NOVARTIS AG
Form 20-F
January 30, 2019

As filed with the Securities and Exchange Commission on January 30, 2019
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington D.C. 20549

Form 20-F

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o REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR 12(g) OF THE SECURITIES EXCHANGE ACT OF 1934
OR
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 for the fiscal year ended December 31, 2018
OR
o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
OR
o SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission file number 1-15024
Novartis AG
(Exact name of Registrant as specified in its charter)
NOVARTIS Inc.
(Translation of Registrant's name into English)
Switzerland
(Jurisdiction of incorporation or organization)
Lichtstrasse 35
4056 Basel, Switzerland
(Address of principal executive offices)
Shannon Thyme Klinger
Group General Counsel
Novartis AG
CH 4056 Basel
Switzerland
Tel.: 011-41-61-324-1111
Fax: 011-41-61-324-7826
(Name, Telephone, E mail and/or Facsimile number and Address of Company Contact Person)
Securities registered pursuant to Section 12(b) of the Act:

Title of class	**Name of each exchange on which registered**
American Depositary Shares each representing 1 share	**New York Stock Exchange**
Ordinary shares, nominal value CHF 0.50 per share*	**New York Stock Exchange***

Securities registered or to be registered pursuant to Section 12(g) of the Act:
None
Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:
None
Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report:
2,311,171,429 shares
Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.
Yes x **No** o

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 o **No** x

Note—Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

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 x **No** o

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes x **No** o

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

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

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

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

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

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

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 o **Item 18** o

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 o **No** x

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

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Introduction and use of certain terms

Novartis AG and its consolidated affiliates publish consolidated financial statements expressed in US dollars. Our consolidated financial statements responsive to Item 18 of this Annual Report on Form 20-F (Annual Report) are prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB). “Item 5. Operating and Financial Review and Prospects,” together with the sections on products in development and key development projects of our businesses (see “Item 4. Information on the Company—Item 4.B. Business overview”), constitute the Operating and Financial Review (“Lagebericht”), as defined by the Swiss Code of Obligations.

Unless the context requires otherwise, the words “we,” “our,” “us,” “Novartis,” “Group,” “Company,” and similar words or ph in this Annual Report refer to Novartis AG and its consolidated affiliates. However, each Group company is legally separate from all other Group companies and manages its business independently through its respective board of directors or similar supervisory body or other top local management body, if applicable. Each executive identified in this Annual Report reports directly to other executives of the Group company that employs the executive, or to that Group company’s board of directors.

In this Annual Report, references to “US dollars,” “USD” or “$” are to the lawful currency of the United States of America, and references to “CHF” are to Swiss francs; references to the “United States” or to “US” are to the United States of America, references to the “European Union” or to “EU” are to the European Union and its 28 member states, references to “Latin America” are to Central and South America, including the Caribbean, and references to “Australasia” are to Australia, New Zealand, Melanesia, Micronesia and Polynesia, unless the context otherwise requires; references to the “EC” are to the European Commission; references to “associates” are to employees of our affiliates; references to the “SEC” are to the US Securities and Exchange Commission; references to the “FDA” are to the US Food and Drug Administration, references to “EMA” are to the European Medicines Agency, an agency of the EU, and references to the “CHMP” are to the Committee for Medicinal Products for Human Use of the EMA; references to “ADR” or “ADRs” are to Novartis American Depositary Receipts, and references to “ADS” or “ADSs” are to Novartis American Depositary Shares; references to the “NYSE” are to the New York Stock Exchange, and references to “SIX” are to the SIX Swiss Exchange; references to “ECN” are to the Executive Committee of Novartis; references to “GSK” are to GlaxoSmithKline plc, references to “AAA” are to Advanced Accelerator Applications S.A., references to “AveXis” are to AveXis, Inc., and references to “Endocyte” are to Endocyte, Inc.

All product names appearing in italics are trademarks owned by or licensed to Group companies. Product names identified by a “®” or a “™” are trademarks that are not owned by or licensed to Group companies and are the property of their respective owners.

Forward-looking statements

This Annual Report contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934, and the United States Private Securities –Litigation Reform Act of 1995, each as amended from time to time. Other written materials filed with or furnished to the SEC by Novartis, as well as other written and oral statements made to the public, may also contain forward-looking statements. Forward-looking statements can be identified by words such as “potential,” “expected,” “will,” “planned,” “pipelin “outlook,” or similar terms, or by express or implied discussions regarding potential new products, potential new indications for existing products, or regarding potential future revenues from any such products; or regarding the potential outcome, or financial or other impact on Novartis, of the proposed spin-off of our Alcon Division, or of the proposed divestiture of certain portions of our Sandoz Division business in the US; or regarding the potential impact of the share buyback plan; or regarding potential future sales or earnings of the Group or any of its divisions or potential shareholder returns; or regarding potential future credit ratings of the Group; or by discussions of strategy, plans, expectations or intentions. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the –forward-looking statements. You should not place undue reliance on these statements.

In particular, our expectations could be affected by, among other things:

• Global trends toward healthcare cost containment, including ongoing government, payer and general public pricing and reimbursement pressures and requirements for increased pricing transparency;

• Regulatory actions or delays or government regulation generally, including potential regulatory actions or delays with respect to the proposed transactions or the development of the products described in this Annual Report;

• The potential that the strategic benefits, synergies or opportunities expected from the proposed transactions may not be realized or may take longer to realize than expected;

• The inherent uncertainties involved in predicting shareholder returns;

• The uncertainties inherent in the research and development of new healthcare products, including clinical trial results and additional analysis of existing clinical data;

• Our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products that commenced in prior years and will continue this year;

• Safety, quality or manufacturing issues;

• Uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential litigation with respect to the proposed transactions, product liability litigation, litigation and investigations regarding sales and marketing practices, intellectual property disputes and government investigations generally;

• Uncertainties involved in the development or adoption of potentially transformational technologies and business models;

• Our performance on environmental, social and governance measures;

• General political, economic and trade conditions, including uncertainties regarding the effects of ongoing instability in various parts of the world;

• Uncertainties regarding future global exchange rates;

• Uncertainties regarding future demand for our products; and

• Uncertainties regarding potential significant breaches of data security or data privacy, or disruptions of our information technology systems.

Some of these factors are discussed in more detail in this Annual Report, including under “Item 3. Key Information—Item 3.D. Risk factors,” “Item 4. Information on the Company,” and “Item 5. Operating and Financial Review and Prospects.” Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described in this Annual Report as anticipated, believed, estimated or expected. We provide the information in this Annual Report as of the date of its filing. We do not intend, and do not assume any obligation, to update any information or forward-looking statements set out in this Annual Report as a result of new information, future events or otherwise.

Part I

Item 1. Identity of Directors, Senior Management and Advisers

Not applicable.

Item 2. Offer Statistics and Expected Timetable

Not applicable.

Item 3. Key Information

3.A Selected financial data

The selected financial information set out below has been extracted from our consolidated financial statements prepared in accordance with IFRS as issued by the IASB. Our consolidated financial statements for the years ended December 31, 2018, 2017 and 2016, are included in "Item 18. Financial Statements" in this Form 20-F.
All financial data should be read in conjunction with "Item 5. Operating and Financial Review and Prospects." All financial data presented in this Form 20-F are qualified in their entirety by reference to the consolidated financial statements and their notes.

	Year ended December 31,				
(USD millions, except per share information)	2018	2017	2016	2015	2014
INCOME STATEMENT DATA					
Net sales to third parties from continuing operations	51 900	49 109	48 518	49 414	52 180
Operating income from continuing operations	8 169	8 629	8 268	8 977	11 089
Income from associated companies	6 438	1 108	703	266	1 918
Interest expense	– 957	– 777	– 707	– 655	– 704
Other financial income and expense	185	39	– 447	– 454	– 31
Income before taxes from continuing operations	13 835	8 999	7 817	8 134	12 272
Taxes	– 1 221	– 1 296	– 1 119	– 1 106	– 1 545
Net income from continuing operations	12 614	7 703	6 698	7 028	10 727
Net income/(loss) from discontinued operations[1]				10 766	– 447
Group net income	12 614	7 703	6 698	17 794	10 280
Attributable to:					
Shareholders of Novartis AG	12 611	7 703	6 712	17 783	10 210
Non-controlling interests	3	0	– 14	11	70
Basic earnings per share (USD)					
Continuing operations	5.44	3.28	2.82	2.92	4.39
Discontinued operations				4.48	– 0.18
Total	5.44	3.28	2.82	7.40	4.21
Diluted earnings per share (USD)					
Continuing operations	5.38	3.25	2.80	2.88	4.31
Discontinued operations				4.41	– 0.18
Total	5.38	3.25	2.80	7.29	4.13
Cash dividends[2]	6 966	6 495	6 475	6 643	6 810
Cash dividends per share in CHF[3]	2.85	2.80	2.75	2.70	2.60
Personnel cost[4, 5]	15 651	13 932	13 681	13 540	14 569
Full-time equivalent associates at year-end[5]	125 161	121 597	118 393	118 700	117 809

[1] In 2015, Novartis completed a series of portfolio transformation transactions, including the divestments of its Animal Health and Vaccines business. In addition, a combined consumer healthcare business was created through the combination of the Novartis OTC and GlaxoSmithKline (GSK) Consumer Healthcare businesses. On March 2, 2015 a new entity, GlaxoSmithKline Consumer Healthcare Holdings Ltd. (GSK Consumer Healthcare) was formed via contribution of businesses from both Novartis and GSK. Novartis had a 36.5% interest in the newly created entity. To reflect these transactions, Novartis reported the Group's financial results for 2015 and 2014 as "continuing operations" and "discontinued operations", as required by IFRS.

[2] Cash dividends represent cash payments in the applicable year that generally relates to earnings of the previous year.

[3] Cash dividends per share represent dividends proposed that relate to earnings of the current year. Dividends for 2014 through 2017 were approved at the respective AGMs and dividends for 2018 will be proposed to the Annual General Meeting on February 28, 2019 for approval.

[4] Personnel cost include wages, salaries, allowances, commissions and bonuses to staff, overtime, awards, holiday pay, severance payments and social welfare expenses.

[5] Own employees

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	Year ended December 31,				
(USD millions)	2018	2017	2016	2015	2014
BALANCE SHEET DATA					
Cash, cash equivalents and marketable securities & derivative financial instruments	15 964	9 485	7 777	5 447	13 862
Inventories	6 956	6 867	6 255	6 226	6 093
Other current assets	11 836	11 856	10 899	11 172	10 805
Non-current assets	110 000	104 871	105 193	108 711	87 826
Assets of disposal group held for sale[1]	807				
Assets related to discontinued operations[2]					6 801
Total assets	145 563	133 079	130 124	131 556	125 387
Trade accounts payable	5 556	5 169	4 873	5 668	5 419
Other current liabilities	24 000	18 234	17 336	18 040	19 136
Non-current liabilities	37 264	35 449	33 024	30 726	27 570
Liabilities of disposal group held for sale[1]	51				
Liabilities related to discontinued operations[2]					2 418
Total liabilities	66 871	58 852	55 233	54 434	54 543
Issued share capital and reserves attributable to shareholders of Novartis AG	78 614	74 168	74 832	77 046	70 766
Non-controlling interests	78	59	59	76	78
Total equity	78 692	74 227	74 891	77 122	70 844
Total liabilities and equity	145 563	133 079	130 124	131 556	125 387
Net assets	78 692	74 227	74 891	77 122	70 844
Outstanding share capital	875	869	896	890	898
Total outstanding shares (millions)	2 311	2 317	2 374	2 374	2 399

[1] The disposal group held for sale relate to the assets and liabilities of the pending divestment of the Sandoz US dermatology business and generic US oral solids portfolio to Aurobindo Pharma USA Inc., as announced on September 6, 2018 (see “item 18. Financial Statements – Note 2 Significant pending transactions).
[2] A description of discontined operations can be found in footnote 1 of the table above.

Cash dividends per share
Cash dividends are translated into US dollars at the Bloomberg Market System Rate on the payment date. Because we pay dividends in Swiss francs, exchange rate fluctuations will affect the US dollar amounts received by holders of ADRs.

Year earned	Month and year paid	Total dividend per share (CHF)	Total dividend per share (USD)
2014	March 2015	2.60	2.67
2015	March 2016	2.70	2.70
2016	March 2017	2.75	2.72
2017	March 2018	2.80	2.94
2018 [1]	March 2019	2.85	2.89 [2]

[1] Dividend to be proposed at the Annual General Meeting on February 28, 2019 and to be distributed March 6, 2019
[2] Translated into US dollars at the December 31, 2018 rate of USD 1.014 to the Swiss franc. This translation is an example only, and should not be construed as a representation that the Swiss franc amount represents, or has been or could be

converted into US dollars at that or any other rate.

3.B Capitalization and indebtedness

Not applicable.

3.C Reasons for the offer and use of proceeds

Not applicable.

3.D Risk factors

Our businesses face significant risks and uncertainties. You should carefully consider all of the information set forth in this Annual Report and in other documents we file with or furnish to the SEC, including the Form 20-F filed with the SEC by our subsidiary Alcon Inc. in connection with our planned spin-off of the Alcon business, as well as the following risk factors, before deciding to invest in or to maintain an investment in any Novartis securities. Our business, as well as our financial condition or results of operations, could be materially adversely affected by any of these risks, as well as other risks and uncertainties not currently known to us or not currently considered material.

Risks facing our business

Our products face losses of intellectual property protection.

Major products of our Innovative Medicines Division, as well as certain products of our Sandoz and Alcon Divisions, are protected by patent and other intellectual property rights, which provide us with exclusive rights to market the products, and give us an opportunity to recoup our investments in research and development. However, the strength and duration of those intellectual property rights can vary significantly from product to product and country to country, and they may be successfully challenged by third parties or governmental authorities. Loss of market exclusivity for one or more important products has had, and can be expected to continue to have, a material adverse effect on our results of operations.

The introduction of generic competition for a patented branded medicine typically results in a significant and rapid reduction in net sales and operating income for the branded product because generic manufacturers typically offer their unpatented versions at sharply lower prices. Such competition can occur after successful challenges to intellectual property rights or the regular expiration of the term of the patent or other intellectual property rights. Such competition can also result from the entry of generic versions of another medicine in the same therapeutic class as one of our drugs or in another competing therapeutic class, from a Declaration of Public Interest or the compulsory licensing of our drugs by governments, or from a general weakening of intellectual property laws in certain countries around the world. In addition, generic manufacturers sometimes take an aggressive approach to challenging intellectual property rights, including conducting so-called “launches at risk” of products that are still under legal challenge for infringement, before final resolution of legal proceedings.

We also rely in all aspects of our businesses on unpatented proprietary technology, know how, trade secrets and other confidential information, which we seek to protect through various measures, including confidentiality agreements with licensees, employees, third-party collaborators, and consultants who may have access to such information. If these agreements are breached or our other protective measures should fail, then our contractual or other remedies may not be adequate to cover our losses.

Some of our best-selling products have begun or are about to face significant competition due to the end of market exclusivity resulting from the expiry of patent or other intellectual property protection.

• Our former top-selling products *Gleevec/Glivec, Diovan* and *Exforge* all face continued and increasing generic competition in major markets.

• Patent protection for the marketed forms of our *Sandostatin* products has expired. Generic versions of *Sandostatin* SC are available in the US, the EU and Japan. While there is currently no generic competition in the US, the EU or Japan for *Sandostatin* LAR, the long-acting version of *Sandostatin* that represents the majority of our *Sandostatin* sales, such generic competition may arise in the future.

• Intellectual property protecting a number of additional major products is either being challenged or will expire at various times in the coming years, raising the possibility of generic competition. Among these products that may begin to face generic competition in one or more major markets during the next three years are *Gilenya*, our everolimus products (*Afinitor/Votubia* and *Zortress/Certican*), *Exjade* and *Jadenu*, and *Lucentis*.

For more information on the patent and generic competition status of our Innovative Medicines Division’s products, see “Item 4. Information on the Company—Item 4.B Business overview—Innovative Medicines—Intellectual property.”

In 2019, we expect a potentially significant impact on our net sales from products that have already lost intellectual property protection, as well as products that will lose protection during the year. Because we typically have substantially reduced marketing and research and development expenses related to products that are in their final years of exclusivity, the initial loss of intellectual property protection for a product during the year could also have an impact on our 2019 operating income in an amount corresponding to a significant portion of the product’s lost sales.

The magnitude of the impact of generic competition on our income could depend on a number of factors, including the time of year at which the generic competitor is launched; the ease or difficulty of manufacturing a competitor product and obtaining regulatory approval to market it; the number of generic competitor products approved, including whether, in the US, a single competitor is granted an exclusive marketing period; whether an authorized generic is launched; the geographies in which generic competitor products are approved, including the strength of the market for generic pharmaceutical products in such geographies and the comparative profitability of branded

pharmaceutical products in such geographies; and our ability to successfully develop and launch profitable new products to replace the income lost to generic competition. See also "—Our research and development efforts may not succeed," below, with respect to the development and launch of new products.

Clearly, with respect to major products for which the patent terms are expiring, the loss of exclusivity of these products could have a material adverse effect on our business, financial condition, or results of operations. In addition, should we unexpectedly lose exclusivity on additional products as a result of patent litigation or other reasons, this could also have a material adverse effect on our business, financial condition, or results of operations, both due to the loss of revenue and earnings, and the difficulties in planning for such losses.

Our financial performance depends on the commercial success of key products.

Our financial performance, including our ability to replace revenue and income lost to generic and other competition and to grow our business, depends heavily on the commercial success of our products. If any of our major products were to become subject to problems such as changes in prescription growth rates, unexpected side effects, loss of intellectual property protection, supply chain issues or other product shortages, regulatory proceedings, changes in labeling, publicity affecting doctor or patient confidence in the product, material product liability litigation, or pressure from new or existing competitive products, the adverse impact on our revenue and profit could be significant. In addition, our revenue and profit could be significantly impacted by the timing and rate of commercial acceptance of key new products.

See also "—Our business is affected by pressures on pricing and reimbursement for our products," below, with regard to the impact of pricing and reimbursement issues on the commercial success of our products.

All of our businesses face intense competition from new products and technological advances from competitors, and physicians, patients and third-party payers may choose our competitors' products instead of ours if they perceive them to be safer, more effective, easier to administer, less expensive, more convenient or more cost-effective. Products that compete with ours are launched from time to time. We cannot predict with accuracy the timing of the introduction of such competitive products or their possible effect on our sales. However, products significantly competitive to our major products – including *Cosentyx, Lucentis, Gilenya, Sandostatin, Tasigna, Afinitor, Kisqali* and *Kymriah*– are on the market, and others are in development. In addition, numerous companies from around the world are seeking to enter the healthcare field to take advantage of their expertise in digital and other new technologies.

See "—We may fail to develop or take advantage of transformational technologies and business models," below.

Such competitive products could significantly affect the revenue from our products and our results of operations. This impact could also be compounded to the extent such competition results in us making significant additional investments in marketing and sales, or in research and development.

For example, our US Sandoz business has suffered significant declines in sales and profits in recent years due, at least in part, to increased competition in its product segments. There can be no certainty that Sandoz US sales will recover in the coming years. In any event, such competition and the costs of our efforts to improve the business's performance, as well as other factors, can be expected to affect the business, financial condition, or results of operations of this organization, at least in the near term. In addition, despite the devotion of significant resources to our efforts to improve the performance of Sandoz US, those efforts may ultimately prove insufficient. Should our efforts fail to accomplish their goals, or fail to do so in a timely manner, it could have a material adverse impact on our business, financial condition, or results of operations beyond the near term, as well.

See also "—Our research and development efforts may not succeed," and "—Competition and failure to successfully develop biosimilars and other differentiated products may impact the success of our Sandoz Division," below.

Our research and development efforts may not succeed.

We engage in extensive and costly research and development activities, both through our own dedicated resources and through collaborations with third parties, in an effort to identify and successfully and cost-effectively develop new products that address unmet and changing medical needs, are accepted by patients and physicians, are reimbursed by payers, and are commercially successful. Our ability to continue to maintain and grow our business; to replace sales lost due to competition, entry of generics or other reasons; and to bring to market products and medical advances that take advantage of new and potentially disruptive technologies, depends in significant part upon the success of these efforts. However, developing new healthcare products and bringing them to market is a highly costly, lengthy and uncertain process. In spite of our significant investments, there can be no guarantee that our research and development activities will produce commercially successful new products that will enable us to replace revenue and income lost to

generic and other competition and to grow our business. See also "—We may not successfully achieve our goals in transactions or reorganizations," below, with regard to our efforts to reorganize our Innovative Medicines product development organization.

Using the products of our Innovative Medicines Division as an example, the research and development process for a new product can take up to 15 years, or even longer, from discovery to commercial product launch – and with limited available intellectual property protections, the longer it takes to develop a product, the less time there may be for us to recoup our research and development costs. New products must undergo intensive preclinical and clinical testing, and must be approved by means of highly complex, lengthy and expensive approval processes that can vary from country to country.

During each stage, there is a substantial risk that we will encounter serious obstacles that will further delay us and add substantial expense, that we will develop a

product with limited potential for commercial success, or that we will be forced to abandon a product in which we have invested substantial amounts of time and money. These risks may include failure of the product candidate in preclinical studies, difficulty enrolling patients in clinical trials, clinical trial holds or other delays in completing clinical trials, insufficient clinical trial data to support the safety or efficacy of the product candidate or to differentiate our product candidate from competitors, delays in completing formulation and other testing and work necessary to support an application for regulatory approval, adverse reactions to the product candidate or other safety concerns, an inability to manufacture sufficient quantities of the product candidate for development or commercialization activities in a timely and cost-effective manner, and failure to obtain, or delays in obtaining, the required regulatory approvals for the product candidate or the facilities in which it is manufactured.

In addition, following the "Brexit" vote in the UK, the EU decided to move the headquarters of the EU's health authority, the EMA, from the UK to the Netherlands by March 2019. It is expected that a significant percentage of the current employees of the EMA will decide not to make the move to the Netherlands. This raises the possibility that new drug approvals in the EU could be delayed as a result.

Further, in recent years, in order to achieve approvals of new products and new indications, governmental authorities around the world have increasingly required more clinical trial data than they had in the past, the inclusion of significantly higher numbers of patients in clinical trials, and more detailed analyses of the trials. In addition, in order for a product to be reimbursed and to be commercially successful, payers and prescribers have increasingly required additional data that differentiates the product from other drugs on the market. As a result, despite significant efforts by health authorities such as the FDA to accelerate the development of new drugs, the already lengthy and expensive process of obtaining regulatory approvals and reimbursement for pharmaceutical products has in many cases become even more challenging.

Similarly, the post-approval regulatory burden has also increased. Approved drugs are subject to various requirements such as risk evaluation and mitigation strategies (REMS), risk management plans, comparative effectiveness studies, health technology assessments, and requirements to conduct post-approval Phase IV clinical trials to gather additional safety and other data on products. These requirements have the effect of making the maintenance of regulatory approvals for our products increasingly expensive, and further heightening the risk of recalls, product withdrawals, loss of market share, and loss of revenue and profitability.

There is also the risk that we may fail to identify significant new product candidates for development or potentially disruptive new technologies, and so may fail to take advantage of a potential new wave of innovation.

Our Alcon Division faces similar challenges in bringing new products to market, including both the products and components that have been developed in house, as well as those that have been acquired from third parties. Alcon's Surgical and Vision Care products face medical device development and approval processes that are often similarly as difficult as those faced by our Innovative Medicines Division. For example, in 2017 the EU published a new EU Medical Devices Regulation, which has introduced substantial changes to the requirements for medical device manufacturers bringing new products to the EU market, including with respect to clinical development, labeling, technical documentation and quality management systems. The regulation has a three-year implementation period. Further, the FDA is also pursuing various efforts to modernize its regulation of devices, including potential changes to existing regulatory approval pathways that could impact our device approval efforts. Alcon has taken steps to increase its innovation power and the success of its research and development efforts. But these efforts are costly and require extensive efforts over time. There can be no certainty that Alcon will be successful in these efforts, in either the short term or the long term, and if Alcon is not successful, there could be a material adverse effect on the success of the Alcon Division.

In addition, our Sandoz Division has made, and expects to continue to make, significant investments in the development of biotechnology-based, "biologic" medicines intended for sale as bioequivalent or "biosimilar" versions of currently marketed biotechnology products, as well as other differentiated, "difficult-to-make" generic products. While the development of such products typically is significantly less costly and complex than the development of the equivalent originator medicines, it is nonetheless often significantly more costly and complex than that for non-differentiated generic products. In addition, many countries do not yet have fully developed legislative or regulatory pathways to facilitate the development of biosimilars and permit biosimilars to be sold in a manner in which the biosimilar product would be readily substitutable for the originator product. Further delays in the development and completion of such regulatory pathways, or any significant impediments that may ultimately be built

into such pathways, or any other significant difficulties that may arise in the development or marketing of biosimilars or other differentiated products, could put at risk the significant investments that Sandoz has made, and will continue to make, in the development of differentiated products in general, and in its Biopharmaceuticals business in particular. Sandoz also achieves significant revenue opportunities when it secures and maintains exclusivity periods granted for generic products in certain markets – particularly the 180-day exclusivity period granted in the US by the Hatch Waxman Act for first-to-file generics. Failure to obtain and maintain such exclusivity periods or to successfully develop and market biosimilars and differentiated generic products could have a material adverse effect on the success of the Sandoz Division and the Group as a whole.

See also "—Competition and failure to successfully develop biosimilars and other differentiated products may impact the success of our Sandoz Division," below.

Further, in all of our divisions, our research and development activities must be conducted in an ethical and compliant manner. Among other things, we must be concerned with patient safety, data privacy, Good Clinical Practices requirements, data integrity requirements, the fair treatment of patients in developing countries, and animal welfare requirements. Should we fail to properly

manage such issues, we risk injury to third parties, damage to our reputation, negative financial consequences as a result of potential claims for damages, sanctions and fines, and the potential that our investments in research and development activities could have no benefit to the Group.

If we are unable to maintain a flow of successful, cost-effective new products and new indications for existing products that will sustain and grow our business, cover our substantial research and development costs and the decline in sales of older products that become subject to generic or other competition, and take advantage of technological and medical advances, then this could have a material adverse effect on our business, financial condition, or results of operations.

For a further description of the approval processes that must be followed to market our products, see the sections headed "Regulation" included in the descriptions of our operating divisions under "Item 4. Information on the Company—Item 4.B Business overview."

Our business is affected by pressures on pricing and reimbursement for our products.

Our businesses are operating in an ever more challenging environment, with significant pressures on the pricing of our products and on our ability to obtain and maintain satisfactory rates of reimbursement for our products by governments, insurers and other payers. The growth of overall healthcare costs as a percentage of gross domestic product in many countries means that governments and payers are under intense pressure to control healthcare spending even more tightly than in the past. These pressures are particularly strong given the increasing demand for healthcare resulting from the aging of the global population and associated increases in noncommunicable diseases, and the resulting impact on healthcare budgets. These pressures are further compounded by significant controversies and intense political debate and publicity about prices for pharmaceuticals that some consider excessive, including government regulatory efforts, funding restrictions, legislative proposals, policy interpretations, investigations and legal proceedings regarding pharmaceutical pricing practices.

See also "—Ongoing consolidation among our distributors and retailers is increasing both the purchasing leverage of key customers and the concentration of credit risk," below, with regard to the impact of the consolidation among our customers on our pricing; "—Our products face losses of intellectual property protection," above, with regard to the impact of the loss or risk of loss of intellectual property protections on our pricing; and "—Political and economic instability may impact our results," below, with regard to the impact of economic conditions on our pricing.

As a result, in addition to ongoing public and political pressures to limit the prices we charge for our products, we face numerous cost-containment measures imposed by governments and other payers, including government-imposed industrywide price reductions, mandatory pricing systems, reference pricing systems, payers limiting access to treatments based on cost-benefit analyses, imports of drugs from lower-cost countries to higher-cost countries, shifting of the payment burden to patients through higher co-payments, limiting physicians' ability to choose among competing medicines, mandatory substitution of generic drugs for the patented equivalent, growing pressure on physicians to reduce the prescribing of patented prescription medicines, increasing pressure on intellectual property protections, and requirements for increased transparency on pricing. For more information on such price controls, see "Item 4. Information on the Company—Item 4.B Business overview—Innovative Medicines—Price controls."

We expect these challenges to continue and to increase in 2019 and following years as political pressures mount, and healthcare payers around the globe, including government-controlled health authorities, insurance companies and managed care organizations, step up initiatives to reduce the overall cost of healthcare, restrict access to higher-priced new medicines, increase the use of generics and impose overall price cuts. These factors may materially affect our ability to achieve an acceptable return on our investments in the research and development of our products, may impact our ability to invest in the research and development of new products, and could have a material adverse impact on our business, financial condition, or results of operations, as well as on our reputation.

We could be impacted by new laws and regulations, and by failures to comply with law, legal proceedings and government investigations.

We are obligated to comply with the laws of all of the countries around the world in which we operate and sell products with respect to an extremely wide and growing range of activities. Such legal requirements can vary from country to country, and new requirements may be imposed on us from time to time as a result of changing government and public expectations regarding the healthcare industry, and acceptable corporate behavior generally.

For example, we are faced with increasing pressures, including new laws and regulations from around the world, to be more transparent with respect to how we do business, including with respect to our interactions with healthcare

professionals and organizations. These laws and regulations include requirements that we disclose payments or other transfers of value made to healthcare professionals and organizations, as well as information relating to the prices for our products. Such measures, including any additional such measures that may be put in place, could have a material adverse impact on our business, financial condition, or results of operations.

In addition, companies and executives in our industry continue to face significant government investigations, legal proceedings and law enforcement activities, both in the US and in countries around the world. Increasingly, such activities can involve criminal proceedings, and can retroactively challenge practices previously considered to be legal. A number of our subsidiaries across each of our divisions are, or may in the future be, subject to various investigations and legal proceedings,

including proceedings regarding sales and marketing practices, pricing, corruption, trade regulation and embargo legislation, product liability, commercial disputes, employment and wrongful discharge, antitrust matters, securities, insider trading, occupational health and safety, environmental matters, tax, cybersecurity, data privacy and intellectual property.

Our Sandoz Division may from time to time seek approval to market a generic version of a product before the expiration of patents claimed by the marketer of the patented product. We do this in cases where we believe that the relevant patents are invalid or unenforceable, or would not be infringed by our generic product. As a result, affiliates of our Sandoz Division frequently face patent litigation, and in certain circumstances, we may elect to market a generic product even though patent infringement actions are still pending. Should we elect to proceed in this manner and conduct a "launch at risk," we could face substantial damages if the final court decision is adverse to us.

For information on significant legal matters pending against us, see "Item 18. Financial Statements—Note 19. Provisions and other non-current liabilities" and "Item 18. Financial Statements—Note 27. Commitments and contingencies." See also "—Our reliance on outsourcing key business functions to third parties heightens the risks faced by our businesses," below.

To help us in our efforts to comply with the many requirements that impact us, we have a significant global ethics and compliance program in place, and we devote substantial time and resources to efforts to ensure that our business is conducted in a lawful and publicly acceptable manner. Nonetheless, despite our efforts, any actual or alleged failure to comply with law or with heightened public expectations could lead to substantial liabilities that may not be covered by insurance, or to other significant losses, and could affect our business, financial position and reputation.

Such proceedings are inherently unpredictable, and large judgments sometimes occur. As a consequence, we may in the future incur judgments that could involve large cash payments, including the potential repayment of amounts allegedly obtained improperly, and other penalties, including treble damages. In addition, such legal proceedings and investigations, even if meritless, may affect our reputation, may create a risk of potential exclusion from government reimbursement programs in the US and other countries, and may lead to civil litigation. As a result, having taken into account all relevant factors, we have in the past and may again in the future enter into major settlements of such claims without bringing them to final legal adjudication by courts or other such bodies, despite having potentially significant defenses against them, in order to limit the risks they pose to our business and reputation. Such settlements may require us to pay significant sums of money and to enter into corporate integrity or similar agreements, which are intended to regulate company behavior for extended periods.

Any such judgments or settlements, and any accruals that we may take with respect to potential judgments or settlements, could have a material adverse impact on our business, financial condition, or results of operations, as well as on our reputation.

The manufacture of our products is highly regulated and complex.

The manufacture of our products is complex and heavily regulated by governmental health authorities around the world, including the FDA. Whether our products and the related raw materials are manufactured at our own dedicated manufacturing facilities or by third parties, we must ensure that all manufacturing processes comply with our own quality standards, as well as with current Good Manufacturing Practices (cGMP) and other applicable regulations.

