for adult and pediatric patients (label extension for pediatric use was granted in the EU in 2012) aged two years and over with type 1 diabetes.

Lantus® is the most-studied basal insulin, with 16 years of clinical evidence in diabetes treatment and a well-established safety profile.

Lantus® can be administered subcutaneously using syringes or specific pens including:

- Lantus® SoloSTAR®, a pre-filled disposable pen available in over 120 countries worldwide, that combines a low injection force of up to 80 units per injection with ease of use;

- AllSTAR®, a reusable insulin pen developed specially for people with diabetes in emerging markets, indicated for use with Sanofi's insulin portfolio. AllSTAR® is currently available in a dozen countries, mostly in emerging markets.

Lantus® remains the world's no. 1 selling insulin brand in terms of both sales and units and is available in over 130 countries worldwide. The leading countries for sales of Lantus® in 2016 were the US, China, France and Germany.

A biosimilar of Lantus® from Eli Lilly and Company (Lilly) was launched in several European markets in the third quarter of 2015 (including Germany, the UK, Spain and eight other countries), and has also been launched in Japan. Lilly's insulin glargine drug, Basaglar® (as it is known in the US), was launched in the US in December 2016; it has now been launched in several countries worldwide and approved in several additional countries. On September 16, 2016, we announced that we had filed a patent infringement suit against Merck Sharp & Dohme Corp. (Merck) in the US to defend our patent rights on Lantus® and Lantus® SoloSTAR® following Merck's filing of a New Drug Application with the FDA for their insulin glargine drug product. For further information, see Item 8 – "Information on Legal or Arbitration Proceedings – Lantus® and Lantus® SoloSTAR® Patent Litigation".

**Toujeo®**

Toujeo® (insulin glargine 300 units/mL) has been granted marketing authorization by the FDA (February 2015), the European Commission (April 2015), and by the Ministry of Health, Labor and Welfare (J-MHLW) in Japan where its approved brand name is Lantus® XR (June 2015).

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 compared to Lantus® SoloSTAR®. The maximum single injection dose of 80 IU meets the needs of the vast majority of patients on basal insulin in the US, who require 80 IU or less per day.

Toujeo® has now been launched in more than 40 countries, including the US, Germany, Spain, France, the UK and Japan. Toujeo® is currently pending marketing authorization with other health authorities around the world and it is expected that additional countries including Italy, Mexico and Russia will launch Toujeo® in 2017, making this next-generation insulin glargine treatment for type 1 and type 2 diabetes widely available.

**Apidra®**

Apidra® (insulin glulisine) is a rapid-acting analog of human insulin. Apidra® is indicated for the treatment of adults with type 1 or type 2 diabetes for supplementary glycemic control. Apidra® has a more rapid onset and shorter duration of action than fast-acting human insulin and can be used in combination with long-acting insulins such as Lantus® 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.

**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.

**Lyxumia® / Adlyxin™**

Lyxumia® (lixisenatide) is a once-daily 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.

In February 2013, the European Commission granted marketing authorization in Europe for Lyxumia®. On completion of pricing and reimbursement discussions, Sanofi initiated a phased launch of Lyxumia® in most EU countries. Lixisenatide was approved by the FDA in July 2016 under the brand name of Adlyxin™ after the results of the ELIXA trial demonstrated cardiovascular safety in type 2 diabetes patients with high cardiovascular risk. Adlyxin™ availability in the US is anticipated early 2017. Lixisenatide is approved under the proprietary name Lyxumia® in more than 60 countries and marketed in over 40. Commercial launches include most EU countries, Japan, Brazil, Mexico and India. 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. It has been studied in a Phase III program of more than 1,900 patients.

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. Soliqua™ 100/33 is now available in the US

(since January 5, 2017) in a single pre-filled pen for once-daily dosing covering 15 to 60 units of insulin glargine 100 units/mL and 5 to 20 mcg of lixisenatide using SoloSTAR® technology, the most frequently used disposable insulin injection pen platform in the world.

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.

Applications for regulatory approval have also been submitted in several other countries and are being reviewed.

**Afrezza®**

Afrezza® is a rapid-acting inhaled insulin indicated to improve glycemic control in adult patients with diabetes. The product was launched in the US at the beginning of February 2015. Sanofi exercised its option to terminate the license and collaboration agreement with MannKind Corporation, the developer of Afrezza®, in January 2016 and transferred the rights for Afrezza® back to MannKind on April 4, 2016.

**Integrated Care Solutions**

This approach integrates therapeutic innovations, connected devices and technology, personalized services and support solutions, such as the My Dose Coach App which was submitted to the FDA in November 2016. In line with our partnership strategy, we have partnered with AgaMatrix to co-develop MyStar Dose Coach®, a dose helper for insulin glargine with an integrated blood glucose meter, which has obtained the CE mark.

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. The joint venture is based in Cambridge, Massachusetts (United States). Onduo's mission is to help people with diabetes live full, healthy lives by developing comprehensive solutions that combine devices, software, medicine, and professional care to enable simple and intelligent disease management.

**e) Cardiovascular Diseases**

**Praluent®**

Praluent® (alirocumab) is a human monoclonal antibody (mAb) 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.

Praluent® has been extensively studied through the ODYSSEY Phase III program with 16 global trials including more than 23,500 patients in more than 40 countries to evaluate the product's efficacy and safety across various high cardiovascular risk patients (due to but not limited to diabetes, family hypercholesterolemia or previous cardiovascular events) including patients with heterozygous familial hypercholesterolemia (HeFH), patients with primary hypercholesterolemia uncontrolled on statins and/or other lipid-modifying therapies, post acute coronary syndrome (ACS) patients and as a monotherapy for patients who are unable to tolerate an effective dose of statins.

The effect of Praluent® on cardiovascular morbidity and mortality within the post ACS patient population is being investigated in the ongoing ODYSSEY OUTCOMES trial.

Praluent® has been granted marketing authorization by the FDA (July 2015), the European Commission (September 2015) and the Japanese Ministry of Health, Labor and Welfare (J-MHLW) (July 2016). Praluent® is indicated as an adjunct to diet and maximally tolerated statin therapy in certain adult patients with uncontrolled LDL cholesterol. Praluent® is available in 75 mg and 150 mg dose injections for self-administration every two weeks.

As of December 2016, Praluent® had been approved in 44 countries and launched in 16 countries including the US, Canada, Japan, Germany, the UK, Spain, Austria, the Nordic countries, Mexico and the UAE.

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 and "Item 8. Financial Information – B. Significant changes of this annual report for more information".

**Multaq®**

Multaq® (dronedarone) is an oral multichannel blocker with anti-arrhythmic properties for prevention of atrial fibrillation recurrences. Multaq® is among the most extensively studied anti-arrhythmic drugs in atrial fibrillation: it demonstrated a unique cardiovascular outcome benefit in the ATHENA study and effective rhythm control in the EURIDIS and ADONIS studies which was confirmed in real world investigations.

In August 2016, the District Court of Delaware ruled in favor of Sanofi in the Multaq® patent litigation holding that the defendants infringe both of the patents at suit; the

'800 Formulation patent and the '167 Method of Use patent, expiring in 2018 and 2029, respectively. Both defendants appealed that ruling in September 2016. For further information, see Item 8 – "Information on Legal or Arbitration Proceedings – Multaq® Patent Litigation".

**f) 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).

Plavix® is indicated for patients with acute coronary syndrome (ACS):

- For patients with non-ST-segment elevation ACS, including unstable angina/nonQ-wave myocardial infarction, Plavix® has been shown to decrease the rate of a combined endpoint of cardiovascular death, MI or stroke, as well as the rate of a combined endpoint of cardiovascular death, MI, stroke, or refractory ischemia. This applies equally to patients who are to be managed medically, and those who are to be managed with percutaneous coronary intervention (with or without stent) or coronary artery bypass grafting.
- For patients with ST-segment elevation acute myocardial infarction, Plavix® has been shown to reduce the rate of death from any cause and the rate of a combined endpoint of death, re-infarction or stroke.

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 and other markets. In Japan, generics were launched in June 2015 for the stroke indication, in October 2015 for MI and in December 2016 for the PAD indication, the last protected indication.

Plavix® is the leading anti-platelet in the Chinese market. The main countries contributing to sales of Plavix® / Iscover® in 2016 were China and Japan.

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

**Lovenox® / Clexane®**

Lovenox® or Clexane® (enoxaparin sodium) is registered for a wider range of clinical indications than any other 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. In the prevention of venous thromboembolism, the use of Lovenox® continues to grow, particularly in prophylaxis of deep vein thrombosis (DVT) in patients hospitalized for an acute medical condition.

In the US, three enoxaparin generics have been approved in addition to our own authorized generic. In the EU, the European Commission granted marketing authorizations to two enoxaparin biosimilars in September 2016; one national marketing authorization has been granted in Poland where this biosimilar is available and other enoxaparin biosimilar dossiers are under assessment, but as of January 31, 2017 no enoxaparin biosimilars have been launched in Europe except in Poland.

Lovenox® or Clexane® is marketed in more than 100 countries. In 2016, Lovenox® was the leading injectable anti-thrombotic in all European countries.

**Aprovel® / Avapro® / Karvea®**

Aprovel® or Avapro® or Karvea® (irbesartan) is an anti-hypertensive belonging to the class of angiotensin II receptor antagonists. These highly effective and well tolerated antagonists act by blocking the effect of angiotensin II, the hormone responsible for blood vessel contraction, thereby enabling blood pressure to return to normal. In addition to Aprovel® / Avapro® / Karvea®, we also market CoAprovel® / Avalide® / Karvezide®, a fixed-dose combination of irbesartan and hydrochlorothiazide (HCTZ), a diuretic that increases the excretion of water and sodium by the kidneys and provides an additional blood pressure lowering effect.

Aprovel® and CoAprovel® tablets are available in a wide range of dosages to fit the needs of patients with different levels of hypertension severity.

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.

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

The main countries contributing to sales of Aprovel® / Avapro® / Karvea® in 2016 were China and Japan.

**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 a condition called hyperphosphatemia, or elevated phosphorus levels, which is associated with heart and bone disease. Renvela® is a second-generation buffered phosphate binder.

In the US, there are an estimated 395,000 dialysis patients, approximately 90% of whom receive a phosphate binder. There are an estimated 350,000 dialysis patients in the EU and 65,000 in Brazil. In the EU, Renvela® is also approved to treat CKD patients not on dialysis.

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.

As of January 31, 2017, there have been no approvals of generics in the US. However, we expect potential generics approvals in the US in 2017. Generics of sevelamer carbonate are currently marketed in some European countries.

The main countries contributing to sales of Renagel® and Renvela® in 2016 were the US, France, Canada, Spain and Italy.

**Allegra® / Telfast®**

Allegra® or Telfast® (fexofenadine hydrochloride) is a long-lasting (12- and 24-hour) non-sedating prescription anti-histamine for the treatment of seasonal allergic rhinitis (hay fever) and uncomplicated hives. It offers patients significant relief from allergy symptoms without causing drowsiness.

We also market Allegra-D® 12 Hour and Allegra-D® 24 Hour, anti-histamine/decongestant combination products with an extended-release decongestant for effective non-drowsy relief of seasonal allergy symptoms, including nasal congestion. This combination is marketed in Japan under the Dellegra® brand name.

Generics of most forms of Allegra® / Telfast® have been approved in our major markets.

In the US, the Allegra® family moved to over-the-counter (OTC) use in adults and children aged two and over in 2011. Allegra® was also launched on the OTC market in Japan in November 2012, though it also remains available on prescription. See "– g) Consumer Healthcare" below.

Allegra® / Telfast ® is marketed in approximately 80 countries. The largest market for prescriptions of Allegra® is Japan, where competing generics entered the market in early 2013.

**Stilnox® / Ambien® / Myslee®**

Stilnox® (zolpidem tartrate) is indicated for the short-term treatment of insomnia. Stilnox® rapidly induces sleep that is qualitatively close to natural sleep and devoid of certain side effects that are characteristic of the benzodiazepine class as a whole. Its action lasts for a minimum of six hours and it is generally well tolerated, allowing the patient to awaken without notably impaired attention, alertness or memory throughout the day.

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.

In 2016, the main countries contributing to Stilnox® / Ambien® / Myslee® sales were Japan and the US.

**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. Currently the main viscosupplementation market is for the treatment of pain associated with osteoarthritis of the knee.

Synvisc® is a triple-injection product and Synvisc-One® a single-injection product. Both are administered directly into the intra-articular space of the joint to temporarily restore synovial fluid.

In 2016, the main countries contributing to Synvisc® and Synvisc-One® sales were the US, Mexico, France, Brazil and Canada.

**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 and, in numerous countries, in the prevention of mood episodes.

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

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

**g) Consumer Healthcare**

Consumer Healthcare (CHC) became a growth platform of Sanofi in 2009. At the end of 2013, a Global CHC Division was created following the acquisition of Chattem (in 2010) and the US launch of self-care versions of Allegra® products (in 2011) that had previously been available only by prescription.

The sustained growth of our CHC business is based on three complementary development priorities:

- **Maximize the potential of existing brands** by accelerating our consumer-driven innovation processes and by geographical expansion of our portfolio. Highlights of our product launches throughout the world in 2016 include the following extensions: Aspercreme® Lidocaine Patch (US), Depura™ High Strength (Brazil), Ibupradoll® (France), Enterogermina® 4 Billion (Italy), Bio-Organics Glycemix™ (Australia) and the roll-out of Doliprane® line extensions including for example, Doliprane Orodoz™ 500 mg or Doliprane® Vitamine C.
- **Shape new categories** by enhancing our strategy of launching self-care versions of products previously available only by prescription. A license agreement signed in 2014 with Lilly granted us exclusive rights to apply for approval of Cialis® as an OTC product in the US, Europe, Canada and Australia, and to sell it in those markets on receipt of all necessary regulatory approvals and once certain patents protecting the product have expired. On February 1, 2017, we announced the FDA approval of Xyzal® Allergy 24HR as an over-the-counter (OTC) treatment for the relief of symptoms associated with seasonal and year-round allergies.
- **Pursue external growth opportunities** to reach critical scale in key countries and optimize the portfolio in priority categories. Our aim was to achieve leadership in consumer healthcare, and we have done so by completing a business swap with Boehringer Ingelheim (BI). The transaction closed in most markets on January 1, 2017. With this transaction, Sanofi acquired BI's CHC business in all countries except China. The deal enhanced our position in four of our strategic categories – Nutritionals, Cough & Cold, Digestive Health, and Pain Care – by bringing in iconic BI brands (Buscopan®, Pharmaton®, Bisolvon®, Mucosolvan®, Dulcolax®, Lysopaine®/Mucoangin®), and enabled us to achieve critical scale in key geographies.

  To drive performance and ensure the successful integration of the Sanofi and BI businesses, we have created a separate CHC Global Business Unit.

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

- Allegra® is a range of fexofenadine HCl–based products. Fexofenadine is an antihistamine for relief from allergy symptoms including sneezing, runny nose, itchy nose or throat, and itchy, watery eyes. Allegra® OTC is mainly sold in the US, and is also sold in more than 80 countries across the world.
- Nasacort® Allergy 24H is an intranasal steroid indicated for allergic rhinitis in adults and children aged 2 and older. Nasacort Allergy® 24H is sold mainly in the US.
- 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.
- No-Spa® (drotaverine hydrochloride) is an abdominal anti-spasmodic, indicated for intestinal spasms, menstrual pain and bladder spasm. No-Spa® is sold mainly in Russia and Eastern Europe.
- Enterogermina® is a probiotic in the form of a drinkable suspension in 5 ml bottles or capsules containing two billion Bacillus clausii spores and also powder sachets (six billion). Enterogermina® is indicated for the maintenance and restoration of intestinal flora in the treatment of acute or chronic intestinal disorders (in babies and adults). Enterogermina® is sold primarily in Europe and also 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. Essentiale® is sold mainly in Russia, Eastern Europe, various countries in Southeast Asia and China.
- Maalox® contains two antacids, aluminum hydroxide and magnesium hydroxide, available in various forms, for the relief of heartburn and acid indigestion (symptoms of gastroesophageal reflux). Maalox® is available in 55 countries in Europe, Latin America and Asia.
- Magne B6® is a food supplement offering a wide range of magnesium and vitamin B6 based products. The therapeutic indication is primarily relief of symptoms associated with magnesium deficiency, such as irritability, anxiety, sleep disorders and women's health issues (premenstrual syndrome and menopausal problems). Magne B6® is available primarily in Europe and Russia.

**h) Generics**

As announced in our 2020 strategic roadmap, we carefully reviewed all options for our European Generics business in 2016. In October 2016, we announced that we would initiate a carve-out process in order to divest this European Generics business. We have also confirmed our commitment to our Generics business in other parts of the world, and will further focus on emerging markets in order to develop this business in those countries.

## B.3. VACCINE PRODUCTS

Sanofi Pasteur, the vaccines division of Sanofi, offers a broad range of vaccines. In 2016, Sanofi Pasteur provided more than one billion doses of vaccines immunizing more than 500 million people across the globe against 20 serious diseases, and generated net sales of €4,577 million. Sales were favorably impacted by record sales of influenza vaccines, a strong performance from the Pediatric Combinations and Meningitis franchises, and the launch of Dengvaxia®.

Sanofi Pasteur is a world leader in the vaccine industry in terms of sales. In the US, Sanofi Pasteur is the leading producer of influenza and meningitis vaccines.

In Europe, Sanofi Pasteur's vaccine products have historically been developed and marketed by Sanofi Pasteur MSD (SPMSD), a joint venture that served 19 countries. Created in 1994 and held equally by Sanofi Pasteur and Merck & Co., Inc. (Merck), SPMSD also distributed Merck vaccines such as Gardasil® and Zostavax®. In 2016, SPMSD net sales amounted to €940 million. The vaccines market has undergone significant changes since the creation of SPMSD, leading Sanofi Pasteur and Merck to adjust their strategic priorities. Over time, the decreasing complementarity between the two companies' vaccine portfolios made the joint venture model less relevant for both parties. Consequently, Sanofi Pasteur and Merck terminated the SPMSD joint venture at the end of December 2016, reintegrating their European vaccine activities into their own operations. Sanofi Pasteur is now directly managing its portfolio, which includes the following products: primary and booster pediatric vaccines for diphtheria, tetanus, pertussis, polio and Hib such as Pediacel®, Pentavac™, Repevax®, Revaxis®, Tetravac®, and Imovax® Polio; two 6-in-1 combination pediatric vaccines marketed as Hexyon® and Vaxelis®; the influenza vaccines Vaxigrip® / Mutagrip®; travel vaccines for hepatitis A, typhoid and yellow fever marketed as Avaxim®, Typhim VI®, Stamaril® and Viatim®; and the rabies vaccines Verorab® and Imovax® Rabies.

Outside of Europe, Sanofi Pasteur continues to expand in Asia, Latin America, Africa and the Middle East. In addition, Sanofi Pasteur is a key supplier to publicly funded international markets such as UNICEF, the Pan American Health Organization (PAHO) and the Global Alliance for Vaccines and Immunization (GAVI).

See "– B.5.3. Vaccines Research and Development" below for a presentation of the Sanofi Pasteur R&D portfolio.

The table below lists net sales of vaccines by product range.

| (€ million) | 2016 Net Sales |
|---|---|
| Polio/Pertussis/Hib Vaccines | 1,495 |
| Influenza Vaccines | 1,521 |
| Meningitis/Pneumonia Vaccines | 633 |
| Adult Booster Vaccines | 417 |
| Travel and Other Endemic Vaccines | 368 |
| Dengue Vaccine | 55 |
| Other Vaccines | 88 |
| **Total Vaccines[a]** | **4,577** |

*(a) Due to a change in accounting presentation, VaxServe sales of non-Sanofi products are included in Other revenues from 2016 onwards. The presentation of prior period Net sales and Other revenues has been amended accordingly; refer to Note A.5. to our consolidated financial statements. VaxServe, a Sanofi Pasteur company, acts as US distributor for a broad portfolio of products from Sanofi Pasteur and other manufacturers, giving access to channels not otherwise served by Sanofi Pasteur.*

**a) Pediatric, Combination and Poliomyelitis (Polio) 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.

Pentaxim®, a pediatric combination vaccine protecting against diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b (Hib), was first marketed in 1997. To date, more than 260 million doses of Pentaxim® have been distributed in over 100 countries, and the vaccine has been included in the national immunization programs of more than 25 countries.

Hexaxim® is the only fully liquid, ready-to-use 6-in-1 (hexavalent) pediatric vaccine that provides protection against diphtheria, tetanus, pertussis, polio, Hib and hepatitis B. In 2013, the EMA approved this hexavalent pediatric vaccine in the EU, where it is sold under the brand name Hexyon® in Western Europe and under the brand name Hexacima™ in Eastern Europe. The rollout of this new hexavalent vaccine began in July 2013 in Germany and has since ramped up significantly, with 27 countries having launched Hexaxim® in their public or private immunization programs. 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. In

February 2016, SPMSD obtained a European license for its PR5i hexavalent combination vaccine, which will be marketed by a partnership between Sanofi Pasteur and Merck under the trademark Vaxelis®. PR5i antigens are manufactured by Sanofi Pasteur (Diphtheria, Tetanus, Pertussis (5acP) and Polio (IPV)), and by Merck (Hib and HepB).

Pentacel®, a pediatric combination vaccine protecting against five diseases (diphtheria, tetanus, pertussis, polio and Hib), was launched in the US in 2008. There has been a tight supply of Pentacel® since 2013, which has required careful supply management to meet strong market demand. Supply constraints were in place throughout 2016. However, Pentacel® supply is improving in the US.

Pediacel® is a fully liquid pentavalent vaccine protecting against diphtheria, tetanus, pertussis, polio and Hib.

Act-HIB®, for the prevention of Haemophilus influenzae type b (Hib), is also an important growth driver within the pediatric product line.

Quadracel™ is a combination vaccine against diphtheria, tetanus, pertussis and polio. It is used as a booster to be administered as the fifth dose in the primary series of vaccines, allowing children to complete the entire childhood schedule with as few injections as possible. Quadracel™ was already licensed in Canada (1997) and Australia (2002), before being licensed in the US in April 2015. On January 31, 2017, Sanofi Pasteur announced that Quadracel™ had become available in the US.

Shan5™, developed by Shantha, is a fully-liquid 5-in-1 vaccine protecting against five diseases (diphtheria, tetanus, pertussis, polio and Hepatitis B). Following improvements made to key manufacturing steps in the production of the antigen components of the vaccine, Shan5™ regained its prequalification from the WHO in May 2014 and was launched in the Indian market in the last quarter of 2014. Over 46 million doses have been delivered to customers (including UNICEF) since the relaunch of Shan5™ in 2014. Shan5™ has also been retained for the GAVI/UNICEF tender for the 2017-2019 period.

In Japan, a key milestone was achieved in July 2014 with the licensing of Squarekids®, a quadrivalent pediatric combination vaccine offering protection against diphtheria, tetanus, pertussis and polio. Squarekids® was co-developed with our partner Kitasato Daiichi Sankyo Vaccine. The commercial launch took place in December 2015.

Sanofi Pasteur is the world's leading developer and manufacturer of polio vaccines, with both oral polio vaccines (OPVs) and injectable inactivated polio vaccines (IPVs) in its portfolio. Sanofi Pasteur's polio production capacity and historic commitment have enabled us to serve as an important industrial partner in helping to achieve the goal of worldwide polio eradication. The combined use of OPVs and IPVs is expected to improve the level of protection in countries threatened by the possible resurgence of polio. In November 2013, GAVI announced its support for the introduction of IPV in the national immunization programs of the world's 71 poorest countries. The WHO expert group on immunization recommended that all countries introduce at least one dose of IPV in their routine immunization schedule by the first half of 2016. In September 2014, Nepal became the first GAVI supported country to introduce IPV. By the end of 2015, all 71 eligible countries had been approved for IPV support and 38 had completed their introductions, with the remaining countries to complete their introductions in the next several years. Sanofi Pasteur continues to partner with public health authorities, supplying much-needed vaccines and making substantial efforts to register Imovax® Polio, Shan IPV™ Polio and bivalent OPV in an impressive number of countries in record time. Sanofi Pasteur delivered 45 million doses of standalone IPVs to UNICEF for GAVI countries in 2016. As of today, polio remains endemic in three countries: Afghanistan, Pakistan and Nigeria.

**b) Influenza Vaccines**

Sanofi Pasteur is a world leader in the production and marketing of influenza vaccines, with about 200 million doses delivered in 2016. In terms of sales, 2016 was a record year for our influenza campaign. In recent years, demand for influenza vaccine has experienced strong growth in many countries, particularly in the US, Brazil and Mexico. Sanofi Pasteur expects the global demand for influenza vaccines to continue to grow within the next decade due to increased disease awareness, growth in emerging markets, and expanded recommendations by governmental and advisory bodies to be vaccinated against seasonal influenza.

Sanofi Pasteur has two distinct influenza vaccines that are sold globally, Fluzone® and Vaxigrip®, and is also focused on meeting the increasing demand for seasonal influenza vaccines through the launch of innovative vaccines. This differentiated product strategy, which is strengthening Sanofi Pasteur's leadership in the influenza market, has delivered the following products:

- Fluzone® High-Dose vaccine, launched in the US in 2010, was specifically designed to generate a more robust immune response against influenza in people aged 65 and older and provide greater protection against influenza. In November 2014, the FDA changed the prescribing information for Fluzone® High-Dose to document its superior clinical benefit compared to the standard Fluzone® dose (the high-dose vaccine was 24% more effective than standard Fluzone® in a large-scale efficacy study). In 2016, Fluzone® High-Dose continued to generate strong sales growth.
- Fluzone® Quadrivalent is a quadrivalent inactivated influenza vaccine containing two type A antigens and two type B antigens. Compared to the trivalent influenza vaccine, the addition of a second B strain to the vaccine

provides increased protection against the most prevalent circulating strains. In June 2013, Sanofi Pasteur obtained FDA authorization for Fluzone® Quadrivalent to be commercialized in the US for children aged over six months, adolescents and adults. Fluzone® Quadrivalent/FluQuadri® has since expanded its reach and is now available in 24 countries.

- Intradermal (ID) trivalent influenza vaccines (Intanza®/ IDflu®, launched in 2010 in Australia, Canada, the EU and several other countries, and Fluzone® ID launched in the US in 2011) also contribute to Sanofi Pasteur's influenza differentiation strategy. These innovative ID vaccines offer efficiency and simplicity of administration. In 2015, Fluzone® ID Quadrivalent was launched in the US.
- Vaxigrip® is a trivalent vaccine licensed in over 150 countries globally for people aged six months and over. A quadrivalent formulation of Vaxigrip® (QIV) for people aged 3 years and over was licensed in 2016, with the launch scheduled for 2017. An EU license application for Vaxigrip® QIV in the 6 to 35 months age group is expected to be submitted in 2017.

**c) Adult and Adolescent Boosters**

Many countries now recommend pertussis immunization for adolescents and adults. These recommendations, combined with immunization awareness initiatives, have led to increased pertussis vaccination rates in these populations in recent years.

Adacel®, the first trivalent adolescent and adult booster offering protection against diphtheria, tetanus and pertussis, was launched in Canada in 2000, Germany in 2002 and the US in 2005. Adacel® has expanded globally, and is now licensed in over 65 countries with over 175 million doses distributed since launch. This vaccine plays an important role in efforts to better control pertussis, by preventing the disease in adolescents and adults and reducing exposure to infants who are not immunized or only partially immunized.

Repevax® (also marketed under the trademark Adacel-Polio®) is a combination vaccine that provides the same benefits as Adacel® but also offers protection against polio. Repevax® is useful in markets that recommend adolescent and/or adult immunizations to protect against both pertussis and polio. This vaccine is licensed in more than 30 countries worldwide.

**d) Meningitis and Pneumonia Vaccines**

Sanofi Pasteur is at the forefront of the development of vaccines to prevent bacterial meningitis and in 2014 celebrated 40 years of providing meningitis vaccines. In 2005, Sanofi Pasteur introduced Menactra®, the first quadrivalent conjugate vaccine against meningococcal meningitis, which is considered the deadliest form of meningitis in the world. In 2011, the FDA granted Sanofi Pasteur a license to expand the indication of Menactra® to children as young as nine months of age. Menactra® is now indicated for people aged nine months through 55 years in the US, Canada, several Middle Eastern countries such as Saudi Arabia, and numerous other countries in all regions of the world. In most markets, a conjugated quadrivalent vaccine like Menactra® offers the best value proposition by protecting against four of the most common serogroups: A, C, Y, and W-135.

Menactra® is registered in 67 countries worldwide, with 11 years of clinical experience and over 89 million doses shipped since launch. The most recent launches in key countries include Russia, South Korea and Japan. The product once again performed strongly in 2016.

**e) Travel and Endemic Vaccines**

Sanofi Pasteur provides a wide range of travel and endemic vaccines including hepatitis A, typhoid, cholera, yellow fever, and Japanese encephalitis, as well as rabies vaccines and immunoglobulins. These vaccines and immunoglobulins 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. Sanofi Pasteur is the leader in most of the world's travel and endemic vaccine markets and benefits from long-term expertise in this domain.

In 2009, Shantha launched Shanchol®, the first oral cholera vaccine produced in India for use in children and adults. Shanchol® received WHO prequalification in 2011. In 2013, the first oral cholera vaccine stockpile (which Shanchol® is part of) was created by the WHO, to respond to outbreaks and vaccine needs in areas of heightened risk.

IMOJEV®, a Japanese encephalitis vaccine, is the most recent addition to our travel and endemic vaccines portfolio and was successfully launched in Australia and Thailand in 2012. In 2014, IMOJEV® obtained an extension of indication for use in children aged nine months and over, and obtained WHO prequalification which provides access to the product in low-income countries. IMOJEV® is being progressively rolled out in endemic countries throughout Asia.

For yellow fever, we shipped a significant part of the outbreak prevention stockpile in record time in 2016 to support our WHO/UNICEF/GAVI partners in their fight against expansion of the ongoing outbreak confirming our key role in combatting this important public health threat.

**f) Dengue**

Dengue fever constitutes a major public health and economic burden in the endemic areas of the Asia-Pacific region and in Latin America. More than 100 countries, representing nearly half of the world's population, are at risk. Over the last 50 years, the incidence of the disease has increased 30-fold, an alarming rate given there was no

specific treatment available. In response to this global threat, which can impact children, adolescents and adults, the WHO has set ambitious objectives to reduce the burden of the disease on society. One of these objectives is to reduce morbidity by 25% and mortality by 50% by 2020. Following 20 years of innovative research and collaboration with local at-risk communities and dengue scientists around the world, Sanofi Pasteur has developed a dengue vaccine candidate and embarked on a global, multinational clinical development program.

In 2014, the results of two large-scale Phase III efficacy studies conducted in 10 countries in Asia and Latin America were published in *The Lancet* and *The New England Journal of Medicine,* respectively. These studies involved 31,000 participants aged two to 16 years living in highly endemic countries. The results showed an overall efficacy against symptomatic dengue of 56.5% in Asia and 60.8% in Latin America, with a favorable safety profile during the 25-month active surveillance period. Overall, the combined results of these studies showed efficacy against all four dengue serotypes. Importantly, these studies consistently showed highly significant reductions in severe dengue and hospitalization due to dengue during the 25-month active surveillance periods (80% reduction in severe disease and 67.2% reduction in hospital cases in Asia, and 95% protection against severe dengue and 80.3% reduction in risk of hospitalization in Latin America).

Based on those results, we have continued to work closely with local health authorities in various endemic countries to bring this important vaccine to people. Dengvaxia® has been approved in 14 countries to date: Mexico, the Philippines and Brazil in December 2015; El Salvador in February 2016; Costa Rica in June 2016; Guatemala, Paraguay and Indonesia in August 2016; Peru and Thailand in September 2016; Singapore, Bolivia and Cambodia in October 2016; and Venezuela in January 2017.

Dengvaxia® has also garnered support from medical societies. A recent WHO vaccine position paper provides global vaccine and immunization recommendations for infectious diseases. The WHO vaccine position paper for dengue endorses the recommendation of the WHO Strategic Advisory Group of Experts (SAGE) on dengue, advising that countries with high dengue transmission consider introduction of the dengue vaccine as part of an integrated disease prevention strategy including vector control to effectively lower their dengue disease burden. Dengvaxia® has also received recommendations from medical societies, including the Latin American Society of Pediatric Infectious Disease and five other medical societies (three in Brazil, one in the Philippines and one in Indonesia).

Dengvaxia® has been launched in a public vaccination campaign in Parana State (Brazil), as well as in a public program targeting students in public schools in the Philippines.

### B.4. ANIMAL HEALTH

On January 1, 2017, we exited the animal health business through the Boehringer Ingelheim transaction. See "Item 5. Operating and Financial Review and Prospects – A. Operating results".

### B.5. GLOBAL RESEARCH & DEVELOPMENT

The mission of Sanofi's R&D organization is to discover and develop therapies that prevent, treat or cure diseases. Our day-to-day commitment is to respond to patients' needs and to provide them with adapted therapeutic solutions in order to improve their well-being and extend their lives.

Sanofi R&D is a global organization integrating all R&D activities across two major segments: Pharmaceuticals and Vaccines.

To carry out our mission and maximize its impact, we strive to bring innovation to patients and to build a pipeline of high value projects. Its approach is neutral to the source of innovation, whether it comes from internal research or external innovation.

Medical value, scientific quality and operational effectiveness are the three drivers that underpin the strategy. The focus is on projects that have the potential to provide the best added medical value to patients and payers and to reduce healthcare costs for society.

By using a translational medicine approach, ensuring that research hypotheses are validated in humans as early as possible, R&D can translate basic research findings into medical practice more quickly and efficiently and improve the scientific quality of our projects.

#### 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.

Seven therapeutic areas (TAs) have been rolled out:

- Diabetes
- Oncology

- Cardiovascular and Metabolism
- Immunology & Inflammation
- Multiple Sclerosis, Neurology & Ophthalmology
- Infectious Diseases
- 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 has been introduced that works across multiple disease areas and methods. This platform 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 internal 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.

Projects are assessed using two key criteria which allow management to rapidly understand how the portfolio is performing in terms of innovation, unmet medical needs, risk and value:

- relative medical value, which encompasses the extent of the unmet need, the market dynamics and the likelihood of getting satisfactory market conditions; and
- science translation, which includes the level of innovation and translatability of the science including likelihood of development success.