The technically complex manufacturing processes required to manufacture many of our products increase the risk of production failures and product recalls, and can increase the cost of producing our goods. Many of our products require a supply of highly specialized raw materials. For some of our products and raw materials, we may rely on a single source of supply. In addition, we manufacture and sell a number of sterile products, biologic products and products involving advanced therapy platforms, such as CAR-T therapies, gene therapy and radioligand therapy products, all of which are particularly complex and involve highly specialized manufacturing technologies. As a result, even slight deviations at any point in their production process or in material used may lead to production failures or recalls. For example, for our new CAR-T therapy product *Kymriah,* manufacturing-related issues have impacted the product's sales. In sum, because the production process for some of our products is complex and sensitive, the cost of production of these products can be high, and the chance of production failures, lengthy supply interruptions, product recalls or voluntary market withdrawals is increased.

In addition, due to the inherent complexities of our production processes, we are required to plan our production activities well in advance. If we should suffer from raw material shortages, or if we should underestimate market demand for a product, or should fail to accurately predict when the product would be approved for sale, then we may not be able to produce sufficient product to meet demand. Alternatively, if we overestimate the quantity or timing of

product to be produced, then we may be required to dispose of excess product, which would result not only in the loss of the product but also in the resources spent to produce it.

These complex production processes are also heavily regulated by health authorities around the world. And in recent years, these health authorities have substantially intensified their scrutiny of manufacturers' compliance with such requirements. Any significant failure by us or our third-party suppliers to comply with these requirements, or with the health authorities' expectations, may cause us to shut down the production facilities or production lines and recall previously shipped products. Alternatively, we may be forced to do so by a government health authority, or could be prevented from importing our products from one country to another. In addition, health authorities have in some cases imposed significant penalties for such failures to comply with cGMP. A failure to comply fully with cGMP could also lead to a delay in the approval of new products to be manufactured at the impacted site.

Further, because our products are intended to promote the health of patients, for some of our products, a

supply disruption or other production issue could endanger our reputation and subject us to lawsuits or to allegations that the public health, or the health of individuals, has been harmed.

In sum, complex production processes and compliance with regulatory requirements can increase our cost of producing our products, and any significant disruption in the supply of our products could impact patient health and our sales, which could have a material adverse effect on our business, financial condition, or results of operations, as well as our reputation.

See also "—We may not successfully achieve our goals in transactions or reorganizations," below, with regard to our efforts to reorganize our product manufacturing organization, and "—Climate change, extreme weather events, earthquakes and other natural disasters could adversely affect our business," below.

We devote substantial time and resources to meeting these challenges. However, there can be no guarantee as to the success of our efforts, or that we or our third-party suppliers will not face significant manufacturing issues, or that we will successfully manage such issues when they arise. Such issues could lead to shutdowns, to product shortages, or to our being entirely unable to supply products to patients for an extended period of time. Such shortages or shutdowns have led to, and could continue to lead to, significant losses of sales revenue and to potential third-party litigation.

We may not successfully achieve our goals in transactions or reorganizations.

As part of our strategy, from time to time we acquire and divest products or entire businesses in order to expand or complement our existing businesses, or to enable us to focus more sharply on our strategic businesses. For example, we recently completed the acquisitions of AveXis, Inc., a gene therapy company, and Endocyte, Inc., a radioligand therapy company, as well as the divestment of our stake in the GSK consumer healthcare joint venture. We also announced plans to spin off our Alcon Division and to divest the Sandoz US dermatology business and US oral solids portfolio.

Despite expending significant efforts and resources in this area, we cannot ensure that we will identify products or businesses that are suitable for acquisition. In addition, acquisition activities can be thwarted by governmental regulation, including market concentration limitations, political interference, overtures from competitors for the targeted assets, potentially increasing prices demanded by sellers, and other issues. Once an acquisition is agreed upon with a third party, we may not be able to complete the acquisition in the expected form or within the expected timeframe, or at all, due to a failure to obtain required regulatory approvals or a failure to achieve contractual or other required closing conditions. Further, after an acquisition, efforts to develop and market acquired products or to integrate the acquired business may not meet expectations, or may otherwise not be successful, as a result of difficulties in retaining key personnel, customers and suppliers; difference in corporate culture, standards, controls, processes and policies; the price at which we acquired the business; or other reasons. Acquisitions and divestments can also divert management's attention from our existing businesses, and could result in the existing businesses failing to achieve expected results, or in liabilities being incurred that were not known at the time of acquisition, or the creation of tax or accounting issues.

Similarly, we cannot ensure that we will be able to successfully divest or spin off businesses or other assets that we have identified for this purpose. Neither can we ensure that we will correctly select businesses or assets as candidates for divestment or spin-off, that we will be able to successfully complete any planned divestments or spin-offs, or that any completed divestment or spin-off will achieve the expected strategic benefits, synergies or opportunities, or that the divestment or spin-off will ultimately maximize shareholder value.

In addition, as part of our strategy, from time to time we reassess the optimal organization of our business, such as our ongoing efforts to centralize and optimize our manufacturing and business services organizations, in order to better align our organization with the capabilities and expertise required for competitive advantage. But the expected benefits of such reorganizations may never be fully realized or may take longer to realize than expected. There can be no certainty that the businesses and functions involved will be successfully integrated into the new organizations or that key personnel will be retained. Disruption from the reorganizations may make it more difficult to maintain relationships with customers, employees or suppliers; could result in shortfalls in program oversight; and may result in the Group not achieving the expected productivity and financial benefits.

Both with respect to the transactions and reorganizations previously announced, and to potential future transactions and reorganizations, if we fail to successfully address these risks, or to devote adequate resources to them, we may fail to achieve our strategic objectives, including our growth strategy, or otherwise may not realize the intended benefits of the acquisition, divestiture, spin-off or reorganization.

Significant breaches of information security and the use of electronic communications technologies could adversely affect our business and expose people's personal information.

We are heavily dependent on critical, complex and interdependent information technology systems, including internet-based systems, to support our business processes. In addition, we rely on internet and social media tools and mobile technologies as a means of communications and to gather information, which can include people's personal data. We also increasingly seek to develop technology-based products such as mobile applications and other digital health products that go "beyond the pill" to improve patient welfare in a variety of ways, which could also result in us collecting personal information about individual patients and others.

The size, age and complexity of our information technology systems make them potentially vulnerable to external and internal security threats; outages; malicious intrusions and attacks; cybercrimes, including state-sponsored cybercrimes; malware; misplaced or lost data; programming or human errors; or other similar events. Although we have devoted and continue to devote significant resources and management attention to cybersecurity, information management and business

continuity efforts, like many companies, we have experienced certain of these events and expect to continue to experience them in the future, as the external and internal information security threat continues to grow. We believe that the information security incidents we have experienced to date have yet to result in significant disruptions to our operations, and have not had a significant adverse effect on our results of operations, or on third parties. However, we may not be able to prevent future outages, security incidents or other breaches in our systems from having a material adverse effect on our business, financial condition, results of operations, or reputation.

A significant information security or other such event could negatively impact important business processes, such as the conduct of scientific research and clinical trials, the submission of the results of such efforts to health authorities in support of requests for product approvals, the functioning of our manufacturing and supply chain processes, our compliance with legal obligations, communication between employees and with third parties, and other key business activities. Information technology issues could also lead to the compromise of trade secrets or other intellectual property that could be sold and used by competitors to accelerate the development or manufacturing of competing products; to the compromise of personal financial and health information that could be misused for fraud and identity theft; and to the compromise of information technology security data such as usernames, passwords and encryption keys, as well as security strategies and information about network infrastructure, which could allow unauthorized parties to gain access to additional information on our systems. In addition, malfunctions in software or medical devices that make significant use of information technology, including our Alcon surgical equipment, could lead to a risk of direct harm to patients.

In addition, our routine business operations increasingly involve our gathering personal information (including sensitive personal information) about patients, vendors, customers, employees, collaborators and others, through the use of information technologies such as the internet, social media, mobile technologies and technology-based medical devices. Breaches of our systems or those of our third-party contractors, or other failures to protect such information, could expose such people’s personal data to unauthorized persons. Any event involving the substantial loss of personal data could give rise to significant liability, reputational harm, damaged relationships with business partners, and potentially substantial monetary penalties under laws enacted or being enacted around the world. Such events could also lead to restrictions on our ability to transfer personal data across country borders.

We also use internet, social media and mobile tools as a means to communicate with the public, including about our products or about the diseases our products are intended to treat. However, such uses create risks, such as potential violations of rules regulating the promotion of prescription medicines and the potential loss of trade secrets or other intellectual property. In addition, there continues to be significant uncertainties as to the rules that apply to such communications, and as to the interpretations that health authorities will apply in this context to the rules that do exist. As a result, despite our efforts to comply with applicable rules, there is a significant risk that our use of internet, social media and mobile technologies for such purposes may cause us to nonetheless be found in violation of them.

Our dependence upon information technology, including any breaches of data security, technology disruptions, privacy violations, or other impacts from the use of interconnected technologies, could give rise to the loss of trade secrets or other intellectual property, to the public exposure of personal information, and to interruptions to our operations, and could result in enforcement actions or liability, including potential government fines, claims for damages, and shareholders’ litigation. Any significant events of this type could require us to expend significant resources beyond those we already invest to remediate any damage, to further modify or enhance our protective measures, and to enable the continuity of our business, and could have a material adverse effect on our business, financial condition, results of operations, and reputation.

We may fail to develop or take advantage of transformational technologies and business models.

Rapid progress in medical and digital technologies and in the development of sometimes radical new business models is substantially transforming numerous industries around the world, creating new businesses and new opportunities for revenue and profit, while sometimes quickly rendering established businesses uncompetitive or obsolete. Such transformations, both positive and negative, may impact the healthcare industry, and numerous companies from the digital technology and other industries are seeking to enter the healthcare field.

To take advantage of these opportunities, Novartis has embarked upon a digital transformation strategy, with the goal of making Novartis an industry leader in leveraging advanced analytics and other new technologies. As part of this effort, we have created a new role of Chief Digital Officer, reporting directly to the CEO, charged with creating and executing a Companywide digital strategy, to be led by the Executive Committee of Novartis.

In order to reach our goal, we expect to invest substantial resources into efforts to improve the way we use data in drug discovery and development; to improve the ways we engage with patients, doctors and other stakeholders; and to automate business processes. With our commitment to using innovative science and digital technologies to help create transformative treatments for patients, together with our expertise and the extensive data we have and continue to amass, we believe that we have an opportunity to transform our business model using digital technologies.

There is no guarantee that our efforts toward a digital transformation will succeed, or that we will successfully transform our business model, or that we will be able to do so at any particular cost or any particular time. In order to succeed, we will be required to encourage a cultural change among our employees, attract and retain employees with appropriate skills and mindset, and successfully innovate across a variety of technology fields.

At the same time, other companies with specialized expertise or business models are entering the

healthcare field, from research and development to pharmaceutical distribution, potentially disrupting our relationships with patients, healthcare professionals, customers, distributors and suppliers, with unknown potential consequences for us. For example, companies such as Amazon, which acquired PillPack; IBM, with its Watson project; Alphabet, with its subsidiaries Verily and Calico; and Amazon, Berkshire Hathaway and JPMorgan, with their healthcare joint venture, as well as other established technology companies and specialized startup organizations, are aggressively seeking to move forward in this field. In addition, we face new competitors from different regions of the world, including China, which is moving aggressively to expand its role in the sciences and in many industries. Such new competitors may successfully impact our share of the healthcare value chain, or even develop products or technologies that could make our products uncompetitive or obsolete.

In an effort to maintain and advance our position as a leader in healthcare and related technology, we have made significant efforts to develop and to collaborate with other organizations in the development of advanced therapy platforms, including CAR-T therapy, developed in collaboration with the University of Pennsylvania; gene therapy, through our acquisition of AveXis and the licensing of *Luxturna* outside the US from Spark Therapeutics; and radioligand therapy, through our acquisitions of Advanced Accelerator Applications and Endocyte, Inc.

If we should fail in our efforts at a digital transformation of our Company, or in bringing advanced therapy platforms to market, then there is a risk that we may fail to create the innovative new products, tools or techniques that the new medical and digital technologies may make possible, or may fail to create them as quickly and efficiently as such technologies may enable. We may also lose opportunities to engage with our stakeholders and to profit from improved business processes, and may lose the resources devoted to these efforts to transform our business. At the same time, should third parties successfully enter the healthcare field with disruptive new technologies or business models, then we potentially may see our business supplanted in whole or in part by these new entrants. Any such events could have a material adverse effect on our business, financial condition, or results of operations.

Environmental, social and governance matters may impact our business and reputation.

Increasingly, in addition to the importance of their financial performance, companies are being judged by their performance on a variety of environmental, social and governance (ESG) matters, which are considered to contribute to the long-term sustainability of companies' performance.

A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized, including, for example, MSCI, Sustainalytics, the Dow Jones Sustainability Index and, in the healthcare industry, the Access to Medicine Index. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors, such as BlackRock, have publicly emphasized the importance of such ESG measures to their investment decisions. Topics taken into account in such assessments include the company's efforts and impacts on climate change and human rights, ethics and compliance with law, and the role of the company's board of directors in supervising various sustainability issues. In addition to the topics typically considered in such assessments, in our healthcare industry, issues of the public's ability to access our medicines are of particular importance.

We actively manage a broad range of such ESG matters, taking into consideration their expected impact on the sustainability of our business over time, and on the potential impact of our business on society. For a description of our activities on such topics, see "Item 4. Information on the Company—Item 4.B Business overview—Overview—Corporate responsibility." However, in a rapidly changing world, there can be no certainty that we will manage such issues successfully, or that we will successfully meet society's expectations as to our proper role. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation and on our business, financial condition, or results of operations, including the sustainability of our business over time.

See also "—Our reliance on outsourcing key business functions to third parties heightens the risks faced by our businesses," and "—Climate change, extreme weather events, earthquakes and other natural disasters could adversely affect our business," below.

Intangible assets and goodwill on our books may lead to significant impairment charges.

We carry a significant amount of goodwill and other intangible assets on our consolidated balance sheet, primarily due to acquisitions, including, in particular, substantial goodwill and other intangible assets obtained as a result of our acquisitions of Alcon and of certain oncology assets from GSK. As a result, we may incur significant impairment charges in the future if the fair value of the intangible assets and the groupings of cash-generating units containing goodwill would be less than their carrying value on the Group's consolidated balance sheet at any point in time.

We regularly review for impairment our long-lived intangible and tangible assets, including identifiable intangible assets, investments in associated companies, and goodwill. Goodwill, intangible assets with an indefinite useful life, acquired research projects not ready for use, and acquired development projects not yet ready for use are subject to impairment review at least annually. Other long-lived assets are reviewed for impairment when there is an indication that an impairment may have occurred. Impairment testing under IFRS may lead to impairment charges in the future. Any significant impairment charges could have a material adverse effect on our results of operations and financial condition. In 2018, for example, we recorded intangible asset impairment charges of USD 1.2 billion.

For a detailed discussion of how we determine whether an impairment has occurred, what factors could result in an impairment, and the impact of impairment charges on our results of operations, see “Item 5. Operating and Financial Review and Prospects—Item 5.A Operating results—Critical accounting policies and

estimates—Impairment of goodwill, intangible assets and property, plant and equipment" and "Item 18. Financial Statements—Note 1. Significant accounting policies" and "Item 18. Financial Statements—Note 10. Goodwill and intangible assets."

Political and economic instability may impact our results.

Unpredictable political conditions currently exist in various parts of the world, including a backlash in certain areas against free trade, anti-immigrant sentiment, social unrest, fears of terrorism, and the risk of direct conflicts between nations. In the US, the presidential administration's imposition of tariffs and opposition to free-trade agreements could have a negative impact on international trade. Similarly, there is a risk that barriers to free trade and the free movement of people may rise in Europe as a result of the UK's "Brexit" efforts and the rise of nationalist, separatist and populist sentiment in various countries, sometimes exacerbated by large-scale migration flows. Furthermore, significant conflicts continue in parts of the Middle East, including conflicts involving Saudi Arabia and Iran, and with respect to places such as Russia, Ukraine and North Korea. Collectively, such difficult conditions could, among other things, disturb the international flow of goods and increase the costs and difficulties of international transactions.

In addition, local economic conditions may adversely affect the ability of payers, as well as our distributors, customers, suppliers and service providers, to pay for our products, or otherwise to buy necessary inventory or raw materials, and to perform their obligations under agreements with us. Although we make efforts to monitor these third parties' financial condition and their liquidity, our ability to do so is limited, and some of them may become unable to pay their bills in a timely manner, or may even become insolvent, which could negatively impact our business or results of operations. These risks may be elevated with respect to our interactions with fiscally challenged government payers, or with third parties with substantial exposure to such payers. See also "—Our reliance on outsourcing key business functions to third parties heightens the risks faced by our businesses," below.

Financial market issues may also result in a lower return on our financial investments, and a lower value on some of our assets. Alternatively, inflation could accelerate, which could lead to higher interest rates, increasing our costs of raising capital. Uncertainties around future central bank and other economic policies in the US and EU, as well as high debt levels in certain other countries, could also impact world trade. Sudden increases in economic, currency or financial market volatility in different countries have also impacted, and may continue to unpredictably impact, our business or results of operations, including the conversion of our operating results into our reporting currency, the US dollar, as well as the value of our investments in our pension plans.

For further information on such risks, see "—Foreign exchange fluctuations may adversely affect our earnings and the value of some of our assets," and "—Any inaccuracy in the assumptions and estimates used to calculate our pension plan obligations could substantially increase our pension-related expenses," below. See also "—Our business is affected by pressures on pricing and reimbursement for our products," above, and "Item 5. Operating and Financial Review and Prospects—Item 5.B Liquidity and capital resources—Effects of currency fluctuations."

There is also a risk that countries facing local financial difficulties, including countries experiencing high inflation rates and highly indebted countries facing large capital outflows, may impose controls on the exchange of foreign currency. Such exchange controls could limit our ability to distribute retained earnings from our local affiliates, or to pay intercompany payables due from those countries.

See also "Item 5. Operating and Financial Review and Prospects—Item 5.B Liquidity and capital resources—Condensed consolidated balance sheets," and "Item 18. Financial Statements—Note 14. Trade receivables" and "Item 18. Financial Statements—Note 28. Financial instruments—additional disclosures."

Similarly, increased scrutiny of corporate taxes and executive pay may lead to significant business disruptions or other adverse business conditions, and may interfere with our ability to attract and retain qualified personnel. See "—Changes in tax laws or their application could adversely affect our results of operations" and "—An inability to attract and retain qualified personnel could adversely affect our business," below.

To the extent that economic and financial conditions directly affect consumers, then our Innovative Medicines and Sandoz Divisions may be impacted. Given the requirements in certain countries that patients directly pay an increasingly large contribution toward their own healthcare costs, there is a risk that consumers may cut back on prescription drugs to help cope with rising costs. In addition, the elective surgical and contact lens businesses of our Alcon Division may be particularly sensitive to declines in consumer spending.

At the same time, significant changes and potential future volatility in the financial markets, in the consumer and business environment, in the competitive landscape, and in the global political and security landscape make it

increasingly difficult for us to predict our revenues and earnings into the future. As a result, any revenue or earnings guidance or outlook that we have given or might give may be overtaken by events, or may otherwise turn out to be inaccurate. Though we endeavor to give reasonable estimates of future revenues and earnings at the time we give such guidance, based on then-current knowledge and conditions, there is a significant risk that such guidance or outlook will turn out to be, or to have been, incorrect.

Separately and collectively, such factors may have a material adverse effect on our revenues, results of operations, financial condition and, if circumstances worsen, our ability to raise capital at reasonable rates.

Our indebtedness could adversely affect our operations.

As of December 31, 2018, we had USD 22.5 billion of non-current financial debt and USD 9.7 billion of current

financial debt. Our current and long-term debt requires us to dedicate a portion of our cash flow to service interest and principal payments and, if interest rates rise, this amount may increase. As a result, our existing debt may limit our ability to use our cash flow to fund capital expenditures, to engage in transactions, or to meet other capital needs, or otherwise may place us at a competitive disadvantage relative to competitors that have less debt. Our debt could also limit our flexibility to plan for and react to changes in our business or industry, and increase our vulnerability to general adverse economic and industry conditions, including changes in interest rates or a downturn in our business or the economy. We may also have difficulty refinancing our existing debt or incurring new debt on terms that we would consider to be commercially reasonable, if at all.

Our reliance on outsourcing key business functions to third parties heightens the risks faced by our businesses.

We outsource the performance of certain key business functions to third parties, and invest a significant amount of effort and resources into doing so. Such outsourced functions can include research and development collaborations, manufacturing operations, warehousing and distribution activities, certain finance functions, marketing activities, data management and others. We may particularly rely on third parties in developing countries, including for the sales, marketing and distribution of our products, and to obtain the intermediate and raw materials used in the manufacture of our products.

Our reliance on outsourcing and third parties for the research and development or manufacturing of our products may reduce the potential profitability of such products.

In addition, governments and the public are increasingly placing pressure on major corporations, including Novartis, to take responsibility for compliance with human rights and appropriate environmental practices, as well as other actions, of their third-party contractors around the world. Examples of this include the Conflict Minerals rule in the US, and the UK Modern Slavery Act.

We place strict contractual requirements on such contractors to comply with law and with our high standards. We also expend significant resources on efforts to screen out inappropriate contractors, to monitor the activities of those we have retained, and to seek their compliance with the law and with our expectations. Nonetheless, many of these companies have limited resources, and, in particular, do not have internal compliance resources comparable to those within our organization.

Ultimately, if the third parties fail to meet their obligations to us, we may lose our investment in the collaborations and fail to receive the expected benefits. In addition, should any of these third parties fail to comply with the law or should they act inappropriately in the course of their performance of services for us, there is a risk that we could be held responsible for their acts, that our reputation may suffer, and that penalties may be imposed upon us. Any such failures by third parties could have a material adverse effect on our business, financial condition, results of operations, or reputation.

Competition and failure to successfully develop biosimilars and other differentiated products may impact the success of our Sandoz Division.

Our Sandoz Division faces intense competition from companies that market patented pharmaceutical products, which sometimes take aggressive steps to delay the introduction of generic and biosimilar medicines, to limit the availability of exclusivity periods or to reduce their value. At the same time, Sandoz faces strong competition from other generic and biosimilar pharmaceutical companies, which aggressively compete for market share, including through significant price competition. Such competitive actions by other patented, generic and biosimilar pharmaceutical manufacturers may increase the costs and risks associated with our efforts to introduce and market such products, may delay the introduction or marketing of such products, and may further limit the prices at which we are able to sell these products and impact our results of operations. In particular, in the US in recent years, industrywide price competition among generic pharmaceutical companies and consolidation of buyers have significantly hurt Sandoz sales. Expecting these trends to continue, we agreed to sell the Sandoz US dermatology business and generic US oral solids portfolio to Aurobindo Pharma USA Inc.

In addition, Sandoz has invested heavily in the development of biosimilar drugs and other differentiated products, with the expectation that such products offer the potential for higher profitability than less complex products. Sandoz has invested in the development of such products despite the fact that their development is more difficult and expensive than the development of standard generic drugs, and despite the fact that regulations concerning the approval, marketing and sale of biosimilars in certain countries, including in the US, are still under development or not entirely clear. If Sandoz should fail in its efforts to develop and market biosimilars or other such differentiated

products, or if the developing biosimilars regulations do not ultimately favor the development and sale of such products, or if we are unable to sell our biosimilar products for a sufficient price, then this could have an adverse effect on the success of our Sandoz Division, and we may fail to achieve expected returns on the investments by Sandoz in the development of biosimilars and other differentiated products.

See also "—Our research and development efforts may not succeed" above, with regard to the risks involved in our efforts to develop biosimilars and differentiated generic products and to obtain exclusivity periods; and "—Ongoing consolidation among our distributors and retailers is increasing both the purchasing leverage of key customers and the concentration of credit risk," below, with respect to the impact of such consolidation on our pricing.

Any inaccuracy in the assumptions and estimates used to calculate our pension plan and other post-employment obligations could substantially increase our pension-related expenses.

We sponsor pension and other post-employment benefit plans in various forms. These plans cover a significant portion of our current and former associates. While most of our plans are now defined contribution plans, certain of our associates remain participants in defined benefits

plans. For these defined benefits plans, we are required to make significant assumptions and estimates about future events in calculating the present value of expected future plan expenses and liabilities. These include assumptions used to determine the discount rates we apply to estimated future liabilities and rates of future compensation increases. Assumptions and estimates used by Novartis may differ materially from the actual results we experience in the future, due to changing market and economic conditions, higher or lower withdrawal rates, or longer or shorter life spans of participants, among other variables. For example, in 2018, a decrease in the interest rate we apply in determining the present value of expected future defined benefit obligations of one-quarter of 1% would have increased our year-end defined benefit pension obligation for plans in Switzerland, the US, the UK, Germany and Japan, which represent 94% of the Group total defined benefit pension obligation, by USD 0.8 billion. Any differences between our assumptions and estimates and our actual experience could require us to make additional contributions to our pension funds. Further, additional employer contributions might be required if plan funding falls below the levels required by local rules. Either such event could have a material effect on our results of operations and financial condition.

For more information on obligations under retirement and other post-employment benefit plans and underlying actuarial assumptions, see “Item 5. Operating and Financial Review and Prospects—Item 5.A Operating results—Critical accounting policies and estimates—Retirement and other post-employment benefit plans” and “Item 18. Financial Statements—Note 24. Post-employment benefits for associates.” See also “—Political and economic instability may have a material adverse effect on our results,” above.

Changes in tax laws or their application could adversely affect our financial results.

Our multinational operations are taxed under the laws of the countries and other jurisdictions in which we operate. However, the integrated nature of our worldwide operations can produce conflicting claims from revenue authorities in different countries as to the profits to be taxed in the individual countries, including potential disputes relating to the prices our subsidiaries charge one another for intercompany transactions, known as transfer pricing. The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the impact of double taxation on our revenues and capital gains. However, mechanisms developed to resolve such conflicting claims are largely untried, and can be expected to be very lengthy.

In recent years, tax authorities around the world have increased their scrutiny of company tax filings, and have become more rigid in exercising any discretion they may have. As part of this, the Organization for Economic Co-operation and Development (OECD) has proposed a number of tax law changes under its Base Erosion and Profit Shifting (BEPS) Action Plans to address issues of transparency, coherence and substance.

At the same time, the European Commission is finalizing its Anti Tax Avoidance Directive, which seeks to prevent tax avoidance by companies and to ensure that companies pay appropriate taxes in the markets where profits are effectively made and business is effectively performed. The EU also adopted a new Directive on Administrative Cooperation (DAC6) in 2018, which seeks additional reporting. In addition, the European Commission continues to extend the application of its policies seeking to limit fiscal aid by member states to particular companies, and the related investigation of the member states’ practices regarding the issuance of rulings on tax matters relating to individual companies.

These OECD and EU tax reform initiatives also need local country implementation, including in our home country of Switzerland, which may result in significant changes to established tax principles. Although we have taken steps to be in compliance with the evolving OECD and EU tax initiatives, and will continue to do so, significant uncertainties remain as to the outcome of these efforts.

Switzerland is in the process of considering the implementation of corporate tax reform, which could become effective as early as the first quarter of 2019. However, the outcome of these efforts remains subject to change and could be enacted in a materially different form from what is currently proposed, or could be administered or implemented in a manner different from our expectations. There is also a risk that the EU may not be satisfied with the outcome of Switzerland’s tax reform efforts, and take steps to seek further changes. Accordingly, there can be no assurance that Swiss corporate tax reform will not adversely affect our business or financial condition.

In addition, in the US, the Tax Cuts and Jobs Act, enacted at the end of 2017, included substantial changes to the US taxation of individuals and businesses. Although the law substantially decreased tax rates applicable to corporations in the US, we do not yet know what all of the consequences of this new statute will be, including whether the law will have any unintended consequences. In particular, significant uncertainties remain as to how the US government will implement the new law, including with respect to the tax qualification of interest deductions, the concept of a

territorial tax regime, royalty payments and cost of goods sold.

In general, such tax reform efforts, including with respect to tax base or rate, transfer pricing, intercompany dividends, cross-border transactions, controlled corporations, and limitations on tax relief allowed on the interest on intercompany debt, will require us to continually assess our organizational structure against tax policy trends, and could lead to an increased risk of international tax disputes and an increase in our effective tax rate, and could adversely affect our financial results.

Counterfeit versions of our products could harm our patients and reputation.

Our industry continues to be challenged by the vulnerability of distribution channels to illegal counterfeiting and the presence of counterfeit products in a growing number of markets and over the internet. Counterfeit products are frequently unsafe or ineffective, and can potentially be life-threatening. To distributors and patients, counterfeit products may be visually indistinguishable from the authentic version. Reports of product

ineffectiveness or adverse reactions to counterfeit drugs, or increased levels of counterfeiting could affect patient confidence in our authentic products, and could harm our business or lead to litigation. In addition, it is possible that a lack of efficacy or adverse events caused by unsafe counterfeit products could mistakenly be attributed to the authentic product. If a product of ours was the subject of counterfeits, we could incur substantial reputational and financial harm.

Foreign exchange fluctuations may adversely affect our earnings and the value of some of our assets.

Changes in exchange rates between the US dollar, our reporting currency, and other currencies can result in significant increases or decreases in our reported sales, costs and earnings as expressed in US dollars, and in the reported value of our assets, liabilities and cash flows.

In addition to ordinary market risk, there is a risk that countries could take affirmative steps that could significantly impact the value of their currencies. Such steps could include "quantitative easing" measures and potential withdrawals by countries from common currencies. In addition, countries facing local financial difficulties, including countries experiencing high inflation rates and highly indebted countries facing large capital outflows, may impose controls on the exchange of foreign currency. Such exchange controls could limit our ability to distribute retained earnings from our local affiliates, or to pay intercompany payables due from those countries. See "—Political and economic instability may have a material adverse effect on our results," below.

Despite measures undertaken to reduce or hedge against foreign currency exchange risks, because a significant portion of our earnings and expenditures are in currencies other than the US dollar, including expenditures in Swiss francs that are significantly higher than our revenue in Swiss francs, any such exchange rate volatility may negatively and materially impact our results of operations and financial condition, and may impact the reported value of our net sales, earnings, assets and liabilities. In addition, the timing and extent of such volatility can be difficult to predict. Further, depending on the movements of particular foreign exchange rates, we may be materially adversely affected at a time when the same currency movements are benefiting some of our competitors.

For more information on the effects of currency fluctuations on our consolidated financial statements and on how we manage currency risk, see "Item 5. Operating and Financial Review and Prospects—Item 5.B Liquidity and capital resources—Effects of currency fluctuations," "Item 11. Quantitative and Qualitative Disclosures About Market Risk," and "Item 18. Financial Statements—Note 28. Financial instruments—additional disclosures."

Ongoing consolidation among our distributors and retailers is increasing both the purchasing leverage of key customers and the concentration of credit risk.

Increasingly, a significant portion of our global sales is made to a relatively small number of drug wholesalers, retail chains and other purchasing organizations. For example, our three most important customers globally are all in the US, and accounted for approximately 16%, 13% and 7%, respectively, of Group net sales in 2018. The largest trade receivables outstanding were for these three customers, amounting to 12%, 10% and 6%, respectively, of the Group's trade receivables at December 31, 2018. The trend has been toward further consolidation among distributors and retailers, both in the US and internationally. As a result, we may be affected by fluctuations in the buying patterns of such customers, and these customers are gaining additional purchasing leverage, increasing the pricing pressures facing our businesses. These pressures can particularly impact our Sandoz Division, the generic products of which can often be obtained from numerous competitors. Moreover, we are exposed to a concentration of credit risk as a result of this concentration among our customers. If one or more of our major customers experienced financial difficulties, the effect on us would be substantially greater than in the past, and could include a substantial loss of sales and an inability to collect amounts owed to us. Such events could have a material adverse effect on our business, financial condition, or results of operations.

An inability to attract and retain qualified personnel could adversely affect our business.

We highly depend upon skilled personnel in key parts of our organization, and we invest heavily in recruiting, training and retaining qualified individuals, including significant efforts to enhance the diversity of our workforce. The loss of the service of key members of our organization – including senior members of our scientific and management teams, high-quality researchers and development specialists, and skilled personnel in developing countries – could delay or prevent the achievement of major business objectives.

Our future growth will demand talented associates and leaders, yet the market for talent has become increasingly competitive. In particular, Emerging Growth Markets are expected to continue to be an important source of growth, but in many of these countries there is a limited pool of executives with the training and international experience

needed to work successfully in a global organization like Novartis.