The clinical portfolio is the result of decisions taken during these 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

The clinical portfolio for new products can be summarized as follows as of February 8, 2017:

| | Phase I | Phase II | Phase III /registration |
|---|---|---|---|
| **Diabetes** | SAR341402<br>SAR438335 | efpeglenatide /<br>SAR493977<br>SAR425899 | SAR342434 /insulin lispro<br>sotagliflozin /SAR439954 |
| **Oncology** | SAR408701<br>SAR428926<br>SAR566658 | SAR439684 | isatuximab /SAR650984 |
| **Cardiovascular & Metabolism** | SAR247799<br>SAR407899 | SAR100842<br>SAR439152 | |
| **Immunology & Inflammation** | SAR439794<br>SAR440340 | SAR156597<br>GZ389988 | sarilumab /SAR153191<br>dupilumab /SAR231893 |
| **Multiple Sclerosis**<br>**Neurology**<br>**Ophthalmology** | GZ402668<br>SAR228810<br>UshStat® /SAR421869 | SAR422459 | |
| **Infectious diseases** | | ferroquine (combo OZ439) /SSR97193 | |
| **Rare diseases** | fitusiran/SAR439774 | olipudase alfa /<br>GZ402665<br>GZ402671 | patisiran (SAR438027)<br>GZ402666 |

Phase I studies are the first studies performed in humans, who are mainly healthy volunteers. 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

**Main compounds currently in Phase III and in the registration phase**

**SAR342434 (Insulin lispro):** The program entered Phase III in November 2014. The Phase III clinical program compares SAR342434 rapid-acting solution to Humalog® (insulin lispro, Lilly) in patients with type 1 diabetes (SORELLA 1) and patients with type 2 diabetes (SORELLA 2), also using Lantus®. The entry into Phase III followed successful completion of the Phase I study, in which SAR342434 rapid-acting solution demonstrated similar pharmacodynamic activity and pharmacokinetic exposure as compared to Humalog®. The dossier was submitted in 2016.

**Sotagliflozin (SAR439954):** new investigational oral dual inhibitor of SGLT1/2, which could be a potential treatment option for people with diabetes. The product was in-licensed from Lexicon in November 2015 and is in Phase III in the treatment of type 1 diabetes. The Phase III program in the treatment of type 2 diabetes was initiated in December 2016.

**Main products in early stage**

**Efpeglenatide (SAR439977),** a long-acting GLP1 receptor agonist derived from our license agreement with Hanmi, currently in Phase II.

**Dual GLP-1/glucagon receptor (SAR425899),** which entered Phase IIb in December 2016 for the treatment of patients with type 2 diabetes.

**Dual GLP-1/GIP receptor agonist (SAR438335),** in Phase I for the treatment of patients with type 2 diabetes.

**Rapid Acting Insulin (SAR341402),** in Phase I in the treatment of type 1 and type 2 diabetes

**Product discontinued in 2016**

**Stable glucagon analog (SAR438544),** assessed for the treatment of diabetes patients with severe hypoglycemia, was discontinued in Phase I.

### Collaborations

Sanofi Diabetes maintains a significant network of R&D collaborations with world leading academic institutions and startup companies, including collaborations with Joslin Diabetes Center (Cambridge, USA), and Gubra (a Danish biotech company specialized in gut hormone R&D). Sanofi and the Juvenile Diabetes Research Foundation (JDRF) continue to jointly fund selected innovation projects in the field of type 1 diabetes research and specifically Glucose Sensing Insulins.

Sanofi remains strongly committed to bringing integrated care to people with diabetes, and will continue to establish partnerships with a view to creating new solutions to improve patient outcomes.

Sanofi is continuing its collaboration with Evotec in an effort to develop beta cell-modulating diabetes treatments, which may reduce or even eliminate the need for insulin injections and may be a step towards a cure for type 1 diabetes.

Sanofi and Verily (formerly Google Life Sciences) have started a collaboration to improve care and outcomes for people with type 1 and type 2 diabetes. The collaboration pairs Sanofi's leadership in diabetes treatments and devices with Google's expertise in analytics, miniaturized electronics and low power chip design. This includes health indicators such as blood glucose and hemoglobin A1c levels, patient-reported information, medication regimens and sensor devices.

## b) Oncology

### Main compounds currently in Phase III

**Isatuximab (SAR650984)** is a naked chimeric immunoglobulin G1 (IgG1) monoclonal antibody (mAb) that is being developed under a license and collaboration agreement with Immunogen Inc. Isatuximab 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 (i) antibody-dependent cellular-mediated cytotoxicity (ADCC); (ii) complement-dependent cytotoxicity (CDC); (iii) antibody-dependent cellular phagocytosis (ADCP); and (iv) 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. There are eight ongoing studies in multiple myeloma, two as a single agent and five trials investigating isatuximab in combinations with (i) lenalidomide/dexamethasone, (ii) carfilzomib, (iii) pomalidomide/ dexamethasone, and (iv) cyclophosphamide/bortezomib/dexamethasone. The ICARIA-MM Phase III trial compares isatuximab in combination with pomalidomide and dexamethasone against pomalidomide and dexamethasone in patients with relapsed and refractory multiple myeloma.

### Main products in early stage

**SAR439684**, a PD-1 inhibitor derived from our alliance with Regeneron, is currently in Phase IIb to support registration in the treatment of cutaneous squamous cell carcinoma.

**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. The compound is in Phase I.

**SAR566658** is an antibody drug conjugate (ADC) loaded with a maytansinoid derivative DM4 (huDS6-SPDB-DM4) targeting CA6. CA6 is a tumor specific epitope highly expressed on some solid tumors. The Phase I program has been completed, and Phase II in the treatment of breast cancer is scheduled to start in the first quarter of 2017.

**SAR428926** is an Antibody Drug Conjugate (ADC) that binds to Lysosomal Associated Membrane Protein 1 (LAMP1), a protein localized in the lumen of the lysosomes in normal tissue and which is found aberrantly expressed at the cell surface in a number of tumor tissues. SAR428926 is expected to selectively deliver its cytotoxic to LAMP1-expressing tumor cells. The compound is in Phase I.

### Collaborations

Sanofi Oncology has a large number of collaborations and alliances to support its R&D portfolio.

In 2015, we entered into a strategic collaboration and license agreement with Regeneron focusing on cancer immunotherapy. The objective of the collaboration is to generate high value development candidates in the emerging field of immuno-oncology, providing us with an opportunity to expand and accelerate our development pipeline and build a strong position in one of the most attractive segments of the oncology market. To date SAR439684, a PD-1 inhibitor monoclonal antibody derived from this collaboration, has entered Phase II clinical development.

Also in 2015, we entered into an exclusive strategic collaboration with the German biotech company BioNTech (Mainz) in the field of active immunization. The goal of the alliance is to discover and develop messenger RNA (mRNA) therapeutics for cancer immunotherapy by leveraging the scientific expertise of the two organizations. The first clinical candidate is expected in 2017.

These two ambitious alliances have the potential to address some of the unmet medical needs that remain in cancer treatment.

Sanofi Oncology has also established various alliances with leading academic cancer centers such as Institut Gustave

Roussy, Institut Curie and the Dana Farber Cancer Institute, and with biotechnology companies like Immunogen and Evotec.

In 2016, we entered into a collaboration with Innate Pharma to develop innovative bispecific antibody formats engaging natural killer (NK) cells to kill tumor cells, and a collaboration with Warp Drive Bio to develop drugs targeting human oncogenes including RAS. Both these collaborations are in line with our ongoing commitment to the discovery and development of new cancer drugs and therapeutic strategies that will make a difference in the lives of cancer patients.

**c) Cardiovascular & Metabolism**

**Main products in early stage**

**SAR439152**, a myosin inhibitor derived from our partnership with MyoKardia, entered Phase IIa in October 2016 in the treatment of obstructive hypertrophic cardiomyopathy.

**SAR100842**, an LPA1 receptor antagonist, has completed the Phase I program in the treatment of diffuse cutaneous systemic sclerosis (dcSSc).The Phase IIa study is due to start in 2017.

**SAR407899**, a Rho-kinase inhibitor, has completed the Phase I program in the treatment of microvascular angina. The Phase IIa study is due to start in 2017.

**SAR247799**, an S1P1 agonist, entered Phase I in August 2016 in the treatment of cardiovascular diseases.

**d) Immunology & Inflammation**

**Main products in Phase III and the registration phase**

**Sarilumab (SAR153191)**, a monoclonal antibody against the Interleukin-6 Receptor derived from our alliance with Regeneron, is under development for moderate to severe rheumatoid arthritis (RA). The US Biological License Application (BLA) was submitted on October 30, 2015. On October 28, 2016, the U.S. Food and Drug Administration (FDA) issued a Complete Response Letter (CRL) regarding the Biologics License Applications (BLA) for sarilumab for the treatment of adult patients with moderately to severely active rheumatoid arthritis. The CRL refers to certain deficiencies identified during a routine good manufacturing practice inspection of the Sanofi Le Trait facility where sarilumab is filled and finished, one of the last steps in the manufacturing process. Satisfactory resolution of these deficiencies is required before the BLA can be approved. Based on review of Sanofi's responses to the FDA 483 letters as well as proposed corrective actions, the FDA has classified the Le Trait 'fill and finish' facility as "acceptable". Sanofi plans to re-submit the sarilumab BLA in the first quarter of 2017 subject to successful FDA preapproval inspection of Le Trait for dupilumab.

A European Marketing Authorization Application (MAA) was submitted on June 24, 2016 and the Japan NDA filing occurred on October 7, 2016.

In January 2017, Kevzara™ (sarilumab) was approved in Canada for the treatment of moderate to severe rheumatoid arthritis in adults.

The Global Phase III RA program (SARIL-RA) includes seven core trials enrolling more than 2,600 patients. Two pivotal RA trials (SARIL-RA-MOBILITY in methotrexate inadequate responders, assessing signs and symptoms and inhibition of structural damage; SARIL-RA-TARGET in inadequate responders to anti-TNF treatment, assessing signs and symptoms and effect on physical function) met all primary endpoints. Sarilumab was also administered as monotherapy in two studies, SARIL-RA-MONARCH and SARIL-RA-ONE.

Additional studies are:

- The SARIL-RA-EXTEND study aims to evaluate the long term safety and efficacy of sarilumab in combination with DMARDs in patients with active RA. This is an uncontrolled extension study that enrolled patients from earlier studies: MOBILITY, TARGET, ONE and ASCERTAIN (to benchmark safety against tocilizumab).
- SARIL-RA-EASY, a usability study comparing two devices: the auto-injector and the pre-filled syringe.

In addition to these international studies in adult RA:

- A Japanese program has been conducted with two Phase III studies in Japanese patients with RA (SARIL-RA-KAKEHASI and SARIL-RA-HARUKA).
- Two Phase II pediatric studies have been initiated, aimed at defining a suitable dose regimen in patients with polyarticular-course juvenile idiopathic arthritis (pJIA) and systemic juvenile arthritis (sJIA).

**Dupilumab (SAR231893)**, a monoclonal antibody against the Interleukin-4 alpha receptor, is derived from our alliance with Regeneron. Dupilumab modulates signaling of both the IL-4 and IL-13 pathways. It is currently being developed in several indications: atopic dermatitis in review, asthma in Phase III, nasal polyposis in Phase III, and eosinophilic esophagitis in Phase II.

- In **atopic dermatitis**, a submission has been filed with the FDA and accepted for priority review. The target action date is March 29, 2017. The product has also been accepted for review by the European Medicines Agency (EMA). The EMA and FDA have conditionally accepted Dupixent™ as the trade name for dupilumab.
- In **asthma**, the Phase III program consists of:
  - a randomized, double-blind, placebo-controlled, dose-ranging study to evaluate dupilumab in patients with moderate to severe uncontrolled asthma, completed in May 2015;

- a 52-week Phase III randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of dupilumab in patients with moderate to severe uncontrolled asthma; and
- an open-label extension study of dupilumab in patients with asthma who have previously participated in dupilumab asthma clinical studies.

- In **nasal polyposis,** the Phase III program consists of:
  - 24-week and 52-week controlled clinical studies of dupilumab in patients with nasal polyposis to evaluate the efficacy of dupilumab compared to placebo on a background of mometasone furoate nasal spray (MFNS) in reducing nasal congestion/obstruction (NC) severity and endoscopic nasal polyp score (NPS) in patients with bilateral nasal polyposis. In addition the studies will evaluate as key secondary endpoints the reduction in computed tomography (CT) scan opacification of the sinuses, improvement in loss of smell and patient reported quality of life, and reduction in need for steroids or surgery.
- In **eosinophilic esophagitis:** Phase II study of dupilumab in adult patients with active eosinophilic esophagitis. A randomized, double-blind, parallel, placebo-controlled study to assess the efficacy, safety and tolerability of dupilumab in this population is ongoing.

### Main products in early stage

**SAR156597** (humanized bi-specific monoclonal antibody targeting the cytokines IL-4 and IL-13) is currently in Phase IIB for the treatment of idiopathic pulmonary fibrosis and in Phase IIA for the treatment of diffuse systemic sclerosis.

**GZ389988** (TrKA) is a small molecule which inhibits binding of nerve growth factor (NGF) to its primary TrkA receptor, and is being developed as a treatment for pain resulting from osteoarthritis. The molecule entered Phase IIa in August 2016.

**SAR439794,** a TLR4 agonist, entered Phase I in September 2016 for the treatment of peanut allergy.

**SAR440340,** a human anti-IL33 monoclonal antibody derived from our alliance with Regeneron, entered Phase I

### Product discontinued in 2016

**SAR113244,** an anti-CXCR5 humanized monoclonal antibody, was discontinued in Phase I in the treatment of systemic lupus erythematosus (SLE).

#### e) Multiple Sclerosis, Neurology & Ophthalmology

**Multiple sclerosis**

- **GZ402668 (GLD52),** an IgG1 monoclonal antibody binding to CD52 (a cell surface antigen present at high levels on T and B lymphocytes) for the treatment of relapsing forms of multiple sclerosis (MS), is in Phase Ib in patients suffering from progressive MS.

**Neurology**

- **SAR228810,** an anti-protofibrillar Abeta monoclonal antibody, has completed the Phase I program in mild cognitive impairment due to Alzheimer's Disease (AD) and in mild AD. The Phase IIa study is due to start in 2017.

**Ophthalmology**

- **SAR422459,** 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.
- **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. A Phase I/IIA clinical study is ongoing.
- **Sarilumab,** the anti-IL6 receptor monoclonal antibody (also developed for rheumatoid arthritis, see above) is in Phase IIa in the treatment of non-infectious uveitis.

### Product discontinued in 2016

**SAR366234,** an EP2 receptor agonist of the prostaglandin $E_2$ (activation of which induces an increased outflow of aqueous humor outflow and a reduction of intra ocular pressure), was discontinued in Phase I.

#### f) Infectious Diseases

**Ferroquine** (OZ439) is a first in class combination for malaria, developed in collaboration with the Medicines for Malaria Venture (MMV). Ferroquine is a new 4 amino quinoline being developed for the treatment of acute uncomplicated malaria, and is active against chloroquine sensitive and chloroquine resistant Plasmodium strains. Due to its long half-life it has the potential to be part of single dose cure regimens for the treatment of both P. vivax and P. falciparum malaria. OZ439 is a synthetic peroxide antimalarial drug candidate from MMV designed to provide a single dose oral cure in humans. A Phase IIB clinical study of the combination of the two products, conducted in adults and children with P. falciparum malaria, started in July 2015 in Africa and is expected to start in the second half of 2017 in Asia.

### g) Rare Diseases

#### Main products in Phase III

**Alnylam collaboration:** In October 2012, Genzyme entered into an exclusive license agreement with Alnylam, covering the ALN-TTR programs in the Asia-Pacific-Japan region. ALN-TTR01 and ALN-TTR02 Phase I results were published in the New England Journal of Medicine in August 2013. Results showed that RNAi therapeutics targeting transthyretin (TTR) achieved rapid, dose-dependent, durable, and specific knockdown of TTR, the disease-causing protein in TTR-mediated amyloidosis (ATTR). Genzyme's exclusive territory rights for the ALN-TTR programs were extended to the rest of the world excluding North America and Western Europe on January 14, 2014. The January 2014 agreement also included exclusive rights for Sanofi to opt into future Alnylam rare disease pipeline programs including fitusiran (see early stage products) for which we exercised a regional option in September 2015 and then stepped up to a co-development, co-commercialization option on November 14, 2016.

**Patisiran (SAR438027)** (mRNA inhibition – Alnylam – ALN-TTR02). The Phase III clinical trial is ongoing in the treatment of familial amyloid polyneuropathy, with results expected in the second half of 2017.

**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 late onset Pompe disease patients.

#### Main products in early stage

**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. A Phase I/II study in the pediatric population has dosed nine out of twelve patients to date. These nine patients are in the adolescent cohort (12 years old to less than 18 years old) and child cohort (six years old to less than 12 years old). The infant cohort (birth to less than 6 years old) began enrollment in January 2017. The Phase II/III trial to support registration in the adult population started enrolling patients in 2016. To date, a total of 16 clinical trial sites have been initiated globally.

**GZ402671 (GCS Inhibitor)** is in development in several indications. A Phase II trial for the treatment of Fabry disease has entered its extension phase. A Phase II trial in Parkinson's disease patients carrying a glucerobrosidase gene (GBA) mutation (GBA-PD) started in December 2016. This is the first clinical trial in a genetic form of Parkinson's disease. The Phase II trial in Gaucher disease type 3 started in January 2017.

**Fitusiran (SAR439774 –** Alnylam (ALN-AT3): Alnylam is developing a siRNA therapeutic to treat hemophilia (A and B) using a novel approach targeting antithrombin (AT) with AT knockdown leading to increase in thrombin generation. On November 14, 2016 Sanofi Genzyme, which already had regional rights to this program under the overall alliance agreement, exercised its option to increase its rights to co-commercialization and co-development. The Phase III program is expected to start in 2017.

#### Product discontinued in 2016

**Revusiran (SAR438714)** (mRNA inhibition, Alnylam: ALN-TTRsc). This product was discontinued in Phase III in the treatment of familial amyloidotic cardiomyopathy.

### B.5.2. Vaccines

Our Human Vaccines R&D is focused on developing new prophylactic vaccines and improving existing ones.

The Sanofi Pasteur R&D portfolio includes 15 vaccines currently in advanced development as shown in the table below. The portfolio is well balanced, with seven vaccine products for novel targets and eight vaccines which are enhancements of existing vaccine products.

| PHASE I | PHASE II | PHASE III | REGISTRATION |
|---|---|---|---|
| **Respiratory Syncytial Virus*** RSV infant vaccine | **Rabies VRVg** Purified vero rabies vaccine | **VaxiGrip® QIV IM** Quadrivalent inactivated influenza vaccine (6-35 months) | **VaxiGrip® QIV IM** Quadrivalent inactivated influenza vaccine (3 years+) |
| **Herpes Simplex virus Type 2*** HSV-2 vaccine | **Fluzone® QIV HD** Quadrivalent inactivated influenza vaccine – High dose | **Clostridium difficile*** Toxoid vaccine against *Clostridium difficile* | **Dengvaxia®*** Mild-to-severe dengue fever vaccine (ongoing international registrations) |
| **Zika Virus*** Inactivated Zika vaccine | **Tuberculosis*** Recombinant subunit vaccine | **Japan Penta** DTP-Polio-Hib[(a)] Pediatric pentavalent vaccine | **PR5i** DTP-HepB-Polio-Hib[(a)] Pediatric hexavalent vaccine (US) |
| | **HIV*** Prevention of HIV infections in at-risk adults | **MenQuadTT** Second generation meningococcal ACYW conjugate vaccine | |
| | **Adacel®+** Tdap booster | | |
| | **Shan6** DTP-HepB-Polio-Hib[(a)] Pediatric hexavalent vaccine, Shantha | | |

*(a) D=Diphtheria, T=Tetanus, P=Pertussis, Hib=Haemophilus influenzae b, HepB=Hepatitis B.*
** New targets*

#### Influenza Vaccine

To sustain our global leadership in the development of influenza vaccines, our R&D efforts are focused on innovative approaches. Following up on the development of quadrivalent flu vaccines (see "B.3. Vaccine Products"), Sanofi Pasteur will continue to assess new formulations and alternative delivery systems, as well as approaches that broaden protective efficacy versus standard of care in order to address specific patient needs and offer innovative solutions for the future.

#### Meningitis Vaccine

*Neisseria meningitidis* bacteria are a leading cause of meningococcal disease in the US, Europe, the African meningitis belt and other endemic regions such as Brazil and Australia.

Sanofi Pasteur is developing a second-generation quadrivalent conjugated meningococcal vaccine. This vaccine uses an alternative technology to diptheria conjugation as currently used in the commercialized vaccine. Phase II clinical trial results have demonstrated its safety and immunogenicity. Sanofi Pasteur is continuing the development of this vaccine to suit a wider range of age groups and a flexible range of vaccination schedules. The project has advanced to Phase III.

#### Rabies Vaccine

A new generation serum-free Vero cell human rabies vaccine (VRVg, also known as VerorabVax®) is under development to allow both of our currently available human rabies vaccines, Verorab® and Imovax® Rabies, to be replaced globally by a single vaccine offering. The results of a Phase II clinical trial demonstrated the non-inferiority of VRVg versus Verorab® in pre-exposure prophylaxis. VRVg was approved in France as a line extension of Verorab® in 2011. More recent Phase II studies, conducted to license

VerorabVax® in countries where Verorab® was not previously licensed, have provided data indicating a requirement to adjust the formulation.

**Pediatric Vaccine**

Sanofi Pasteur, in partnership with Kitasato (KDSV) and Daiichi Sankyo (DS), is developing a pediatric pentavalent vaccine for the Japanese market. The vaccine includes diphtheria, tetanus, acP (DTaP) from KDSV, and inactivated polio IPV & Hib from Sanofi Pasteur. It is anticipated that this product, to be distributed by DS, will be the first pentavalent pediatric combination vaccine in the Japanese market. It would serve as a primary series and booster vaccine for Japanese children up to two years old. The project is currently in Phase III.

**PR5i (hexavalent vaccine)**

Sanofi Pasteur is co-developing with Merck & Co., Inc. (Merck) a hexavalent combination vaccine (PR5i 6-in-1 vaccine) to protect against diphtheria, tetanus, pertussis, polio, Hib and hepatitis B. A license application for this vaccine was submitted to the European Medicines Agency (EMA) by Sanofi Pasteur MSD (SPMSD) in January 2015. On December 17, 2015 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending marketing authorization for the product, to be commercialized as Vaxelis® in the European Union. On February 19, 2016, SPMSD was granted marketing authorization for Vaxelis®, which will be commercialized through a partnership of Merck and Sanofi Pasteur. A Biologics License Application was submitted to the US FDA in August 2014, and on November 2, 2015 the FDA issued a Complete Response Letter (CRL) for PR5i, which is to be commercialized through a partnership of Merck and Sanofi Pasteur. Sanofi Pasteur and Merck are currently reviewing the CRL and plan to further communicate with the FDA. PR5i is expected to be the first hexavalent vaccine in the US market.

**Shan6**:

A cost-effective, all-in-one liquid hexavalent combination vaccine (Shan6) is in development. This product, which is being developed for the Indian market and WHO pre-qualification, comprises a detoxified whole-cell pertussis component as well as diphtheria toxoid, tetanus toxoid, Haemophilus influenza type b PRP-T, inactivated poliovirus types 1, 2, and 3 and hepatitis B virus components. A Phase I/II trial was initiated in India in October 2016, and Phase III preparations are underway.

**Adacel+ (Pertussis Vaccine)**

To sustain our global leadership in the development of pertussis vaccines, our R&D efforts are focused on developing an improved Tdap (tetanus toxoid, diphtheria toxoid, and 5-component Acellular pertussis containing formulation), for use in individuals aged 10 and over in the US market.

**New Vaccine Targets**

**C.diff Toxoid** – *Clostridium difficile* (C.diff) is a major public health concern in North America and Europe. In hospitals, it is the leading cause of infectious diarrhea in adults, particularly the elderly. The epidemiology of C.diff associated disease has been increasing at a worrying rate since 2003, driven primarily by the emergence of a treatment-resistant, highly virulent strain: CD027. There is currently no vaccine available and our toxoid based C.diff vaccine is the only candidate in Phase III. Sanofi Pasteur received a positive response from the FDA Center for Biologics Evaluation & Research (CBER) on the Fast Track Development Program submission in 2010. A multinational, large scale Phase III study, named Cdiffense™, began in August 2013. This trial is focused on evaluating the vaccine's efficacy in preventing the first episode of C.diff infection in at-risk individuals, including adults with imminent hospitalization or current or impending residence in a long-term care or rehabilitation facility. We voluntarily paused enrollment in the trial in July, 2016 while the data were thoroughly examined and assessed by the Independent Data Monitoring committee (IDMC). In December 2016 the IDMC recommended that the trial continue. We are currently in the process of seeking regulatory approval from the many countries where the trial is in progress to reinitiate enrolling more volunteers. Importantly, the trial did not stop and the existing volunteers continued to maintain protocol-specified visits. Phase II results were communicated in May 2014 showing the C.diff vaccine candidate to be generally well tolerated and immunogenic in the target population.

**Tuberculosis** – Statens Serum Institute (SSI) of Denmark has granted Sanofi Pasteur a license to its technology for the use of certain fusion proteins in the development of a tuberculosis vaccine. The candidate vaccine is made up of recombinant protein units. Results from a 2008 Phase I trial found that the candidate vaccine was safe when administered to healthy adults living in a region of high endemic tuberculosis. A Phase I/II study in infants was initiated in South Africa in July 2013. A Phase II proof of concept study was initiated in young adolescents in South Africa in March 2014. Results are expected in 2018.

**Herpes Simplex Virus** – Herpes simplex virus type 2 is a member of the herpes virus family and as such establishes life-long infections, with latent virus established in neural ganglia. Although antivirals currently exist to treat infections, no vaccine exists, greatly limiting options in disease management. The vaccine candidate is a live attenuated virus and is being assessed as a therapeutic and possibly prophylactic vaccine to reduce recurrence and transmission. A Phase I trial, sponsored by the US National Institutes of

Health (NIH), was initiated in October 2013 to evaluate the vaccine. In October 2014, Sanofi Pasteur signed a contract with Immune Design Corp. to collaborate on the development of a therapeutic herpes simplex virus vaccine.

**HIV**: Existing treatments for HIV are able to extend the life-span of an infected individual but unable to cure the disease. Prevention is considered a key approach to abating the HIV pandemic by reducing new infection. Prevention through the use of a prophylactic vaccine still remains an important unmet medical need. Due to the enormity of the disease burden in developing countries and the potential for initial licensing of an efficacious vaccine in the developing world, Sanofi Pasteur is working in a "pox-protein public-private partnership" (P5) to document efficacy of a pox-protein based HIV prophylactic vaccine in the Republic of South Africa. Specifically, following the modest success of RV144 (the first trial to show supporting evidence that vaccines could lower the risk of contracting HIV), the P5 partnership adopted a pox-protein based vaccine candidate as potentially providing greater protection for South Africa and conducted a Phase I/II study (HVTN 100). This study met all pre-specified safety and immunogenicity criteria and supported moving the vaccine regimen to a pivotal efficacy study (HVTN702), which started on October 26, 2016 in South Africa and will continue until 2021. HVTN702 will not only assess the vaccine's safety and efficacy, it will also help in discovering immune correlates of protection.

**RSVi**: Respiratory Syncytial Virus (RSV) is the most common cause of bronchiolitis in young children. Globally, RSV accounts for 22%-40% of lower tract respiratory illnesses, 50%-90% of bronchiolitis cases and 19%-40% of pneumonia cases, and causes up to 199,000 deaths each year. It is estimated that in the US alone, about 172,000 RSV hospitalizations occur each year in children under 5 years of age, resulting in significant health care costs. Sanofi Pasteur has signed a Cooperative Research and Development Agreement (CRADA) with the US NIH to develop a live attenuated RSV vaccine for routine immunization in infants aged 4 months and older. The lead candidate(s) are currently under Phase 1a evaluation and scheduled to enter Phase 1b evaluation by end of 2017.

**Zika**: Sanofi Pasteur entered into a Cooperative Research and Development Agreement (CRADA) with the Walter Reed Army Institute of Research (WRAIR) on a Zika vaccine project in 2016, under which WRAIR is transferring its Zika purified inactivated virus (ZPIV) vaccine technology to Sanofi Pasteur. The Biomedical Advanced Research and Development Authority (BARDA) of the US Department of Health and Human Services has agreed to provide $43.2 million in funding for the manufacture of the inactivated Zika vaccine and the Phase I-II clinical trials. WRAIR and NIAID are conducting a series of Phase I ZPIV trials while the technology is transferred to Sanofi Pasteur.

Sanofi Pasteur committed to researching and developing a vaccine to prevent Zika shortly after the World Health Organization declared an emergency last year, and believes that coordination among researchers, developers, manufacturers, regulatory agencies, the WHO, national health authorities, governments and non-governmental agencies is essential to combat public health emergencies. The inactivated Zika virus candidate entered Phase I in October 2016, and we are scheduled to enter Phase II with Sanofi Pasteur produced material by early 2018.

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

Expenditures on research and development amounted to €5,172 million in 2016, comprising €4,618 million in the Pharmaceuticals segment and €554 million in Human Vaccines. Research and development expenditures were the equivalent of about 15.3% of net sales in 2016, compared to about 14.9% in 2015 and in 2014. The stability in R&D expenditure as a percentage of sales over the past three years is attributable to active management of the portfolio and close cost control, and has been achieved despite a greater proportion of products being in late stage development. Preclinical research in the pharmaceutical segment amounted to €1,094 million in 2016 compared to €1,072 million in 2015 and €986 million in 2014. Of the remaining €3,523 million relating to clinical development in the Pharmaceuticals segment (€3,458 million in 2015 and €3,188 million in 2014), the largest portion was generated by Phase III or post-marketing studies, reflecting the cost of monitoring large scale clinical trials.

For each of our current late stage (Phase III in 2016) compounds in the Pharmaceuticals segment, we set out below the date at which this compound entered into Phase III development, information concerning any compound patent in the principal markets for innovative pharmaceutical products (the US, the EU and Japan) as well as comments regarding significant future milestones that are reasonably determinable at this date. Because the timing of such milestones typically depends on a number of factors outside of our control (such as the time to validate study protocols and recruit subjects, the speed with which endpoints are realized, as well as the substantial time taken by regulatory review) it is frequently not possible to provide such estimates, and any such estimates as are given should be understood to be indicative only. See also "Item 3. Key Information – D. Risk Factors – Risks Relating to Our Business".

| Phase III | Entry into Phase III[a] | Compound Patent Term[b] | | | Comments |
|---|---|---|---|---|---|
| | (month/year) | US | EU | Japan | |
| SAR342434 insulin lispro | November 2014 | N/A | N/A | N/A | Phase III program in Type 1 & 2 diabetes completed<br>Dossier submitted |
| sotagliflozin (SAR439954) | November 2015 | 2028 | 2027 | 2027 | Phase III program ongoing in Type 1 & 2 diabetes. |
| sarilumab (SAR153191) | August 2011 | 2028 | 2027 | 2027 | First approval in Canada on January 12, 2017 in Rheumatoid Arthritis<br>Submitted in US in October 2015, and accepted for review in January 2016<br>Submission in EU in June 2016 and validated for review in July 2016 |
| dupilumab (SAR231893) | October 2014 | 2027 | 2029 | 2029 | Atopic Dermatitis: Submitted in US and accepted for priority review, expected approval date is March 2017. Submitted in EU and accepted for review.<br>Phase III program in Asthma & Nasal polyposis ongoing. |
| patisiran (SAR438027) | December 2013 | 2029 | 2029 | 2029 | Phase III program ongoing in Familial Amyloid Polyneuropathy. |
| GZ402666 | November 2016 | 2029 | 2028 | 2028 | Phase III program ongoing in Pompe Disease |
| isatuximab (SAR650984) | December 2016 | 2028 | 2027 | 2027 | Phase III program ongoing in multiple myeloma |

*(a) First entry into Phase III in any indication.*
*(b) Subject to any future supplementary protection certificates and patent term extensions.*

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 in many cases may provide more 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 2016, 2015, and 2014 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 2016 MAT (Moving Annual Total) basis. The data are mainly from QuintilesIMS (MIDAS), supplemented by country-specific sources: Knobloch (Mexico), GERS (France hospital channel), and HMR (Portugal). Market share data for the Consumer Healthcare business are from Nicholas Hall, June 2016 MAT. 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. 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. Sanofi is the fifth largest pharmaceutical company in China.
- The US: we rank eleventh with a market share of 3.9% (3.9% in 2015).

- Europe: we are the second largest pharmaceutical company in France where our market share is 7.5% (7.8% in 2015), and we rank third in Germany with a 4.6% market share.
- Other countries: our market share in Japan is 2.0% (2.7% in 2015).

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, 2016 Compared with Year Ended December 31, 2015."

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.

We use a range of channels from in-person to digital to disseminate information about and promote our products among healthcare professionals and patients, 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 advertise in medical journals and 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. As of December 31, 2016, we had a global sales force of 30,815 people excluding the Animal Health business.

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."

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.

### 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 in Item 18 of this annual report.

Sanofi is the sixth largest pharmaceutical company globally by sales. 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; Lilly in diabetes and oncology; Bristol-Myers Squibb in oncology; Novartis in diabetes, multiple sclerosis, and oncology; Shire in rare diseases; Pfizer in rare diseases and oncology; Biogen, Teva and Merck Serono in multiple sclerosis; Bayer in multiple sclerosis and oncology; Roche and Johnson & Johnson in oncology; AstraZeneca in diabetes, cardiovascular disease and oncology; and Amgen in cardiovascular disease.

Following our acquisition of Boehringer Ingelheim's consumer healthcare business, we will be one of the leaders in the consumer healthcare market, tied at 4.4% market share with GSK and Bayer. Other key competitors include Johnson & Johnson, Pfizer, and Reckitt Benckiser, as well as local players, especially in emerging markets.

Our generics business is the seventh largest globally by sales and competes with multinational corporations such as Teva, Sandoz (a division of Novartis), Mylan and Actavis and local players, especially in emerging markets.

In our Human 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, these 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 these 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 counterfeit drugs. The WHO estimates that counterfeit products account for 10% of the market worldwide, rising to 30% in some countries. However, in markets where powerful regulatory controls are in place, counterfeit 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, product withdrawals and 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.