In addition, shifting demographic trends are expected to result in fewer students, fewer graduates and fewer people entering the workforce in the Western world in the next 10 years. Moreover, many members of younger generations around the world have changing expectations toward careers, engagement and the integration of work in their overall lifestyles.

The supply of talent for certain key functional and leadership positions is decreasing, and a talent gap is visible for some professions and geographies – engineers in Germany, for example. Recruitment is increasingly regional or global in specialized fields such as clinical development, biosciences, chemistry and information technology. In addition, the geographic mobility of talent is expected to decrease in the future, with talented individuals in developed and developing countries anticipating ample career opportunities closer to home than in the past. This decrease in mobility may be worsened by anti-immigrant sentiments in many countries, and laws discouraging immigration. See "—Political and economic instability may impact our results," above.

In addition, our ability to hire qualified personnel also depends on the flexibility to reward superior performance and to pay competitive compensation. Laws and regulations on executive compensation, including legislation in our home country, Switzerland, may restrict our ability to attract, motivate and retain the required level of qualified personnel. We face intense competition for an increasingly limited pool of qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities, other research institutions, other companies seeking to enter the healthcare space, and companies in other industries. As a result, despite significant efforts on our part, we may be unable to attract and retain qualified individuals in sufficient numbers, which could have an adverse effect on our business, financial condition, or results of operations.

Environmental liabilities may adversely impact our financial results.

The environmental laws of various jurisdictions impose actual and potential obligations on us to remediate contaminated sites, in some cases over many years. While we have set aside substantial provisions for worldwide environmental liabilities, there is no guarantee that additional costs will not be incurred beyond the amounts for which we have provided in the Group consolidated financial statements. If environmental contamination related to our facilities or products adversely impacts third parties, if we fail to properly manage the safety of our facilities and the environmental risks, or if we are required to further increase our provisions for environmental liabilities in the future, this could have a material adverse effect on our business, financial condition, results of operations, and reputation. See also “Item 4. Information on the Company—Item 4.D Property, plants and equipment—Environmental matters” and “Item 18. Financial Statements—Note 19. Provisions and other non-current liabilities.”

Climate change, extreme weather events, earthquakes and other natural disasters could adversely affect our business.

In recent years, extreme weather events and changing weather patterns such as storms, flooding, droughts and temperature changes have become more common. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as hurricanes, tornadoes, droughts or floods, or other events that may result from the impact of climate change on the environment, such as sea level rise. For example, some of our production facilities that depend on the availability of significant water supplies are located in areas where water is increasingly scarce. Other facilities are located in places that, because of increasingly violent weather events, sea level rise, or both, are increasingly at risk of substantial flooding. As a result, we could experience increased production or other costs, business interruptions, destruction of facilities, and loss of life, all of which could have a material adverse effect on our business, financial condition, or results of operations.

In addition, our corporate headquarters, the headquarters of our Innovative Medicines Division, and certain of our major Innovative Medicines Division production and research facilities are located near earthquake fault lines in Basel, Switzerland. Other major facilities are located near major earthquake fault lines in various locations around the world. In the event of a major earthquake, we could experience business interruptions, destruction of facilities, and loss of life, all of which could have a material adverse effect on our business, financial condition, or results of operations.

Risks related to our ADRs

The price of our ADRs and the US dollar value of any dividends may be negatively affected by fluctuations in the US dollar/Swiss franc exchange rate.

Our American Depositary Shares (ADSs), each representing one Novartis share and evidenced by American Depositary Receipts (ADRs), trade on the NYSE in US dollars. Since the shares underlying the ADRs are listed in Switzerland on the SIX Swiss Exchange (SIX) and trade in Swiss francs, the value of the ADRs may be affected by fluctuations in the US dollar/Swiss franc exchange rate. In addition, since dividends that we may declare will be denominated in Swiss francs, exchange rate fluctuations will affect the US dollar equivalent of dividends received by holders of ADRs. If the value of the Swiss franc decreases against the US dollar, the price at which our ADRs trade may – and the value of the US dollar equivalent of any dividend will – decrease accordingly.

Holders of ADRs may not be able to exercise pre-emptive rights attached to shares underlying ADRs.

Under Swiss law, shareholders have pre-emptive rights to subscribe for issuances of new shares on a *pro rata* basis. Shareholders may waive their pre-emptive rights in respect of any offering at a general meeting of shareholders. Pre-emptive rights, if not previously waived, are transferable during the subscription period relating to a particular offering of shares and may be quoted on the SIX. US holders of ADRs may not be able to exercise the pre-emptive rights attached to the shares underlying their ADRs unless a registration statement under the US Securities Act of 1933 is effective with respect to such rights and the related shares, or an exemption from this registration requirement

is available. In deciding whether to file such a registration statement, we would evaluate the related costs and potential liabilities, as well as the benefits of enabling the exercise by ADR holders of the pre-emptive rights associated with the shares underlying their ADRs. We cannot guarantee that a registration statement would be filed, or, if filed, that it would be declared effective. If pre-emptive rights could not be exercised by an ADR holder, JPMorgan Chase Bank, N.A., as depositary, would, if possible, sell the holder's pre-emptive rights and distribute the net proceeds of the sale to the holder. If the depositary determines, in its discretion, that the rights could not be sold, the depositary might allow such rights to lapse. In either case, the interest of ADR holders in Novartis would be diluted and, if the depositary allowed rights to lapse, holders of ADRs would not realize any value from the pre-emptive rights.

Item 4. Information on the Company

4.A History and development of Novartis

Novartis AG

Novartis AG was incorporated on February 29, 1996, under the laws of Switzerland as a stock corporation (*Aktiengesellschaft*) with an indefinite duration. On December 20, 1996, our predecessor companies, Ciba-Geigy AG and Sandoz AG, merged into this new entity, creating Novartis. We are domiciled in and governed by the laws of Switzerland. Our registered office is located at the following address:

Novartis AG
Lichtstrasse 35
CH-4056 Basel, Switzerland
Telephone: 011-41-61-324-1111
Web: www.novartis.com

Novartis is a multinational group of companies specializing in the research, development, manufacturing and marketing of a broad range of healthcare products led by innovative pharmaceuticals and also including high-quality generic pharmaceuticals and eye care products. Novartis AG, our Swiss holding company, owns, directly or indirectly, all of our significant operating companies. For a list of our significant operating subsidiaries, see “Item 18. Financial Statements—Note 31. Principal Group subsidiaries and associated companies.”

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

Important corporate developments 2016-2018

2018

December

Novartis announces that on December 21, 2018, it completed the previously-announced acquisition of Endocyte, a US-based biopharmaceutical company focused on developing targeted therapeutics for cancer treatment, in a transaction valued at approximately USD 2.1 billion.

Novartis announces that on December 19, 2018, it completed the acquisition of Tear Film Innovations, Inc., a privately-held company and manufacturer of the *iLux* Device, a therapeutic device used to treat meibomian gland dysfunction (MGD), a leading cause of dry eye.

Novartis announces the appointment of Susanne Schaffert, Ph.D., as CEO Novartis Oncology and a member of the Executive Committee of Novartis (ECN), effective January 1, 2019. Dr. Schaffert succeeds Liz Barrett, who stepped down effective December 31, 2018.

Novartis announces an offer to acquire Cell*for*Cure from LFB. Cell*for*Cure, a French company, is one of the first and largest contract development and manufacturing organizations producing cell and gene therapies in Europe. The transaction is subject to usual and customary closing conditions, including employee consultation process and necessary regulatory approvals.

November

Novartis announces that Alcon had filed an initial Form 20-F registration statement with the US Securities and Exchange Commission (SEC) in relation to the previously announced intention of Novartis to spin off the Alcon Division as an independent, publicly traded company. We expect to make an application to list the shares in Alcon on SIX and the NYSE under the ticker symbol “ALC.” Completion of the planned spin-off is subject to general market conditions, receipt of necessary authorizations, tax rulings and opinions, and shareholder approval at the 2019 Novartis annual shareholder meeting. If approvals are secured and conditions are met, the spin-off is expected to be completed in the first half of 2019.

October

Novartis announces that it has entered into a clinical development agreement with Pfizer that will include a study combining tropifexor and one or more Pfizer compounds for the treatment of nonalcoholic steatohepatitis (NASH).

Novartis announces that it has entered into a licensing and equity agreement with Boston Pharmaceuticals for the development of three novel anti-infective drug candidates that are part of the Novartis Infectious Diseases portfolio, which have the potential to address the need for new agents to treat antibiotic-resistant Gram-negative infections. Under the terms of the agreement, Boston Pharmaceuticals acquired worldwide rights to two complementary candidates targeting carbapenem-resistant enterobacteriaceae (CRE) and one candidate targeting Pseudomonas infections.

September

Novartis announces it has agreed to sell selected portions of its Sandoz US portfolio, specifically the Sandoz US dermatology business and generic US oral solids portfolio, to Aurobindo Pharma USA Inc., for USD 0.9 billion in cash plus USD 0.1 billion in potential earn-outs. This transaction is expected to close in 2019, subject to the completion of customary closing conditions.

Novartis announces that it plans to continue the transformation of its manufacturing network and services businesses, including a planned workforce reduction in Switzerland over a four-year period. Novartis also plans to continue the ongoing transfer of transactional activities to the five global service centers within Novartis Business Services, and to begin to transfer managerial service capabilities to these service centers.

August

Novartis announces the appointment of Dr. Klaus Moosmayer as Chief Ethics, Risk and Compliance Officer and a member of the ECN, reporting to the CEO of Novartis, effective December 1, 2018.

July

Novartis announces that it has signed a renewed Memorandum of Understanding with the World Health Organization to extend its agreement for the donation of *Egaten* (triclabendazole) for the treatment of liver fluke (fascioliasis) until 2022.

Novartis announces that it has entered into an exclusive in-license agreement with Galapagos NV and MorphoSys AG for an investigational biologic compound, MOR106, a novel antibody directed against IL-17C. This transaction became effective on September 10, 2018, upon the expiration of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976.

June

Novartis announces its intention to seek shareholder approval for a 100% spin-off of its Alcon Division into a standalone public company. In addition to shareholder approval, completion of the proposed Alcon spin-off remains subject to certain conditions precedent, such as no material adverse events, receipt of necessary authorizations as well as tax rulings and opinions.

Novartis announces that it will initiate a share buyback of up to USD 5 billion to be executed by the end of 2019.

Novartis announces the completion on June 1, 2018, of its previously announced divestment to GlaxoSmithKline PLC of its 36.5% stake in GSK Consumer Healthcare Holdings Ltd. for a payment of USD 13.0 billion in cash. The divestment brings to an end Novartis participation in its consumer healthcare joint venture with GSK, which was formed in 2015 as part of the Novartis portfolio transformation.

May

Novartis announces that Shannon Thyme Klinger, previously Chief Ethics, Risk and Compliance Officer, was appointed Group General Counsel effective June 1, 2018, and will continue as a member of the ECN, following the decision by Felix R. Ehrat to retire from the Company.

Novartis announces that Robert Weltevreden will be appointed as Head of Novartis Business Services (NBS) and a member of the ECN, reporting to the CEO of Novartis, effective June 1, 2018.

Novartis announces the completion of its previously announced cash tender offer to purchase all the outstanding shares of common stock of AveXis, Inc., a US-based clinical stage gene therapy company. The lead AveXis product candidate, AVXS-101, has the potential to be the first-ever one-time gene replacement therapy for spinal muscular atrophy. This acquisition was completed on May 15, 2018.

April

Novartis announces the appointment of John Tsai, M.D., as Head of Global Drug Development (GDD) and Chief Medical Officer of Novartis, and a member of the ECN, reporting to the CEO of Novartis, effective May 1, 2018. Dr. Tsai succeeds Dr. Narasimhan, who became CEO of Novartis on February 1, 2018. Dr. Robert Kowalski, who led GDD ad interim from February 1, 2018, will resume his responsibilities as Head of Global Regulatory Affairs for GDD.

Novartis announces that its Sandoz Division has entered into a collaboration with Pear Therapeutics to commercialize and continue development of novel prescription digital therapeutics, including *reSET* for patients with substance use disorder and *reSET-O* for patients with opioid use disorder who are currently receiving buprenorphine. Novartis announced the commercial launch of *reSET* for patients with substance use disorder in November 2018 and announced FDA clearance of *reSET-O* for patients with opioid use disorder in December 2018 and launch in January

2019.

Novartis announces a five-year commitment to the fight against malaria in conjunction with the 7th Multilateral Initiative on Malaria Conference and the Malaria Summit of the Commonwealth Heads of Government meeting. As part of its commitment, Novartis will invest more than USD 100 million over the next five years to advance research and development of next-generation treatments to combat emerging resistance to artemisinin and other currently used antimalarials. The Company will also implement an equitable pricing strategy to maximize patient access in malaria-endemic countries when these new treatments become available.

25

March

Novartis announces that it has entered into a collaboration and licensing agreement with the Wyss Institute for Biologically Inspired Engineering at Harvard University and the Dana-Farber Cancer Institute to develop biomaterial systems for its portfolio of immuno-oncology therapies.

Novartis announces that Bertrand Bodson, Chief Digital Officer; Steffen Lang, Global Head Novartis Technical Operations; and Shannon Klinger, Chief Ethics, Risk and Compliance Officer, have been appointed to the ECN effective as of April 1, 2018. André Wyss, President Novartis Operations, has decided to step down from the ECN on April 1, 2018, to pursue his career outside of Novartis.

Novartis announces an additional strategic alliance with Science 37 to design and initiate up to 10 new clinical trials over the next three years, which are intended to blend virtual and traditional clinical trial models, with increasing degrees of decentralization toward a mostly “site-less” model.

Novartis announces a collaboration with Pear Therapeutics to develop novel prescription digital therapeutics, software applications designed to effectively treat disease and improve clinical outcomes for patients, for schizophrenia and multiple sclerosis.

February

Novartis announces an alliance with the Bill & Melinda Gates Foundation to advance development of Novartis drug candidate KDU731 for the treatment of cryptosporidiosis.

Novartis completes euro (EUR) denominated bond offerings totaling EUR 2.25 billion.

January

Novartis announces on January 22, 2018, that it had successfully completed its previously announced tender offer for all of the then-outstanding ordinary shares, including ordinary shares represented by American Depositary Shares (ADSs), of AAA. As of the expiration of the offer on January 19, 2018, approximately 97% of the then-outstanding fully diluted ordinary shares, including ordinary shares represented by ADSs, were validly tendered. In addition, on January 22, 2018, Novartis commenced a subsequent offering period that expired as scheduled on January 31, 2018. As of the expiration of the subsequent offering period, an additional 1.8% of the outstanding shares were validly tendered, resulting in an increase in Novartis ownership in AAA to 98.7% of all outstanding ordinary shares, including ordinary shares represented by ADSs. AAA is a radiopharmaceutical company headquartered in Saint Genis-Pouilly, France, that develops, produces and commercializes molecular nuclear medicines – including *Lutathera* (USAN: lutetium Lu 177 dotatate/INN: lutetium (^{177}Lu) oxodotreotide), a first-in-class radioligand therapy product for neuroendocrine tumors – and diagnostic products.

Novartis announces a licensing agreement and a manufacturing and supply agreement with Spark Therapeutics to develop, register and commercialize in markets outside the US voretigene neparvovec, a gene therapy approved as *Luxturna* in the EU in November 2018 for the treatment of patients with vision loss due to a genetic biallelic mutation of the RPE65 (retinal pigment epithelial 65kDa protein) gene and who have enough viable retinal cells.

Novartis announces a global collaboration between Sandoz and Biocon Ltd. to develop, manufacture and commercialize multiple biosimilars in immunology and oncology.

Novartis announces that Elizabeth (Liz) Barrett has been appointed CEO Novartis Oncology and a member of the ECN, effective February 1, 2018.

2017

December

Novartis announces that Bruno Strigini, CEO Novartis Oncology, has decided to retire from Novartis for personal reasons.

November

Novartis announces an expanded collaboration with Amgen and the Banner Alzheimer’s Institute to collaborate on a new Generation Study 2 to assess whether investigational BACE1 inhibitor CNP520 can prevent or delay the symptoms of Alzheimer’s disease in a high-risk population.

October

Novartis announces that it has made significant progress in its ongoing strategic review of the Alcon Division and has examined all options, ranging from retaining the business to a capital markets solution (e.g., an IPO or a spin-off). As part of this, we updated Alcon’s strategic plan, which confirms that it has the potential to grow sales at or above market while delivering profitability at least in line with the industry.

Novartis announces that its over-the-counter ophthalmic products and certain surgical diagnostic products will transfer from the Innovative Medicines Division to the Alcon Division effective January 1, 2018.

September

Novartis announces a collaboration with UC Berkeley to establish the Novartis-Berkeley Center for Proteomics and Chemistry Technologies.

Novartis announces that, effective February 1, 2018, Vasant (Vas) Narasimhan, M.D., will succeed Joseph Jimenez as CEO of Novartis, who had indicated his desire to retire after eight years as CEO. Robert Kowalski, Pharm.D., Head of Global Regulatory Affairs, will assume ad-interim leadership of our Global Drug Development organization, effective February 1, 2018.

August

Novartis announces that, effective January 1, 2018, Bertrand Bodson has been appointed to the new role of Chief Digital Officer, reporting to the CEO of Novartis. Mr. Bodson is responsible for creating and executing a companywide digital strategy. As part of this strategy, we plan to improve the ways we use data in drug discovery and development, engage with patients, doctors and other stakeholders, as well as to automate business processes.

June

Novartis announces that it has entered into a clinical research collaboration in which Bristol-Myers Squibb is to investigate the safety, tolerability and efficacy of *Mekinist* (trametinib) in combination with Opdivo® (nivolumab) and Opdivo® + Yervoy® (ipilimumab) regimen as a potential treatment option for metastatic colorectal cancer in patients with microsatellite stable tumors where the tumors are proficient in mismatch repair (MSS mCRC pMMR).

Novartis announces a collaboration with IBM Watson Health to explore development of a cognitive solution that uses real-world data and advanced analytical techniques with the aim to provide better insights on the expected outcomes of breast cancer treatment options.

May

Novartis announces the launch of Better Hearts Better Cities, an innovative initiative to address the high rates of high blood pressure in low-income urban communities.

April

Novartis announces an expanded collaboration agreement with Amgen to co-commercialize erenumab (AMG 334) in the US, currently being investigated for the prevention of migraine. This agreement builds on the previously announced 2015 global collaboration between Novartis and Amgen.

Novartis announces that it has entered into a clinical trial agreement with Allergan plc to conduct a Phase IIb study involving the combination of a Novartis FXR agonist and Allergan’s cenicriviroc for the treatment of nonalcoholic steatohepatitis (NASH).

Novartis announces that it has exercised an option to in-license ECF843, a recombinant form of human lubricin from Lubris, LLC, for ophthalmic indications worldwide (outside Europe). This transaction closed and Novartis received its exclusive license on April 21, 2017.

March

Novartis completes euro-denominated bond offerings in an amount equivalent to approximately USD 2 billion.

February

Novartis completes a USD 3 billion bond offering under its SEC Registration Statement on Form F-3.

January

Novartis announces that it is considering options for the Alcon Division. The review will explore all options, ranging from retaining all or part of the business to separation via a capital markets transaction (e.g., IPO or spin-off), in order to determine how to best maximize value for our shareholders.

Novartis announces that it is initiating a share buyback of up to USD 5.0 billion in 2017 under existing shareholder authority.

Novartis announces that it has entered into a collaboration and option agreement with Ionis Pharmaceuticals, Inc. (Ionis), and its affiliate Akcea Therapeutics, Inc. (Akcea), to license two investigational treatments with the potential to significantly reduce cardiovascular risk in patients suffering from high levels of lipoproteins known as Lp(a) and ApoCIII. In addition, Novartis entered into a stock purchase agreement with Ionis and Akcea. This transaction was completed on February 14, 2017.

2016

December

Novartis announces that it has entered into a definitive agreement for the acquisition of Encore Vision, Inc., a privately held company focused on the development of UNR844 (formerly EV06), an investigational, first-in-class, potentially disease-modifying topical treatment for presbyopia. This acquisition was completed on January 20, 2017.

Novartis announces the signing of an exclusive option, collaboration and license agreement with Conatus Pharmaceuticals Inc., for the global rights to emricasan, an investigational, first-in-class, oral, pan-caspase inhibitor for the treatment of nonalcoholic steatohepatitis (NASH) with advanced fibrosis and cirrhosis of the liver. Novartis

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exercised the option on May 4, 2017. Novartis obtained an exclusive, worldwide license to develop and commercialize products containing emricasan on July 5, 2017.

Novartis announces that it has entered into a definitive agreement for the acquisition of Ziarco Group Limited, a privately held company focused on the development of novel treatments in dermatology, including ZPL389 (adriforant), a once-daily oral H4 receptor antagonist in development for atopic dermatitis. This acquisition was completed on January 20, 2017.

November

Novartis announces that it has acquired Reprixys Pharmaceuticals Corporation and SEG101 (crizanlizumab) for reduction of pain crises in sickle cell disease.

September

Novartis completes two euro-denominated bond offerings totaling EUR 1.75 billion.

June

Novartis announces that it has entered into a collaboration and licensing agreement with Xencor for the development of bispecific antibodies for treating cancer.

Novartis announces that it will further expand its longstanding partnership with Medicines for Malaria Venture. Novartis will lead the development of antimalarial compound KAF156 (ganaplacide) with scientific and financial support from Medicines for Malaria Venture in collaboration with the Bill & Melinda Gates Foundation.

May

Novartis announces changes to focus its Pharmaceuticals Division by creating two business units: Novartis Pharmaceuticals and Novartis Oncology. These business units form the Innovative Medicines Division of Novartis. The CEO of each business unit reports directly to the CEO of Novartis, and both joined the ECN effective July 1, 2016.

February

Shareholders authorize the Novartis Board of Directors to execute share buybacks within the framework of a seventh share repurchase program that will allow Novartis to repurchase shares for cancellation up to a maximum of CHF 10 billion.

Novartis announces that it has entered into an agreement to acquire Transcend Medical, Inc., a privately held, US-based company focused on developing minimally invasive surgical devices to treat glaucoma, such as the *CyPass* Micro-Stent. This acquisition was completed on March 23, 2016.

Novartis announces that it has acquired from Pfizer the rights for the development and commercialization of PF-06438179 (biosimilar infliximab) in the European Economic Area.

January

Novartis announces leadership changes effective February 1, 2016. Mike Ball has been appointed Division Head and CEO Alcon, succeeding Jeff George; Dr. Vas Narasimhan has been appointed Global Head Drug Development and Chief Medical Officer, a new position in the ECN; and André Wyss has been appointed President, Novartis Operations.

Novartis announces that it is taking a number of steps to further build on its strategy, including focusing the Alcon Division on its Surgical and Vision Care franchises and strengthening the ophthalmic medicines business by transferring Alcon's Ophthalmic Pharmaceuticals products to the Innovative Medicines Division, and by shifting selected mature, non-promoted pharmaceutical products from the Innovative Medicines Division into the Sandoz Division, which changes were operationally completed as of April 1, 2016; and by centralizing manufacturing operations across divisions within a single technical operations unit; increasing Group-wide coordination of drug development by establishing a single Global Head of Drug Development and centralizing certain common functions such as the Chief Medical Office, which changes were operationally completed as of July 1, 2016.

Novartis announces a collaboration and licensing agreement with Surface Oncology, which gives Novartis access to four preclinical programs in immuno-oncology.

For information on our principal expenditures on property, plants and equipment, see "Item 4. Information on the Company—Item 4.D Property, plants and equipment." For information on our significant expenditures in research and development, see the sections headed "Research and Development" included in the descriptions of our Innovative Medicines Division and Alcon Division, and the section headed "Development and Registration" included in the description of our Sandoz Division under "Item 4. Information on the Company—Item 4.B Business overview." For

information on other principal capital expenditures and divestitures, see “Item 5. Operating and Financial Review and Prospects—Item 5.A Operating results—Factors affecting comparability of year-on-year results of operations.”

4.B Business overview

Overview

As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach more than 800 million people globally and we are finding innovative ways to expand access to our latest treatments. Our purpose is to reimagine medicine to improve and extend people's lives. Our vision is to be a trusted leader in changing the practice of medicine. Our strategy is to focus Novartis as a leading medicines company powered by advanced therapy platforms and data science.

In 2018, Novartis achieved net sales of USD 51.9 billion, while net income amounted to USD 12.6 billion. Headquartered in Basel, Switzerland, our Group companies employed 125,000 full-time equivalent associates as of December 31, 2018. Our products are sold in approximately 155 countries around the world.

The Group comprises three global operating divisions:

• Innovative Medicines: innovative patent-protected prescription medicines
• Sandoz: generic pharmaceuticals and biosimilars
• Alcon: surgical and vision care products

In June 2018, we announced that we plan to spin off Alcon into a separately-traded standalone company. As two distinct publicly traded companies, we believe Novartis and Alcon will be better positioned to capitalize on significant growth opportunities and focus resources on their respective businesses and strategic priorities.

Our divisions are supported by the following cross-divisional organizational units: the Novartis Institutes for BioMedical Research, Global Drug Development, Novartis Technical Operations and Novartis Business Services. The financial results of these organizational units are included in the results of the divisions for which their work is performed. As part of the planned spin-off of Alcon, efforts are being undertaken to prepare for the separation of Alcon from Novartis and to enable Alcon to operate as a standalone public company. As part of these efforts, Alcon has formed, and will continue to form, its own support functions, including its own service organization.

The Novartis Institutes for BioMedical Research (NIBR) is the innovation engine of Novartis, which conducts drug discovery research and early clinical development trials for our Innovative Medicines Division and also collaborates with our Sandoz Division. Approximately 6 000 full-time equivalent scientists and associates at NIBR are working to discover new medicines for various diseases at sites located in the US, Switzerland and China. For more information about NIBR, see "—Innovative Medicines—Research and development—Research program" below.

Our Global Drug Development (GDD) organization oversees all drug development activities for our Innovative Medicines Division and the biosimilars portfolio of our Sandoz Division. The development of products for the Surgical and Vision Care franchises within our Alcon Division and of small-molecule generics for our Sandoz Division is not included in GDD. GDD works collaboratively with NIBR, Innovative Medicines and Sandoz to execute our overall pipeline strategy and takes an enterprise approach to pipeline portfolio management. GDD incorporates centralized global functions such as Regulatory Affairs and Global Development Operations, as well as Global Development units aligned with our business franchises. GDD includes approximately 11 000 full-time equivalent associates worldwide.

Novartis Technical Operations (NTO) was established to centralize management of our manufacturing operations and supply chain across our Innovative Medicines and Sandoz Divisions, with a goal of further improving efficiency. Manufacturing for Alcon's Surgical and Vision Care franchises continues to be managed by our Alcon Division. NTO is expected to optimize capacity planning and adherence to quality standards, and to lower costs through simplification, standardization and external spend optimization. Centralization is also expected to improve our ability to develop next-generation technologies, implement continuous manufacturing and share best practices across divisions. NTO includes approximately 25 200 full-time equivalent associates and 64 manufacturing sites across our Innovative Medicines and Sandoz Divisions.

Novartis Business Services (NBS), our shared services organization, delivers integrated solutions to all Novartis divisions and units worldwide. NBS seeks to drive efficiency and effectiveness across Novartis by simplifying and standardizing services across six service domains: human resources, real estate and facility services, procurement,

information technology, commercial and medical support activities, and financial reporting and accounting operations. NBS has approximately 10 500 full-time equivalent associates in more than 30 countries. NBS works to leverage the full scale of Novartis to create value across the Company and to free up resources to invest in innovation and our product pipeline. NBS continues to transfer the delivery of selected services to its five Global Service Centers in Dublin, Ireland; Hyderabad, India; Kuala Lumpur, Malaysia; Mexico City, Mexico; and Prague, Czech Republic.
As of January 1, 2019, Novartis Internal Audit, Business Practices Office and Global Security were combined into one function called Novartis Business Assurance & Advisory (NBAA).

Innovative Medicines Division

Our Innovative Medicines Division researches, develops, manufactures, distributes and sells patented prescription medicines to enhance health outcomes for patients and healthcare providers. Innovative Medicines is organized into two global business units: Novartis Oncology and Novartis Pharmaceuticals. Novartis Pharmaceuticals consists of the global business franchises Ophthalmology; Neuroscience; Immunology, Hepatology and Dermatology; Respiratory; Cardio-Metabolic; and Established Medicines.

Sandoz Division

Our Sandoz Division develops, manufactures, distributes and sells prescription medicines as well as pharmaceutical active substances that are not protected by valid and enforceable third-party patents. Sandoz is organized globally into three franchises: Retail Generics, Anti-Infectives and Biopharmaceuticals. In Retail Generics, Sandoz develops, manufactures and markets active ingredients and finished dosage forms of pharmaceuticals to third parties. Retail Generics includes the areas of cardiovascular, central nervous system, dermatology, gastrointestinal and hormonal therapies, metabolism, oncology, ophthalmics, pain, and respiratory, as well as finished dosage form anti-infectives sold to third parties. In Anti-Infectives, Sandoz manufactures and supplies active pharmaceutical ingredients and intermediates – mainly antibiotics – for internal use by Retail Generics and for sale to third-party customers. In Biopharmaceuticals, Sandoz develops, manufactures and markets protein- or other biotechnology-based products, including biosimilars, and provides biotechnology manufacturing services to other companies.

Alcon Division

Our Alcon Division, a global leader in eye care, researches, develops, manufactures, distributes and sells eye care products. Alcon is organized into two global business franchises: Surgical and Vision Care. Surgical researches, develops, manufactures, distributes and sells ophthalmic products for cataract surgery, vitreoretinal surgery, refractive laser surgery and glaucoma surgery. The Surgical portfolio also includes implantables, consumables and surgical equipment required for these procedures and supports the end-to-end procedure needs of the ophthalmic surgeon. Vision Care researches, develops, manufactures, distributes and sells daily disposable, reusable, and color-enhancing contact lenses and a comprehensive portfolio of ocular health products, including products for dry eye, contact lens care and ocular allergies, as well as ocular vitamins and redness relievers. Alcon also provides services, training, education and technical support for both the Surgical and Vision Care businesses.

Effective January 1, 2018, we transferred our over the counter ophthalmic products and certain surgical diagnostic products (2017 sales of USD 747 million) from the Innovative Medicines Division to the Alcon Division. Our prescription Ophthalmic medicines business remains with the Innovative Medicines Division. In compliance with IFRS, beginning with our first-quarter 2018 results, Novartis updated its segment financial information to reflect this transfer, both for the current and prior years, to aid comparability of year on year results.

Corporate activities

We separately report the results of Corporate activities. The financial results of our Corporate activities include the costs of the Group headquarters and those of corporate coordination functions in major countries. In addition, Corporate includes other items of income and expense that are not attributable to specific segments, such as certain revenues from intellectual property rights and certain expenses related to post-employment benefits, environmental remediation liabilities, charitable activities, donations and sponsorships.

Corporate responsibility

We are taking steps to continue to build trust with key stakeholders and society. We aim to hold ourselves to the highest ethical standards, be part of the solution on pricing and access to medicines, help tackle global health challenges, and be a responsible citizen wherever we operate.

Holding ourselves to the highest ethical standards

We continue to embed a principles based approach to compliance through the new Professional Practices Policy (P3), which in 2018 replaced separate divisional compliance policies. We believe this approach will help ensure that employees act in the best interest of patients, physicians and Novartis.

Since 2016, we have adjusted the ratio of fixed to variable total compensation for our sales force to help ensure that the target variable component is a maximum of 35% of total compensation, on a country average basis. To receive any form of variable compensation, each employee, including the sales force, must perform to a minimum standard with regard to our Values and Behaviors, which include acting with integrity. For our sales force, in particular, 20% of target variable pay is based on demonstration of our Values and Behaviors. We are in the process of implementing

these standards in every country in which Novartis operates. Ultimately, no sales representative will receive the variable compensation unless he or she meets expectations with respect to Values and Behaviors. In 2018, we assessed the rollout of the new incentive system with positive results. Across divisions, there was a 54% reduction in the number of reported complaints of fraud or professional practices in the sales force in 2018 compared to 2017.
Despite this progress, we are still facing questions about our business practices. Following the issue with Essential Consultants, when our political consultancy practices came into question, we took steps to improve oversight and help prevent similar matters in the future. We have strengthened the relevant contracting and due diligence processes to help ensure more ownership and

transparency at a senior management level. For example, before Novartis engages political consultants, we will secure an independent due diligence report from an external partner.