In 2016, the International Council for Harmonization (ICH) started implementing 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 observers; and facilitate the involvement of additional regulators and industry associations around the world. Eight countries, four Regional Harmonization Initiatives and five interested organizations have joined as observers since then.

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" (i.e. pediatrics, oncology, advanced therapy medicinal products, vaccines, pharmacogenomics, orphan drugs, biosimilars, and blood products).

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 Trans-Pacific Partnership, under discussion since 2008, was finalized on October 5, 2015. This free trade agreement,

which was negotiated between Australia, New Zealand, the US, Peru, Chile, Mexico, Canada, Singapore, Brunei, Malaysia, Vietnam and Japan, covers 40% of the global economy. Provisions affecting the BioPharma industry include a patent exclusivity term for biologics. Recent changes in the US political landscape, with the introduction of the new administration, have brought uncertainties to the future of the agreement.

The Transatlantic Trade and Investment Partnership (TTIP) is still being negotiated. This proposed free trade agreement between the EU and the US is intended to promote multilateral economic growth. Specifically with respect to the BioPharma industry, the agreement aims to enable regulators to work together more closely to ensure medicines are safe and effective.

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 approvals for new pharmaceutical products in the EU have been largely centralized within the European Medicines Agency (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.

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 applications can be filed and approved in the EU only after the originator product 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 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 2016, the EMA recommended 81 medicines for marketing authorization (versus 93 in 2015), including 27 new active substances.

Among the 81 medicines recommended, 17 (21%) had an orphan designation (versus 18 in 2015 and 17 in 2014), providing medicines for patients with rare diseases. Seven medicines were evaluated under accelerated assessment in 2016 (versus five in 2015 and seven in 2014); this mechanism is reserved for medicines that have the potential to address unmet medical needs. Eight medicines were 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 marketing authorization holders (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.

The pharmacovigilance legislation was amended in 2012. The amendments aim to further strengthen the protection of patient health by promoting prompt and appropriate regulatory action on European medicines. In particular, the amendments included major changes to notification requirements: MAHs of human medicines now have to notify EU regulators of any action to withdraw a product from a market, together with the reason for this action. Changes also included the creation of a Pharmacovigilance Risk Assessment Committee (PRAC), a scientific advisory committee at EMA level, with a key role in the assessment of all aspects of the risk management relating to the use of medicinal products for human use approved in the European Economic Area (EEA). This includes measures relating to the detection, assessment, minimization and communication of the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product. This committee is also responsible for the design and evaluation of post-authorization safety studies (PASS) and pharmacovigilance audits.

In Europe, the PRAC has performed reviews of marketed products (by class or on ad hoc basis) through various procedures. For Sanofi 153 products underwent PRAC review through signal and referral procedures from July 2012 to December 2016, generating 99 labeling variations (26 new variations in 2016) and five 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.

The EU pharmacovigilance legislation also strengthens the legal basis for regulators to require post-authorization safety and efficacy studies throughout the life cycle of a medicinal product, with regulatory supervision of protocols and results. Such studies are aimed at collecting data to enable the safety or efficacy of medicinal products to be assessed in everyday medical practice. The granting of marketing authorization is conditional on such studies being performed. Consequently, the pharmaceutical industry now has to build the need for PASS and post-authorization efficacy studies (PAES) into development and life cycle management plans. Sanofi has put in place robust processes to ensure that PASS and PAES can be properly implemented as required, either as part of a Risk Management Plan (RMP) or following a health authority request.

A further requirement introduced by the EU pharmacovigilance legislation is for pharmaceutical companies to prepare Periodic Safety Update Reports (PSURs). These are not limited to safety data, but instead present a critical analysis of the risk-benefit balance of a medicinal product, taking into account new or emerging information in the context of cumulative information on risks and benefits.

There is in addition a legal requirement for an enhanced adverse reaction collection and management system (EudraVigilance) that delivers better health protection through simplified reporting, higher quality data, and improved search, analysis and tracking functionalities. Associated with this is a legal requirement for MAHs to monitor EudraVigilance data, to the extent to which they have access to such data. Following an EudraVigilance functionalities audit for the first quarter of 2017, a move to EMA centralized reporting is planned for November 2017.

The database of medicinal products aims to deliver structured and quality assured information on medicinal products authorized in the EU supporting the terminologies of products, substances, and organizations that underpin pharmacovigilance and regulatory systems. Since January 1, 2015, MAHs have been required to notify the EMA of any new marketing authorizations within 15 calendar days from the date of authorization, and to notify the EMA of any change in the terms of a marketing authorization as soon as possible within 30 calendar days following the date on which the changes were authorized.

The EMA's medical literature monitoring (MLM) service was launched on September 1, 2015 to monitor selected medical literature for reports of suspected adverse drug reactions containing certain active substances, and to enter reports into EudraVigilance database.

There is a legal requirement for EMA to set up a repository for Periodic Safety Update Reports (PSURs) and their assessment reports on PSURs in order to facilitate centralized PSUR reporting and to enhance access to data and information, thereby supporting risk/benefit assessments of medicines. The PSUR Repository achieved full functionality in June 2015 and its use in the EU became mandatory on June 13, 2016.

**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 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 require 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 22 novel drugs in 2016 (versus 45 in 2015, 41 in 2014, 27 in 2013 and 39 in 2012). Designations and pathways to expedite drug development and review include Fast Track (8), Breakthrough Therapy (7), Accelerated Approval (6), and Priority Review (15). Of the 22 novel drugs approved in 2016, 16 (73%) were designated in one or more expedited categories.

CDER identified eight of the 22 novel drugs approved in 2016 (36%) as First-in-Class, one indicator of the innovative nature of a drug. Approximately 41% of the novel drugs approved in 2016 (9 of 22) were approved to treat rare or "orphan" diseases that affect 200,000 or fewer Americans.

Congress encouraged development of new human drugs and biological products for prevention and treatment of certain tropical diseases (FDAAA 2007) and rare pediatric diseases (FDASIA 2012) by offering additional incentives for obtaining FDA approval of such products. To date four tropical disease priority review vouchers (PRVs) and seven pediatric rare disease PRVs have been granted. In 2014, Regeneron purchased a pediatric rare disease PRV from BioMarin which was redeemed for the priority review of their PCSK9 product Praluent®, thus cutting short the review time by 4 months. Sanofi purchased a second pediatric rare disease PRV from Retrophin in the summer of 2015, which was redeemed in December 2015 for the priority review of its diabetes fixed combination product Soliqua™ 100 / 33, which was approved by FDA in November 2016. In December 2016, Congress extended the rare pediatric disease priority review voucher program to 2020 for designation and 2022 for marketing approval authorization.

**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. These additional procedures have created a significant delay in the registration of some innovative products in Japan compared to the EU and the US. In order to solve this drug-lag problem, the Japanese Ministry of Health, Labor and Welfare (J-MHLW) introduced a new National Health Insurance (NHI) pricing system on a trial basis in April 2010. 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, the 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. Otherwise, a fine equivalent to 105% (with 5% representing interest) of sales based on the premium would have to be paid back to the government.

To promote the development of innovative drugs and bring them into early practical use in Japan ahead of the world, *Sakigake* (a Japanese term meaning "forerunner") review designation program was introduced from April 2015 on a trial basis. The Pharmaceuticals and Medical Devices Agency (PMDA) will review designated products on a priority basis with the aim of reducing their review time from the normal 12 months to 6 months.

Based on the reform of the NHI price system finalized in 2013, the "Premium" classification will be 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. The "Premium" policy will continue its trial stage.

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 9 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 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.

For new drugs and biosimilar products with approval applications submitted on 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. Pharmaceutical 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 will be mandatory from 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**, a 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 2016, 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 the US**, the Patient Protection and Affordable Care Act (Affordable Care Act), signed into law by President Obama 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 2016 the FDA published for consultation two biosimilar draft guidance documents on labeling and transition products. Sanofi submitted comments to the public docket on both guidance documents. Of particular interest to Sanofi was the draft guidance, "Implementation of the "Deemed to be a License" Provision of the Biologics Price Competition and Innovation Act of 2009," which covers the transition of "Legacy Protein Products" from the drug approval system to the biologics system by March 23, 2020. Sanofi transition products include insulin products, Cerezyme® and Thyrogen®. The Biosimilar Guidance on interchangeability was published in January 2017.

To date four biosimilar products have been approved by the FDA.

US Federal and state officials, including the new 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 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. Generics

**In the EU** 16 positive opinions were issued under the centralized procedure for generics in 2016 (versus 21 in 2015, 8 in 2014 and 16 in 2013). 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. For the period October 1, 2015 through September 30, 2016 the FDA planned to review and act on 75% of original ANDA submissions within 15 months from the date of submission. For this period, 651 ANDAs were approved, 184 received tentative approval and 1725 complete responses were issued. To date, the FDA has met or exceeded its goals.

**In Japan,** the 2014 reforms to the NHI price system included a new special price reduction rule for long-listed drugs. The new rule reduces the NHI prices of long-listed drugs whose generic replacement rates are less than 20% five years after their first generics join the NHI price list. Reductions are 2.0% in the first NHI price revision, 1.75% if the substitution rate is 20% or higher but less than 40%, and 1.5% if the rate is 40% or higher but less than 60%. The rule was introduced in April 2014.

Under the new price system, 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, a maximum "*Sakigake premium*" of 20% 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.6.3.4. 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. Medical devices are currently regulated by three core Directives.

In September 2012, the European Commission adopted proposals to introduce two regulations to overhaul and tighten the current EU rules on medical devices (EU Medical Device Directive 93/42/EC, amended in 2007 as Directive 2007/47/EC).

In 2013, the European Parliament endorsed essential measures to strengthen patient safety. These measures are supported by the industry and include: improving the competence and control of NBs; introducing unannounced site visits by NBs; increasing the transparency and traceability of medical devices; introducing stricter post-market follow-up, and improved stakeholder engagement. In addition, a "scrutiny procedure" was introduced at least for high-risk Class III devices (novel technologies or specific public health threats).

The revised framework also formally introduced the concept of "companion diagnostic", which is expected to deliver a more accurate definition of the patient population that will benefit from a given product. Sanofi has several "companion diagnostics" in development.

On June 15, 2016, the medical device (MD) and in vitro diagnostics (IVD) regulation texts were approved by the European Council. The texts are expected to be formally adopted in 2017. The regulations would then apply to the medical devices and in vitro diagnostics sectors with an expected 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. Regulatory control increases from Class I to Class III. The device classification regulation defines the regulatory requirements for a 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.

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.

### B.6.3.5. OTC drugs

**In the EU**, four European centralized prescription to OTC (Rx-to-OTC) switches have occurred since 2009. GlaxoSmithKline Consumer Healthcare's Alli (orlistat) weight-loss medicine was the first in January 2009, followed by Nycomed's 20mg pantoprazole tablets in June 2009, AstraZeneca's Nexium Control (esomeprazole) in 2013 and EllaOne, an emergency contraceptive, in January 2015. No new centralized OTC switch was granted in 2016. For nationally authorized products, switches follow national rules for OTC classification.

**In the US**, the FDA approved two prescription to OTC switches in 2016: Differin Gel (adapalene) and Flonase Sensimist Allergy Relief (fluticasone).

**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 (the previous safety evaluation period was four years). 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 the 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 that would 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 will be publicly reviewed by the new panel in order to minimize pressures from medical societies. Based on its deliberations, the panel would refer the shortlisted requests to the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) committee on nonprescription drugs, which effectively makes decisions on marketing approval for OTCs. The ministry is also planning to seek public comments.

### B.6.3.6. Transparency and public access to documents

**Transparency regarding regulatory information and clinical trials**

Over recent years the pharmaceutical industry has been subject to growing pressure for greater transparency about clinical trials (conduct and results). Regulatory authorities are also being pushed for more openness and transparency, for example by making more comprehensive disclosures about the rationale and basis of 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 and results of clinical studies performed 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. We have 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. The new 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.

The EMA has committed to continuously extending 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 a EU-wide marketing authorization is complete.

Early October 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, and article 58 applications (medicines that are intended exclusively for markets outside the EU) submitted after that date.

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.

There is a two-step approach for the implementation of the policy:

- The first phase concerns the publication of clinical reports only, the data from which will be 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.

In order to operationalize EMA Policy 70, Sanofi launched an internal project to define, develop, implement and control a sustainable process, supported by associated tools and documents, as well as resourcing, training and communication plans to manage clinical documents and data redaction in compliance with Policy 70. In 2016, the EMA Policy 70 process was fully transitioned to the business operational teams; and awareness communication is ongoing not only for current submissions, but also to streamline the process for ongoing and future studies.

**In the US**, the FDA launched a Transparency Initiative in June 2009. The objective of the initiative was to render the FDA much 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 were 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 scope of results reporting requirements to include trials of unapproved products; clarifies and expands results data elements; and revises Quality Control (QC) and posting process.

**In Japan**, the J-MHLW/PMDA actively publishes information concerning approvals of medicinal products (ethical drugs, nonprescription drugs, and quasi-drugs) and medical devices. For ethical drugs discussed at the J-MHLW's Pharmaceutical Affairs and Food Sanitation Council, the redacted clinical trials data modules 1&2 (except for commercial confidential information and personal data) have been made publicly available on the PMDA website.

**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, or Portugal).

The European Federation of Pharmaceutical Industries Association (EFPIA) released in mid-2013 a new Code on Disclosure of Transfers of Value from Pharmaceutical Companies to HCPs and Healthcare Organizations (HCOs), the "EFPIA HCP/HCO Disclosure Code". EFPIA members were required to comply with this new code and transpose it into their national codes in full by December 2013.

This new 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.

**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, 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 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 to 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.6.3.7. Other new legislation proposed or pending implementation

**In the US**, former President Obama signed on December 13, 2016 the 21st Century Cures Act, intended to promote biomedical innovation and personalized medicines. The 21st Century Cures Act includes increased funding for the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) and provides for the implementation of, among other reforms, enhanced pathways for medical product approval and the modernization and harmonization of clinical trial procedures over a period of several years.

In the United States, user fees for manufacturers of medical products are reauthorized on a five-year cycle. The current fee programs, approved under FDASIA in 2012, will sunset September 30, 2017. The fees, known as PDUFA VI, MDUFA IV, BsUFA II and GDUFA II, will be delivered to Congress in 2017 as an omnibus bill. A fifth possible human health user fee, OMUFA, is currently being negotiated.

**Clinical trial regulation in the EU**

The new Clinical Trial Regulation ((EU) 536/2014) of the European Parliament and of the Council of 16 April 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.

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 will streamline the rules on clinical trials across Europe, facilitating cross-border cooperation to enable larger, more reliable trials, as well as trials on 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 as a more stringent form of regulation instead of a directive in order to reach better harmonization between countries, without interfering with Member States' competences in terms of ethical aspects.

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). This can be seen as a setback for the industry, as the Commission's proposal was based on 41 days without questions and a maximum of 74 days including all possible delays. 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. The fact that this feature was accepted by all parties can be seen as a positive outcome for the industry.
- 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). A single EU submission portal and database fully operational is the prerequisite for regulation implementation: go-live is currently scheduled for September 2018, making the Regulation applicable in October 2018.

During the three-year transition period, both sets of rules will apply in parallel.

**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 were adopted: the establishment of a common EU logo for online pharmacies was adopted in June 2014, giving Member States until July 2015 to prepare for its application. The 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.

**Nagoya Protocol**

The Nagoya Protocol to the Convention on Biological Diversity on "Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization" was adopted in Nagoya at the tenth Conference of the Parties of the Convention on Biological Diversity (CBD) on

October 29, 2010. The Nagoya Protocol came into force in October 2014 and at end December 2016 had 96 ratifications/accessions. The Nagoya Protocol is 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.

On April 16, 2014, the European Parliament and the Council adopted the new regulation (EU 511/2014) on compliance measures for users, based on the Nagoya Protocol on Access to Genetic resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization in the Union. It came into force in October 2014.

In October 2015, the European Commission published the implementation Act (Regulation 2015/1866).

The pharmaceutical industry is due to implement compliance procedures for non-human biological materials used in the discovery, development, manufacturing and packaging of medicinal products to be submitted in the EU, starting after 2015. These will also include documentation from the originating country and acquisition date for materials that were acquired before the Regulation came into force.

Within Sanofi, a **Nagoya ready** project was launched mid-2015 to ensure compliance with international treaties on the sustainable use of biodiversity.

**In Japan**, the relevant ministries are currently considering local measures for the ratification of the Nagoya Protocol. The schedule for ratification has yet to be determined. The details of local measures for the implementation of the Nagoya Protocol cannot be disclosed due to ongoing discussion, but the relevant ministries are considering a framework where terms and conditions can be set for mutual agreement and a consent can be obtained in advance from providers in accordance with laws and regulations in a source country when genetic resources from the source country are used in Japan.

**NDA electronic clinical trial data submission**

**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 is also mandatory for all other EU marketing authorization procedures (i.e. MRP, DCP 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 nonclinical toxicity study data in one of the Standard for the Exchange on Non clinical Data (SEND) formats in due course.

### B.6.4. Pricing & Reimbursement

Rising overall healthcare costs are leading to efforts to curb drug expenditures in most markets in which we operate. Increasingly, these efforts 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/relative effectiveness data 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 enforce transparency and tight compliance with these regulations and controls. 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 continues to grow more complex each year.

While a drive to expand healthcare coverage has become a noticeable feature in many regions, providing opportunities for industry, it has also brought 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, through technology transfer agreements or through preferential conditions for local production, is equally a growing issue.

Significant trends:

In the United States there is increased scrutiny on the price of branded pharmaceutical products, and therefore heightened sensitivity to patient exposure to high out-of-pocket expense.

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 is widespread. 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 a Part D plan.
- Medicaid, which provides health insurance for those on low incomes.

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).

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 rollout of former President Obama's healthcare reform package pursuant to The Affordable Care Act is increasing the government's role with respect to price, reimbursement, and coverage levels for healthcare services and products within the large government healthcare sector. This law also imposed cost containment measures and rebates and fees on pharmaceutical companies. Some US states are also considering legislation that would influence the marketing and prices of, and access to, drugs. US Federal and state officials, including the new 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.

Affordable access for patients is critical to our industry's success; however, the cost of access via third party intermediaries – Pharmaceutical Benefit Managers (PBMs), Health Plans and Government Markets – is calling into question the integrity of the healthcare system and the sustainability of our business.

As the US approached the so-called "Patent Cliff" major market insurers realized the traditional business revenue model was threatened and there was an immediate shift to a model that would increase enrollment and cut costs. In recent years mergers and acquisitions have been the largest source of payer revenue growth, as acquired patients translate to increased demand. Industry consolidation now appears to have stabilized in the US, and there are currently three major PBMs and three major health insurers who will remain dominant.

With a decline in generic conversion and no further scope for consolidation, payers are seeking alternative methods to cut costs. As payers consolidate they can leverage their size and market share to demand higher rebates in return for increased access. If a manufacturer is reluctant to offer a higher rebate, the insurer will resort to interventions to enforce formulary controls.

- As a soft measure to control access, payers use step therapy (to ensure use of low-cost therapies) and prior authorization (to require proof of medical necessity). For example, some US payers have placed significant restrictions on usage of Praluent®, which has resulted in significant out-of-pocket expenditures for Medicare patients.
- A more extreme tactic, initially provoked by pharma coupons, is adding a product to an exclusion list; this means that (i) a patient has to pay out of pocket and (ii) manufacturer coupons are rejected at the pharmacy. For example, since 2014, we have increased the level of rebates granted for Lantus® in order to maintain favorable formulary positions with key payers in the US. Despite these efforts, in 2016 CVS and UnitedHealthcare (a PBM and MCO, respectively) decided that effective January 1, 2017 and April 1, 2017, respectively, Lantus® and Toujeo® will be excluded from the formulary across the commercial and MMC (Medicaid Managed Care) template formularies covering approximately 34.7 million people, thus reducing the potential patient populations to whom Lantus® may be prescribed.

US insurers have prioritized the need to control costs in specialty categories, and will maximize exclusions and protocols to achieve savings. There is a particular focus on all chronic disease states, which will limit the ability of new entrants to achieve coverage without demonstration of comparative effectiveness. Finally, US insurers are quick to adopt Follow-On-Biologic (copycat) versions of branded drugs as a "good enough" alternative to leverage higher rebates as compared with incumbent products.

In addition, distributors have increased their capacity to negotiate price and other terms as a consequence of the growing number of mergers of retail chains and distributors, resulting consolidation of the distribution channel.

The industry in China is going through a transformative period. The most significant changes as regards innovation in the industry are the highly-publicized price negotiations with the NHFPC (National Health and Family Planning Commission), and the subsequent order to list drugs on provincial formularies. The first update of the NRDL

(National Reimbursement Drug List) since 2009 is expected in 2017. The CFDA (China Food and Drugs Administration) has also made clear its intent to clear the backlog of regulatory reviews. The market itself is due to transform through a series of smaller measures. For example, a two-invoice policy will simplify the supply chain, and tax reform has reallocated funds to poorer provinces for healthcare. While these can be viewed as positive, there are many uncertainties. The CFDA finally abandoned a proposal to tie regulatory approval to price commitments based on international price referencing, while it has been announced that the NRDL will use the lowest provincial tender price as a reimbursement basis, which is strongly contested. Whatever the outcome, we can expect many other measures in the Chinese market following a call to step up the pace of reforms.

Recent trends in European policy have been towards joint procurement and joint negotiations, ignited by the controversy on funding Hepatitis C drugs. At the same time, political instability (such as the post-Brexit UK and new measures in Greece) is ever-present. However, some positive signs have begun to appear, such as a dedicated budget for innovative medicines in Italy, though these remain exceptions in a political environment that is increasingly hostile to the industry.

Japan has made high-profile price cuts this year outside of the biennial review, and seems set to move to a yearly price review with the overall objective of cutting costs; again, this reflects budget pressure induced by the funding of Hepatitis C drugs.

In South America, inflation has had a major effect on the sustainability of the industry in the region, most notably in Venezuela.

The Eurasian Economic Union has signed a final agreement on a single market for medicines (Armenia, Belarus, Kazakhstan, Kyrgyzstan and Russia), which should streamline processes but also increase the region's negotiating power. Similar developments have been taking place in South America: UNASUR (Union of South American Nations) has announced a centralized pricing database, while discussions are ongoing on joint procurement of expensive oncology medicines.

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:

- In compliance with local law we actively engage with our key stakeholders to define criteria for assessing the value of our products to them. These stakeholders, including physicians, patient groups, pharmacists, government authorities and third-party payers, can have a significant impact on market access for our products.
- We continue to add flexibility and adaptability to our operations so as to better prepare, diagnose, and address issues in individual markets.

Conscious of the importance of recognizing the value of our products and the high cost of research and development, we continue to analyze innovative pricing and access strategies that balance patient access with appropriate rewards for innovation. Specifically, we are involved in risk-sharing agreements with payers, whereby part of the financial risk related to a treatment's success is carried by the marketing company. Those agreements provide that clinical efficacy be monitored after launch, for a specified period of time and patient population. The price and reimbursement level of the drug is then either confirmed or revised based on the post-marketing results.

We are also actively testing and running tiered pricing models where this is possible, allowing wider access to therapies for populations that would otherwise be denied this.

## B.7. PATENTS, INTELLECTUAL PROPERTY AND OTHER RIGHTS

### 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 approval. 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 (a Supplementary Protection Certificate or SPC), the US (a Patent Term Extension or PTE) and Japan (also a PTE).

Additionally, the product may benefit from the protection of patents obtained during development or after the product's initial marketing approval. The protection a patent provides 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 2015, an EPO patent application may cover the 38 European Patent Convention member states, including all 28 member states of the EU. The "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 by country. 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 patent (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, 12 countries including France have ratified the agreement.

The Unitary Patent will provide unitary protection within the participating states of the EU (when ratified by the member states with the exception of Spain). 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 by 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 – A.3. 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 obtain commercial benefits from product manufacturing trade secrets or from other types of patents, such as patents on processes, intermediates, structure, formulations, methods of treatment, indications or delivery systems. Certain categories of products, such as traditional vaccines and insulin, have been historically relatively less reliant on patent protection and may in many cases have no patent coverage, although it is increasingly frequent for novel vaccines and insulins to be patent protected. Patent protection is of comparatively lesser importance to our Consumer Healthcare and generics businesses, which rely principally on trademark protection.

**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 approval 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. 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 much larger health care reform legislation known as 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 notwithstanding minor differences in clinically inactive components, 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 new 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, to eight years for drugs containing a new chemical entity, to 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, although it provided a limited number of developing countries an extension to 2016. 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 regarding 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.

**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. If the FDA approves the drug for the designated indication, the drug will generally receive orphan drug exclusivity.

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 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 regulatory delay, the extended dates are presented below. US patent expirations presented below reflect US Patent and Trademark Office dates, and also reflect six month pediatric extensions as applicable. Where patent terms have expired we indicate such information and mention if 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.

***Aldurazyme® (laronidase)***

**US**
Compound: November 2019

Later filed patents: ranging through July 2020

**EU**
Compound: November 2020 in some EU countries only

**Japan**
Compound: November 2020

***Allegra® (fexofenadine hydrochloride)***

**US**
Compound: expired
Generics on the market
Converted to Over-the-Counter

**EU**
Compound: expired
Generics on the market

**Japan**
Compound: expired
Generics on the market
Converted to over-the counter

***Amaryl® (glimepiride)***

**US**
Compound: expired

**EU**
Compound: expired

**Japan**
Compound: expired

***Apidra® (insulin glulisine)***

**US**
Compound: June 2018

Later filed patents: ranging through September 2027

**EU**
Compound: September 2019 with SPC in most of the EU countries
Later filed patent: March 2022

**Japan**
Compound: May 2022 with PTE

Later filed patent: July 2022

Regulatory exclusivity: April 2017

***Aprovel® (irbesartan)***

**US**
Compound: expired
Generics on the market

**EU**
Compound: expired
Generics on the market

**Japan**
Compound: expired

***Aubagio® (teriflunomide)***

**US**
Compound: expired
Later filed patents: coverage ranging through September 2034
Regulatory exclusivity: September 2017

**EU**
Compound: expired
Later filed patent: coverage ranging through September 2030
Regulatory exclusivity: August 2023

**Japan**
Compound: expired
Later filed patent: coverage ranging through March 2024

***Cerdelga® (eliglustat)***

**US**
Compound: April 2022
(2026 with PTE when granted)
Later filed patent: November 2030 (pending)
Regulatory exclusivity: August 2019
Orphan Drug Exclusivity: August 2021

**EU**
Compound: July 2022
(2027 with SPC when granted)
Later filed patent: November 2030

Regulatory/Orphan exclusivity: January 2025

**Japan**
Compound: March 2025 with PTE

Later filed patent: November 2030 (pending)
Regulatory exclusivity: March 2023

***Cerezyme® (imiglucerase)***

**US**
Compound: expired

**EU**
Compound: N/A

**Japan**
Compound: N/A

***Depakine® (sodium valproate)***

**US**
Compound: N/A[a]

**EU**
Compound: N/A[a]
Later filed patent: Depakine® Chronosphere formulation (October 2017)

**Japan**
Compound: N/A[a]
Later filed patent: Depakine® Chronosphere formulation (October 2017)

*(a) No rights to compounds in the US, EU and Japan.*

***Fabrazyme® (agalsidase beta)***

**US**
Compound: N/A
Later filed patents: expired

**EU**
Compound: N/A

**Japan**
Compound: N/A
Later filed patents: expired

***Insuman® (human insulin)***

**US**
Compound: N/A

**EU**
Compound: N/A
Later filed patent: August 2018

**Japan**

Compound: N/A

***Jevtana® (cabazitaxel)***

**US**
Compound: March 2021 with PTE
Later filed patents: coverage ranging through October 2030

**EU**
Compound: expired
Later filed patents: coverage ranging through October 2030 (pending)
Regulatory exclusivity: March 2021

**Japan**
Compound: March 2021 with PTE
Later filed patents: coverage ranging through October 2030
Regulatory exclusivity: July 2022

***Lantus® (insulin glargine)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Later filed patents[a] ranging through March 2028 | Compound: Expired<br>Later filed patents ranging through June 2023 | Compound: expired<br>Later filed patents ranging through June 2023 |

*(a) On September 16, 2016, several Sanofi entities filed a patent infringement suit against Merck Sharp & Dohme Corp. ("Merck") in the United States District Court for the District of Delaware. In its suit, Sanofi alleges infringement of ten patents. The suit was triggered by a notification received from Merck in early August, in which Merck stated that it had filed an NDA (505(b)(2) New Drug Application) with FDA for an insulin glargine drug product. Merck also stated that its NDA included a paragraph IV certification challenging all of the ten Sanofi patents then listed in the FDA Orange Book for Sanofi's Lantus® and Lantus® SoloStar® products. This suit resulted in a stay during which the FDA cannot approve Merck's NDA. The 30 month stay is expected to expire on the earlier of (1) February 8, 2019 or (2) a court decision in favor of Merck. The Court has scheduled a bench trial to begin on May 29, 2018, a claim construction hearing for August 21, 2017 and briefing on summary judgment motions on certain issues pertaining to some of the patents-in-suit to begin on October 2, 2017.*

***Lemtrada® (alemtuzumab)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Later filed patents: ranging through September 2027 (pending) | Compound: expired<br>Later filed patent: September 2027 | Compound: expired<br>Later filed patent: September 2027 (pending) |

***Lovenox® (enoxaparin sodium)***

| US | EU | Japan |
|---|---|---|
| Compound: N/A<br>Generics on the market | Compound: expired | Compound: expired |

***Lumizyme® / Myozyme® (alglucosidase alpha)***

| US | EU | Japan |
|---|---|---|
| Compound: N/A<br>Later filed patents: coverage ranging through February 2023[a]<br>Biologics Regulatory Exclusivity: April 2018 | Compound: N/A<br>Later filed patents: July 2021 | Compound: N/A<br>Later filed patents: July 2021<br>Orphan Regulatory Exclusivity: April 2017 |

*(a) Genzyme filed a notice of appeal to the Federal Circuit to challenge successful inter partes review (IPR). For more information refer to Item 8 – Consolidated Financial Statements and other Financial Information – Information on Legal and Arbitration Proceedings – Genzyme Myozyme® Lumizyme Patent Litigation (United States).*

***Lyxumia®/Adlyxin™ (lixisenatide)***

| US | EU | Japan |
|---|---|---|
| Compound: July 2020[a] (July 2025 with PTE when granted)<br>Later filed patents: coverage ranging through December 2033 (pending)<br>Regulatory Exclusivity: July 2021 | Compound: July 2020[a] (2025 with SPC in most EU countries)<br>Later filed patents: coverage ranging through March 2034 (pending)<br>Regulatory Exclusivity: February 2023 | Compound: July 2024[a] with PTE<br>Later filed patents: coverage ranging through November 2030<br>Regulatory Exclusivity: June 2021 |

*(a) Lixisenatide compound patent licensed exclusively from Zealand Pharma*

***Mozobil® (plerixafor)***

| US | EU | Japan |
|---|---|---|
| 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: July 2022 |

***Multaq® (dronedarone hydrochloride)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Later filed patents: coverage ranging through December 2031 | Compound: expired<br>Later filed patent: June 2018 (2023 with SPC in most EU countries)<br>Regulatory exclusivity: December 2019 | Compound: expired<br>Later filed patent: June 2018 |

***Soliqua™100/33 / Suliqua™ (lixisenatide + insulin glargine)***

| US | EU | Japan |
|---|---|---|
| Compound: July 2020[a]<br>(July 2025 with PTE when granted)<br>Later filed patents: coverage ranging through November 2030 (pending)<br>Regulatory Exclusivity: July 2021 | Compound: July 2020[a]<br>(2025 with SPC in most EU countries)<br>Later filed patents: coverage ranging through November 2030<br>Regulatory Exclusivity: January 2027 | Compound: July 2024[a] with PTE<br><br>Later filed patents: coverage ranging through November 2030<br>Regulatory Exclusivity: to be determined |

*(a) Lixisenatide compound patent licensed exclusively from Zealand Pharma*

***Plavix® (clopidogrel bisulfate)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Generics on the market | Compound: expired<br>Generics on the market | Compound: expired |

***Praluent® (alirocumab)***

| US | EU | Japan |
|---|---|---|
| Compound: December 2029<br>Later filed patents: coverage ranging through September 2032 (pending)<br><br>Biologics Regulatory Exclusivity: July 2027 | Compound: December 2029<br>Later filed patents: coverage ranging through September 2032 (pending)<br>Regulatory exclusivity: September 2025 | Compound: December 2029<br>Later filed patents: coverage ranging through September 2032 (pending) |

***Renagel® (sevelamer hydrochloride)***

| US | EU | Japan |
|---|---|---|
| Compound: N/A<br>Later filed patent: October 2020 | Compound: N/A<br>Later filed patent: October 2020<br>Generics on the market | Compound: N/A<br>Later filed patent: October 2020 |

***Renvela® (sevelamer carbonate)***

| US | EU | Japan |
|---|---|---|
| Compound: N/A<br>Later filed patents: October 2025 (tablet) and December 2030 (sachet) | Compound: N/A<br>Later filed patent: September 2026 (sachet)<br>Generics on the market | Compound: N/A<br>Later filed patents: November 2025 (tablet) and September 2026 (sachet) |

***Stilnox® (zolpidem tartrate)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Generics on the market | Compound : expired<br>Generics on the market | Compound : expired<br>Later filed patent: Ambien® CR formulation (December 2019) – not commercialized |

***Synvisc® (hyaline G-F 20)***

| US | EU | Japan |
|---|---|---|
| Compound: expired | Compound: N/A | Compound: expired |

***Synvisc-One® (hyaline G-F 20)***

| US | EU | Japan |
|---|---|---|
| Compound: expired | Compound: N/A<br>Later filed patent: December 2025 | Compound: expired<br>Later filed patent: December 2025 |

***Toujeo® (insulin glargine)***

| US | EU | Japan |
|---|---|---|
| Compound: expired<br>Later filed patents:<br>coverage ranging through May 2031<br><br>Regulatory exclusivity: February 2018 | Compound: expired<br>Later filed patents:<br><br>coverage ranging through May 2031 | Compound: expired<br>Later filed patents:<br>coverage ranging through July 2033 with PTE<br>Regulatory exclusivity: July 2019 |

***Zaltrap® (aflibercept)***

| US | EU | Japan |
|---|---|---|
| Compound: May 2020 (July 2022 with PTE when granted)*<br><br>Later filed patents: coverage ranging through April 2032 (applications pending)<br>Biologics Regulatory Exclusivity: November 2023 | Compound: May 2020 (May 2025 with SPC in some EU countries)*<br>Later filed patents: coverage ranging through April 2032 (pending)<br>Regulatory Exclusivity: February 2023 | Compound: May 2020* (PTE to be determined once product is approved)<br><br>Later filed patents: coverage ranging through April 2032 (pending) |

** Patents under license of Regeneron Pharmaceuticals, Inc.*

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" below. 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 following the initial US marketing authorization of the original product. 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" below. We seek to defend our patent rights vigorously in these cases. Success or failure in the assertion of a 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 FDA publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (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 approval 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.