In addition, we continue to strengthen our Integrity & Compliance (I&C) function. In 2018, we combined our risk management and compliance functions in a single organization to help enable more effective risk management and mitigation efforts. We created the role of Chief Ethics, Risk and Compliance Officer to head the combined organization, and we elevated this role to the Executive Committee of Novartis (ECN).

To help monitor and enforce our integrity standards, we added more than 100 people to the I&C function in recent years. The expanded team has increased the number of country visits to share learnings from across the organization, reaching about 220 in 2018. We also harmonized our I&C risk assessment and monitoring process and control activities into a single, continuous process supported by an online tool.

We continue to evolve our reporting and data analytics to provide centralized and aggregated data across the risk functions to identify trends and help improve risk mitigation. For instance, in the last two years, we have seen a positive trend in generally effective internal compliance audits. At the same time, our whistleblower hotline continues to receive reports of suspected cases where employees may have failed to follow our ethical guidelines. However, the proportion of substantiated allegations related to ethics and compliance matters remains stable. We believe these are indications that our efforts are starting to pay off. We also started to employ data analytics for better monitoring and risk prevention. For example, in the US and China, the team leverages big data to monitor various aspects of engagement with healthcare professionals.

Being part of the solution on pricing and access

Our medications reach more than 800 million people worldwide every year, but billions more still lack access to essential medicines and healthcare. We are making a fundamental shift in the way we do business and are reimagining how to expand access to critical healthcare innovations.

We launched the Novartis Access Principles, embarking on a journey to systematically integrate access strategies into how we research, develop and deliver our new medicines globally. These strategies include adopting innovative pricing and access models, refocusing research and development based on society's healthcare needs, and supporting approaches to strengthen healthcare systems. We made significant progress in setting up our internal systems and training our internal teams on our new business standards. The ECN reviewed plans for key brands in launch phase to assess access strategies targeting underserved populations. For example, *Aimovig,* our innovative medicine for the treatment of migraine, is supported by programs designed to help accelerate access both before and after reimbursement, as well as to speed up introduction and access in low- and middle-income countries (LMICs). We are also co-creating employer-based access schemes in selected markets, including Russia and Mexico.

We aim to price our medicines responsibly, based on the value they deliver to patients, healthcare systems and society. In the US we recently implemented guidelines for limiting average net price increases across our portfolio to the healthcare inflation rate, and we publish average price increases annually in the Novartis in Society US report.

In addition, we take local affordability into account when pricing our medicines. In LMICs, for instance, we introduced more affordable local brands of many innovative therapies, such as our heart failure treatment *Entresto*, to help speed up and improve access where there is inadequate healthcare coverage or reimbursement. Through our continued efforts and an impactful access strategy, the number of patients reached with *Entresto* in LMICs grew two-and-a-half-fold in the last 12 months. Overall, we have launched more than 60 local brands across more than 30 developing markets, reaching more than 220 000 additional patients to date. In addition, we are now able to reduce the time lag between availability of medicines in higher- and lower-income countries. For example, the first *Entresto* local brand was launched within 12 months of the launch in the European Union. We plan to further expand these strategies.

Through our Novartis Social Business (NSB) group, we continue to pursue unique social business models, such as the Novartis Access and Healthy Family programs, to help expand access to healthcare in lower-income countries. Novartis Access, which offers a portfolio of 15 medicines to governments, nongovernmental organizations and other institutional customers for USD 1 per treatment, per month, delivered almost 2.3 million monthly treatments to five countries in 2018, and Healthy Family reached 7.8 million people with health education initiatives. Since January, NSB has adapted its product and price offering in six African and Asian countries, expanding reach to patients across all income levels.

Novartis does not file or enforce patents in least developed countries or low-income countries. In late 2018, we reviewed our approach to patent filing in LMICs in an effort to better align it with the local socio-economic circumstances that exist in many of these countries. As a result, effective 2019, we decided to stop filing patent applications in nine LMICs, where Novartis had previously filed. In addition, in the remaining LMICs, we will aim to restrict patent filings to those patent applications covering new molecules or new chemical entities. Novartis is also a founding member of the Patent Information Initiative for Medicines (Pat-INFORMED), a unique public online resource launched in September 2018 that provides basic patent information for medicines of participating companies, and that aims to help procurement agencies around the world better understand patent status to help inform procurement decisions. As of December, Novartis has listed patent information for all of our small-molecule medicines, which goes significantly beyond Pat-INFORMED's near-term goal of capturing information for medicines in a more limited number of disease areas.

We regularly review our early- and late-stage development programs to identify further opportunities for adapting our existing medicines to address unmet patient needs in countries with a high disease burden. In 2018,

14 project proposals were endorsed to move forward. They include the development of a child-friendly formulation of hydroxyurea for treatment of sickle cell disease in Africa; the use of *Entresto* in heart failure related to Chagas disease; a project to identify potential differences in the pharmacokinetics of drugs in African patients, where such data is lacking; and the creation of a new *Coartem* formulation to treat infants below 5 kilograms of body weight.

Tackling global health challenges

Novartis has a long history of helping tackle some of the biggest global health challenges, particularly leprosy and malaria.

The Novartis Foundation helped found the Global Partnership for Zero Leprosy in 2018. It brings together international organizations and national leprosy programs, with support from the World Health Organization, to accelerate progress toward eliminating the disease. The Novartis Foundation and Microsoft are partnering to develop a proof-of-concept digital health tool, enabled by artificial intelligence, and a Leprosy Intelligent Image Atlas – in collaboration with local investigators from the Oswaldo Cruz Foundation in Brazil – to aid in the early detection of leprosy. The launch of the first public version of the atlas is planned for 2019.

In April, we renewed our commitment to malaria elimination, pledging USD 100 million to research and develop next-generation antimalarials over the next five years. In addition, we will help expand access to antimalarials formulated for children, and we plan to implement programs to strengthen healthcare systems in four sub-Saharan countries.

We also launched efforts in other areas where we believe we can have significant impact. In October, in Latin America, we kicked off our partnership with the World Heart Federation to develop a roadmap for addressing Chagas disease, the second most common cause of chronic heart failure in Latin America.

In Ghana, we kicked off a collaboration with the government and local partners to establish our commitment to sickle cell disease (SCD) in Africa. This collaboration aims to support the development of treatment guidelines; strengthen the healthcare system by establishing centers of excellence to advance newborn screening and train scientists; accelerate registration and launch of hydroxyurea for the treatment of SCD; and integrate the needs of patients into our drug development strategy. We plan to launch our commitment in 2019 and to also expand our efforts to other countries in sub-Saharan Africa.

Being a responsible citizen

Building trust with society requires doing business responsibly wherever we operate. This includes minimizing our environmental impact, managing risk in our supply chain, respecting human rights and being transparent.

We have adopted a more ambitious 2030 environmental sustainability strategy, aiming for carbon neutrality, plastic neutrality and water sustainability. We have already taken steps to mitigate our exposure to environmental risk, completing a series of comprehensive supplier audits and taking relevant actions. For example, in the Hyderabad area of India, we are severing ties with six suppliers that failed to comply with our Supplier Code, and we are working with nine suppliers to improve their performance in critical areas such as operational efficiency, waste management, and use of natural resources. These suppliers share our values for environmental stewardship and employee health and safety.

In October, our Third-Party Risk Management program went live in Mexico. The program is to be rolled out globally in 2019 in a phased regional approach, beginning in the Americas (including the US) and followed by Asia-Pacific and Europe later in the year.

After completing human rights impact assessments in our own operations in Egypt, Turkey, China and Malaysia, we have established that we have strong policies and solid processes to identify and manage potential human rights risks. We have also identified common risk areas that require additional follow up action in 2019. For example, we need more regular and broader engagement and consultation with external stakeholders at a local level – including representatives from patient groups, local communities, health authorities and third-party partners – to gain a better understanding of issues; to help ensure that formal grievance mechanisms and processes are in place for communities living close to our manufacturing operations; and, in some markets, to address risks associated with our outsourced workforce.

For additional information, see “—Item 4.B Business overview—Sandoz.”

Innovative Medicines

Overview

Our Innovative Medicines Division is a world leader in offering innovation-driven, patent-protected medicines to patients and physicians. The Innovative Medicines Division researches, develops, manufactures, distributes and sells patented pharmaceuticals, and is composed of two global business units: Novartis Oncology and Novartis Pharmaceuticals.

The Novartis Oncology business unit is responsible for the commercialization of products in the areas of cancer and hematologic disorders. The Novartis Pharmaceuticals business unit is organized into the following global business franchises responsible for the commercialization of various products in their respective therapeutic areas: Ophthalmology; Neuroscience; Immunology, Hepatology and Dermatology; Respiratory; Cardio-Metabolic; and Established Medicines.

Following an internal reorganization announced on January 27, 2016, 19 mature products were transferred from our Innovative Medicines Division to the Retail Generics franchise of our Sandoz Division, and the

Ophthalmic Pharmaceuticals products of Alcon were transferred to our Innovative Medicines Division, effective as of January 1, 2018.

We subsequently transferred our over-the-counter ophthalmic products and certain surgical diagnostic products (2017 sales of USD 747 million) from the Innovative Medicines Division to the Alcon Division, effective January 1, 2018. Our prescription Ophthalmic medicines business remains with the Innovative Medicines Division. In compliance with IFRS, beginning with our first-quarter 2018 results, Novartis updated its segment financial information to reflect this transfer, both for the current and prior years, to aid comparability of year-on-year results.

The Innovative Medicines Division is the largest contributor among the divisions of Novartis and reported consolidated net sales of USD 34.9 billion in 2018, which represented 67% of the Group's net sales.

The product portfolio of the Innovative Medicines Division includes more than 60 key marketed products, many of which are leaders in their respective therapeutic areas.

Innovative Medicines Division products

The following table and summaries describe certain key marketed products in our Innovative Medicines Division. While we typically seek to sell our marketed products throughout the world, not all products and indications are currently available in every country. In addition, a product may be available under different brand names depending on country and indication. Some of the products listed below have lost patent protection or are otherwise subject to generic competition. Others are subject to patent challenges by potential generic competitors. Please see "—Intellectual property" for general information on intellectual property and regulatory data protection, and for further information on the status of patents and exclusivity for Innovative Medicines Division products.

Selected marketed products
Novartis Oncology business unit

Business franchise	Product	Common name	Indications (vary by country and/or formulation)	Formulation
Oncology	*Afinitor/Votubia* and *Afinitor Disperz/Votubia* dispersible tablets	everolimus	In combination with exemestane for postmenopausal women with advanced hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer after failure of treatment with letrozole or anastrozole, or after recurrence or progression following treatment with a non-steroidal aromatase inhibitor Advanced renal cell carcinoma after failure of treatment with VEGF-targeted therapy, or after failure of treatment with sunitinib or sorafenib Advanced neuroendocrine tumors of gastrointestinal, lung or pancreatic origin Renal angiomyolipoma associated with tuberous sclerosis complex (TSC) in patients not requiring immediate surgery Subependymal giant cell astrocytoma associated with TSC in patients not requiring immediate surgery Adjunctive treatment of patients aged 2 years and older with TSC-associated partial-onset and refractory seizures	Tablet Dispersible tablet for oral suspension
	Arzerra	ofatumumab	Treatment of patients with chronic lymphocytic leukemia (CLL) who are refractory to fludarabine and alemtuzumab In combination with an alkylator-based regimen for the treatment of patients with CLL who have not received prior therapy and are not eligible for fludarabine-based therapy Maintenance/extended treatment for patients with CLL who are in complete or partial response after at least two lines of induction therapy In combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL	Intravenous infusion
	Exjade and *Jadenu*	deferasirox	Chronic iron overload due to blood transfusions and non-transfusion-dependent thalassemia	Dispersible tablet for oral suspension Oral film-coated tablet

			Granules
Farydak	panobinostat	Relapsed and/or refractory multiple myeloma, in combination with bortezomib and dexamethasone, after at least two prior regimens including bortezomib and an immunomodulatory agent	Capsule
Femara	letrozole	HR+ early breast cancer in postmenopausal women following surgery (upfront adjuvant therapy) Early breast cancer in postmenopausal women following standard tamoxifen therapy (extended adjuvant therapy) Advanced breast cancer in postmenopausal women (both as first- and second-line therapies)	Tablet
Gleevec/Glivec	imatinib mesylate/ imatinib	Certain forms of Philadelphia chromosome-positive chronic myeloid leukemia Certain forms of KIT-positive gastrointestinal stromal tumors Certain forms of acute lymphoblastic leukemia Dermatofibrosarcoma protuberans Hypereosinophilic syndrome Aggressive systemic mastocytosis Myelodysplastic/myeloproliferative diseases	Tablet Capsule
Jakavi	ruxolitinib	Disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis Polycythemia vera in adult patients who are resistant to or intolerant of hydroxyurea	Tablet
Kisqali	ribociclib	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of pre-, peri- or postmenopausal women with HR+/HER2- locally advanced or metastatic breast cancer In combination with fulvestrant as first- or second-line therapy for the treatment of postmenopausal women with HR+/HER2- advanced or metastatic breast cancer	Tablet
Kymriah	tisagenlecleucel	Children and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia Adult patients with relapsed or refractory diffuse large B-cell	Suspension for intravenous infusion Dispersion for intravenous

		lymphoma Treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in adults	infusion
Lutathera	USAN: lutetium Lu 177 dotatate/ INN: lutetium (^{177}Lu) oxodotreotide	Treatment of unresectable or metastatic, progressive, well-differentiated (G1 and G2), somatostatin receptor-positive GEP-NETs in adults	Solution for intravenous infusion
Promacta/Revolade	eltrombopag	Thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune (idiopathic) thrombocytopenia who have had an insufficient response to corticosteroids or immunoglobulins Thrombocytopenia in patients with chronic hepatitis C to allow initiation and maintenance of interferon-based therapy As first-line therapy in patients with severe aplastic anemia, and as second-line therapy in patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy	Film-coated tablet

Business franchise	Product	Common name	Indications (vary by country and/or formulation)	Formulation
	Rydapt	midostaurin	In combination with standard cytarabine and daunorubicin induction and cytarabine consolidation chemotherapy for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who are FLT3 mutation-positive, as detected by an FDA-approved test (*Rydapt* is not indicated as a single-agent induction therapy for the treatment of patients with AML)	Capsule
	Sandostatin LAR and *Sandostatin* SC	octreotide acetate	For the treatment of adult patients with aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm, or mast cell leukemia Acromegaly Symptom control for certain forms of neuroendocrine tumors Treatment of advanced neuroendocrine tumors of the midgut or of unknown primary origin	Vial Ampoule/pre-filled syringe Solution for subcutaneous injection in ampoule
	Signifor and *Signifor* LAR	pasireotide	Cushing's disease Acromegaly	Powder and solvent for suspension for IM injection
	Tafinlar + *Mekinist*	dabrafenib + trametinib	Unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by a validated test Adjuvant treatment of patients with stage III melanoma with a BRAF V600 mutation, following complete resection Locally advanced or metastatic anaplastic thyroid cancer with a BRAF V600E mutation and no satisfactory locoregional treatment options Metastatic non-small cell lung cancer with a BRAF V600E mutation, as detected by a validated test	Capsule *(Tafinlar)* Tablet *(Mekinist)*
	Tasigna	nilotinib	Certain forms of chronic myeloid leukemia in adult and pediatric patients resistant or intolerant to prior treatment, including *Gleevec/Glivec* First-line chronic myeloid leukemia in adult and	Capsule

			pediatric patients In combination with capecitabine for the treatment of patients with human epidermal growth factor receptor 2-positive (HER2+) advanced or metastatic breast cancer who have progressed on prior trastuzumab therapy In combination with an aromatase inhibitor (specifically letrozole in the US) for the treatment of patients with hormone-sensitive metastatic breast cancer	
	Tykerb/Tyverb	lapatinib	In combination with trastuzumab for patients with hormone receptor-negative (HR-) metastatic disease that has progressed on prior trastuzumab therapy/ therapies plus chemotherapy In combination with paclitaxel for first-line treatment of patients with HER2+ metastatic breast cancer for whom trastuzumab is not appropriate	Tablet
	Votrient	pazopanib	Advanced renal cell carcinoma Certain types of advanced soft tissue sarcoma after prior chemotherapy	Tablet
	Zometa	zoledronic acid	Skeletal-related events from bone metastases Hypercalcemia of malignancy	Vial/4 mg ready-to-use
	Zykadia	ceritinib	Advanced or metastatic non-small cell lung cancer that is anaplastic lymphoma kinase-positive	Capsule

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Novartis Pharmaceuticals business unit

Business franchise	Product	Common name	Indications (vary by country and/or formulation)	Formulation
Ophthalmology	Azarga/Azorga	brinzolamide and timolol	Decrease of intraocular pressure in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provides insufficient intraocular pressure reduction	Eye drops
	Ciprodex	ciprofloxacin and dexamethasone	Treatment of bacterial ear infections	Ear drops
	Duotrav	travoprost and timolol	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Eye drops
	Durezol	difluprednate	Treatment of inflammation and pain associated with ocular surgery Treatment of endogenous anterior uveitis	Eye drops
	Lucentis	ranibizumab	Neovascular age-related macular degeneration Visual impairment due to diabetic macular edema Visual impairment due to macular edema secondary to central retinal vein occlusion Visual impairment due to macular edema secondary to branch retinal vein occlusion Visual impairment due to choroidal neovascularization secondary to pathologic myopia Visual impairment due to choroidal neovascularization secondary to other pathologies	Intravitreal injection
	Luxturna	voretigene neparvovec	Treatment of adult and pediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells	Subretinal injection
	Pataday and *Pazeo*	olopatadine	Signs and symptoms of allergic conjunctivitis Ocular itching associated with allergic conjunctivitis	Eye drops
	Patanol	olopatadine	Signs and symptoms of allergic conjunctivitis	Eye drops
	Simbrinza	brinzolamide and brimonidine tartrate	Decrease of elevated intraocular pressure in adult patients with open-angle	Eye drops

			glaucoma or hypertension for whom monotherapy provides insufficient intraocular pressure reduction	
	Travatan, Travatan Z, Travatan BAK-Free, *Izba*	travoprost	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension	Eye drops
Immunology, Hepatology and Dermatology	Cosentyx	secukinumab	Active ankylosing spondylitis Active psoriatic arthritis Moderate-to-severe plaque psoriasis Pustular psoriasis	Auto-injector Lyophilized, pre-filled syringe
	Ilaris	canakinumab	Cryopyrin-associated periodic syndromes Tumor necrosis factor receptor-associated periodic syndrome Hyperimmunoglobulin D syndrome/mevalonate kinase deficiency Familial Mediterranean fever Systemic juvenile idiopathic arthritis Gouty arthritis Adult-onset Still's disease	Solution for injection Lyophilized powder for reconstitution for subcutaneous injection
	Xolair	omalizumab	Chronic spontaneous urticaria/chronic idiopathic urticaria See also "Respiratory"	Liquid formulation in pre-filled syringe Lyophilized powder in vial Subcutaneous injection
Neuroscience	Aimovig	erenumab	Preventive treatment of migraine	
	Extavia	interferon beta-1b	Relapsing-remitting and/or relapsing forms of multiple sclerosis (MS) in adult patients, and for patients who have had a single clinical event suggestive of MS and are at high risk of developing clinically definite MS	Subcutaneous injection
	Gilenya	fingolimod	Relapsing forms of MS	Capsule
Respiratory	Onbrez Breezhaler	indacaterol	Chronic obstructive pulmonary disease	Inhalation powder hard capsules
	Seebri Breezhaler	glycopyrronium bromide	Chronic obstructive pulmonary disease	Inhalation powder hard capsules
	Ultibro Breezhaler	indacaterol and glycopyrronium bromide	Chronic obstructive pulmonary disease	Inhalation powder hard capsules
	Xolair	omalizumab	Moderate to severe allergic asthma See also "Immunology, Hepatology and Dermatology"	Lyophilized powder in vial Liquid

				formulation in pre-filled syringe
Cardio-Metabolic 36	Entresto	sacubitril/valsartan	Symptomatic chronic heart failure with reduced ejection fraction in adults	Tablet

Business franchise	Product	Common name	Indications (vary by country and/or formulation)	Formulation
Established Medicines	Cibacen	benazepril hydrochloride	Hypertension Adjunct therapy in congestive heart failure Progressive chronic renal insufficiency	Tablet
	Comtan	entacapone	Parkinson's disease patients who experience end-of-dose motor (or movement) fluctuations	Tablet
	Diovan	valsartan	Hypertension Heart failure Post-myocardial infarction	Tablet Capsule Oral solution
	Diovan HCT/Co-Diovan	valsartan and hydrochlorothiazide	Hypertension	Tablet
	Eucreas	vildagliptin and metformin	Type 2 diabetes	Tablet
	Exelon	rivastigmine	Mild-to-moderate Alzheimer's disease dementia Severe Alzheimer's disease dementia Dementia associated with Parkinson's disease	Capsule Oral solution Transdermal patch
	Exforge	valsartan and amlodipine besylate	Hypertension	Tablet
	Exforge HCT	valsartan, amlodipine besylate and hydrochlorothiazide	Hypertension	Tablet
	Focalin and *Focalin XR*	dexmethylphenidate HCl and dexmethylphenidate extended release	Attention deficit hyperactivity disorder	Tablet Capsule
	Galvus	vildagliptin	Type 2 diabetes	Tablet
	Lescol and *Lescol XL*	fluvastatin sodium	Hypercholesterolemia and mixed dyslipidemia in adults Secondary prevention of major adverse cardiac events Slowing the progression of atherosclerosis Heterozygous familial hypercholesterolemia in children and adolescents	Capsule *(Lescol)* Tablet *(Lescol XL)*
	Myfortic	mycophenolic acid (as mycophenolate sodium)	Prophylaxis of organ rejection in patients receiving allogeneic renal transplants	Gastro-resistant tablet
	Neoral/Sandimmune	cyclosporine, USP Modified	Prevention of rejection following certain organ transplantation Non-transplantation autoimmune conditions such as severe psoriasis	Capsule Oral solution Intravenous *(Sandimmune)*

		and severe rheumatoid arthritis	
Ritalin	methylphenidate HCl	Attention deficit hyperactivity disorder and narcolepsy	Tablet
Ritalin LA	methylphenidate HCl-modified release	Attention deficit hyperactivity disorder	Capsule
Simulect	basiliximab	Prevention of acute organ rejection in de novo renal transplantation	Vial for injection or infusion
Stalevo	carbidopa, levodopa and entacapone	Parkinson's disease patients who experience end-of-dose motor (or movement) fluctuations	Tablet
Tegretol	carbamazepine	Epilepsy Pain associated with trigeminal neuralgia Acute mania and bipolar affective disorders Alcohol withdrawal syndrome Painful diabetic neuropathy Diabetes insipidus centralis Polyuria and polydipsia of neurohormonal origin	Tablet Chewable tablet Oral suspension Suppository
Trileptal	oxcarbazepine	Epilepsy	Tablet Oral suspension
Tyzeka/Sebivo	telbivudine	Chronic hepatitis B	Tablet Oral solution
Voltaren/Cataflam	diclofenac sodium/ potassium/resinate/ free acid	Inflammatory and degenerative forms of rheumatism Post-traumatic and postoperative pain, inflammation and swelling Painful and/or inflammatory conditions in gynecology Other painful and/or inflammatory conditions such as renal and biliary colic; migraine attacks; and as adjuvant in severe ear, nose and throat infections Post-traumatic inflammation of the tendons, ligaments, muscles and joints Localized forms of soft-tissue and degenerative rheumatism	Tablet Capsule Oral drops/ oral suspension Ampoule for injection Suppository Gel Powder for oral solution Transdermal patch
Zortress/Certican	everolimus	Prevention of organ rejection (heart, liver and kidney)	Tablet Dispersible tablet

Key marketed products
Novartis Oncology business unit
Oncology
• *Tasigna* (nilotinib) is a signal transduction inhibitor of the BCR-ABL tyrosine kinase. Since its launch in 2007, *Tasigna* has been approved in more than 125 countries to treat patients with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in the chronic and/or accelerated phase who are resistant or intolerant to existing treatment, including *Gleevec/Glivec*, and to treat newly diagnosed patients in the chronic phase. In June 2017, the European Commission (EC) approved the inclusion of treatment-free remission data in the summary of product characteristics for *Tasigna*. In December 2017, the FDA also approved the inclusion of treatment-free remission data in the US label for *Tasigna*. In November 2017, the EC approved *Tasigna* for the treatment of newly diagnosed pediatric patients with Ph+ CML in the chronic phase (CP), and Ph+ CML-CP pediatric patients with resistance or intolerance to prior therapy including imatinib. In March 2018, the FDA approved *Tasigna* for this pediatric indication.
• *Sandostatin* SC (octreotide acetate for injection) and *Sandostatin* LAR (octreotide acetate for injectable suspension) are somatostatin analogs indicated for the treatment of patients with acromegaly, a chronic disease caused by the over-secretion of growth hormone in adults. *Sandostatin* is also indicated for the treatment of patients with certain symptoms associated with carcinoid tumors and other types of gastrointestinal and pancreatic neuroendocrine tumors. Additionally, *Sandostatin* LAR is approved in more than 60 countries for the treatment of patients with advanced neuroendocrine tumors of the midgut or unknown primary tumor location. *Sandostatin* SC was first launched in 1988 and is approved in more than 100 countries.
• *Gleevec/Glivec* (imatinib mesylate/imatinib) is a kinase inhibitor approved as a targeted therapy for adult and pediatric patients with Ph+ CML in the chronic phase. It is also approved to treat patients with Ph+ CML in the blast, accelerated or chronic phase after failure with interferon; to treat patients with metastatic and/or unresectable gastrointestinal stromal tumors (GIST) that are KIT (CD117)-positive (KIT+); and as an adjuvant treatment for certain adult patients following resection of KIT+ GIST. First launched in 2001, *Gleevec/Glivec* is approved in approximately 125 countries. It is approved in more than 80 countries as a post-surgery therapy for certain adult patients with KIT+ GIST. Additionally, *Gleevec/Glivec* is approved in the US, the EU and Japan to treat Ph+ acute lymphoblastic leukemia (a rapidly progressive form of leukemia); in the US and EU to treat dermatofibrosarcoma protuberans (a rare solid tumor), hypereosinophilic syndrome, myelodysplastic/myeloproliferative diseases and other rare blood disorders; and in the US (as *Gleevec*) to treat aggressive systemic mastocytosis.
• *Afinitor/Votubia* (everolimus) is an oral inhibitor of the mTOR pathway. *Afinitor* is approved in more than 120 countries, including the US, EU member states and Japan, for patients with advanced renal cell carcinoma whose disease has progressed during or after treatment with vascular endothelial growth factor-targeted therapy (in the EU), or after failure of treatment with sunitinib or sorafenib (in the US). Additionally, *Afinitor* is approved in more than 110 countries, including the US, EU member states and Japan, for patients with progressive neuroendocrine tumors (NETs) of pancreatic origin that are unresectable, locally advanced or metastatic; in more than 45 countries, including the US and EU member states, for patients with progressive, well-differentiated, nonfunctional NETs of gastrointestinal or lung origin that are unresectable, locally advanced or metastatic; and in 117 countries, in combination with exemestane, for postmenopausal women with advanced hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) breast cancer after recurrence or progression following treatment with a nonsteroidal aromatase inhibitor (in the EU), or after failure of treatment with letrozole or anastrozole (in the US). All oncology indications are approved under the trade name *Afinitor,* in the tablet formulation. Everolimus, under the trade name *Afinitor* in the US and *Votubia* in the EU, is also approved in more than 100 countries to treat patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) not requiring immediate surgery, and in more than 95 countries to treat patients with TSC who have renal angiomyolipoma not requiring immediate surgery. The dispersible tablets for oral suspension formulation are approved in more than 40 countries – including the US (under the trade name *Afinitor Disperz*), EU member states (under the trade name *Votubia*) and Japan (under the trade name *Afinitor*) – for patients with TSC who have SEGA. Dispersible tablets are also approved in more than 30 countries – including EU member states (as *Votubia*) and the US (as *Afinitor Disperz*) – as adjunctive treatment for patients aged 2 years and older with TSC-associated partial-onset seizures. Everolimus is available under the trade names *Zortress/Certican* for use in transplantation in the US and EU,

respectively. It is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.
• *Promacta/Revolade* (eltrombopag) is a once-daily oral thrombopoietin receptor agonist that works by stimulating bone marrow cells to produce platelets. It is the only approved once-daily oral thrombopoietin receptor agonist, and is marketed under the brand name *Promacta* in the US and *Revolade* in most countries outside the US. It is approved in more than 90 countries for the treatment of thrombocytopenia in adult patients with chronic immune (idiopathic) thrombocytopenia (ITP) who have had an inadequate response or are intolerant to other treatments. In the US and EU, *Promacta/Revolade* is approved for pediatric patients 1 year and older with chronic ITP who have had an insufficient response to other treatments. *Promacta/Revolade* is also approved in more than 40 countries for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. It is approved in the US and Japan for aplastic anemia as first-line therapy, and in 45 countries for the treatment of patients with severe

aplastic anemia (SAA) who are refractory to other treatments (including in the EU for adults with acquired SAA who were either refractory to prior immunosuppressive therapy or heavily pretreated and are unsuitable for hematopoietic stem cell transplant). *Promacta/Revolade* is marketed under a collaboration agreement between Ligand Pharmaceuticals, Inc. and Novartis.

• *Tafinlar + Mekinist* (dabrafenib + trametinib) is a combination therapy approved for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600 mutation; the adjuvant treatment of patients with stage III melanoma with a BRAF V600 mutation; the treatment of patients with advanced non-small cell lung cancer with a BRAF V600 mutation; and the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer with a BRAF V600 mutation. Usage in the adjuvant treatment of melanoma was approved in the US, the EU, Japan and other countries worldwide in 2018, making *Tafinlar + Mekinist* the first targeted therapy approved in this setting. The 2018 FDA approval of *Tafinlar + Mekinist* for the treatment of anaplastic thyroid cancer represented the first approval of any therapy in the US for this aggressive form of thyroid cancer. *Tafinlar* and *Mekinist* are kinase inhibitors of BRAF and MEK1/2, respectively, and are also indicated as single agents to treat patients with unresectable or metastatic melanoma with a BRAF V600 mutation. Novartis has worldwide exclusive rights to develop, manufacture and commercialize trametinib granted by Japan Tobacco Inc.

• *Exjade* and *Jadenu* (deferasirox) is an oral iron chelator approved for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older, and of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia. *Exjade,* a dispersible tablet for oral suspension, was first approved in 2005 and is now approved in more than 100 countries, including the US, the EU and Japan. An oral film-coated tablet formulation that can be swallowed or crushed is also approved in countries including the US and Canada (under the *Jadenu* or *Exjade* trade name, depending on the country). Additionally, the formulation has been developed as granules and is approved in the US, the EU and Japan.

• *Jakavi* (ruxolitinib) is an oral inhibitor of the JAK1 and JAK2 tyrosine kinases. It is the first JAK inhibitor indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis, and for the treatment of adult patients with polycythemia vera who are resistant or intolerant to hydroxyurea. *Jakavi* is currently approved in more than 100 countries for patients with myelofibrosis, and in more than 75 countries – including EU member states and Japan – for patients with polycythemia vera. Novartis licensed ruxolitinib from Incyte Corporation for development and commercialization in the indications of oncology, hematology and Graft-versus-host disease outside the US. Ruxolitinib, marketed in the US as Jakafi® by Incyte Corporation, was approved by the FDA for the treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. Jakafi® was also approved by the FDA for the treatment of patients with polycythemia vera who have had an inadequate response or are intolerant to hydroxyurea.

• *Votrient* (pazopanib) is a small-molecule tyrosine kinase inhibitor that targets a number of growth factors to limit new blood vessel and tumor growth and cell survival. *Votrient* is approved in the US for the treatment of patients with advanced renal cell carcinoma (RCC), and in the EU for first-line treatment of adult patients with advanced RCC and for patients who have received prior cytokine therapy for advanced disease. *Votrient* is also indicated for the treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy (efficacy in adipocytic STS or gastrointestinal stromal tumors has not been demonstrated), and in the EU for the treatment of adult patients with selective subtypes of advanced STS who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo)adjuvant therapy. *Votrient* is approved in more than 100 countries worldwide for advanced RCC and in more than 90 countries for advanced STS.