**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.

### B.8. Production and Raw Materials

For many years, we have chosen, as often as possible, to keep the manufacture of our products in-house in order to ensure better quality management. Our production process consists of three principal stages: the manufacture of pharmaceutical active ingredients, the transformation of those ingredients into drug products, and packaging those products.

Our general policy is to produce our main active ingredients and principal drug products at our own plants in order to reduce our dependence on external manufacturers and to maintain strict and precise control over the entire production cycle. In significant cases, however, we 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 main pharmaceutical subcontractors are Famar, MSD, Unither, Delpharm and Saneca. Those 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".

We also obtain active ingredients from third parties under partnership agreements. This applies 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 drug products, and a number of our main solid-form drug 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, Thailand, Argentina and India. The pharmaceutical sites at Le Trait (France) and Anagni (Italy) also contribute to Sanofi Pasteur's industrial operations by making available their aseptic filling and freeze-drying facilities.

All of our production facilities – whether in Pharmaceuticals, Sanofi Genzyme or Vaccines – are good manufacturing practice (GMP) compliant, in line with international guidelines.

Many of our industrial sites are approved by the US Food and Drug Administration (FDA):

- our Pharmaceuticals facilities in France (Ambarès, Tours, Le Trait, Maisons Alfort, Compiègne and Lyon Gerland), the United Kingdom (Haverhill and Holmes Chapel), Ireland (Waterford), Germany (Frankfurt), Italy (Anagni) and the United States (Saint Louis and Chattanooga);
- the Sanofi Genzyme facilities in the United States (Allston, Framingham, Ridgefield, Northpointe-Lynnwood and Northborough) and in Belgium (Geel); and
- our Vaccines sites in France (Marcy l'Étoile, and Le Trait which handles filling and packaging of Fluzone® ID for the US market), the United States (Swiftwater, Canton and Rockville) 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 FDA following FDA inspections at the facility that resulted in observations and a warning letter raising Current Good Manufacturing Practices (CGMP) deficiencies. A consent decree is a court order entered into by agreement between a company and the government (in this case the FDA) that requires the company to take certain actions as set out in the decree.

Under the terms of the consent decree, Genzyme Allston was permitted to continue manufacturing during the remediation process subject to compliance with the terms of the consent decree.

The consent decree required Genzyme to implement a plan to bring operations at the Allston facility into compliance with applicable laws and regulations. The plan had to address all deficiencies reported to Genzyme or identified as part of an inspection completed by a third-party expert in February 2011. This workplan was submitted to the FDA in April 2011 and accepted by the FDA in January 2012. Modifications to the remediation workplan were accepted by the FDA in March 2012 and April 2015.

The workplan was successfully completed on March 31, 2016. The next step in the consent decree is a third-party certification process; this is ongoing, and is due to be finalized by the end of 2017.

Once the certification process is finalized, the Allston facility will remain under consent decree for an additional period of at least five years, with yearly inspections by the FDA.

In April 2014, the FDA withdrew the warning letter relating to the Sanofi Pasteur sites at Toronto (Canada) and Marcy l'Étoile (France). Sanofi Pasteur is implementing an ongoing program to improve compliance at those sites by applying a Global Quality Plan. This has already resulted in important improvements, as acknowledged in the most recent CGMP inspection conducted by the FDA at the Marcy l'Étoile site in September 2015.

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 captive 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 program operated by our captive insurance company. This approach shares risk between our entities, enabling us to set deductibles and guarantees that are appropriate to the needs of local entities. It also incorporates a prevention program, including a comprehensive site visit program covering our production, storage, research and distribution facilities and standardized repair and maintenance procedures across all sites. Specialist site visits are conducted every year to address specific needs, such as testing of sprinkler systems or emergency plans to deal with flooding risks.

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 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. This program, which is led by our captive insurance company, has substantial capacity, largely to deal with the growth in sea freight which can lead to a concentration of value in a single ship.

Our General & Product Liability program has been renewed for all our subsidiaries worldwide wherever it was possible to do so, despite the increasing 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 insuring some products that have been subject to numerous claims. These products are excluded from the cover provided by insurers, and hence from the cover obtained by us on the insurance market. This applies to a few of our products, principally those described in Note D.22.a) to our consolidated financial statements included at Item 18 in this annual report. Because of these market conditions we have increased, 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 by our captive insurance company. The level of risk self-insured by Sanofi – including via our captive reinsurance company – 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 with very low exposure 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 lines of business of 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 the company's 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 the Bornhuetter-Ferguson method; these 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. Our captive insurance company 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 on a continuous basis. 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, the Czech Republic, 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; Merial Barceloneta in Puerto Rico; Frankfurt in Germany; Brindisi in Italy; Dagenham in the United Kingdom; Ujpest in Hungary; Prague in the Czech Republic; Beaucaire, Valernes, Limay, Romainville, Neuville, Vitry and Merial Toulouse 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.e to the consolidated financial statements. In 2016, Sanofi spent €81 million (including €0.3 million related to the held-for-exchange Animal Health business) 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 €737 million as of December 31, 2016 (including €5 million related to the held-for-exchange Animal Health business) versus €720 million as of December 31, 2015. 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 2016 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 (52 in 2016, including 3 at Merial sites) are carried out by Sanofi in order to assess compliance with our standards (which implies compliance with regulations) and to initiate corrective measures. Additionally, 10 specialized audits covering biosafety (including two for Merial) and 111 prevention visits (including seven for Merial) were carried out by our teams in 2016. Moreover, 91 specific visits were performed jointly with experts representing our insurers (including 18 at Merial sites).

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, 78 rules (policies) have been drawn up in the key fields of HSE management, Good HSE Practices, 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).

**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**

The main objectives of our environmental policy are to implement clean manufacturing techniques, minimize the use of natural resources and reduce the environmental impact of our activities. In order to optimize and improve our environmental performance, we have a strategy of continuous improvement practiced at all our sites through the annual implementation of HSE progress plans. We believe that this strategy clearly expresses the commitment of both management and individuals to health, safety and the environment. In 2016, five of our European sites were included in the scope of the European $CO_2$ Emissions Credit Trading Scheme aimed at helping to reach the targets set by the Kyoto protocol.

Our recent efforts in terms of environmental protection have mainly targeted reductions in energy consumption, greenhouse gas emissions control, improvements in the performance of water treatment installations, reduction of volatile organic compound emissions, raw material savings and recycling, and reductions in waste materials or increases in the percentage being recycled. Measured against the benchmark year for our targets (2010), direct and indirect emissions from our production and research facilities (scope 1 & 2 and excluding vehicle fleets) have fallen by 19.2% overall. We are targeting a 20% reduction in $CO_2$ emissions in 2020 vs. 2010 on a constant structure basis.

An internal committee of experts called ECOVAL assesses the environmental impact of the pharmaceutical agents found in products marketed by Sanofi. It has developed an environmental risk assessment methodology and runs programs to collect the necessary data for such assessments. Additional ecotoxicity assessments are being performed on certain substances which predate current regulations, in order to obtain information that was not gathered when they were launched (as regulatory requirements were different at that time) and evaluate environmental risks resulting from their use by patients.

## C. Organizational Structure

### C.1. SIGNIFICANT SUBSIDIARIES

Sanofi is the holding company of a consolidated group consisting of over 400 companies. The table below sets forth our significant subsidiaries as of December 31, 2016.

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% |
| Merial, Inc. | 08/01/1997 | United States | Animal Health | 100% |
| Merial SAS | 02/25/1941 | France | Animal Health | 100% |
| Sanofi-Aventis Amérique du Nord | 09/20/1985 | France | Pharmaceuticals | 100% |
| Sanofi-Aventis Deutschland GmbH | 06/30/1997 | Germany | Pharmaceuticals | 100% |
| Sanofi-Aventis Europe | 07/15/1996 | France | 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 | 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 and Merial in September 2009. 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. During 2016, Sanofi and Boehringer Ingelheim (BI) finalized the negotiations initiated in December 2015 with a view to swapping Sanofi's Animal Health business for BI's Consumer Healthcare business. The financial effects of this transaction, which closed on January 1, 2017, are presented in Note G. to our consolidated financial statements, included at Item 18 of this annual report on Form 20 F. 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.

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 immuno-oncology; and (ii) with BMS, relating to Plavix®. For further information, refer to Note C. to our consolidated financial statements, "Principal Alliances".

### C.2. INTERNAL ORGANIZATION OF ACTIVITIES

Sanofi and its subsidiaries collectively form a group organized around two activities: Pharmaceuticals and Human Vaccines (Vaccines).

The Animal Health business, which was divested on January 1, 2017 as part of the transaction with Boehringer Ingelheim, is no longer an operating segment within the meaning of IFRS 8.

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 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, Aventis Pharma SA, Sanofi Biotechnology SAS (France), Sanofi-Aventis Deutschland GmbH (Germany) and Genzyme Corporation (US);
- 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, Sanofi, Merial SAS France, 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, 2016, the Sanofi parent company held 92% of our external financing and 83% 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[a]**

| | |
|---|---|
| *Industrial* | *59%* |
| *Research* | *14%* |
| *Offices* | *14%* |
| *Logistics* | *9%* |
| *Other* | *4%* |

**(a) Includes sites of the Animal Health business.*

**Breakdown of sites by ownership status**

| | |
|---|---|
| *Leasehold* | *27%* |
| *Owned* | *73%* |

**(a) Includes sites of the Animal Health business.*

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 lean 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 2016, we were carrying out industrial production at 86 sites in 38 countries (including 35 sites in emerging markets):

- 74 sites for our Pharmaceuticals activity, including Sanofi Genzyme; and
- 12 sites for the industrial operations of Sanofi Pasteur in vaccines.

In 2016, we produced the following quantities:

- Pharmaceuticals: 4,292 million units, comprising:
  - units manufactured and packaged: 2,956 million;
  - units packaged only: 275 million;
  - bulk products in unit equivalents: 396 million;
  - outsourced units: 666 million; and
- Vaccines: 500 million containers (syringes and ampoules) 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.

***Industrial Sites: Pharmaceuticals***

Production of chemical and pharmaceutical products is the responsibility of our Industrial Affairs department, which is also in charge of most of our logistics facilities (distribution and storage centers).

Major drugs, active ingredients, specialties and medical devices are manufactured at the following sites:

- France: Ambarès, Amilly, Aramon, Le Trait, Lyon Gerland, Maisons-Alfort, Sisteron, Tours, Vitry-sur-Seine and Vertolaye;
- Germany: Frankfurt Injectable, Frankfurt Pharma, Frankfurt Device and Frankfurt Chemistry;
- Ireland: Waterford;
- Italy: Scoppito, Anagni and Brindisi;
- United Kingdom: Haverhill and Holmes Chapel;
- Hungary: Ujpest and Csanyikvölgy;
- Japan: Kawagoe;
- Singapore: Jurong;
- China: Beijing and Hangzhou;
- Brazil: Campinas;
- Russia: Orel;
- India: Goa, Ankleshwar Pharma and Ankleshwar Chemistry;
- Belgium: Geel; and
- United States: Allston, Framingham Biologics, Framingham Biosurgery, Ridgefield, Northborough and Lynnwood, Washington State.

***Industrial sites: Consumer Healthcare***

Major drugs for our Consumer Healthcare portfolio are manufactured at the following sites:

- France: Compiègne and Lisieux;
- Germany: Cologne;
- Italy: Origgio;
- Hungary: Veres;
- Poland: Rzeszow;
- United States: Chattanooga;
- Brazil: Suzano;
- Mexico: Ocoyoacac;
- Vietnam: ACE; and
- Australia: Virginia.

***Industrial Sites: Vaccines (Sanofi Pasteur)***

The headquarters of our Vaccines division, Sanofi Pasteur, is located in Lyon, France. Sanofi Pasteur has 12 industrial sites in eight countries:

- France: Marcy l'Étoile, Val de Reuil and Neuville;
- United States: Swiftwater, Canton and Rockville;
- Canada: Toronto;
- India: Hyderabad (Shantha);
- China: Shenzhen;
- Argentina: Pilar;
- Mexico: Ocoyoacac; and
- Thailand: Chachoengsao.

Sanofi Pasteur also has its own R&D and production sites, either freehold or under finance leases with a purchase option exercisable on expiration of the lease.

**Research & Development sites**

In Pharmaceuticals, research and development activities are conducted at 14 sites:

- six operational sites in France: Chilly/Longjumeau, Marcy l'Etoile, Montpellier, Strasbourg, Toulouse and Vitry/Alfortville;
- two sites in the rest of Europe (Germany and the Netherlands), the larger of which is in Frankfurt (Germany);

- four sites in the United States, the Bridgewater, Cambridge, Framingham and Great Valley sites; and
- two sites in Asia (a clinical research unit in Beijing, China and a unit in Japan).

Vaccines research and development sites are:

- United States: Swiftwater, Cambridge, Orlando;
- France: Marcy L'Etoile/Lyon;
- Canada: Toronto.

### D.3. ACQUISITIONS, CAPITAL EXPENDITURES AND DIVESTITURES

The carrying amount of our property, plant and equipment at December 31, 2016 was €10,019 million. During 2016, we invested €1,093 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 2014, 2015 and 2016 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, 2016, our firm commitments in respect of future capital expenditures amounted to €545 million. The principal locations involved were: for the Pharmaceuticals segment, the industrial facilities at Frankfurt (Germany), Framingham and Allston (United States), Geel (Belgium), Waterford (Ireland), Sisteron and Elbeuf (France) ; and for the Vaccines segment, the facilities at Swiftwater (United States), Toronto (Canada) and Marcy L'Étoile (France).

In the medium term and assuming no changes in the scope of consolidation, we expect to invest on average some €1.8 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.

#### Pharmaceuticals

The Frankfurt facility, our principal site for the manufacture of **diabetes** treatments, is now equipped with an additional aseptic filling unit that uses isolator technology. Toujeo®, launched in 2015, is among the diabetes products handled in this new filling unit. The Diabetes industrial network has a solid base in emerging markets, both in Russia with the Orel site (now our second largest insulin pen production site after Frankfurt) and at the Beijing site in China. As part of the integration of Shantha (India) into our Injectables platform, the Indian site uses our proprietary manufacturing technology to handle filling and packaging for insulin products.

Our prefilled syringes network mainly delivers Lovenox®/ Clexane® from Le Trait (France) and Maisons Alfort (France) to global markets and from Csanyikvölgy (Hungary) to non-FDA/EMA regulated markets.

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), Origgio (Italy), Cologne (Germany) and Veresegyház (Hungary). Regional markets are supplied from our Suzano facility in Brazil, our Rzeszow facility in Poland and our ACE facility in Vietnam. Our facilities at Lisieux (France, production of Doliprane® for the French market), Hangzhou (China), Virginia (Australia), and the Chattem facility in Tennessee (United States), mainly supply their local markets. 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, and transforming the Origgio site into a facility dedicated to a single product family (Enterogermina®).

In 2014, a dedicated **Biologics** platform was launched to develop synergies between Pharmaceuticals, Sanofi Pasteur, Sanofi Genzyme and our Biotherapeutic activities. 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 through 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.

The development of our **Emerging Markets** platform is built on a network of over 30 regional and local industrial sites in 25 countries, supporting growth in those markets.

At Sidi Abdellah in Algeria we are building a new facility that will become our largest industrial complex in Africa, mainly producing dry and liquid formulations.

In Vietnam, we have completed construction of our new facility in Ho Chi Minh City, which manufactures specialty pharmaceuticals and CHC products.

The Industrial Affairs Department has an ongoing policy of adapting our industrial facilities to market needs. As part of this process, we closed our facilities at Fawdon (United Kingdom) and Bogota (Colombia) in 2015 and at Kansas City (United States) in 2016, and we have announced the closure of our facility at Saint Louis (United States) in 2017. We sold our facilities at Quetigny (France) in 2015 and at

Mirador (Argentina) in 2016, and reached agreement with a third party to sell our facility at Dakar (Senegal) in 2016.

**Vaccines (Sanofi Pasteur)**

Sanofi Pasteur's industrial operations are in a major investment phase, preparing for the upcoming growth of our flu and Polio/Pertussis/Hib franchises. Major investments are being launched in France, Canada, the US and Mexico.

**Innovation and culture of industrial excellence**

In 2016, we highlighted industrial innovation in our various facilities by organizing our eighth 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.

### D.4. OFFICE SPACE

As part of the worldwide rationalization of our office space we are reassessing our real estate needs across all our sites to bring our people closer together, with a responsible environmental footprint and new working practices.

Following the completion in 2015 of our office space master plan for the Greater Paris area, which brought some 3,000 of our people together on our new urban campus at Gentilly, we are now rolling out a similar master plan for the Lyon area. This plan will bring teams from Sanofi Pasteur and support staff together on the "Carteret" campus, featuring environmentally-certified buildings with dynamic workspaces similar to those at Gentilly. The final spaces on this site are due to be delivered in 2017.

Further office space rationalization will be achieved by a master plan for Cambridge, Massachusetts (United States), under which Genzyme and Sanofi operations will be brought together under a single roof in an environmentally-certified building currently being developed for delivery in 2018. During 2016, other major projects designed to encourage new working practices and optimize our real estate footprint were delivered in Ireland, the Philippines, Bulgaria and Westborough (United States). Further projects launched in 2016 and due for delivery in 2017 – at Sao Paulo (Brazil) and Tokyo (Japan) for example – are intended to meet the same objectives: rationalizing space while promoting teamwork and innovation.

Over 25 non-operational sites were divested during 2016, the main ones being Romainville and Bagneux (France), Guadalajara (Mexico), Kansas City (United States) and Algiers (Algeria).

# Item 4A. Unresolved Staff Comments

N/A

# 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, 2016.

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. 2016 Overview

Throughout 2016 we continued to make progress towards our key strategic objectives: reorganizing our operations, successfully launching new products, enhancing innovation in R&D and streamlining our organization.

During 2016, Sanofi and Boehringer Ingelheim (BI) finalized the negotiations initiated in December 2015 with a view to swapping our Animal Health business for BI's Consumer Healthcare business. This transaction closed on January 1, 2017, strengthening our position in the consumer healthcare market[1]. In 2016, the portfolio of BI Consumer Healthcare products acquired by Sanofi generated net sales estimated to be approximately €1.5 billion. Due to the closing of this transaction, the Animal Health business is no longer an operating segment within the meaning of IFRS 8. In the consolidated income statement, the net income or loss of this business is presented in a separate line item, ***Net income/(loss) of the held-for-exchange Animal Health business***, in accordance with IFRS 5 (see Notes B.7., D.2. and D.36. to the consolidated financial statements, included at Item 18 of this annual report).

At the end of December 2016, Sanofi Pasteur and MSD (known as Merck in the United States and Canada) ended their European joint venture Sanofi Pasteur MSD (SPMSD). This transaction involves the divestment of our share in the joint venture and the acquisition of the vaccines portfolio that reverts to Sanofi. The derecognition of our interest in SPMSD generated a pre-tax gain on disposal of €211 million, included in our consolidated income statement within the line item ***Other gains and losses, and litigation*** (see Note D.28. to the consolidated financial statements). The consolidation of SPMSD's operations relating to the Sanofi vaccines portfolio led to the recognition of intangible assets of €465 million and goodwill of €5 million. We estimate that the additional annual net sales derived from this transaction will be approximately €280 million, based on 2016 figures.

During 2016, we continued our policy of securing research and development alliances and making targeted acquisitions. In immuno-oncology, we entered into a collaboration and license agreement with Innate Pharma, and extended our collaboration with Warp Drive Bio to discover novel oncology therapeutics and antibiotics. In diabetes, we joined forces with Verily Life Sciences LLC (formerly Google Life Sciences) to form Onduo, a joint venture to develop comprehensive diabetes management solutions.

Successes for our R&D efforts in 2016 included the entry into Phase III of dupilumab in nasal polyposis, sotagliflozin in type 2 diabetes, isatixumab for patients with relapsed and refractory multiple myeloma and GZ402666 (NeoGAA) in the treatment of Pompe disease which is a rare disease caused by the deficiency of the enzyme acid alpha-glucosidase. A number of launches were carried out during the year following the granting of regulatory approvals, in particular Praluent® (hypercholesterolemia) in Japan and Adlyxin™ (diabetes) in the United States, followed by Soliqua™ 100/33 (insulin glargine and lixisenatide for diabetes) in the United States at the start of 2017. The launch of Suliqua™, the European trade name for the same association, is planned in Europe in 2017.

Since January 2016, we have been streamlining our organization and rolling out our new structure, composed of five global business units (GBUs): General Medicines & Emerging Markets, Sanofi Genzyme (Specialty Care), Diabetes & Cardiovascular, Sanofi Pasteur (Vaccines), and Animal Health. Following the transaction with BI, this last GBU has been replaced by the Consumer Healthcare GBU, which has been operational since January 1, 2017. To support this new organizational structure, we have embarked on a program to improve the excellence of our delivery by implementing a global information systems solution and by standardizing and consolidating our processes.

*(1) The closing of the acquisition of Merial in Mexico and the exchange of Merial with BI's Consumer Healthcare operations in India have been delayed, and should be finalized in 2017.*

Net sales for the year ended December 31, 2016 were €33,821 million, 0.7% lower than in 2015, but 1.2% higher at constant exchange rates (CER)[1]. This CER growth was driven mainly by the Sanofi Genzyme (Specialty Care) and Sanofi Pasteur (Vaccines) GBUs.

***Net income attributable to equity holders of Sanofi*** reached €4,709 million, up 9.8% (on a reported basis) on 2015, while basic earnings per share was 11.6% higher year-on-year (on a reported basis) at €3.66. Business net income[2] totaled €7,308 million, 0.9% lower (+2.5% CER) than in 2015, while business earnings per share[2] was up 0.7% (+4.1% CER) at €5.68. For a further discussion and definition of "business net income", and business earnings per share for the years ended December 31, 2016, 2015 and 2014, see "– Business Net Income" below.

Our debt, net of cash and cash equivalents[3] increased during 2016 and stood at €8,206 million as of December 31, 2016, compared with €7,254 million a year earlier, due largely to our share repurchase program of €2.9 billion (versus €1.8 billion in 2015), in anticipation of the cash to be received as part of the asset swap with Boehringer Ingelheim. The Annual General Meeting, to be held on May 10, 2017, will be asked to approve a dividend of €2.96 per share for the 2016 financial year, representing a payout of 52.1% 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 2016 due to competition from generics and biosimilars. While 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, we are able to estimate the impact that generic competition has had on each product.

A comparison of our consolidated net sales for the years ended December 31, 2016 and 2015 (see "– Results of Operations – Year Ended December 31, 2016 Compared with Year Ended December 31, 2015" below) shows that in 2016, generic competition led to a loss of €676 million of net sales on a reported basis.

The table below sets forth the impact by product.

| *(€ million)* | 2016 | 2015 | Change on a reported basis (€m) | Change on a reported basis (%) |
|---|---|---|---|---|
| Aprovel® Europe | 127 | 148 | (21) | -14.2% |
| Lantus® Europe | 878 | 991 | (113) | -11.4% |
| Lovenox® Europe | 1,027 | 1,049 | (22) | -2.1% |
| Plavix® Europe | 162 | 184 | (22) | -12.0% |
| Renagel®/Renvela® Europe | 82 | 121 | (39) | -32.2% |
| Ambien® United States | 84 | 74 | 10 | +13.5% |
| Lovenox® United States | 54 | 77 | (23) | -29.9% |
| Taxotere® United States | 4 | (1) | 5 | N/S |
| Allegra® Japan | 174 | 180 | (6) | -3.3% |
| Amaryl® Japan | 36 | 46 | (10) | -21.7% |
| Aprovel® Japan | 82 | 94 | (12) | -12.8% |
| Lantus® Japan | 74 | 112 | (38) | -33.9% |
| Myslee® Japan | 110 | 121 | (11) | -9.1% |
| Plavix® Japan | 355 | 695 | (340) | -48.9% |
| Taxotere® Japan | 26 | 60 | (34) | -56.7% |
| **Total excluding Emerging Markets** | **3,275** | **3,951** | **(676)** | **-17.1%** |

*(1) See definition under "A.1.6. Presentation of Net Sales" below*
*(2) Non-GAAP financial measure: see definition under "A.1.5. Segment information – 3/ Business Net Income" below*
*(3) Non-GAAP financial measure: see definition under "B. Liquidity and Capital Resources" below*

We expect the erosion caused by generic competition to continue in 2017, with a negative impact on our net income. The products likely to be impacted are those that already faced generic competition in 2016, but whose sales can reasonably be expected to be subject to further sales erosion in 2017: Aprovel®, Lantus®, Lovenox®, Plavix® and Renagel®/Renvela® in Europe; Ambien®, Lantus®, Lovenox® and Taxotere® in the United States; and Allegra®, Amaryl®, Aprovel®, Myslee®, Lantus®, Plavix® and Taxotere® in Japan. We also anticipate generic competition for Renagel®/ Renvela® in the United States in the first half of 2017.

Specifically as regards Lantus® in the United States, in September 2015 we reached an out-of-court settlement with Eli Lilly and Company (Lilly) regarding the patents for Lantus® SoloSTAR® (insulin glargine). This settlement brought an end to a patent infringement action in the United States relating to a new drug application by Lilly for a rival product to Lantus® SoloSTAR®. Sanofi and Lilly agreed to terminate that action and other similar proceedings worldwide. Under the terms of the settlement, Lilly will pay royalties to Sanofi in return for a license covering specified Sanofi patents. In the United States, Lilly began commercializing its insulin glargine in mid-December 2016. Lantus® in the United States is not shown in the table above because we believe it would be inaccurate to associate the decline in sales of this product in the United States during 2016 with competition from biosimilars, the decline having been primarily due to a fall in the average selling price of the product. The settlement does not include the injectable solution formulation of Lantus® in vials, Toujeo®, or combination products (for further information see Item 8 – "Information on Legal or Arbitration Proceedings – Lantus® and Lantus SoloSTAR® Patent Litigation").

In 2016, the consolidated net sales of these products in countries where generic competition currently exists or is expected in 2017 amounted to €7,567 million; this comprises €4,434 million in the United States (including €3,528 million in net sales of Lantus® and €764 million in net sales of Renagel®/Renvela®); €2,276 million in Europe; and €857 million in Japan. The negative impact on our 2017 net sales is expected to represent a substantial proportion of this amount, but the actual impact will depend on a number of factors such as the actual launch dates of generic products in 2017, the prices at which they 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, 2016, 2015 and 2014 have been significantly affected by our August 2004 acquisition of Aventis, our April 2011 acquisition of Genzyme and certain subsequent transactions. See "– Critical accounting and reporting policies – Business combinations" below for an explanation of the impact of business combinations on our results of operations.

The Genzyme business combination has generated significant amortization of intangible assets (€866 million in 2016, €890 million in 2015 and €811 million in 2014) and impairment of intangible assets (net reversal of €6 million in 2016, expenses of €214 million in 2015 and net reversal of €309 million in 2014). The Aventis business combination has also generated significant amortization expenses (€482 million in 2016, €638 million in 2015 and €874 million in 2014).

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, human vaccines and active ingredients, 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 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.14. 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

*(1) Non-GAAP financial measure: see definition under "A.1.5. Segment information – 3/ Business Net Income" below*

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 "– Segment Information – 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 Note D.35. ("Segment Information") to our consolidated financial statements, included at Item 18 of this annual report.

Sanofi now has two operating segments: Pharmaceuticals and Human Vaccines (Vaccines) (See Note B.26. to our consolidated financial statements). The Animal Health business was no longer an operating segment as of December 31, 2016, following the exchange deal with Boehringer Ingelheim that was finalized at the start of January 2017 (see Note D.2. to our consolidated financial statements).

The Pharmaceuticals segment comprises the commercial operations of the following franchises: Speciality Care (Rare Diseases, Multiple Sclerosis, Oncology), Diabetes & Cardiovascular, Established Prescription Products, Consumer Healthcare and Generics; and dedicated research and development, production and marketing activities for all of Sanofi's pharmaceuticals operations.

The Sanofi pharmaceuticals portfolio consists of flagship products (see "– A.2. Results of Operations – A.2.2. Net Sales" below), plus a broad range of prescription medicines, generic medicines, and Consumer Healthcare products. This segment also includes all associates whose activities are related to pharmaceuticals, in particular Regeneron Pharmaceuticals, Inc. and the entities majority owned by Bristol-Myers Squibb (BMS).

The Vaccines segment is wholly dedicated to vaccines and includes the commercial operations of Sanofi Pasteur and dedicated research and development, production and marketing activities for Sanofi's vaccines operations. This segment included the Sanofi Pasteur MSD joint venture until December 30, 2016, the date on which the joint venture ended.

Each segment includes global support function costs as allocated for internal reporting purposes within Sanofi.

The "Other" segment includes all activities that do not qualify as reportable segments under IFRS 8. This segment includes the effects of retained commitments in respect of divested activities.

Inter-segment transactions are not material.

#### *2/ Business Operating Income*

We report segment results on the basis of "Business operating income". This indicator is used internally by the chief operating decision maker of the Company to measure the performance of each operating segment and to allocate resources, in accordance with IFRS 8. Business operating income is derived from ***Operating income***, adjusted as follows:

- the amounts reported in the line items ***Restructuring costs and similar items***, ***Fair value remeasurement of contingent consideration liabilities*** and ***Other gains and losses, and litigation*** are eliminated;
- amortization and impairment losses charged against intangible assets (other than software and other rights of an industrial or operational nature) are eliminated;
- the share of profits/losses of associates and joint ventures (excluding restructuring costs relating to associates and joint ventures) is added;
- net income attributable to non-controlling interests is deducted; and
- other acquisition-related effects (primarily the workdown of acquired inventories remeasured at fair value at the acquisition date, and the impact of acquisitions on investments in associates and joint ventures) are eliminated.
- the non-recurring adjustment recognized in 2014 for the annual Branded Prescription Drug (BPD) Fee in the United States (following publication by the US Internal Revenue Service in July 2014 of the final regulations on that fee) is also eliminated.

The table below shows a reconciliation between total "business operating income" for our operating segments and ***Income before tax and associates and joint ventures***, as required by IFRS 8.

| *(€ million)* | 2016 | 2015 | 2014 |
|---|---|---|---|
| **Business operating income** | **9,285** | **9,313** | **8,957** |
| Share of (profit)/loss of associates and joint ventures[a] | (177) | (169) | (146) |
| Net income attributable to non-controlling interests[b] | 113 | 126 | 126 |
| Amortization of intangible assets | (1,692) | (2,137) | (2,081) |
| Impairment of intangible assets | (192) | (767) | 31 |
| Fair value remeasurement of contingent consideration liabilities | (135) | 53 | (303) |
| Restructuring costs and similar items | (879) | (795) | (404) |
| Additional year expense related to US Branded Prescription Drug Fee[c] | - | - | (116) |
| Other gains and losses, and litigation[d] | 211 | - | - |
| **Operating income** | **6,534** | **5,624** | **6,064** |
| Financial expenses[e] | (924) | (559) | (598) |
| Financial income | 68 | 178 | 192 |
| **Income before tax and associates and joint ventures** | **5,678** | **5,243** | **5,658** |

*(a) Excluding restructuring costs of associates and joint ventures and expenses arising from the impact of acquisitions on associates and joint ventures, and after elimination of Sanofi's 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 (€52 million in 2016).*

*(b) Excluding restructuring costs and other adjustments attributable to non-controlling interests.*

*(c) Annual fee related to 2013 sales: the IRS reform of July 2014 altered the date on which the liability is recognized, such that the expense recognized during 2014 was based on both 2013 and 2014 sales.*

*(d) This line item consists of the pre-tax gain on divestment of Sanofi's interest in the Sanofi Pasteur MSD joint venture.*

*(e) In 2016, this line includes the impairment loss of €457 million taken against the investment in Alnylam.*

### *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 financial income/(expense) and the relevant income tax effects. For the year ended December 31, 2016 and comparative periods, "Business net income" consists of (i) "Business net income excluding Animal Health", determined as described above and (ii) "Animal Health business net income", determined on a similar and comparable basis.

We also report "business earnings per share", a non-GAAP financial measure which we define as business net income divided by the weighted average number of shares outstanding.

The table below reconciles our business operating income to our business net income:

| *(€ million)* | 2016 | 2015 | 2014 |
|---|---|---|---|
| **Business operating income** | **9,285** | **9,313** | **8,957** |
| Financial income/(expense) | (399) | (381) | (441) |
| Income tax expense | (2,054) | (1,929) | (2,033) |
| **Business net income excluding Animal Health** | **6,832** | **7,003** | **6,483** |
| Animal Health business net income | 476 | 368 | 364 |
| **Business net income** | **7,308** | **7,371** | **6,847** |

Business net income is defined 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 liabilities relating to business combinations;
- other impacts associated with acquisitions (including impacts of acquisitions on associates and joint ventures);
- the non-recurring adjustment recognized in 2014 for the Annual Branded Prescription Drug (BPD) Fee in the United States (following publication by the US Internal Revenue Service in July 2014 of the final regulations on that fee);
- 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];
- the tax effects related to the items listed above;
- the effects of major tax disputes;
- the 3% tax on the distribution of dividends to equity holders of Sanofi;
- those Animal Health items that are not included in business net income[3];
- the portion attributable to non-controlling interests of the items listed above; and
- the impairment loss taken against our shares in Alnylam in 2016 to reflect a decline in the market value of those shares as of the reporting date relative to their historical cost, mostly resulting from Alnylam's decision to discontinue the revusiran development program on October 5, 2016.

Business net income also includes our share of the business net income of the SPMSD joint venture with effect from the date on which Sanofi and Merck announced their intention to end the joint venture.

(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.*
(3) *Impact of discontinuation of depreciation and impairment of property, plant and equipment from the start date of application of IFRS 5 (Non-current Assets Held for Sale and Discontinued Operations), amortization and impairment of intangible assets until the start date of IFRS 5 application, costs incurred as a result of the divestment, and the tax effects of these items.*