• *Kisqali* (ribociclib) is a cyclin-dependent kinase inhibitor, a class of drugs that helps slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). It is indicated for the treatment of postmenopausal women (and, in the US, pre- or perimenopausal women) with HR+/HER2- locally advanced or metastatic breast cancer as initial endocrine-based therapy in combination with an aromatase inhibitor. In the US and the EU, *Kisqali* is also indicated for use in combination with fulvestrant as first- or second-line therapy in postmenopausal women. *Kisqali* was originally approved in the US in 2017 and is now approved in more than 70 countries, including EU member states. In 2017, the FDA also approved the *Kisqali Femara* Co-Pack (ribociclib tablets and letrozole tablets). *Kisqali* was developed by the Novartis Institutes for BioMedical Research under a research collaboration with Astex Pharmaceuticals.

• *Kymriah* (tisagenlecleucel) suspension for intravenous infusion is a CD19-directed genetically modified autologous chimeric antigen receptor T-cell (CAR-T) therapy. *Kymriah* received FDA approval in 2017 for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse, and in May 2018 for the treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL), high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. *Kymriah* is not indicated for the treatment of patients with primary central nervous system lymphoma. *Kymriah* is also approved in countries including EU

member states and Switzerland for the treatment of children and young adults with r/r B-cell ALL, and adult patients with r/r DLBCL.

• *Lutathera* (USAN: lutetium Lu 177 dotatate/INN: lutetium (177Lu) oxodotreotide) is a lutetium Lu 177-labeled somatostatin analog peptide. It is a radioligand therapy and comprises a targeting molecule that carries a radioactive component. *Lutathera* has received orphan drug designation from the FDA and the EMA. In the US, *Lutathera* is approved for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut and hindgut neuroendocrine tumors, in adults. In Europe, it is approved for the treatment of unresectable or metastatic, progressive, well-differentiated (G1 and G2), somatostatin receptor-positive GEP-NETs in adults.

Novartis Pharmaceuticals business unit

Ophthalmology

• *Lucentis* (ranibizumab) is a recombinant humanized high-affinity antibody fragment that binds to vascular endothelial growth factor A (VEGF-A), a key mediator of intraocular neovascularization. *Lucentis* is an anti-VEGF therapy specifically designed for the eye, minimizing systemic exposure. It is approved for six indications: neovascular (wet) age-related macular degeneration (nAMD), visual impairment due to diabetic macular edema (DME), visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO), visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO), visual impairment due to choroidal neovascularization secondary to pathologic myopia (myopic CNV), and visual impairment due to choroidal neovascularization (CNV) secondary to other pathologies. *Lucentis* is available in more than 110 countries, and the *Lucentis* pre-filled syringe has launched in 37 countries. *Lucentis* is licensed from Genentech, and Novartis holds the rights to commercialize the product outside the US. Genentech holds the rights to commercialize *Lucentis* in the US. For further information, see “Item 18. Financial Statements—Note 26. Transactions with related parties—Genentech/Roche.”

• *Travatan* (travoprost), *Travatan Z* (travoprost) and *Duotrav* (travoprost/timolol) are indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. Single-agent travoprost products (*Travatan*, *Travatan Z*, *Travatan* BAK-Free and *Izba*) are prescribed as first-line agents and are marketed in more than 110 countries, including the US and EU member states. *Duotrav* is a fixed-dose combination solution of the prostaglandin analog travoprost with the beta-blocker timolol, and is approved as a second-line treatment in adults for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogs. *Duotrav* is currently marketed in more than 105 countries, including EU member states.

• *Luxturna* (voretigene neparvovec) is a one-time gene therapy approved in the EU in November 2018 to treat children and adults with vision loss caused by mutations in both copies of the RPE65 gene and who have sufficient viable retinal cells. In January 2018, Spark Therapeutics entered into a licensing agreement and a manufacturing and supply agreement with Novartis covering development, registration and commercialization rights to *Luxturna* in markets outside the US. Upon the transfer of the EU marketing authorization from Spark Therapeutics to Novartis, Novartis plans to commercialize *Luxturna* in the EU/EEA, with Spark Therapeutics as supplier of the gene therapy.

Immunology, Hepatology and Dermatology

• *Cosentyx* (secukinumab) is a fully human monoclonal antibody that selectively inhibits circulating interleukin-17A (IL-17A), a cytokine involved in the pathogenesis of psoriasis, ankylosing spondylitis and psoriatic arthritis. *Cosentyx* is approved in more than 90 countries, including the US, EU member states and Japan, for the treatment of moderate-to-severe plaque psoriasis. It is approved in more than 80 countries, including the US, EU member states and Japan, for the treatment of adults with ankylosing spondylitis and psoriatic arthritis. *Cosentyx* is also approved in Japan for the treatment of pustular psoriasis and psoriasis vulgaris. In 2017, a label update for *Cosentyx* was approved in the EU based on data showing long-term superiority over Stelara® (ustekinumab) in moderate-to-severe plaque psoriasis, along with efficacy in the treatment of moderate-to-severe scalp psoriasis – one of the most difficult-to-treat forms of the disease. In 2018, the FDA approved a label update for *Cosentyx* to include moderate-to-severe scalp psoriasis, and new evidence that *Cosentyx* inhibits progression of joint structural damage in psoriatic arthritis.

• *Xolair* (omalizumab) is a recombinant, DNA-derived, humanized IgG1 monoclonal antibody. *Xolair* is designed to block IgE, which limits the release of mediators in the early and late phases of the allergic cascade. It is currently approved in more than 90 countries, including the US, EU member states and Japan, as a treatment for chronic spontaneous urticaria (CSU), also known as chronic idiopathic urticaria (CIU). In the EU, *Xolair* is indicated as

add-on therapy for the treatment of CSU in adults and adolescents 12 years of age and older with inadequate response to H1 antihistamine treatment. In the US, *Xolair* is approved to treat adults and adolescents 12 years of age and older with CIU who remain symptomatic despite H1 antihistamine treatment. (See also *Xolair* in "Respiratory" below.) We co-promote *Xolair* with Genentech in the US and share a portion of operating income, but we do not record any US sales. Novartis records all sales of *Xolair* outside the US. For further information, see "Item 18. Financial Statements—Note 26. Transactions with related parties—Genentech/Roche."

• *Ilaris* (canakinumab) is a selective, high-affinity fully human monoclonal antibody that inhibits interleukin-1 beta (IL-1 beta), a key cytokine in the inflammatory pathway. *Ilaris* is approved in the US, EU member states and

Japan to treat systemic juvenile idiopathic arthritis and various auto-inflammatory conditions, such as cryopyrin-associated periodic syndromes and other distinct periodic fevers (also known as hereditary periodic fevers). It is also approved in the EU for adult-onset Still's disease and the symptomatic treatment of refractory acute gouty arthritis. *Ilaris* is approved in one or more indications in approximately 70 countries worldwide.

Neuroscience

• *Gilenya* (fingolimod) is an oral disease-modifying therapy approved to treat relapsing forms of multiple sclerosis (MS). It has a reversible lymphocyte redistribution effect targeting both focal and diffuse central nervous system damage caused by MS. In the US, *Gilenya* is indicated for relapsing forms of MS in patients who are 10 years of age and older. In the EU, *Gilenya* is indicated for adult patients who have high disease activity despite treatment with at least one disease-modifying agent, or who have rapidly evolving severe relapsing-remitting MS. Additionally, it received European Commission approval in November 2018 for the treatment of children and adolescents with relapsing-remitting MS. Results from the Phase IIIb ASSESS study, announced in October 2018, showed that *Gilenya* 0.5 mg is superior in reducing relapses to glatiramer acetate in a controlled, head-to-head trial. Treatment with *Gilenya* 0.5 mg resulted in a 40.7% relative reduction in the rate of relapses over one year, compared to patients on glatiramer acetate 20 mg. Adults taking *Gilenya* 0.25 mg achieved a numerical risk reduction in relapses compared to the comparator, but did not reach statistical significance. *Gilenya* is currently approved in more than 80 countries around the world. *Gilenya* is licensed from Mitsubishi Tanabe Pharma Corporation.

• *Aimovig* (erenumab) is designed specifically to block the calcitonin gene-related peptide receptor (CGRP-R), which plays a critical role in migraine. It is the first FDA- and EMA-approved CGRP-targeted therapy for the prevention of migraine in adults. *Aimovig* received US approval in May 2018 and EU approval in July 2018, and is currently approved in 37 countries worldwide. *Aimovig* is co-commercialized with Amgen in the US, where Amgen records sales, and Novartis has exclusive commercialization rights for all territories excluding the US and Japan.

Respiratory

• *Xolair* (omalizumab) is approved for the treatment of moderate-to-severe, or severe, persistent allergic asthma in children (age 6 and older) and adults. It has been approved in more than 90 countries, including the US since 2003, the EU since 2005, Japan since 2009, and China since 2018. *Xolair* is provided as lyophilized powder for resolution, and as liquid formulation in a pre-filled syringe. In December 2018, the European Commission approved the *Xolair* pre-filled syringe for self-administration across all indications. (See also *Xolair* in "Immunology, Hepatology and Dermatology" above.) We co-promote *Xolair* with Genentech in the US and share a portion of operating income, but we do not record any US sales. Novartis records all sales of *Xolair* outside the US. For further information, see "Item 18. Financial Statements—Note 26. Transactions with related parties—Genentech/Roche."

Cardio-Metabolic

• *Entresto* (sacubitril/valsartan) is a first-in-class angiotensin receptor/neprilysin inhibitor indicated for the treatment of symptomatic chronic heart failure with reduced ejection fraction (HFrEF). It acts to enhance the protective neurohormonal systems of the heart (neprilysin system) while simultaneously suppressing the harmful system (the renin-angiotensin-aldosterone system, or RAAS). *Entresto* was approved in the US and in the EU in 2015. It is now approved in more than 100 countries and launched in more than 90 countries. Both European Society of Cardiology heart failure guidelines and US heart failure guidelines have given a Class I recommendation, the strongest class of recommendation, for the use of sacubitril/valsartan in patients with HFrEF.

Established Medicines

• *Galvus* (vildagliptin), an oral DPP-4 inhibitor, and *Eucreas*, a single-pill combination of vildagliptin and metformin, are indicated for the treatment of type 2 diabetes. The products were first approved in 2007. *Galvus* is currently approved in more than 130 countries, including EU member states, Japan (as *Equa*), Latin America and Asia-Pacific. *Eucreas* is currently approved in more than 125 countries. It was the first single-pill combination of a DPP-4 inhibitor and metformin approved in Japan (as *EquMet*) and Europe, and is marketed as *Galvus Met* in most non-EU countries. In the EU, *Galvus* received approval for expanded use as a second-line monotherapy for type 2 diabetes patients who cannot take metformin. The EU also approved *Galvus* in combination with insulin, with or without metformin, for type 2 diabetes when diet, exercise and a stable dose of insulin do not result in glycemic control, and in triple combination with metformin and a sulphonylurea (SU) for type 2 diabetes when diet and exercise plus dual therapy with vildagliptin and metformin do not provide adequate glycemic control. In 2017, *Galvus* was approved as an add-on to insulin and an add-on to SU treatment. *Galvus* and *Eucreas* are co-marketed by Merck KGaA as *Jalra* and

Jalra M, respectively, in some countries in Latin America.

• *Diovan* (valsartan), together with *Diovan HCT/Co-Diovan* (valsartan and hydrochlorothiazide), is an angiotensin II receptor blocker (ARB). *Diovan* is the only agent in its class approved to treat all of the following: patients with high blood pressure (including children 6 to 18 years old), high-risk heart attack survivors, and patients with heart failure. *Diovan* first launched in 1996 and is available in more than 120 countries; *Diovan HCT/Co-Diovan* first launched in 1997 and is available in more than 100 countries.

• *Exforge* (valsartan and amlodipine besylate) is a single-pill combination of the ARB *Diovan* and the calcium channel blocker amlodipine besylate. First approved for the treatment of high blood pressure in Switzerland in 2006, and in the US and EU in 2007, it is now

available in more than 100 countries. *Exforge HCT* (valsartan, amlodipine besylate and hydrochlorothiazide) is a single pill combining three widely prescribed high blood pressure treatments: an ARB, a calcium channel blocker and a diuretic (hydrochlorothiazide). *Exforge HCT* was approved in the EU and the US in 2009, and is now available in more than 75 countries.

• *Zortress/Certican* (everolimus) is an oral inhibitor of the mTOR pathway. *Zortress/Certican* is approved in countries including the US, EU member states and Japan for the prevention of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic kidney or liver transplant. Additionally, it is approved in EU member states and Japan for adult patients receiving a heart transplant. First approved in July 2003, *Zortress/Certican* is now available in more than 80 countries worldwide and is the only mTOR inhibitor approved for liver and heart transplants.

• *Neoral* (cyclosporine, USP Modified) is an immunosuppressant to prevent organ rejection following a kidney, liver or heart transplant. It is approved for use in lung transplant in many countries outside the US. This micro-emulsion formulation of cyclosporine is also indicated for treating certain autoimmune disorders, such as psoriasis and rheumatoid arthritis. First launched in 1995, *Neoral* is marketed in approximately 100 countries.

Compounds in development

The following table and paragraph summaries provide an overview of the key Innovative Medicines Division projects currently in the Confirmatory Development stage and may also describe certain projects in the Exploratory Development stage. Projects include those seeking to develop potential uses of new molecular entities as well as potential additional indications or new formulations for already marketed products. Changes to the selected development projects table are highlighted in the table below entitled “Projects added to and subtracted from the development table since 2017.”

Compounds and new indications in development are subject to required regulatory approvals and, in certain instances, contractual limitations. These compounds and indications are in various stages of development throughout the world. It may not be possible to obtain regulatory approval for any or all of the new compounds and new indications referred to in this Form 20-F in any country or in every country. See “—Regulation” for further information on the approval process.

The year that each project entered the current phase of development disclosed below reflects the year in which the decision to enter the phase was made. This may be different from the year in which the first patient received the first treatment in the related clinical trial. A reference to a project being in registration means that an application has been filed with a health authority for marketing approval.

Selected development projects

Project/ product	Common name	Mechanism of action	Potential indication/ disease area	Business franchise	Formulation/ route of administration	Year project entered current development phase	Planned filing dates/curre phase
ABL001	asciminib	BCR-ABL inhibitor	Chronic myeloid leukemia, 3rd line	Oncology	Oral	2016	2021/III
			Chronic myeloid leukemia, 1st line	Oncology	Oral	2017	≥2023/I
ACZ885	canakinumab	Anti-interleukin-1 beta monoclonal antibody	2nd line non-small cell lung cancer	Oncology	Subcutaneous injection	2017	2021/III
			1st line non-small cell lung cancer	Oncology	Subcutaneous injection	2017	2021/III
			Adjuvant non-small cell lung cancer	Oncology	Subcutaneous injection	2017	2022/III
AVXS-101 (*Zolgensma*)	onasemno-gene abepar-vovec-xxxx	Survival motor neuron (SMN) gene replacement therapy	Spinal muscular atrophy type 1 (IV formulation)	Neuroscience	Intravenous infusion	2018	US/EU registratio
			Spinal muscular atrophy type 2/3 (IT formulation)	Neuroscience	Intrathecal injection	2016	2020/I
AVXS-201	TBD	Methyl-CpG binding protein 2 (MECP2) gene replacement therapy	Rett syndrome	Neuroscience	Intrathecal injection	2018	2022/I
BAF312 (*Mayzent*)	siponimod	Sphingosine-1-phosphate receptor modulator	Secondary progressive multiple sclerosis	Neuroscience	Oral	2018	US/EU registratio
BYL719	alpelisib	PI3K-alpha inhibitor	Hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (postmenopausal women), 2nd line (+ fulvestrant)	Oncology	Oral	2018	US/EU registratio
CAD106	amilomotide	Beta-amyloid-protein therapy	Alzheimer's disease	Neuroscience	Intramuscular injection	2009	≥2023/II/I
CFZ533	iscalimab	Blocking, non-depleting, anti-CD40 monoclonal antibody	Solid organ transplantation	Immunology, Hepatology and Dermatology	Intravenous infusion	2017 2018	≥2023/II ≥2023/II

			Sjögren's syndrome	Immunology, Hepatology and Dermatology	Intravenous infusion		
CNP520	TBD	BACE inhibitor	Alzheimer's disease	Neuroscience	Oral	2016	≥2023/II/I
Cosentyx	secukinumab	Anti-interleukin-17 monoclonal antibody	Non-radiographic axial spondyloarthritis	Immunology, Hepatology and Dermatology	Subcutaneous injection	2015	2019/III
			Psoriatic arthritis head-to-head study versus Humira® (adalimumab)	Immunology, Hepatology and Dermatology	Subcutaneous injection	2015	2020/III
			Ankylosing spondylitis head-to-head study versus Sandoz biosimilar *Hyrimoz* (adalimumab)	Immunology, Hepatology and Dermatology	Subcutaneous injection	2015	2022/III
			Hidradenitis suppurativa	Immunology, Hepatology and Dermatology	Intravenous infusion	2017	2022/III
CSJ117	TBD	Anti-thymic stromal lymphopoietin monoclonal antibody fragment	Severe asthma	Respiratory	Inhalation	2018	≥2023/II
ECF843	TBD	Boundary lubricant	Dry eye	Ophthalmology	Eye drops	2017	2022/II
EMA401	olodanrigan	Angiotensin II type 2 receptor antagonist	Peripheral neuropathic pain	Neuroscience	Oral	2015	≥2023/II
Entresto	valsartan and sacubitril (as sodium salt complex)	Angiotensin receptor/ neprilysin inhibitor	Chronic heart failure with preserved ejection fraction	Cardio-Metabolic	Oral	2012	2019/III
			Post-acute myocardial infarction	Cardio-Metabolic	Oral	2015	2020/III
HDM201	TBD	p53-HDM2 inhibitor	Acute myeloid lymphoma	Oncology	Oral	2017	≥2023/II
INC280	capmatinib	c-MET inhibitor	Non-small cell lung cancer	Oncology	Oral	2014	2019/II
			Non-small cell lung cancer (EGFR mutation)	Oncology	Oral	2016	2022/II
Jakavi	ruxolitinib	JAK1/2 inhibitor	Acute graft-versus-host disease	Oncology	Oral	2016	2020/III
			Chronic graft-versus-host disease	Oncology	Oral	2016	2020/III
KAE609	cipargamin	PfATP4 inhibitor	Malaria		Oral	2012	≥2023/II

Established
Medicines

Project/ product	Common name	Mechanism of action	Potential indication/ disease area	Business franchise	Formulation/ route of administration	Year project entered current development phase	Planned filing dates/curr phase
KAF156	ganaplacide	Imidazolopiperazines derivative	Malaria	Established Medicines	Oral	2014	≥2023/II
Kisqali	ribociclib	CDK4/6 inhibitor	HR+/HER2- breast cancer (adjuvant)	Oncology	Oral	2018	≥2023/III
Kymriah	tisagen-lecleucel	CD19-targeted chimeric antigen receptor T-cell immunotherapy	Relapsed/refractory follicular lymphoma	Oncology	Intravenous infusion	2017	2021/II
			Chronic lymphocytic leukemia	Oncology	Intravenous infusion	2017	2022/II
			Relapsed/refractory diffuse large B-cell lymphoma in 1st relapse	Oncology	Intravenous infusion	2018	2021/III
			Relapsed/refractory diffuse large B-cell lymphoma (+ pembrolizumab)	Oncology	Intravenous infusion	2017	≥2023/I
LAM320	clofazimine	Mycobacterial DNA binding	Multidrug-resistant tuberculosis	Established Medicines	Oral	2016	2021/III
LCI699	osilodrostat	Cortisol synthesis inhibitor	Cushing's disease	Oncology	Oral	2018	EU registrati US 2019/
LJC242	tropifexor, cenicriviroc (in fixed-dose combination)	FXR agonist and CCR2/5 inhibitor	Nonalcoholic steatohepatitis	Immunology, Hepatology and Dermatology	Oral	2017	≥2023/II
LJN452	tropifexor	FXR agonist	Nonalcoholic steatohepatitis	Immunology, Hepatology and Dermatology	Oral	2015	≥2023/II
LMI070	branaplam	SMN2 RNA splicing modulator	Spinal muscular atrophy	Neuroscience	Oral	2017	≥2023/II
LNP023	TBD	Factor B inhibitor	IgA nephropathy	Cardio-Metabolic	Oral	2018	≥2023/II
			Membranous nephropathy	Cardio-Metabolic	Oral	2018	≥2023/II
LOU064	TBD	BTK inhibitor	Chronic spontaneous urticaria	Immunology, Hepatology and Dermatology	Oral	2017	≥2023/II
^{177}Lu-PSMA-617	TBD	Targeted DNA destruction via beta-particle radiation	Metastatic castration-resistant prostate cancer	Oncology	Intravenous infusion	2018	2020/III
Lucentis	ranibizumab	Anti-VEGF monoclonal antibody fragment	Retinopathy of prematurity	Ophthalmology	Intravitreal injection	2018	EU registrati

			Diabetic retinopathy	Ophthalmology	Intravitreal injection	2018	EU registratio
MOR106	TBD	Anti-interleukin-17C monoclonal antibody	Atopic dermatitis	Immunology, Hepatology and Dermatology	Subcutaneous injection	2018	≥2023/II
OMB157	ofatumumab	Anti-CD20 monoclonal antibody	Relapsing multiple sclerosis	Neuroscience	Subcutaneous injection	2015	2019/III
PDR001	spartalizumab	Anti-PD-1 monoclonal antibody	Metastatic BRAF V600+ melanoma (w/ *Tafinlar* + *Mekinist*)	Oncology	Intravenous infusion	2017	2019/III
			Malignant melanoma (combo)	Oncology	Intravenous infusion	2017	2022/II
Promacta/ Revolade	eltrombopag	Thrombopoietin receptor agonist	Severe aplastic anemia, 1st line	Oncology	Oral	2018	US appro EU registratio
QAW039	fevipiprant	DP2 antagonist (CRTH2 antagonist)	Asthma	Respiratory	Oral	2015	2020/III
QBW251	TBD	CFTR potentiator	Chronic obstructive pulmonary disease	Respiratory	Oral	2017	≥2023/II
QGE031	ligelizumab	High-affinity anti-IgE monoclonal antibody	Chronic spontaneous urticaria/ chronic idiopathic urticaria	Immunology, Hepatology and Dermatology	Subcutaneous injection	2017	2021/III
QMF149 44	indacaterol, mometasone furoate (in fixed-dose combination)	Long-acting beta$_2$-adrenergic agonist and inhaled corticosteroid	Asthma	Respiratory	Inhalation	2015	2019/III

Project/ product	Common name	Mechanism of action	Potential indication/ disease area	Business franchise	Formulation/ route of administration	Year project entered current development phase	Planned filing dates/current phase
QVM149	indacaterol, mometasone furoate, glyco-pyrronium bromide (in fixed-dose combination)	Long-acting beta$_2$-adrenergic agonist, long-acting muscarinic antagonist and inhaled corticosteroid	Asthma	Respiratory	Inhalation	2015	2019/III
RTH258	brolucizumab	Anti-VEGF single-chain antibody fragment	Neovascular age-related macular degeneration	Ophthalmology	Intravitreal injection	2014	2019/III
			Diabetic macular edema	Ophthalmology	Intravitreal injection	2017	2020/III
			Retinal vein occlusion	Ophthalmology	Intravitreal injection	2018	2022/III
Rydapt	midostaurin	Signal transduction inhibitor	Acute myeloid leukemia (FLT3 wild type)	Oncology	Oral	2016	2022/III
SEG101	crizanlizumab	P-selectin inhibitor	Sickle cell disease	Oncology	Intravenous infusion	2016	2019/II
UNR844	TBD	Reduction of disulfide bonds	Presbyopia	Ophthalmology	Eye drops	2017	2022/II
VAY736	lanalumab	Anti-BAFF (B-cell-activating factor) monoclonal antibody	Autoimmune hepatitis	Immunology, Hepatology and Dermatology	Subcutaneous injection	2016	≥2023/II
			Primary Sjögren's syndrome	Immunology, Hepatology and Dermatology	Subcutaneous injection	2015	≥2023/II
VAY785	emricasan	Pan-caspase inhibitor	Nonalcoholic steatohepatitis	Immunology, Hepatology and Dermatology	Oral	2017	≥2023/II
VPM087	TBD	Interleukin-1 beta neutralization monoclonal antibody	Colorectal cancer, 1st line; renal cell carcinoma, 1st line	Oncology	Intravenous infusion	2018	≥2023/I
Xolair	omalizumab		Nasal polyps	Respiratory		2017	2019/III

		Anti-IgE monoclonal antibody			Subcutaneous injection		
ZPL389	adriforant	Histamine H4 receptor antagonist	Atopic dermatitis	Immunology, Hepatology and Dermatology	Oral	2017	2022/II

Key development projects

• ACZ885 (canakinumab) was first approved as *Ilaris* in 2009 for cryopyrin-associated periodic syndromes. In 2017, data from CANTOS, a Phase III study evaluating quarterly injections of ACZ885 in people with a prior heart attack and inflammatory atherosclerosis, was presented at the European Society of Cardiology Congress and published simultaneously in The New England Journal of Medicine and The Lancet. A review of a blinded, pre-planned lung cancer safety analysis revealed a 77% reduction in lung cancer mortality and a 67% reduction in lung cancer cases in patients treated with 300 mg of ACZ885. As a result of these findings, Novartis has initiated three Phase III studies of ACZ885 in lung cancer, with data from primary analyses expected to report out in 2021. We received a complete response letter from the FDA in October 2018 regarding our supplemental Biologics License Application for ACZ885 in cardiovascular risk reduction.

• AVXS-101 (onasemnogene abeparvovec-xxxx, *Zolgensma*) is a gene replacement therapy candidate designed to address the genetic root cause of spinal muscular atrophy (SMA), a progressive neuromuscular disease and the leading cause of genetic mortality in infants globally. In December 2018, we announced that the FDA accepted the Biologics License Application for *Zolgensma* for the treatment of SMA type 1, the most severe form of the disease. Delivered as a single, one-time infusion, *Zolgensma* works by replacing the missing or defective SMN1 gene with a functional copy that makes the SMN protein, thereby improving motor neuron function and survival. The Biologics License Application filing is supported by data from the Phase I START trial, which demonstrated an increase in survival and improved achievement of developmental milestones compared to the natural history of SMA type 1. *Zolgensma* is currently being studied in a Phase III trial in patients with SMA type 1 in the US (STR1VE) and in Europe (STR1VE-EU), with a planned Phase III study in the Asia-Pacific region (STR1VE-AP). *Zolgensma* is also being studied in a Phase I trial in the US in patients with SMA type 2 (STRONG), and in a Phase III multinational trial in presymptomatic patients with SMA with two or three copies of the SMN2 gene (SPR1NT). A trial in pediatric patients with SMA types 1, 2 and 3 (REACH) is planned for 2019. Patients from the START trial had the option to voluntarily enroll in a long-term, 15-year observational follow-up study. The brand name *Zolgensma* has been provisionally approved by the FDA for AVXS-101, but the product itself has not received marketing authorization or Biologics License Application approval from any regulatory authorities.

• BAF312 (siponimod, *Mayzent*) is an oral, second-generation sphingosine-1-phosphate (S1P) receptor modulator under development for the treatment of secondary progressive multiple sclerosis (SPMS). It binds selectively to the S1P receptor subtypes 1 and 5, and penetrates effectively to the central nervous system, where it may impact central nervous system inflammation and repair mechanisms. Results from the EXPAND Phase III study, evaluating efficacy and safety for SPMS, demonstrated that *Mayzent* reduced three- and six-month confirmed disability progression against placebo, with a safety profile similar to other S1P1 receptor modulators. The full results from the Phase III EXPAND study of oral, once-daily *Mayzent* in SPMS were published in The Lancet in March 2018. Further analyses from the EXPAND study presented in April 2018 at the American Academy of Neurology showed that the efficacy of *Mayzent* on disability was largely independent from relapse activity in SPMS. The analyses also revealed positive data on cognitive decline. In October 2018, we announced that both the FDA and EMA had accepted our New Drug Application and Marketing Authorization Application, respectively, for review. Submissions are now also underway in Japan and China. If approved, label content will be subject to negotiation with regulatory authorities, but it is expected to reflect the typical SPMS population studied in the EXPAND trial. The brand name *Mayzent* has been provisionally approved by the FDA and EMA for BAF312, but the product itself has not been approved for sale in any country.
• BYL719 (alpelisib) is an investigational, orally bioavailable, alpha-specific PI3K inhibitor. In breast cancer cell lines harboring PIK3CA mutations, BYL719 has been shown to potentially inhibit the PI3K pathway and have antiproliferative effects. In addition, cancer cell lines with PIK3CA mutations were more sensitive to BYL719 than those without the mutation across a broad range of different cancers. At ESMO 2018, positive results from the global Phase III SOLAR-1 trial evaluating BYL719 in combination with fulvestrant were presented. In patients with PIK3CA-mutated HR+/HER2- advanced breast cancer, BYL719 plus fulvestrant nearly doubled median progression-free survival compared to fulvestrant alone. Novartis is also conducting the Phase II open-label BYLieve trial evaluating BYL719 plus fulvestrant or letrozole in patients with PIK3CA-mutated HR+/HER2- advanced breast cancer who have progressed on prior therapy. The study investigates BYL719 in a broader patient population as compared with SOLAR-1, including two cohorts exclusively enrolling patients who have progressed on or after prior CDK4/6 inhibitor therapies.
• *Cosentyx* (secukinumab) is a fully human monoclonal antibody that selectively neutralizes interleukin-17A (IL-17A). *Cosentyx* is in Phase III development in non-radiographic axial spondyloarthritis. We expect results from this trial in 2019. *Cosentyx* is also in a Phase III head-to-head clinical trial in psoriatic arthritis against Humira® (adalimumab), and a Phase III head-to-head clinical trial in ankylosing spondylitis against the Sandoz biosimilar *Hyrimoz* (adalimumab).
• *Entresto* (sacubitril/valsartan) is a first-in-class angiotensin receptor/neprilysin inhibitor approved and marketed for the treatment of chronic heart failure with reduced ejection fraction (HFrEF). Novartis is conducting multiple studies of *Entresto* as part of the FortiHFy clinical program. FortiHFy includes studies to provide reinforcing evidence in HFrEF, such as PIONEER-HF and TRANSITION, which both read out in 2018 and confirmed safety as well as superiority of *Entresto* versus enalapril, an angiotensin-converting enzyme inhibitor (ACE inhibitor), in the hospital setting in a wide range of HFrEF patients hemodynamically stabilized after an acute decompensated heart failure event. FortiHFy also includes studies to investigate *Entresto* use in novel indications and expanded patient populations. These include PARAGON-HF and PARALLAX-HF, Phase III trials of *Entresto* in patients with chronic heart failure with preserved ejection fraction (PARAGON-HF enrollment is completed and results are expected in 2019, while PARALLAX-HF enrollment is ongoing and results are expected in 2020); PARADISE-MI, a Phase III trial for patients at high risk for heart failure after an acute myocardial infarction (enrollment is ongoing and results are expected in 2020); PARALLEL-HF, a Phase III trial in Japan for patients with HFrEF (enrollment is completed and results are expected in 2019); and PANORAMA-HF, a Phase III trial for pediatric patients with heart failure (enrollment is ongoing and results are expected in 2021).
• INC280 (capmatinib) is an investigational, oral and selective MET inhibitor currently in a Phase II study in adult patients with advanced non-small cell lung cancer harboring MET exon 14 skipping mutations, as well as additional early-stage studies in combination with other compounds. In October 2018, Novartis presented preliminary results of the Phase II study at the European Society of Medical Oncology congress. INC280 is licensed by Novartis from Incyte Corporation. Under the licensing agreement, Incyte granted Novartis exclusive worldwide development and commercialization rights to this MET inhibitor compound.

• KAF156 (ganaplacide) belongs to a novel class of antimalarial compounds called imidazolopiperazines. It has the potential to clear malaria infection, including resistant strains, and to block the transmission of the malaria parasite. As demonstrated in a Phase IIa proof-of-concept trial, the compound is fast-acting and potent across multiple stages of the parasite's lifecycle, rapidly clearing both Plasmodium falciparum and Plasmodium vivax parasites. In August 2017, Novartis began a Phase IIb study to test multiple dosing combinations and dosing schedules of KAF156 and lumefantrine, including the feasibility of a single dose therapy in adults, adolescents and children.
• *Kisqali* (ribociclib) is a selective cyclin-dependent kinase inhibitor that inhibits two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). Novartis is continuing to assess *Kisqali* through the MONALEESA clinical trial program, which includes MONALEESA-2, MONALEESA-3 and MONALEESA-7, as well as the NataLEE adjuvant trial. These trials are

evaluating *Kisqali* in multiple endocrine therapy combinations across a broad range of patients, including men and premenopausal women. *Kisqali* was developed by Novartis as part of a drug discovery collaboration with Astex Pharmaceuticals.

• *Kymriah* (tisagenlecleucel) is a CD19-directed genetically modified autologous chimeric antigen receptor T-cell (CAR-T) therapy that uses the patient's own immune system to fight certain types of cancer. CARs are engineered proteins that enable a patient's own T-cells to seek out specific target proteins present on a patient's cancerous cells. When these cells are reintroduced into the patient's blood, they demonstrate the potential to bind to the cancer cells and destroy them. *Kymriah* targets a protein called CD19, which is associated with a number of B-cell malignancies. Novartis is starting pivotal clinical studies of *Kymriah* in relapsed or refractory (r/r) follicular lymphoma, adult r/r acute lymphoblastic leukemia (ALL), first-line high-risk pediatric ALL, diffuse large B-cell lymphoma after first relapse, and r/r chronic lymphoblastic leukemia. Novartis and the University of Pennsylvania's Perelman School of Medicine, which developed *Kymriah*, have a global collaboration to research, develop and commercialize CAR-T therapies, including *Kymriah*, for the investigational treatment of cancers.

• LJN452 (tropifexor) is a potent, non-bile acid, farnesoid X receptor (FXR) agonist that is being developed for the treatment of nonalcoholic steatohepatitis (NASH). LJN452 has been shown to reduce steatosis, inflammation and fibrosis in animal models, alongside a favorable safety profile in first-in-human studies. This oral treatment is designed to break the cycle of fatty buildup in the liver and harness the body's built-in mechanisms for coping with excess bile acid. Recruitment is underway for the first LJN452 clinical study with histological endpoints in NASH patients.

• OMB157 (ofatumumab) is a fully human monoclonal antibody administered by subcutaneous injection. It is in development for multiple sclerosis (MS). OMB157 works by binding to the CD20 molecule on the B-cell surface and inducing B-cell depletion. Positive Phase IIb results in MS patients were presented in 2014 and showed significant reduction in the number of new brain lesions in the first 24 weeks after OMB157 administration. Novartis initiated a Phase III program for OMB157 in relapsing MS in August 2016. The program is fully enrolled and is on track for completion in 2019. In addition, a registration study for Japan was initiated in March 2018.

• PDR001 (spartalizumab) is an investigational PD-1 antagonist that may restore the ability of immune cells to induce cell death and fight cancer. PDR001 is being evaluated in a Phase III trial in combination with *Tafinlar* + *Mekinist* for metastatic BRAF V600+ melanoma, and in combination in other clinical trials across different tumor types.

• QAW039 (fevipiprant) is a once-daily oral therapy that blocks the DP2 pathway, a principal regulator of the inflammatory cascade. By targeting the DP2 pathway, QAW039 blocks the asthma inflammatory cascade at multiple points. In asthma, this results in the reduction of eosinophil activation and migration; in the reduced release of pro-inflammatory cytokines IL-4, IL-5 and IL-13; and in the reduction of smooth muscle cell mass in the airways. Positive Phase II results showed improvement of lung function, reduction of sputum eosinophil levels, and improvement of asthma symptoms. Phase III studies are ongoing, measuring improvement of lung function and reduction of asthma attacks in moderate to severe patients with unresolved asthma despite treatment with inhaled therapies. Phase III development started in 2015, with first pivotal trial readouts expected this year.

• QVM149 (indacaterol acetate, glycopyrronium bromide, mometasone furoate) is a fixed-dose combination of indacaterol acetate (an inhaled long-acting beta2-adrenergic agonist), glycopyrronium bromide (an inhaled long-acting muscarinic antagonist), and mometasone furoate (an inhaled corticosteroid) delivered once-daily via the *Breezhaler* device, a unit dose dry powder inhaler. It is in development as a maintenance treatment for poorly controlled asthmatic patients. All three mono-components have previously been developed as individual drugs for either chronic obstructive pulmonary disease or asthma. QVM149 is currently in Phase III clinical trials to support registration outside the US.

• RTH258 (brolucizumab) is a single-chain antibody fragment that acts as an anti-vascular endothelial growth factor (anti-VEGF) agent. RTH258 is currently in development for neovascular age-related macular degeneration (nAMD) and diabetic macular edema. In nAMD, RTH258 met its primary endpoint of non-inferiority to aflibercept in mean change in best-corrected visual acuity in two Phase III clinical trials, HAWK and HARRIER. Additionally, superiority was shown in three secondary endpoints that are considered key markers of nAMD disease: central subfield retinal thickness, retinal fluid (intraretinal and subretinal), and disease activity. A majority of patients were maintained on a 12-week treatment schedule immediately following the loading phase to Week 48, also assessed by secondary endpoints in the HAWK and HARRIER trials. Year Two data reaffirmed the Year One findings. We expect to make

global regulatory filings for nAMD, starting in the US, the EU and Japan.

• SEG101 (crizanlizumab) is an investigational humanized anti-P-selectin monoclonal antibody that is in late-stage development for the prevention of vaso-occlusive pain crises (VOCs) in patients with sickle cell disease (SCD). SCD is a debilitating genetic blood disorder that affects the shape of red blood cells and can cause VOCs. In December 2018, the FDA granted SEG101 breakthrough therapy designation for the prevention of vaso-occlusive crises in sickle cell disease.

• UNR844 is a potential first-in-class topical treatment in development for presbyopia. It is believed to work through the reduction of disulfide bonds, softening the

crystalline lens. Presbyopia is a common age-related loss of near-distance vision characterized by a progressive inability to focus on objects nearby, making everyday activities (such as reading) a challenge. In a Phase I/II masked, placebo-controlled proof-of-concept study, 50 patients were treated daily for 90 days with topical UNR844, and 25 patients were treated with placebo. UNR844 showed a statistically significant difference to placebo in distance-corrected near vision at all time points measured (from Day Eight). At Day 90, 82% of participants treated with UNR844 had 20/40 near vision (or 0.30 LogMAR) versus 48% in the placebo group. Near vision of 20/40 allows for the majority of near-vision tasks in most people. UNR844 was acquired by Novartis through the acquisition of Encore Vision, Inc. in January 2017.

Projects added to and subtracted from the development table since 2017

Project/product	Potential indication/disease area	Change	Reason
ACZ885	Secondary prevention of cardiovascular events	Removed	Development discontinued
Afinitor/Votubia	Tuberous sclerosis complex seizures	Commercialized	
AMG 334	Prophylaxis of migraine	Commercialized as *Aimovig*	
Arzerra	Refractory indolent non-Hodgkin's lymphoma	Removed	Development discontinued
AVXS-101 (*Zolgensma*)	Spinal muscular atrophy type 1 (IV formulation)	Added	Acquired with acquisition of AveXis, Inc.
	Spinal muscular atrophy type 2/3 (IT formulation)	Added	Acquired with acquisition of AveXis, Inc.
AVXS-201	Rett syndrome	Added	Acquired with acquisition of AveXis, Inc.
BYM338	Hip fracture recovery	Removed	Development discontinued
	Sarcopenia	Removed	Development discontinued
CFZ533	Sjögren's syndrome	Added	Entered Confirmatory Development
Cosentyx	Hidradenitis suppurativa	Added	Entered Confirmatory Development
CSJ117	Severe asthma	Added	Entered Confirmatory Development
EGF816	Non-small cell lung cancer	Removed	Development discontinued
Gilenya	Pediatric multiple sclerosis	Commercialized	
Kisqali	HR+/HER2- advanced breast cancer (postmenopausal women), 1st/2nd line (+ fulvestrant)	Commercialized	
	HR+/HER2- advanced breast cancer (premenopausal women), 1st line (+ tamoxifen + goserelin or NSAI + goserelin)	Commercialized	
Kymriah (CTL019)	Pediatric/young adult acute lymphoblastic leukemia	Commercialized	
		Commercialized	

	Relapsed/refractory diffuse large B-cell lymphoma		
LHW090	Resistant hypertension	Removed	Development discontinued
LIK066	Weight loss	Removed	Development discontinued
LJC242	Nonalcoholic steatohepatitis	Added	Entered Confirmatory Development
LNP023	IgA nephropathy	Added	Entered Confirmatory Development
	Membranous nephropathy	Added	Entered Confirmatory Development
^{177}Lu-PSMA-617	Metastatic castration-resistant prostate cancer	Added	Acquired with acquisition of Endocyte
Lucentis	Diabetic retinopathy	Added	Entered Confirmatory Development
MAA868	Stroke prevention in atrial fibrillation	Removed	Development discontinued
MOR106	Atopic dermatitis	Added	Entered Confirmatory Development
MTV273	Multiple myeloma	Removed	Development discontinued
PDR001	Malignant melanoma (w/ *Tafinlar* + *Mekinist*)	Now disclosed as metastatic BRAF V600+ melanoma (w/ *Tafinlar* + *Mekinist*)	
	Endocrine neoplasm	Removed	Development discontinued
	Malignant melanoma	Now disclosed as malignant melanoma (combo)	
RTH258	Retinal vein occlusion	Added	Entered Confirmatory Development
Signifor LAR	Cushing's disease	Commercialized	
Tafinlar + *Mekinist*	BRAF V600+ melanoma (adjuvant)	Commercialized	
VPM087	Colorectal cancer, 1st line; renal cell carcinoma, 1st line	Added	Entered Confirmatory Development

Principal markets

The Innovative Medicines Division sells products in approximately 155 countries worldwide. Net sales are generally concentrated in the US, Europe, Japan and China. The following table sets forth the aggregate 2018 net sales of the Innovative Medicines Division by region:

Innovative Medicines

	2018 net sales to third parties	
	USD millions	%
Europe	12 296	35
United States	11 864	34
Asia, Africa, Australasia	8 097	23
Canada and Latin America	2 635	8
Total	34 892	100
Of which in Established Markets *	26 258	75
Of which in Emerging Growth Markets *	8 634	25

* Emerging Growth Markets comprise all markets other than the Established Markets of the US, Canada, Western Europe, Japan, Australia and New Zealand.

Many of our Innovative Medicines Division products are used for chronic conditions that require patients to consume the product over long periods of time, ranging from months to years. However, certain of our marketed products and development projects, such as gene therapies, are administered only once. Net sales of the vast majority of our products are not subject to material changes in seasonal demand.

Production

The primary goal of our manufacturing and supply chain management program is to ensure the uninterrupted, timely and cost-effective supply of products that meet all product specifications and quality standards. The manufacture of our products is heavily regulated by governmental health authorities around the world, including the FDA and EMA. In addition to regulatory requirements, many of our products involve technically complex manufacturing processes or require a supply of highly specialized raw materials.

We manufacture our products at facilities worldwide. See also “—Item 4.D Property, plants and equipment.” Active pharmaceutical ingredients are manufactured in our own facilities or purchased from third-party suppliers. We maintain state-of-the-art processes, with quality as a primary goal within our own production network. Those processes include fermentation, chemical syntheses and precipitation processes, such as sterile processing. Many biologic medicines are manufactured using recombinant DNA-derived technology, by which a gene is introduced into a host cell, which then produces a human protein. This manufacturing process requires sophisticated technical expertise. We are constantly working to improve current, and to develop new, manufacturing processes, and to review and adapt our manufacturing network to meet the needs of our Innovative Medicines Division.

Raw materials for the manufacturing process are either produced in-house or purchased from a number of third-party suppliers. Where possible, we maintain multiple supply sources so that the business is not dependent on a single or limited number of suppliers. However, our ability to do so may at times be limited by regulatory or other requirements. We monitor market developments that could have an adverse effect on the supply of essential materials. Our suppliers of raw materials are required to comply with Novartis quality standards.

Because the manufacture of our products is complex and heavily regulated by governmental health authorities, supply is never guaranteed. If we or our third-party suppliers fail to comply with applicable regulations, then there could be a product recall or other shutdown or disruption of our production activities. We have experienced supply interruptions for our products in the past, and there can be no assurance that supply will not be interrupted again in the future. We have implemented a global manufacturing strategy to maximize business continuity in case of such events. However, there can be no guarantee that we will always be able to successfully manage such issues when they arise.

Marketing and sales

The Innovative Medicines Division serves customers with 25 783 field force representatives, as of December 31, 2018, including supervisors and administrative personnel. These trained representatives present the therapeutic risks and benefits of our products to physicians, pharmacists, hospitals, insurance groups, managed care organizations and other healthcare professionals. We continue to see increasing influence of customer groups beyond prescribers, and

Novartis is responding by adapting our business practices to engage appropriately with such constituencies. The marketplace for healthcare is also evolving, with patients becoming more informed stakeholders in their healthcare decisions and looking for solutions to meet their changing needs. Novartis seeks to support the

patient, delivering innovative solutions to drive education, access and improved patient care. Additionally, in the US, certain products can be advertised by way of internet, television, newspaper and magazine advertising.

Although specific distribution patterns vary by country, Novartis generally sells its prescription drugs primarily to wholesale and retail drug distributors, hospitals, clinics, government agencies and managed healthcare providers. The growing number of so-called “specialty” drugs in our portfolio has resulted in increased engagement with specialty pharmacies. In the US, specialty pharmacies continue to grow as a distribution channel for specialty products, with an increasing number of health plans mandating use of specialty pharmacies to monitor specialty drug utilization and costs.

Novartis pursues co-promotion/co-marketing opportunities as well as licensing and distribution agreements with other companies in various markets, when economically attractive.

As a result of continuing changes in healthcare economics and an aging population, the US Centers for Medicare & Medicaid Services (CMS) is the largest single payer for healthcare services in the US. In addition, both commercial and government-sponsored managed care organizations continue to be among the largest groups of payers for healthcare services in the US. In other countries, national health services are often the only significant payer for healthcare services. In an effort to control prescription drug costs, almost all managed care organizations and national health services use formularies that list specific drugs that may be reimbursed and/or the level of reimbursement for each drug. Managed care organizations and national health services also increasingly utilize various cost-benefit analyses to determine whether or not newly approved drugs will be added to a formulary and/or the level of reimbursement for that drug, and to determine whether or not to continue to reimburse existing drugs. We have dedicated teams that actively seek to optimize patient access, including formulary positions, for our products.

Recent trends have been toward continued consolidation among distributors and retailers of Innovative Medicines Division products, both in the US and internationally. This has increased our customers’ purchasing leverage and resulted in increased pricing pressure on our products. Moreover, we are exposed to increased concentration of credit risk as a result of the consolidation among our customers.

Competition

The global pharmaceutical market is highly competitive, and we compete against other major international corporations that have substantial financial and other resources, as well as against smaller companies that operate regionally or nationally. Competition within the industry is intense and extends across a wide range of activities, including pricing, product characteristics, customer service, sales and marketing, and research and development.

In addition, as is the case with other pharmaceutical companies selling patented pharmaceuticals, Novartis faces ever-increasing challenges from companies selling products that compete with our products, including competing patented products and generic forms of our products following the expiry of intellectual property protection. Generic companies may also gain entry to the market through successfully challenging our intellectual property rights, but we vigorously use legally permissible measures to defend those rights. See also “—Intellectual property” below. We also may face competition from over-the-counter (OTC) products that do not require a prescription from a physician. See also “—Regulation—Price controls” below.

There is ongoing consolidation in the pharmaceutical industry. At the same time, new entrants are looking to use their expertise to establish or expand their presence in healthcare, including technology companies hoping to benefit as data and data management become increasingly important in our industry.

Research and development

The discovery and development of a new drug is a lengthy process, usually requiring approximately 10 to 15 years from the initial research to bringing a drug to market, including approximately six to eight years from Phase I clinical trials to market entry. At each of these steps, there is a substantial risk that a compound will not meet the requirements to progress further. In such an event, we may be required to abandon a compound in which we have made a substantial investment.

We manage our research and development expenditures across our entire portfolio in accordance with our strategic priorities. We make decisions about whether or not to proceed with development projects on a project-by-project basis. These decisions are based on the project’s potential to meet a significant unmet medical need or to improve patient outcomes, the strength of the science underlying the project, and the potential of the project (subject to the risks inherent in pharmaceutical development) to generate significant positive financial results for the Company. Once a management decision has been made to proceed with the development of a particular molecule, the level of research

and development investment required will be driven by many factors, including the medical indications for which it is being developed, the number of indications being pursued, whether the molecule is of a chemical or biological nature, the stage of development, and the level of evidence necessary to demonstrate clinical efficacy and safety.

Research program

Our research program is conducted by the Novartis Institutes for BioMedical Research (NIBR), which was established in 2002 and is the research and early development innovation engine of Novartis. NIBR is responsible for the discovery of new medicines for diseases with unmet medical need. We focus our work in areas where we believe we can have the most impact for patients. This requires the hiring and retention of extraordinary talent, a focus on fundamental disease mechanisms that are relevant across different disease areas, continuous improvement in technologies for drug discovery and

potential therapies, close alliances with clinical colleagues, and the establishment of strategic external alliances.
At NIBR sites in Basel, Switzerland; Cambridge, Massachusetts; East Hanover, New Jersey; San Diego, California; Emeryville, California; and Shanghai, China, approximately 6 000 full-time equivalent scientists, physicians and business professionals contribute to research into disease areas such as cardiovascular and metabolic diseases, neuroscience, oncology, muscle disorders, ophthalmology, autoimmune diseases and respiratory diseases. Research at the Friedrich Miescher Institute and the Genomics Institute of the Novartis Research Foundation focuses on basic genetic and genomic research, and the Novartis Institute for Tropical Diseases (NITD), located in Emeryville, California, focuses on discovering new medicines to fight tropical diseases, including malaria and cryptosporidiosis.
All drug candidates are taken to the clinic via proof-of-concept trials to enable an early assessment of the safety and efficacy of the drug while collecting basic information on pharmacokinetics and tolerability, and adhering to the guidance for early clinical testing set forth by health authorities. Following proof of concept, our Global Drug Development unit conducts confirmatory trials on the drug candidates.
In July 2018, we announced the decision to exit antibacterial and antiviral research. While the science for these programs is compelling, we have decided to prioritize our resources in other areas where we believe we are better positioned to develop innovative medicines that will have a positive impact for patients. The San Francisco Bay Area will continue to be home to NITD and global drug discovery teams focused on “undruggable” targets in collaboration with the Novartis-Berkeley Center for Proteomics and Chemistry Technologies. The need for new types of medicines to combat antimicrobial resistance is clear, and following the announcement, we began to explore out-licensing opportunities for compounds within our infectious diseases portfolio.
Development program
Our Global Drug Development (GDD) organization oversees drug development activities for our Innovative Medicines Division. GDD works collaboratively with NIBR to execute our overall pipeline strategy and takes an enterprise approach to pipeline portfolio management. The GDD organization includes centralized global functions such as Regulatory Affairs and Global Development Operations, and Global Development units aligned with our business franchises. GDD was created to improve resource allocation, technology implementation and process standardization to further increase innovation. GDD includes approximately 11 000 full-time equivalent associates worldwide.
Under our Global Drug Development unit, the focus of our development program is to determine and then establish the safety and efficacy of a potential new medicine in humans.
The traditional model of development comprises three phases, which are defined as follows:
Phase I: The first clinical trials of a new compound – generally performed in a small number of healthy human volunteers – to assess the drug’s safety profile, including the safe dosage range. These trials also determine how a drug is absorbed, distributed, metabolized and excreted, and the duration of its action.
Phase II: Clinical studies performed with patients who have the target disease, with the aim of continuing the Phase I safety assessment in a larger group, assessing the efficacy of the drug in the patient population, and determining the appropriate doses for further evaluation.
Phase III: Large-scale clinical studies with several hundred to several thousand patients, which are conducted to establish the safety and efficacy of the drug in specific indications for regulatory approval. Phase III trials may also be used to compare a new drug against a current standard of care to evaluate the overall benefit-risk relationship of the new medicine.
In each of these phases, physicians monitor volunteer patients closely to assess the potential new drug’s safety and efficacy.
Though we use this traditional model as a platform, we have tailored the development process to be simpler, more flexible and efficient. We view the development process as generally consisting of Exploratory Development where proof of concept is established, and Confirmatory Development where this concept is confirmed in large numbers of patients. Exploratory Development consists of clinical proof-of-concept (PoC) studies, which are small clinical trials (typically involving five to 15 patients) that combine elements of traditional Phase I/II testing. These customized trials are designed to give early insights into issues such as safety, efficacy and toxicity for a drug in a given indication and are conducted by NIBR. Once a positive proof of concept has been established, the drug moves to the Confirmatory Development stage and becomes the responsibility of GDD. Confirmatory Development has elements of traditional Phase II/III testing and includes trials aimed at confirming the safety and efficacy of the drug in the given indication,

leading up to submission of a dossier to health authorities for approval. This stage can also include trials that compare the drug to the current standard of care for the disease in order to evaluate the drug's overall risk-benefit profile. Further, with new treatment approaches such as gene therapy, elements of Exploratory and Confirmatory Development may be combined.

The vast amount of data that must be collected and evaluated makes clinical testing the most time-consuming and expensive part of new drug development. The next stage in the drug development process is to seek registration for the new drug. For more information, see "—Regulation."

At each phase of clinical development, our activities are managed by our Innovation Management Board (IMB). The IMB is responsible for oversight over all major aspects of our development portfolio and oversees our drug development budget. In particular, the IMB is responsible for the endorsement of proposals to commence the first clinical trials of a development compound, and of major project phase transitions and milestones following a positive proof-of-concept outcome, including transitions to full development and the decision to submit a regulatory application to the health authorities. The IMB is also responsible for project

discontinuations, the endorsement of overall development strategy, and the endorsement of development project priorities. The IMB is chaired by our Chief Executive Officer and has representatives from Novartis senior management with expertise spanning multiple fields, among its core members and extended membership.

Alliances and acquisitions

Our Innovative Medicines Division enters into business development agreements with other pharmaceutical and biotechnology companies and with academic and other institutions to develop new products and access new markets. We license products that complement our current product line and are appropriate to our business strategy. Therapeutic area strategies have been established to focus on alliances and acquisition activities for key disease areas and indications that are expected to be growth drivers in the future. We review products and compounds we are considering licensing, using the same criteria that we use for our own internally discovered drugs.

On December 21, 2018, we completed our acquisition of Endocyte, a US-based biopharmaceutical company focused on developing targeted therapeutics for cancer treatment. This acquisition expanded our radioligand therapy platform and added ^{177}Lu-PSMA-617 – a potential first-in-class radioligand therapy in Phase III development for metastatic, PSMA-positive castration-resistant prostate cancer – as well as other investigational treatments.

In December 2018, we announced an offer to acquire Cell*for*Cure, a French company that is one of the largest contract development and manufacturing organizations producing cell and gene therapies in Europe. This proposed acquisition builds on an existing agreement with Cell*for*Cure to produce CAR-T therapies, including *Kymriah* (tisagenlecleucel). If completed, the acquisition would bolster our CAR-T therapy manufacturing capacity with the potential to expand to other cell and gene therapies in the Novartis pipeline. This transaction is subject to customary closing conditions, including regulatory approval. For additional information, see “Item 18. Financial Statements—Note 2. Significant transactions—Significant pending transactions.”

In October 2018, we licensed three of our infectious disease programs, with the potential to address the need for new approaches to treat antibiotic-resistant Gram-negative infections, to Boston Pharmaceuticals. This agreement is part of our strategy to collaborate with external innovators to further develop new medicines that fall outside of our strategic direction but have the potential to have a positive impact on the lives of patients.

In August 2018, we closed an agreement with pharmaceutical company Mylan. Under the agreement, Mylan purchased the worldwide rights to commercialize our cystic fibrosis products *TOBI* solution and *TOBI Podhaler*.

In July 2018, we announced an exclusive license agreement with biotech companies Galapagos NV and MorphoSys AG regarding their compound MOR106. Under the agreement, Novartis acquires the exclusive global development and marketing rights to MOR106 for atopic dermatitis and all other potential indications. This transaction became effective on September 10, 2018.

In May 2018, we successfully completed the acquisition of AveXis, Inc., a US-based clinical stage gene therapy company. AveXis has several ongoing clinical studies for the treatment of spinal muscular atrophy (SMA), an inherited neurodegenerative disease. The lead AveXis gene therapy candidate, AVXS-101, has the potential to be the first-ever one-time gene replacement therapy for SMA. For additional information, see “Item 18. Financial Statements—Note 2. Significant transactions—Significant transactions in 2018.”

In March 2018, we announced a collaboration and licensing agreement with the Wyss Institute for Biologically Inspired Engineering at Harvard University and the Dana-Farber Cancer Institute to develop biomaterial systems for our portfolio of immuno-oncology therapies. The implantable and injectable systems aim to overcome barriers to success that have faced traditional cancer vaccines. The work will combine Harvard’s expertise in tumor biology and materials science with our diverse immuno-oncology pipeline.

In March 2018, we announced a collaboration with Pear Therapeutics to develop novel prescription digital therapeutics for patients with schizophrenia and multiple sclerosis. Under the agreement, we are working with Pear Therapeutics to advance clinical development of the Pear-004 prescription digital therapeutic for patients with schizophrenia. We will also work together on the design and development of a new prescription digital therapeutic to address underserved mental health burden in multiple sclerosis patients.

In January 2018, we announced a licensing agreement and a manufacturing and supply agreement with Spark Therapeutics covering development, registration and commercialization rights to *Luxturna* (voretigene neparvovec) in markets outside the US. *Luxturna* received FDA approval in December 2017 as a one-time gene therapy to restore functional vision in children and adult patients with biallelic mutations of the RPE65 gene, which typically lead to blindness. *Luxturna* was approved in the EU in November 2018.

On January 19, 2018, we successfully completed a tender offer for all of the then-outstanding ordinary shares, including ordinary shares represented by American Depositary Shares (ADSs), of Advanced Accelerator Applications S.A. (AAA). In addition, we commenced a subsequent offering period that expired on January 31, 2018. As of December 31, 2018, Novartis held 99.1% of the then outstanding fully-diluted ordinary shares, including ordinary shares represented by ADSs, which were validly tendered during the initial offering period, the subsequent offering period, and afterward. AAA is a radiopharmaceutical company headquartered in Saint-Genis-Pouilly, France, that develops, produces and commercializes nuclear medicines – including *Lutathera* (USAN: lutetium Lu 177 dotatate/INN: lutetium (^{177}Lu) oxodotreotide), a first-in-class radioligand therapy for gastroenteropancreatic neuroendocrine tumors – and diagnostic products. For additional information, see “Item 18. Financial Statements—Note 2. Significant transactions—Significant transactions in 2018.”

In November 2017, we announced an expanded collaboration with Amgen Inc. and Banner Alzheimer’s Institute to collaborate on a new Generation Study 2 to assess whether investigational BACE1 inhibitor CNP520

can prevent or delay the symptoms of Alzheimer's disease in a high-risk population.

In September 2017, we announced a collaboration agreement with the University of California, Berkeley, in the field of covalent chemoproteomics to establish the Novartis-Berkeley Center for Proteomics and Chemistry Technologies, based at Berkeley. The collaboration focuses on discovery of drug targets on proteins inaccessible to conventional therapeutic molecules.

In June 2017, we announced a clinical research collaboration in which Bristol-Myers Squibb is to investigate the safety, tolerability and efficacy of *Mekinist* (trametinib) in combination with Opdivo® (nivolumab) and Opdivo® + Yervoy® (ipilimumab) regimen as a potential treatment option for metastatic colorectal cancer in patients with microsatellite stable tumors where the tumors are proficient in mismatch repair (MSS mCRC pMMR).

In April 2017, we announced an expanded collaboration agreement with Amgen to co-commercialize *Aimovig* (erenumab) in the US. *Aimovig*, formerly known as AMG 334, was approved for the prevention of migraine. Under the agreement, Novartis retained exclusive rights to commercialize *Aimovig* in the rest of the world and gained commercialization rights in Canada. This agreement builds on the previously announced 2015 global collaboration between Novartis and Amgen.

In January 2017, we entered into a collaboration and option agreement with Ionis Pharmaceuticals, Inc. (Ionis) and its affiliate Akcea Therapeutics, Inc. (Akcea) to license two investigational treatments with the potential to significantly reduce cardiovascular risk in patients suffering from high levels of lipoproteins known as Lp(a) and ApoCIII. The two investigational antisense therapies developed by Ionis – called AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx– have the potential to lower both lipoproteins up to 90% and significantly reduce cardiovascular risk in high-risk patient populations. In addition, Novartis entered into a stock purchase agreement with Ionis and Akcea. This transaction was completed on February 14, 2017.

In December 2016, we entered into a definitive agreement for the acquisition of Encore Vision, Inc., a privately held company focused on the development of UNR844 (formerly EV06), an investigational, first-in-class, potentially disease-modifying topical treatment for presbyopia. This acquisition was completed on January 20, 2017.

In December 2016, we signed an exclusive option, collaboration and license agreement with Conatus Pharmaceuticals Inc. for the global rights to VAY785 (emricasan), an investigational, first-in-class, oral, pan-caspase inhibitor for the treatment of nonalcoholic steatohepatitis with advanced fibrosis and cirrhosis of the liver. Novartis exercised the option on May 3, 2017. Novartis obtained an exclusive, worldwide license to develop and commercialize products containing emricasan on July 5, 2017.

In December 2016, we entered into a definitive agreement for the acquisition of Ziarco Group Limited, a privately held company focused on the development of novel treatments in dermatology, including ZPL389 (adriforant), a once-daily oral H4 receptor antagonist in development for atopic dermatitis. This acquisition was completed on January 20, 2017.

In November 2016, we acquired Reprixys Pharmaceuticals Corporation and SEG101 (crizanlizumab), an anti-P-selectin antibody being investigated in the reduction of vaso-occlusive pain crises in patients with sickle cell disease.

In June 2016, we announced a collaboration and licensing agreement with Xencor for the development of bispecific antibodies for treating cancer. We are collaborating with Xencor to co-develop its bispecific T-cell-engaging antibody targeting CD3xCD123 for the treatment of acute myeloid leukemia. As part of the agreement, Novartis also received the right to develop four additional bispecific antibodies and to use other Xencor proprietary antibody engineering technology for up to 10 additional biotherapeutic programs across the Novartis research and development portfolio. The original terms also included co-development of Xencor's bispecific T-cell-engaging antibody targeting CD3xCD20 for the treatment of B-cell malignancies, which we have since agreed to revert to Xencor.

In January 2016, we announced a collaboration and licensing agreement with Surface Oncology. Novartis obtained an exclusive worldwide license to develop and commercialize an anti-CD73 antibody. As part of the collaboration, Novartis has options to license additional next-generation cancer immunotherapies.

As part of our previously announced exclusive global research and development collaboration with the University of Pennsylvania (Penn) to develop and commercialize targeted chimeric antigen receptor (CAR) immunotherapies for the treatment of cancer, in February 2016 Penn opened the Center for Advanced Cellular Therapeutics (CACT) at the Perelman School of Medicine campus in Philadelphia, Pennsylvania. The CACT is a first-of-its-kind research and development center established specifically to develop and manufacture adoptive T-cell immunotherapies under the

research collaboration guided by scientists and clinicians from NIBR and Penn.

On March 2, 2015, we acquired a right of first negotiation over the co-development or commercialization of GSK's current and future oncology R&D pipeline, excluding oncology vaccines, which expires on September 2, 2027. We acquired this right with the completion of our acquisition of the oncology products of GSK and certain related assets.

Regulation

The international pharmaceutical industry is highly regulated. Regulatory authorities around the world administer numerous laws and regulations regarding the testing, approval, manufacturing, importing, labeling and marketing of drugs, and also review the safety and efficacy of pharmaceutical products. Extensive controls exist on the non-clinical and clinical development of pharmaceutical products. These regulatory requirements, and the implementation of them by local health authorities around the globe, are a major factor in determining whether a substance can be developed into a marketable product, and the amount of time and expense associated with that development.

Health authorities, including those in the US, the EU and Japan, have high standards of technical evaluation. The introduction of new pharmaceutical products generally entails a lengthy approval process. Products must be authorized or registered prior to marketing, and such authorization or registration must subsequently be maintained. In recent years, the registration process has required increased testing and documentation for the approval of new drugs, with a corresponding increase in the expense of product introduction.

To register a pharmaceutical product, a registration dossier containing evidence establishing the safety, efficacy and quality of the product must be submitted to regulatory authorities. Generally, a therapeutic product must be registered in each country in which it will be sold. In every country, the submission of an application to a regulatory authority does not guarantee that approval to market the product will be granted. Although the criteria for the registration of therapeutic drugs are similar in most countries, the formal structure of the necessary registration documents and the specific requirements, including risk tolerance, of the local health authorities can vary significantly from country to country. It is possible that a drug can be registered and marketed in one country while the registration authority in another country may, prior to registration, request additional information from the pharmaceutical company or even reject the product. It is also possible that a drug may be approved for different indications in different countries.

The registration process generally takes between six months and several years, depending on the country, the quality of the data submitted, the efficiency of the registration authority's procedures, and the nature of the product. Many countries provide for accelerated processing of registration applications for innovative products of particular therapeutic interest. In recent years, efforts have been made among the US, the EU and Japan to harmonize registration requirements in order to achieve shorter development and registration times for medical products. However, the requirement in many countries to negotiate selling prices or reimbursement levels with government regulators and other payers can substantially extend the time until a product may finally be available to patients.

The following provides a summary of the regulatory processes in the principal markets served by Innovative Medicines Division affiliates:

United States

In the US, applications for drug registration are submitted to and reviewed by the FDA. The FDA regulates the testing, manufacturing, labeling and approval for marketing of pharmaceutical products intended for commercialization in the US. The FDA continues to monitor the safety of pharmaceutical products after they have been approved for sale in the US market. The pharmaceutical development and registration process is typically intensive, lengthy and rigorous. When a pharmaceutical company has gathered data that it believes sufficiently demonstrates a drug's safety, efficacy and quality, then the company may file a New Drug Application (NDA) or Biologics License Application (BLA), as applicable, for the drug. The NDA or BLA must contain all the scientific information that has been gathered about the drug and typically includes information regarding the clinical experiences of patients tested in the drug's clinical trials. A Supplemental New Drug Application (sNDA) or BLA amendment must be filed for new indications for a previously approved drug.

Once an application is submitted, the FDA assigns reviewers from its staff, including experts in biopharmaceutics, chemistry, clinical microbiology, pharmacology/toxicology, and statistics. After a complete review, these content experts provide written evaluations of the NDA or BLA. These recommendations are consolidated and are used by senior FDA staff in its final evaluation of the NDA or BLA. Based on that final evaluation, the FDA then provides to the NDA or BLA's sponsor an approval, or a "complete response" letter if the NDA or BLA application is not approved. If not approved, the letter will state the specific deficiencies in the NDA or BLA that need to be addressed. The sponsor must then submit an adequate response to the deficiencies in order to restart the review procedure.

Once the FDA has approved an NDA, BLA, sNDA or BLA amendment, the company can make the new drug available for physicians to prescribe. The drug owner must submit periodic reports to the FDA, including any cases of adverse reactions. For some medications, the FDA requires additional post-approval studies (Phase IV) to evaluate long-term effects or to gather information on the use of the product under specified conditions.

Throughout the life cycle of a product, the FDA requires compliance with standards relating to good laboratory, clinical and manufacturing practices. The FDA also requires compliance with rules pertaining to the manner in which we may promote our products.

European Union

In the EU, there are three main procedures for application for authorization to market pharmaceutical products in more than one EU member state at the same time: the centralized procedure, the mutual recognition procedure and the

decentralized procedure. It is also possible to obtain a national authorization for products intended for commercialization in a single EU member state only, or for additional indications for licensed products. The procedure used for first authorization must continue to be followed for subsequent changes, e.g., to add an indication for a licensed product.

Under the centralized procedure, applications are made to the EMA for an authorization that is valid for the European Union (all member states). The centralized procedure is mandatory for all biotechnology products; new chemical entities in cancer, neurodegenerative disorders, diabetes, AIDS, autoimmune diseases and other immune dysfunctions; advanced therapy medicines, such as gene therapy, somatic cell therapy and tissue-engineered medicines; and orphan medicines (medicines for rare diseases). It is optional for other new chemical entities, innovative medicinal products, and medicines for which authorization would be in the interest of public health. When a pharmaceutical company has gathered data that it believes sufficiently demonstrates a drug’s safety, efficacy and quality, the company may submit an application to the EMA. The EMA then receives and validates the application, and the specialized committee for human medicines, the CHMP, appoints

a rapporteur and co-rapporteur to review it. The entire review cycle must be completed within 210 days, although there is a “clock stop” at Day 120 to allow the company to respond to questions set forth in the rapporteur and co-rapporteur’s assessment report. When the company’s complete response is received by the EMA, the clock restarts on Day 121. If there are further aspects of the dossier requiring clarification, the CHMP will issue further questions at Day 180, and may also request an oral explanation, in which case the sponsor must not only response to the further questions but also appear before the committee to justify its responses. On Day 210, the CHMP will take a vote to recommend the approval or non-approval of the application, and their opinion is transferred to the European Commission (EC). The final EC decision under this centralized procedure is a decision that is applicable to all member states. This decision occurs 60 days, on average, after a positive CHMP recommendation.

Under both the mutual recognition procedure (MRP) and the decentralized procedure (DCP), the assessment is led by one member state, called the reference member state (RMS) which then liaises with other member states, known as the concerned member states (CMSs). In the MRP, the company first obtains a marketing authorization in the RMS, which is then recognized by the CMSs in 90 days. In the DCP, the application is done simultaneously in the RMS and all CMSs. During the DCP, the RMS drafts an assessment report within 120 days. Within an additional 90 days, the CMSs review the application and can issue objections or requests for additional information. On Day 90, each CMS must be assured that the product is safe and effective, and that it will cause no risks to the public health. Once an agreement has been reached, each member state grants national marketing authorizations for the product.

After the marketing authorizations have been granted, the company must submit periodic safety reports to the relevant health authority (EMA for the centralized procedure, national health authorities for DCP or MRP). In addition, pharmacovigilance measures must be implemented and monitored, including the collection, evaluation and expedited reporting of adverse events, and updates to risk management plans. For some medications, post-approval studies (Phase IV) may be imposed to complement available data with additional data to evaluate long-term effects (called a Post-Approval Safety Study, or PASS) or to gather additional efficacy data (called a Post-Approval Efficacy Study, or PAES).

European marketing authorizations have an initial duration of five years. The holder of the marketing authorization must actively apply for its renewal after this first five-year period. As part of the renewal procedure, the competent authority will perform a full benefit-risk review of the product. Should the authority conclude that the benefit-risk balance is no longer positive, the marketing authorization can be suspended or revoked. Once renewed, the marketing authorization is valid for an unlimited period. If the holder does not apply for renewal, the marketing authorization automatically lapses. Any marketing authorization that is not followed within three years of its granting by the actual placing on the market of the corresponding medicinal product ceases to be valid.

Japan

In Japan, applications for new products are made through the Pharmaceutical and Medical Devices Agency (PMDA). Once an NDA is submitted, a review team is formed, which consists of specialized officials of the PMDA, including chemistry/manufacturing, non-clinical, clinical and biostatistics. While a team evaluation is carried out, a data reliability survey and Good Clinical Practice/Good Laboratory Practice/Good Manufacturing Practice inspection are carried out by the Office of Conformity Audit and Office of GMP/GQP Inspection of the PMDA. Team evaluation results are passed to the PMDA’s external experts, who then report back to the PMDA. After a further team evaluation, a report is provided to the Ministry of Health, Labor and Welfare (MHLW); the MHLW makes a final determination for approval and refers this to the Council on Drugs and Foods Sanitation, which then advises the MHLW on final approvability. Marketing and distribution approvals require a review to determine whether or not the product in the application is suitable as a drug to be manufactured and distributed by a person who has obtained a manufacturing and distribution business license for the type of drug concerned, and to confirm that the product has been manufactured in a plant compliant with Good Manufacturing Practices.

Once the MHLW has approved the application, the company can make the new drug available for physicians to prescribe. After that, the MHLW lists its National Health Insurance price within 60 days (or 90 days) from the approval, and physicians can obtain reimbursement. For some medications, the MHLW requires additional post-approval studies (Phase IV) to further evaluate safety and/or to gather information on the use of the product under specified conditions. The MHLW also requires the drug’s sponsor to submit periodic safety update reports. Within three months from the specified re-examination period, which is designated at the time of the approval of the application for the new product, the company must submit a re-examination application to enable the drug’s safety and

efficacy to be reassessed against approved labeling by the PMDA.

Price controls

In most of the markets where we operate, the prices of pharmaceutical products are subject to both direct and indirect price controls and to drug reimbursement programs with varying price control mechanisms. Due to increasing political pressure and governmental budget constraints, we expect these mechanisms to continue to remain robust – and to potentially even be strengthened – and to have a negative influence on the prices we are able to charge for our products.

Direct governmental efforts to control prices

United States:

• In the US, President Trump declared the reduction of drug prices as one of his key priorities to be addressed by his administration. In May 2018, the Trump administration unveiled its blueprint of potential actions that could be used to lower drug prices and reduce drug out-of-pocket costs for patients. In the second half of 2018, the Trump administration released a series of

prescription drug-related proposals that may ultimately lead to new price restrictions and cost reduction solutions for pharmaceuticals. A key area of focus is Medicare Part B, which includes prescription drugs dispensed by physicians in their offices or in outpatient clinics. The administration is also considering use of an international pricing comparison model for Medicare Part B drugs that would reduce costs of select medications by aligning US drug reimbursements to prices in other countries.

• In November 2018, the Democratic Party regained majority leadership of the US House of Representatives. Democratic Party leaders have outlined prescription drug costs as one of their priorities in the congressional session that began in January 2019.

• The Independent Payment Advisory Board (IPAB), an entity created under the Patient Protection and Affordable Care Act with authority to implement broad actions to reduce future costs of the Medicare program, was repealed in February 2018.

• Additionally, seven states have passed legislation intended to impact pricing or requiring price transparency reporting (California, Connecticut, Louisiana, Maine, Nevada, Oregon and Vermont). The California law requires 60-day advance notification of price increases for products exceeding a specific threshold over the past two years, as well as additional quarterly reporting requirements. Various formats of drug price reporting and disclosure are required in all seven states. It is expected in 2019 that state legislatures will continue to focus on drug pricing and that similar bills will be passed in more states.

Europe: In Europe, our operations are subject to significant price and marketing regulations. Many governments are introducing healthcare reforms in a further attempt to curb increasing healthcare costs. In the EU, governments influence the price of pharmaceutical products through their control of national healthcare systems that fund a large part of the cost of such products to patients. The downward pressure on healthcare costs in general in the EU, particularly with regard to prescription drugs, has become very intense. Increasingly strict analyses are applied when evaluating the entry of new products, and as a result, access to innovative medicines is limited based on strict cost-benefit assessments. In addition, prices for marketed products are referenced within member states and across member state borders, further impacting individual EU member state pricing. As an additional control for healthcare budgets, some EU countries have passed legislation to impose further mandatory rebates for pharmaceutical products and/or financial claw-backs on the pharmaceutical industry. The calculation of these rebates and claw-backs may lack transparency in some cases and can be difficult to predict.

Japan: In 2018, the National Health Insurance price calculation method for new products and the price revision rule for existing products were reviewed by the Japanese government, and new drug tariffs became effective beginning April 2018. Also in 2018, the MHLW implemented a price maintenance scheme with a narrower scope and decreased number of products. The MHLW also increased the frequency of price cuts from every other year to annually beginning in 2021, and plans to introduce a cost-effectiveness assessment in 2019. The Japanese government is continuing deliberations regarding a healthcare reform initiative with a goal of sustaining universal coverage under the National Health Insurance program, and is addressing the efficient use of drugs, including promotion of use of generic drugs.

Rest of world: Many other countries around the world are also taking steps to control prescription drug prices. For example, China – one of our most important Emerging Growth Markets – organized national price negotiations in 2017 for 36 patented drugs and in 2018 for 17 oncology drugs directly linked to national drug reimbursement, which applied nationwide both in public and military hospitals, as well as a national procurement pilot on certain generic drugs at the end of 2018. These efforts resulted in drug price reductions of more than 50% on average for the drugs subject to these programs. Drug prices in China may further decline due to the national health reform, but meanwhile, reimbursement access is expected to accelerate, which aims to resolve the public issue of accessibility and the high cost of healthcare services. In addition, in 2016, the Colombian government took steps to unilaterally reduce the price of *Glivec* by up to 43% through a local procedural mechanism called a Declaration of Public Interest. While the government's use of this exceptional mechanism as a tool to control the price of a prescription drug and to generally manage its healthcare budget is unprecedented, we continue to contest its appropriateness, as its use could become more widespread if upheld in this case, potentially leading to a more systemic impact on drug pricing. In 2018, Canada proposed amendments to its patented medicines regulations to introduce three new economics-based price regulatory factors and the concept of affordability in price assessments; to update the schedule of comparator countries to include 12 countries with similar consumer protection priorities, economic wealth and marketed medicines as

Canada and to exclude Switzerland and the US; and to require reporting of all confidential discounts and rebates.

Regulations favoring generics and biosimilars

In response to rising healthcare costs, most governments and private medical care providers have instituted reimbursement schemes that favor the substitution of generic pharmaceuticals for more expensive brand-name pharmaceuticals. In the US, generic substitution statutes have been enacted by all states and permit or require the dispensing pharmacist to substitute a less expensive generic drug instead of an original patented drug. Other countries, including numerous European countries, have similar laws. We expect that the pressure for generic substitution will continue to increase. In addition, the US, EU and other jurisdictions are increasingly crafting laws and regulations encouraging the development of biosimilar versions of biologic drugs, which can also be expected to have an impact on pricing.

Cross-border sales

Price controls in one country can also have an impact in other countries as a result of cross-border sales. In the EU, products that we have sold to customers in countries with stringent price controls can be legally resold to customers in other EU countries at a lower price than the price at which the product is otherwise available in the importing country (known as parallel trade). In North America, products that we have sold to customers in Canada – which has relatively stringent price controls – are sometimes resold into the US, again at a lower price than the price at which the product is otherwise sold in the US. Such imports from Canada and other countries into the US are currently illegal. Given the increased focus on pharmaceutical prices in the US, the Trump administration, certain members of the US Congress, and select state legislators continue to explore legislation to allow the safe importation of pharmaceutical products into the US from select countries, including Canada.

We expect that pressures on pricing will continue worldwide and will likely increase. Because of these pressures, there can be no certainty that in every instance we will be able to charge prices for a product that, in a particular country or in the aggregate, would enable us to earn an adequate return on our investment in that product.

Intellectual property

We attach great importance to intellectual property – including patents, trademarks, copyrights, know-how and research data – in order to protect our investment in research and development, manufacturing and marketing. In general, we seek intellectual property protection under applicable laws for significant product developments in major markets. Among other things, patents may cover the products themselves, including the product's active ingredient or ingredients and its formulation. Patents may cover processes for manufacturing a product, including processes for manufacturing intermediate substances used in the manufacture of the product. Patents may also cover particular uses of a product, such as its use to treat a particular disease, or its dosage regimen. In addition, patents may cover assays or tests for certain diseases or biomarkers – which can improve patient outcomes when administered with certain drugs – as well as assays, research tools and other techniques used to identify new drugs. The protection offered by such patents extends for varying periods, depending on the grant and duration of patents in the various jurisdictions. The protection afforded, which may vary from country to country, depends upon the type of patent and its scope of coverage.

In addition to patent protection, various countries offer data or marketing exclusivities for a prescribed period of time. Data exclusivity may be available that would preclude a potential competitor from filing a regulatory application for a set period of time that relies on the sponsor's clinical trial data, or the regulatory authority from approving the application. The data exclusivity period can vary depending upon the type of data included in the sponsor's application. When it is available, market exclusivity, unlike data exclusivity, precludes a competitor from obtaining marketing approval for a product even if a competitor's application relies on its own data. Data exclusivity and other regulatory exclusivity periods generally run from the date a product is approved, and so their expiration dates cannot be known with certainty until the product approval date is known.

In the US and other countries, pharmaceutical products are eligible for a patent term extension for patent periods lost during product development and regulatory review. The law recognizes that product development and review by the FDA and other health authorities can take an extended period, and permits an extension of the patent term for a period related to the time taken for the conduct of clinical trials and for the health authority's review. However, the length of this extension and the patents to which it applies cannot be known in advance and can only be determined after the product is approved.

United States

Patents

In the US, a patent issued for an application filed today will receive a term of 20 years from the earliest application filing date, subject to potential patent term adjustments for delays in patent issuance based upon certain delays in prosecution by the United States Patent and Trademark Office (USPTO). A US pharmaceutical patent that claims a product, method of treatment using a product, or method of manufacturing a product may also be eligible for a patent term extension based on the time the FDA took to approve the product. This type of extension may only extend the patent term for a maximum of five years, and may not extend the patent term beyond 14 years from regulatory approval. Only one patent may be extended for any product based on FDA delay.

In practice, however, it is not uncommon for significantly more than the five-year maximum patent extension period to pass between the time that a patent application is filed for a product and the time that the product is approved by the

FDA. As a result, it is rarely the case that, at the time a product is approved by the FDA, it will have the full 20 years of remaining patent life. Rather, in our experience, it is not uncommon that, at the date of approval, a product will have from 13 to 16 years of patent protection remaining, including all extensions available at that time.

Data and market exclusivity

In addition to patent exclusivities, the FDA may provide data or market exclusivity for a new chemical entity or an "orphan drug," each of which runs in parallel to any patent protection. Regulatory data protection or exclusivity prevents a potential generic competitor from relying on clinical trial data generated by the sponsor when establishing the safety and efficacy of its competing product. Market exclusivity prohibits any marketing of the same drug for the same indication.

• A new small-molecule active pharmaceutical ingredient shall have five years of regulatory data exclusivity, during which time a competitor generally may not submit an application to the FDA based on a sponsor's clinical data.

• Orphan drug exclusivity provides seven years of market exclusivity for drugs designated by the FDA as “orphan drugs,” meaning drugs that treat rare diseases, as designated by the FDA. During this period, a potential competitor may not market the same drug for the same indication even if the competitor’s application does not rely on data from the sponsor.
• A new biologic active pharmaceutical ingredient shall have 12 years of market exclusivity, during which time a competitor may not market the same drug for the same indication.
• The FDA may also request that a sponsor conduct pediatric studies, and in exchange, it will grant an additional six-month period of pediatric market exclusivity if the FDA accepts the data, the sponsor makes a timely application for approval for pediatric treatment, and the sponsor has either a patent-based or regulatory-based exclusivity period for the product that can be extended.

European community

Patents

Patent applications in Europe may be filed in the European Patent Office (EPO) or in a particular country in Europe. The EPO system permits a single application to be granted for the EU plus other non-EU countries such as Switzerland and Turkey. When the EPO grants a patent, it is then validated in the countries that the patent owner designates. The term of a patent granted by the EPO or a European country office is generally 20 years from the filing date of the patent application on which the patent is based, subject to potential patent term extensions. Pharmaceutical patents can be granted a further period of exclusivity under the Supplementary Protection Certificate (SPC) system. SPCs are designed to compensate the owner of the patent for the time it took to receive marketing authorization of a product by the European health authorities. An SPC may be granted to provide, in combination with the patent, up to 15 years of exclusivity from the date of the first European marketing authorization. However, an SPC cannot last longer than five years. The SPC duration can additionally be extended by a further Pediatric Extension of six months if the product is the subject of an agreed pediatric investigation plan. The post-grant phase of patents, including the SPC system, is currently administered on a country-by-country basis under national laws that, while differing, are intended to (but do not always) have the same effect.

In practice, as in the US, it is not uncommon for patent term extensions to not fully compensate the owner of a patent for the time it took to develop the product and receive marketing authorization by the European health authorities. Accordingly, it is not uncommon that a pharmaceutical product, at the date of approval, will have patent protection for 10 to 15 years, including extensions available at that time.

Data and market exclusivity

In addition to patent exclusivity, the EU provides a system of regulatory data exclusivity for authorized human medicines, which runs in parallel to any patent protection. The system for drugs being approved today is usually referred to as “8+2+1” because it provides: an initial period of eight years of data exclusivity, during which a competitor cannot rely on the relevant data; a further period of two years of market exclusivity, during which the data can be used to support applications for marketing authorization but the competitive product cannot be launched; and a possible one-year extension of the market exclusivity period if, during the initial eight-year data exclusivity period, the sponsor registered a new therapeutic indication with “significant clinical benefit.” This system applies both to national and centralized authorizations. It has been in force since 2005; therefore, some medicines remain covered by the previous system in which EU member states provided either six or 10 years of data exclusivity.

The EU also has an orphan drug exclusivity system for medicines similar to the US system. If a medicine is designated as an “orphan drug,” then it benefits from 10 years of market exclusivity after it is authorized, during which time a similar medicine for the same indication will not receive marketing authorization. Under certain circumstances, this exclusivity can be extended with a two-year Pediatric Extension.

Japan

Patents

In Japan, a patent can be issued for active pharmaceutical ingredients. Although methods of treatment – such as dosage and administration – are not patentable in Japan, pharmaceutical compositions for a specific dosage or administration method are patentable. Processes to make a pharmaceutical composition are also patentable. The patent term granted is generally 20 years from the filing date of the patent application on which the patent is based, subject to potential patent term extensions and adjustments. A patent term extension can be granted for up to five years under the Japanese Patent Act to compensate for erosion against the patent term caused by the time needed to obtain marketing

authorization from the MHLW. As in the US and EU, patent term extensions in Japan may not fully compensate for the time necessary to develop a product and obtain a marketing authorization. As a result, it is not uncommon for the effective term of patent protection for an active pharmaceutical ingredient in Japan to be approximately 10 to 15 years, including available extensions.

Data and market exclusivity

Japan also has a regulatory data protection system called a “re-examination period” of eight years for new chemical entities and of four to six years for new indications and formulations, and a 10-year orphan drug exclusivity system.

Third-party patents and challenges to intellectual property

Third parties can challenge our patents, patent term extensions and marketing exclusivities, including pediatric extensions and orphan drug exclusivity, through various proceedings. For example, patents in the US can be challenged in the USPTO through various proceedings, including Inter Partes Review (IPR) proceedings. They

may also be challenged through patent infringement litigation under the Abbreviated New Drug Application (ANDA) provisions of the Hatch-Waxman Act, or the Biologics Price Competition and Innovation Act (BPCIA). See generally "—Sandoz—Intellectual property." In the EU, EU patents may be challenged through oppositions in the EPO, or national patents may be challenged in national courts or national patent offices. In Japan, patents may be challenged in the Japanese patent office and in national courts. The outcomes of such challenges can be difficult to predict.

In addition to directly challenging our intellectual property rights, in some circumstances a competitor may be able to market a generic version of one of our products by, for example, designing around our intellectual property or marketing the generic product for non-protected indications. Despite data exclusivity protections, a competitor could opt to incur the costs of conducting its own clinical trials and preparing its own regulatory application, and avoid our data exclusivity protection altogether. There is a risk that some countries may seek to impose limitations on the availability of intellectual property right protections for pharmaceutical products, or on the extent to which such protections may be enforced. For example, a review of several intellectual property rights is currently ongoing in the EU (orphan drug exclusivity, pediatric extensions, SPCs and regulatory data protection), which could lead to legislative changes in the scope and/or term of protection under those rights. Also, even though we may own, co-own or in-license patents protecting our products, and conduct pre-launch freedom-to-operate analyses, a third party may nevertheless claim that one of our products infringes a third-party patent for which we do not have a license.

As a result, there can be no assurance that our intellectual property will protect our products or that we will be able to avoid adverse effects from the loss of intellectual property protection or from third-party patents in the future.

Intellectual property protection for certain key marketed products and compounds in development

We present below certain additional details regarding intellectual property protection for certain Innovative Medicines Division products and compounds in development. For each product and compound in development below, we identify issued, unexpired patents by general subject matter and, in parentheses, years of expiry in, if relevant, the US, EU and Japan that are owned, co-owned or exclusively in-licensed by Novartis and that relate to the product or to the method of its use as it is currently approved and marketed or, in the case of a compound in development, as it is currently filed with the FDA and/or the EMA for approval. Identification of an EU patent refers to national patents in EU countries and/or to the national patents that have been derived from a patent granted by the EPO. Novartis may own or control additional patents relating to, for example, compound forms, methods of use, formulations, processes, synthesis, purification and detection.

We identify unexpired regulatory data protection periods and, in parentheses, years of expiry if the relevant marketing authorizations have been authorized or granted. The term "RDP" refers to regulatory data protection, regulatory data exclusivity (which in the EU refers to the protections under "8+2+1" regulatory data exclusivity), and data re-examination protection systems. We identify certain unexpired patent term extensions and marketing exclusivities and, in parentheses, years of expiry if they are granted; their subject matter scope may be limited and is not specified. Marketing exclusivities and patent term extensions include orphan drug exclusivity (ODE), pediatric exclusivity (PE), patent term extensions (PTE) and SPCs. We designate them as "pending" if they have been applied for but not granted and years of expiry are estimable. Such pending applications may or may not ultimately be granted.

In the case of the EU, identification of a patent, patent term extension, marketing exclusivity or data protection means grant, authorization and maintenance in at least one country and possibly pending or found invalid in others.

For each product below, we indicate whether there is current generic competition – which in the case of products containing biologics, refers to biosimilar competition – for one or more product versions in one or more approved indications in each of the major markets for which intellectual property is disclosed. We identify ongoing challenges to the disclosed intellectual property that have not been finally resolved, including IPRs if instituted by the USPTO. Challenges identified as being in administrative entities, such as national patent offices, include judicial appeals from decisions of those entities. Resolution of challenges to the disclosed intellectual property, which in the EU may involve intellectual property of one or more EU countries, may include settlement agreements under which Novartis permits or does not permit future launch of generic versions of our products before expiration of that intellectual property. We identify certain material terms of such settlement agreements where they could have a material adverse effect on our business. In other cases, such settlement agreements may contain confidentiality obligations restricting what may be disclosed.

For additional information regarding commercial arrangements with respect to these products, see "—Key marketed products."

Novartis Oncology business unit
Oncology
• *Tasigna.* US: Patent on compound (2023), PE (2024); patents on salt forms (2026, 2027, 2028), three PEs (2027, 2028, 2029); patent on polymorph compound form (2026), PE (2027); patents on capsule form (2026, 2027), two PEs (2027, 2028) and patent on method of treatment (2032), PE (2032). EU: Patent on compound (2023); patent on salt form (2026); patent on polymorph compound form (2026); patent on capsule form (2027); patent on method of treatment (2030); ODE (2017), PE (2019). Japan: Patent on compound (2023), PTE (2024); patent on salt form (2026); patent on polymorph compound form (2026); patent on capsule form (2027); patent on method of treatment (2030).
There is currently no generic competition in the US, EU or Japan. In the US, the salt form patents, the polymorph patent, the capsule form patent and the method
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of treatment patent are being challenged in ANDA proceedings against generic manufacturers. The EU method of treatment patent, the capsule form patent, and the polymorph compound patent are being opposed in the EPO.

• *Sandostatin* SC and *Sandostatin* LAR.

Sandostatin SC. There is no patent protection in the US, EU or Japan. There is generic competition in the US, EU and Japan.

Sandostatin LAR. There is no patent protection in the US, EU or Japan. There is currently no generic competition in the US, EU or Japan.

• *Gleevec/Glivec.* US: Patent on polymorphic compound form (2019), PE (2019); patent on GIST method of use (2021), PE (2022). EU: Patent on GIST method of use (2021); patent on tablet formulation (2023). Japan: Patent on polymorphic compound form (2019); patent on GIST method of use (2021); patent on tablet formulation (2023). There is generic competition in the US, EU and Japan. In the US and EU, Novartis has resolved patent litigation with certain generic manufacturers. Novartis is taking steps in some EU countries to enforce the tablet formulation patent and the GIST method of use patent. The EU GIST method of use patent is being challenged in one EU country. The EU tablet formulation patent is being challenged in the EPO and in the patent office of one EU country.

• *Afinitor/Votubia* and *Afinitor Disperz/Votubia* dispersible tablets. US: Patent on compound (2014), PTE (2019), PE (2020); patent on dispersible tablet formulation (2022), PE (2023); patent on antioxidant (2019); patent on antioxidant (2019), PE (2020); patent on tuberous sclerosis complex (TSC)/subependymal giant cell astrocytoma (SEGA) use (2022), PE (2022); patent on breast cancer use (2022), PE (2022); patent on renal cell carcinoma use (2025), PE (2026); patent on pancreatic neuroendocrine tumor use (2028); RDP for neuroendocrine tumors of gastrointestinal or lung origin (2019), PE (2019); ODE for TSC/renal angiomyolipoma (2019), PE (2019). EU: Patent on dispersible tablet formulation (2022); patent on antioxidant (2019); patent on breast cancer use (2022); patent on renal cell carcinoma use (2022); patent on TSC/SEGA use (2022); patent on use in neuroendocrine tumors of lung origin (2022); ODE (*Votubia*) (2021). Japan: Patent on dispersible tablet formulation (2022); patent on antioxidant (2019); patent on breast cancer use (2022); patent on pancreatic neuroendocrine tumor use (2026); patent on renal cell carcinoma use (2022); patent on gastrointestinal and lung neuroendocrine tumor use (2026), PTE (2027); patent on TSC/SEGA and TSC/AML use (2027); ODE (tuberous sclerosis) (2022); ODE (dispersible tablet) (2022).

There is currently no generic competition in the US, EU or Japan. In the US, the compound patent and renal cell carcinoma use patent are being challenged in ANDA proceedings against generic manufacturers. The US renal cell carcinoma use and pancreatic neuroendocrine tumor use patents are being challenged in IPR proceedings in the USPTO. In the US, Novartis has resolved patent litigation with certain generic manufacturers which may result in limited generic competition for *Afinitor* toward the end of 2019, and has resolved patent litigation relating to *Afinitor Disperz*. The EU breast cancer use patent, the EU TSC/SEGA use patent and the EU renal cell carcinoma use patent are being opposed in the EPO. The Japanese breast cancer use patent is being challenged in the Japanese Patent Office.

• *Promacta/Revolade.* US: Patent on compound (2021), PTE (2022), PE (2023); patent on compound (2018), PE (2019); two patents on compound (2021, 2021), PEs (2021, 2021); patent on method of treating thrombocytopenia (2021), PE (2021); patent on method of enhancing platelet production (2021), PE (2021); patent on method of enhancing platelet production (2023), PE (2023); patent on salt form (2025); PE (2026); four patents on formulation of different dose strengths (2027) (4), PE (2028) (4); ODE (2021), two PEs (2022, 2022). EU: Patents on compound (2021); patent on compound (2021), SPC (2025); patent on salt form (2023); patent on formulation (2027); RDP (2020). Japan: Patent on compound (2021), PTE (2025); patent on salt form (2023); PTE (2023), patent on formulation (2027); RDP (2020). There is currently no generic competition in the US, EU or Japan. In the US, generic manufacturers have filed ANDAs challenging certain patents other than the compound patents. The EU formulation patent is being opposed in the EPO.

• *Tafinlar* and *Mekinist.*

Tafinlar. US: Two patents on compound (2030; 2030); patent on method of use (2029); RDP (2018); ODE (2020). EU: Patent on compound (2029); RDP (2023). Japan: Patent on compound (2031). There is currently no generic competition in the US, EU or Japan.

Mekinist. US: Patent on compound (2025), PTE (2027); patent on method of use (2025); three patents on formulation (2032) (3); RDP (2018); ODE (2020). EU: Patent on compound (2025), SPC (2029); RDP (2025). Japan: Patent on compound (2025); patent on method of use (2025); patent on formulation (2031). There is currently no generic

competition in the US, EU or Japan.

Use of *Mekinist* with *Tafinlar* or *Tafinlar* with *Mekinist*. US: Patent on combination (2030); patent on method of use of combination (2030); RDP (2020); ODE on melanoma with certain mutations (2021), ODE on non-small cell lung cancer (2024). EU: RDP (2025). Japan: Patent on method of use of combination (2030). There is currently no generic competition in the US, EU or Japan.

• *Exjade* and *Jadenu.*

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Exjade. US: Patent on compound (2017), PTE (2019), ODE for non-transfusion iron overload (2020). EU: Patent on compound (2017), SPC (2021), PE (2022); patent on dispersible tablet formulation (2023). Japan: Patent on compound (2017), PTE (2021); patent on dispersible tablet formulation (2023). There is currently no generic competition in the US, EU or Japan. In the US, Novartis has resolved patent litigation with generic manufacturers relating to *Exjade*.

Jadenu (marketed as *Exjade* FCT in EU and Japan). The compound patents for *Exjade* also protect *Jadenu* (US), and *Exjade* FCT (EU/Japan). US: Patent on film-coated tablet formulation (2034), ODE for non-transfusion iron overload (2020). EU: Patent on film-coated tablet formulation (2034). There is currently no generic competition in the US, EU or Japan. In the US, the formulation patent is being challenged in ANDA proceedings against a generic manufacturer. Novartis has resolved patent litigation relating to the US formulation patent with a generic manufacturer. In the EU, the formulation patent is being opposed in the EPO.

• *Jakavi.* EU: Patent on compound (2026), SPC (2027); patent on salt (2028); RDP (2023). Japan: Patent on compound (2026), PTE (2028), PTE (2030); patent on salt (2028), PTE (2028), PTE (2030); patent on method of use (2026), PTE (2027); RDP (2022). There is currently no generic competition in the EU or Japan. The EU salt patent is being opposed in the EPO.

• *Votrient.* US: Patent on compound (2021), PTE (2023), two patents on compound (2021, 2021), ODE (2019). EU: Patent on compound (2021), SPC (2025); RDP (2021). Japan: patent on compound (2021), two PTEs (2025, 2026); RDP (2020). There is currently no generic competition in the US, EU or Japan.

• *Kisqali*. US: Three patents on compound (2028, 2030, 2031), pending PTE (2031); three patents on methods of use (2029, 2029, 2031); patent on salt (2031); RDP (2022). EU: Patent on compound (2027); patent on compound (2029), SPC (2032); patent on methods of use (2029); RDP (2027). Japan: Two patents on compound (2027, 2029). *Kisqali* is currently not marketed in Japan. There is currently no generic competition in the US or EU.

• *Kymriah*. US: Seven patents on cells and/or pharmaceutical compositions comprising the cells (2031) (7); four patents on methods of use (2031) (4); RDP (2029), PE (2030); ODE for r/r pedALL (2024); ODE for r/r DLBCL (2025), PE (2025). EU: Two patents on methods of use (2031, 2031); RDP (2028); ODE (2028), PE (2030). Japan: One patent on pharmaceutical compositions (2031); one patent on cells, pharmaceutical compositions and medical uses (2031). *Kymriah* is currently not marketed in Japan. There is currently no generic competition in the US or Europe.

• *Lutathera*. US: RDP (2023), ODE (2025); EU: RDP (2027), ODE (2027). *Lutathera* is currently not marketed in Japan. There is currently no generic competition in the US or EU.

Novartis Pharmaceuticals business unit

Ophthalmology

• *Lucentis.* EU: Patent on compound (2018), SPC (2022). Japan: Patent on compound (2018), PTE for age-related macular degeneration (2019), PTE for pathologic myopia (2021), PTE for retinal vein occlusion (2023). There is currently no generic competition in the EU or Japan.

• *Duotrav, Travatan* and *Travatan Z.*

Duotrav. EU: Six patents on formulations (2029) (6). Japan: Two patents on formulations (2029, 2029). *Duotrav* is not marketed in the US. There is generic competition in some EU countries. There is currently no generic competition in Japan. In the EU, the six formulation patents are being opposed in the EPO.

Travatan. EU: Six patents on formulations (2029) (6). *Travatan* is not marketed in the US or Japan. There is generic competition in the EU. In the EU, the six formulation patents are being opposed in the EPO.

Travatan Z. US: Three patents on formulations (2027, 2027, 2029). Japan: Three patents on formulation (2027) (3). *Travatan Z* is not marketed in the EU. There is currently no generic competition in the US. There is generic competition in Japan. In the US, Novartis has resolved patent litigation with certain generic manufacturers.

• *Luxturna*. EU: ODE (2028).

Immunology, Hepatology and Dermatology

• *Cosentyx.* US: Patent on compound (2026), PTE (2029); patent on method of use (psoriasis) (2032); patent on method of use (ankylosing spondylitis) (2033); RDP (2027). EU: Patent on compound (2025), SPC (2030); patent on method of use (psoriasis) (2031); RDP (2026). Japan: Patent on compound (2025), PTE (2026, 2028, 2029); patent on method of use (psoriasis) (2031), PTE (2032, 2033); patent on method of use (psoriatic arthritis) (2031); RDP (2022). There is currently no generic competition in the US, EU or Japan.

• *Xolair.* US: Two patents on syringe formulation (2021, 2024). EU: Two patents on syringe formulation (2021, 2024). Japan: Two patents on syringe formulation (2021, 2024). There is currently no generic competition in the US, EU or Japan.
• *Ilaris.* US: Patent on compound (2024); patent on method of use in cryopyrin-associated periodic syndromes (CAPS) (2026), patent on method of use in familial Mediterranean fever (FMF) (2026), patent on method of use in systemic onset juvenile idiopathic arthritis (SJIA) (2027), patent on method of use in hyperimmunoglobulin D syndrome (HIDS) and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) (2028); patent on formulation (2029); RDP (2021). EU: Patent on compound (2021), SPC (2024), PE (2025); patent on method of use in SJIA (2026), patent on method of use in FMF (2026), patent

on formulation (2029); RDP (2020). Japan: Patent on compound (2021), PTE for CAPS (2024), PTE for FMF, HIDS and TRAPS (2026); patent on method of use in familial cold urticaria, neonatal onset multisystem inflammatory disease, SJIA and FMF (2026), patent on method of use in Muckle Wells syndrome (2026), patent on formulation (2029); ODE for CAPS (2021); ODE for FMF, HIDS and TRAPS (2026); ODE for SJIA (2028). There is currently no generic competition in the US, EU or Japan.

Neuroscience

• *Gilenya.* US: Patent on compound (2014), PTE (2019), PE (2019); patent on dosage regimen (2027). EU: RDP (2022); patent on formulation (2024), SPC (2026). Japan: RDP (2021); two patents on formulation (2024, 2024). There is currently no generic competition in the US, EU or Japan. In the US, the compound patent is being challenged in ANDA proceedings against generic manufacturers. The US dosage regimen patent is being challenged in an IPR proceeding in the USPTO. Novartis is taking steps to enforce the US dosage regimen patent against generic manufacturers.

• *Aimovig* (formerly AMG 334). US (co-commercialized with Amgen): Patent on compound (2031), RDP (2030). EU: Patent on compound (2029), RDP (2028). There is currently no generic competition in the US or EU.

Respiratory

• *Xolair.* The information set forth in the IP paragraph for *Xolair* under the "Immunology, Hepatology and Dermatology" heading also applies to *Xolair* for respiratory indications. There is currently no generic competition in the US, EU or Japan.

Cardio-Metabolic

• *Entresto.* US: Four patents on combination (2023) (4); two patents on complex (2026; 2027); RDP (2020). EU: Patent on combination (2023), SPC (2028); patent on complex (2026), SPC (2030); RDP (2025). Japan: Patent on combination (2023); patent on complex (2026); patent on formulation (2028). There is currently no generic competition in the US, EU or Japan. The EU complex patent is being opposed in the EPO.

Established Medicines

• *Galvus* and *Eucreas*. EU: Patent on compound (2019), SPC (2022); patent on combination (2021), SPC (2022); patent on *Galvus* formulation (2025); patent on *Eucreas* formulation (2026). Japan: Patent on compound (2019), PTE on mono therapy and combinations with sulfonyureas (2024), PTE on combinations with other antidiabetics (2022), PTE on *Eucreas* combination (2024); patent on combination (2021); patent on *Galvus* formulation (2025), PTE (2025); patent on *Eucreas* formulation (2026), PTE (2028); *Eucreas* RDP (2019). *Galvus/Eucreas* is not marketed in the US. There is generic competition for *Galvus* and *Eucreas* in some EU countries. There is currently no generic competition in Japan. The EU *Eucreas* formulation patent is being opposed in the EPO.

• *Diovan* and *Co-Diovan/Diovan HCT. Diovan*: There is generic competition in the US, EU and Japan.
Co-Diovan/Diovan HCT: There is generic competition in the US, EU and Japan.

• *Exforge* and *Exforge HCT.*
Exforge. US: Patent on *Exforge* combination (2019). EU: Patent on *Exforge* combination/*Exforge HCT* combination (2019), SPC (2021). There is generic competition in the US, EU and Japan. The EU *Exforge* combination/*Exforge HCT* combination patent is being challenged in the EPO and in the patent offices and courts of some EU countries. In the EU, Novartis has resolved patent litigation with certain generic manufacturers. Novartis is taking steps to enforce the EU *Exforge* combination/*Exforge HCT* combination patent against generic manufacturers.
Exforge HCT. US: Patent on *Exforge HCT* combination (2023); patent on formulation (2023). EU: patent on *Exforge* combination/*Exforge HCT* combination (2019), SPC (2021); RDP (2019). Japan: Patent on *Exforge HCT* combination (2023). There is generic competition in the US. There is currently no generic competition in the EU. *Exforge HCT* is not currently marketed in Japan. The EU *Exforge* combination/*Exforge HCT* combination patent is being challenged in the EPO and in the patent offices and courts of some EU countries. In the EU, Novartis has resolved patent litigation with certain generic manufacturers.

• *Zortress/Certican*. US: Patent on compound (2014), PTE (2019), PE (2020); patent on dispersible tablet formulation (2022), PE (2023); patent on antioxidant (2019); patent on antioxidant (2019), PE (2020); EU: Patent on dispersible tablet formulation (2022); patent on antioxidant (2019). Japan: Patent on dispersible tablet formulation (2022); patent on antioxidant (2019). There is currently no generic competition in the US, EU or Japan. In the US, the compound patent is being challenged in ANDA proceedings against generic manufacturers.

• *Neoral.* There is no patent protection for *Neoral* in the US, EU or Japan. There is generic competition in the US, EU and Japan.

Compounds in development

We provide the following information for non-marketed compounds in development that have been filed with the FDA and/or the EMA for registration but have not yet been approved by either agency for any indication.

• AVXS-101 (onasemnogene abeparvovec-xxxx, *Zolgensma*). US: Patent on vector (2026). EU: Two patents on vector (2024, 2028); patent on method of treatment (2028). Japan: Patent on vector (2024); two patents on method of treatment (2028, 2028).

• BAF312 (siponimod, *Mayzent*). US: Patent on compound (2024); patent on dosage regimen (2030). EU: Patent on compound (2024); patent on solid form (2029); patent on dosage regimen (2029). Japan: Patent on compound (2024); patent on solid form (2029); patent on dosage regimen (2029); two patents on formulation (2032).
• BYL719 (alpelisib). US: Patent on compound (2029); patent on compound and method of treatment (2030). EU: Patent on compound and method of treatment (2029). Japan: Patent on compound and method of treatment (2029).
• LCI699 (osilodrostat). US: Patent on compound (2028), patent on method of treatment (2031), patent on tablet form (2035). EU: Patent on compound (2026), patent on method of treatment (2031); patent on polymorph compound form (2033); patent on tablet form (2035). Japan: Patent on compound (2026), patent on method of treatment (2031); patent on polymorph compound form (2033).

Sandoz

Our Sandoz Division is a global leader in generic pharmaceuticals and biosimilars and sells products in well over 100 countries. In 2018, the Sandoz Division achieved consolidated net sales of USD 9.9 billion, representing 19% of the Group's total net sales. Sandoz develops, manufactures and markets finished dosage form medicines as well as intermediary products including active pharmaceutical ingredients.
Sandoz is organized globally into three franchises: Retail Generics, Anti-Infectives and Biopharmaceuticals. In Retail Generics, Sandoz develops, manufactures and markets active ingredients and finished dosage forms of pharmaceuticals to third parties. Retail Generics includes the areas of cardiovascular, central nervous system, dermatology, gastrointestinal and hormonal therapies, metabolism, oncology, ophthalmics, pain and respiratory, as well as finished dosage form anti-infectives sold to third parties. In Anti-Infectives, Sandoz manufactures and supplies active pharmaceutical ingredients and intermediates – mainly antibiotics – for internal use by Retail Generics and for sale to third-party customers. In Biopharmaceuticals, Sandoz develops, manufactures and markets protein- or other biotechnology-based products, including biosimilars, and provides biotechnology manufacturing services to other companies.
The Sandoz strategic goal is to be a leader in off-patent medicines, driving sustainable and profitable growth. The divisional strategy focuses simultaneously on two pillars: leading the development of an emerging segment of the healthcare market between innovation-driven originator medicines and cost-driven commodity generic medicines, such as biosimilars, complex generics, value-added medicines and digital therapeutics, and excellence in the development, manufacturing and marketing of medicines in selected parts of the standard generics segment.
Sandoz executes on its divisional strategy by focusing on several key priorities, including investing in key markets and therapeutic areas where it is best positioned to make a real difference, increasing the performance of its small-molecule Development and Regulatory organization, and maximizing opportunities in biosimilars. Sandoz also focuses on products that can add more value for patients, payers and healthcare professionals than standard generics, including seeking opportunities to leverage digital therapeutics.
In 2018, in a key strategic step to evolve the Sandoz portfolio toward more differentiated products, Novartis announced an agreement to sell selected portions of its Sandoz US portfolio, specifically the Sandoz US dermatology business and generic US oral solids portfolio, to Aurobindo Pharma USA Inc., for USD 0.9 billion in cash plus USD 0.1 billion in potential earn-outs. The Sandoz US portfolio to be sold to Aurobindo includes approximately 300 products, as well as additional development projects. The sale includes the Sandoz US generic and branded dermatology businesses as well as its dermatology development center. As part of the transaction, Aurobindo agreed to acquire the manufacturing facilities in Wilson, North Carolina, as well as Hicksville, New York, and Melville, New York. These businesses had net sales of approximately USD 1.2 billion in 2018. The transaction is expected to close in the course of 2019 following the satisfaction of customary closing conditions.
Sandoz has a strong and continued strategic focus on biosimilars, which it began developing in 1996 and today sells in more than 80 countries. Sandoz is a market leader in biosimilars, with a total of eight approved and marketed products. Availability of our biosimilars varies by country.
We launched *Hyrimoz* (biosimilar adalimumab) in the EU in October 2018, and *Zessly* (biosimilar infliximab) in the EU in November 2018. *Hyrimoz* was also approved in the US in October 2018. However, under the terms of our settlement with AbbVie, we are not entitled to launch *Hyrimoz* in the US until October 2023. Please see "—Item 4.B Business overview—Sandoz—Intellectual property" below for additional information.

The FDA approved biosimilar *Erelzi* (etanercept-szzs) in 2016 to treat multiple inflammatory diseases. The launch of this biosimilar in the US is pending litigation with Amgen, which markets Enbrel®.

Our biosimilar pegfilgrastim was approved and launched in the EU as *Ziextenzo* in November 2018, and we plan to submit additional data for biosimilar pegfilgrastim to the FDA in 2019 to address a complete response letter (CRL) received from the FDA in June 2016.

We received a CRL from the FDA in May 2018 for our biosimilar rituximab, and subsequently announced in November 2018 that we do not plan to pursue our submission for biosimilar rituximab in the US at this time.

Separately, we received a CRL from the FDA in 2018 for our submission for a generic form of fluticasone propionate and salmeterol inhalation powder, for oral inhalation (GSK's Advair®).

According to IQVIA (formerly IMS Health), as of November 2018, Sandoz holds a leading global position in sales of biosimilars and of generic anti-infectives and oncology medicines. In addition, Sandoz holds leading global positions in key therapeutic areas, including generic cardiovascular, central nervous system, gastrointestinal, metabolism, pain and respiratory medicines.

In 2018 and January 2019, key Retail Generics product launches in the US included *Glatopa* 40 mg/mL (generic Copaxone® 40 mg/mL), palonesetron hydrochloride injection (generic Aloxi®), generic bupropion XL, and *SYMJEPI* (epinephrine) 0.15 mg injection (pediatric formulation), as well as innovative digital therapeutics *reSET* and *reSET-O* (together with Pear Therapeutics).

In 2018, Retail Generics product launches in various European countries included generic versions of rosuvastatin film-coated tablets, ezetimide and simvastatin film-coated tablets, and ezetimide film-coated tablets, as well as buprenorphine and naloxone sublingual tablets.

Following an internal reorganization announced on January 27, 2016, 19 mature products were transferred from our Innovative Medicines Division to the Retail Generics franchise of Sandoz.

Sandoz also holds operational responsibility for the Novartis Social Business unit. Novartis Social Business aims to help improve public health in lower-income countries by developing novel, sustainable business models that enable access to high-quality medicines against infectious and chronic diseases while also strengthening healthcare capacity. Everything Novartis Social Business does is rooted in the local communities it serves and relies on its network of partners who share the same purpose. The unit comprises several legacy programs (Novartis Access, the Novartis Malaria Initiative, and Novartis Healthy Family) supported by digital enabling platforms, and has full responsibility for the entire Novartis product range for seven countries in Asia and Africa. For additional information, see "—Item 4.B Business overview—Overview—Corporate responsibility."

New products

Sandoz launched a number of products in various countries in 2018 and January 2019, including:

- *reSET* (FDA-authorized prescription digital therapeutic for the treatment of patients with substance use disorder in the US)
- *reSET-O* (FDA-cleared prescription digital therapeutic for the treatment of patients with opioid use disorder in the US)
- *Ziextenzo* (biosimilar pegfilgrastim), approved in Europe in 2018 to reduce the duration of neutropenia and incidence of febrile neutropenia in adult patients treated with cytotoxic chemotherapy for malignancy with the exception of chronic myeloid leukemia and myelodysplastic syndromes
- *Hyrimoz* (biosimilar adalimumab), approved in Europe in 2018 to treat multiple inflammatory diseases
- *Zessly* (biosimilar infliximab), approved in Europe in 2018 to treat multiple immunological diseases
- *Glatopa* 40 mg/mL (generic Copaxone® 40 mg/mL)
- Palonesetron hydrochloride injection
- Bupropion XL
- Rosuvastatin film-coated tablets
- Ezetimide and simvastatin film-coated tablets
- Ezetimide film-coated tablets
- Buprenorphine and naxolone sublingual tablets

Key marketed products

Sandoz markets approximately 1 000 molecules in countries around the world. The following are some of the Sandoz key marketed products in each of its franchises (availability varies by market):

Retail Generics

Product	Originator drug	Description
Amoxicillin/clavulanic acid	Augmentin®	Antibiotic
Cyclophosphamide	Endoxan®	Breast, ovarian and non-small cell cancer treatment
Leuprorelin	Various	Hormonal treatment
Levothyroxine sodium	Synthroid®; Levoxyl®	Hypothyroidism treatment
Potassium	Klor-Con®	Hypokalemia treatment

Zoledronic acid 64	Aclasta	Osteoporosis treatment

Anti-Infectives

Active ingredients	Description
Oral and sterile penicillins	Anti-infectives
Oral and sterile cephalosporins	Anti-infectives
Clavulanic acid and mixtures with clavulanic acid	ß-lactam inhibitors
Classical and semisynthetic erythromycins	Anti-infectives

Intermediates	Description
Various cephalosporin intermediates	Anti-infectives
Erythromycin base	Anti-infectives
Various crude compounds produced by fermentation	Cyclosporine, ascomysin, rapamycin, mycophenolic acid, etc.

Biopharmaceuticals

Product	Originator drug	Description
Omnitrope	Genotropin®	Recombinant human growth hormone
Binocrit and Epoetin alfa *Hexal*	Eprex®/Erypo®	Recombinant protein used for anemia
Zarzio, Zarxio and *Filgrastim Hexal*	Neupogen®	Recombinant protein used in oncology
Glatopa	Copaxone®	Treatment for multiple sclerosis (MS)
Erelzi	Enbrel®	Treatment for multiple inflammatory diseases
Rixathon	MabThera®	Treatment for blood cancers and immunological diseases
Hyrimoz	Humira®	Treatment for multiple inflammatory diseases
Zessly	Remicade®	Treatment for gastroenterological, rheumatological and dermatological diseases
Ziextenzo	Neulasta®	Treatment to reduce duration of chemotherapy-induced neutropenia and incidence of chemotherapy-induced febrile neutropenia with the exception of chronic myeloid leukemia and myelodysplastic syndromes

Biosimilars in Phase III development and registration

The following table describes Sandoz biosimilar projects that are in Phase III clinical trials (including filing preparation) and registration:

Project/ product	Common name	Mechanism of action	Potential indication/indications	Therapeutic areas	Route of administration	Current phase
GP2017	adalimumab	TNF- inhibitor	Arthritides (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis), plaque psoriasis and others (same as originator)	Immunology	Subcutaneous	EU: Approved US: Registration
LA-EP2006	pegfilgrastim	Pegylated granulocyte colony-stimulating factor	Chemotherapy-induced neutropenia and others (same as originator)	Oncology	Subcutaneous	EU: Approved US[1]: Registration

[1] Resubmission planned for 2019 to address FDA complete response letter received June 2016

Principal markets

The two largest generics markets in the world – the US and Europe – are the principal markets for Sandoz. The following table sets forth the aggregate 2018 net sales of Sandoz by region:

Sandoz

	2018 net sales to third parties	
	USD millions	%

Europe	4 963	50
United States	2 754	28
Asia, Africa, Australasia	1 363	14
Canada and Latin America	779	8
Total	9 859	100
Of which in Established Markets *	7 233	73
Of which in Emerging Growth Markets *	2 626	27

* Emerging Growth Markets comprise all markets other than the Established Markets of the US, Canada, Western Europe, Japan, Australia and New Zealand.

Many Sandoz products are used for chronic conditions that require patients to consume the product over long periods of time, from months to years. Sales of our anti-infective products and over-the-counter cough and cold products are subject to seasonal variation. Sales of the vast majority of our other products are not subject to material changes in seasonal demand.

Production

The primary goal of our manufacturing and supply chain management program is to ensure the uninterrupted, timely and cost-effective supply of products that meet all product specifications and quality standards. The manufacture of our products is heavily regulated by governmental health authorities around the world, including the FDA and EMA. In addition to regulatory requirements, many of our products involve technically complex manufacturing processes or require a supply of highly specialized raw materials.

We manufacture our products at facilities worldwide. See also "—Item 4.D Property, plants and equipment." Active pharmaceutical ingredients are manufactured in our own facilities or purchased from third-party suppliers. We maintain state-of-the-art and cost-competitive processes, with quality as a primary goal within our own production network. Those processes include fermentation, chemical syntheses and precipitation processes, as well as sterile processing. Many biologic medicines are manufactured using recombinant DNA-derived technology, by which a gene is introduced into a host cell, which then produces a human protein. This manufacturing process requires sophisticated technical expertise. We are constantly working to improve current, and develop new, manufacturing processes, and to review and adapt our manufacturing network to meet the needs of our Sandoz Division.

Raw materials for the manufacturing process are either produced in-house or purchased from a number of third-party suppliers. Where possible, we maintain multiple supply sources so that the business is not dependent on a single or limited number of suppliers. However, our ability to do so may at times be limited by regulatory or other requirements. We monitor market developments that could have an adverse effect on the supply of essential materials. Our suppliers of raw materials are required to comply with Novartis quality standards.

Because the manufacture of our products is complex and heavily regulated by governmental health authorities, supply is never guaranteed. If we or our third-party suppliers fail to comply with applicable regulations, then there could be a product recall or other shutdown or disruption of our production activities. We have experienced supply interruptions for our products in the past, and there can be no assurance that supply will not be interrupted again in the future. We have implemented a global manufacturing strategy to maximize business continuity in case of such events. However, there can be no guarantee that we will always be able to successfully manage such issues when they arise.

Due to impurities found in valsartan, losartan, and ibersartan active ingredient batches sourced from a third party manufacturer, we recalled Sandoz valsartan, losartan and ibersartan products in the third and fourth quarters of 2018 in several countries, in line with our quality standards for all of our marketed products, and in agreement with local health authorities.

Marketing and sales

Sandoz sells a broad portfolio of products, including the products of our Retail Generics franchise and biosimilars, to wholesalers, pharmacies, hospitals and other healthcare outlets. Sandoz adapts its marketing and sales approach to local decision-making processes, depending on the structure of the market in each country.

In response to rising healthcare costs, many governments and private medical care providers, such as health maintenance organizations, have instituted reimbursement schemes that favor the substitution of bioequivalent generic versions of originator pharmaceutical products, such as those sold by our Retail Generics franchise. In the US, statutes have been enacted by all states that permit or require pharmacists to substitute a less expensive generic product for the brand-name version of a drug that has been prescribed to a patient. Generic use is growing in Europe, but penetration rates in many EU countries (as a percentage of volume) remain well below those in the US.

Recent trends have been toward continued consolidation among distributors and retailers of Sandoz products, both in the US and internationally, which has increased our customers' purchasing leverage.

Legislative or regulatory changes can have a significant impact on our business in a country. In Germany, for example, healthcare reforms have increasingly shifted decision-making from physicians to insurance funds.

Our Anti-Infectives franchise supplies active pharmaceutical ingredients and intermediates – mainly antibiotics – for internal use by Retail Generics and for sale to the pharmaceutical industry worldwide.

Our Biopharmaceuticals franchise operates in an emerging business environment, particularly in the US. Regulatory pathways for approving biosimilar products are either relatively new or still in development, and policies have not yet

been fully defined or implemented for the automatic substitution and reimbursement of biosimilars in many markets, including the US. As a result, in many of these markets, our biosimilar products are marketed as branded competitors to the originator products.

Competition

The market for generic products is characterized by increasing demand for high-quality pharmaceuticals that can be marketed at lower costs due to comparatively minimal initial research and development investments. Increasing pressure on healthcare expenditures and numerous patent and data exclusivity period expirations have encouraged more generic product launches,

resulting in increased competition among the companies selling generic pharmaceutical products, leading to ongoing price pressure. In particular, Sandoz faces increased industrywide pressure on prices for generic products, particularly in the US, driven by factors including customer consolidation and growing competition from other manufacturers of generic medicines. These factors contributed to a decline in US sales that began in 2017 and continued in 2018.

In addition, research-based pharmaceutical companies are participating directly in the generic conversion process by licensing their patented products to generic companies (so-called “authorized generics”). Consequently, generic companies that were not otherwise in a position to launch a specific product may participate in the market using the innovator’s product authorization. Authorized generics serve as a business opportunity for Sandoz when the product of a research-based pharmaceutical company loses patent protection and Sandoz secures a license from the research-based pharmaceutical company to launch the authorized generic of that product.

Development and registration

Development of Sandoz Biopharmaceuticals products is jointly overseen by Sandoz and by Novartis Global Drug Development. Development and registration activities for Retail Generics products, and certain registration activities for Biopharmaceuticals products, continue to be overseen directly by Sandoz.

Before a generic pharmaceutical may be marketed, intensive technical and clinical development work must be performed to demonstrate, in bioavailability studies, the bioequivalence of the generic product to the reference product. Nevertheless, research and development costs associated with generic pharmaceuticals generally are much lower than those of the originator pharmaceuticals, as no preclinical studies or clinical trials on dose finding, safety and efficacy must be performed by the generic company. As a result, generic pharmaceutical products can be offered for sale at prices often much lower than those of products protected by patents and data exclusivity, which must recoup substantial research and development costs through higher prices over the life of the product’s patent and data exclusivity period.

While generic pharmaceuticals are follow-on versions of chemically synthesized molecules, biosimilar products contain a version of the active substance of an already approved biological reference medicine. Due to the inherent variability and complexity of biologic products, including batch-to-batch differences and variations following manufacturing changes, the development and the regulatory pathway of biosimilars differ significantly from that of generics.

The development of a biosimilar product is much more technically challenging than the development of a typical generic pharmaceutical. While generic pharmaceuticals normally do not require clinical studies in patients, regulators worldwide do require such targeted studies for biosimilar products. Biosimilars are engineered to match the reference medicine in quality, safety and efficacy. This is achieved by systematically defining the target range of the reference medicine and then comparing the biosimilar to the reference medicine at various development stages to confirm biosimilarity and to establish that there are no clinically meaningful differences between the proposed biosimilar and the reference biologic. Because the purpose of a biosimilar clinical development program is to confirm biosimilarity and not to establish efficacy and safety de novo, the clinical studies required are less than those required for a reference biologic. Therefore, the cost of development for a biosimilar is usually less than that of a reference biologic.

The Development and Registration staff employed by affiliates of the Sandoz Division are based worldwide, including at facilities in Holzkirchen, Germany; Rudolstadt, Germany; Kundl, Austria; Ljubljana, Slovenia; Melville, New York; and Hicksville, New York. In 2018, the divestment of the Boucherville, Canada, development (and associated manufacturing) facility to Avara Pharmaceutical Services was announced and subsequently completed, including a long-term agreement to secure supply of key products to the Canadian market. Also in 2018, Sandoz announced the planned opening of a new development center in Hyderabad, India, initially focused on oral solid medicines.

Regulation

Generics

The Hatch-Waxman Act in the US (and similar legislation in the EU and in other countries) eliminated the requirement that manufacturers of generic pharmaceuticals repeat the extensive clinical trials required for reference products, so long as the generic version could be shown in bioequivalence studies to be of identical quality and purity, and to be therapeutically equivalent to the reference product.

In the US, the decision on whether a generic pharmaceutical is bioequivalent to the original patented product is made by the FDA based on an Abbreviated New Drug Application (ANDA) filed by the generic product’s manufacturer. The process typically takes nearly two years from the filing of the ANDA until FDA approval. However, delays can occur

if issues arise regarding the interpretation of bioequivalence study data, labeling requirements for the generic product, or qualifying the supply of active ingredients. In addition, the Hatch-Waxman Act requires a generic manufacturer to certify in certain situations that the generic product does not infringe on any current applicable patents on the product held by the holder of the marketing authorization for the reference product, or to certify that such patents are invalid or that the product is non-infringing. This certification often results in a patent infringement lawsuit being brought by the patent holder against the generic company. In the event of such a lawsuit, the Hatch-Waxman Act imposes an automatic 30-month delay in the approval of the generic product to allow the parties to resolve the intellectual property issues. For generic applicants who are the first to file their ANDA containing a certification claiming non-infringement or patent invalidity, the Hatch-Waxman Act provides those applicants with

180 days of marketing exclusivity to recoup the expense of challenging the patents on the reference product. However, generic applicants must launch their products within certain timeframes or risk losing the marketing exclusivity that they had gained by being a first-to-file applicant.

In the EU, decisions on the granting of a marketing authorization are made either by the European Commission based on a positive recommendation by the EMA under the centralized procedure, or by a single member state under the national or decentralized procedure. See "—Innovative Medicines—Regulation—European Union." Companies may submit Abridged Applications for approval of a generic medicinal product based upon its "essential similarity" to a medicinal product authorized and marketed in the EU following the expiration of the product's data exclusivity period. In such cases, the generic company is able to submit its Abridged Application based on the data submitted by the innovator company for the reference product, without the need to conduct extensive Phase III clinical trials of its own. For all products that received a marketing authorization in the EU after late 2005, the Abridged Application can be submitted throughout the EU. However, the data submitted by the innovator company in support of its application for a marketing authorization for the reference product will be protected for 10 years after the first grant of marketing authorization in all member states, and can be extended for an additional year if a further innovative indication has been authorized for that product, based on preclinical and clinical trials filed by the innovator company that show a significant clinical benefit in comparison to the existing therapies.

Biosimilars

The regulatory pathways for approval of biosimilar medicines are still being developed and established in many countries of the world. A regulatory framework for the approval of biosimilars has been established in the EU, Japan, Canada and the US, while the World Health Organization (WHO) has issued guidance. Sandoz has successfully registered and launched the first biosimilar (or biosimilar-type) medicine in Europe, the US, Canada, Japan, Taiwan, Australia, and many countries in Latin America and Asia. Sandoz was the first company to secure approval for and launch a biosimilar under the US biosimilar pathway that was established as part of the Biologics Price Competition and Innovation Act (BPCIA).

The approval of biosimilars in Europe follows a process similar to that followed for small molecules. However, biosimilars usually have to be approved through the centralized procedure because they are manufactured using recombinant DNA technology. As part of the approval process in the EU, biosimilars have to demonstrate comparability to the reference medicine in terms of safety, efficacy and quality through an extensive comparability exercise, based on strict guidelines set by the authorities. Regulators will only approve a biosimilar based on data that allows the regulators to conclude that there are no clinically meaningful differences between the reference medicine and the biosimilar.

In the US, under the BPCIA, a biosimilar must be highly similar with no clinically meaningful differences compared to the reference medicine. Approval of a biosimilar in the US requires the submission of a BLA to the FDA, including an assessment of immunogenicity, and pharmacokinetics or pharmacodynamics. The BLA for a biosimilar can be submitted as soon as four years after the initial approval of the reference biologic, but can only be approved 12 years after the initial approval of the reference biologic. This pathway is still relatively new, and some aspects remain untried and controversial.

Intellectual property

We take all reasonable steps to ensure that our products do not infringe valid intellectual property rights held by others. Nevertheless, competing companies commonly assert patent and other intellectual property rights. As a result, we can become involved in significant litigation regarding our products. If we are unsuccessful in defending these suits, we could be subject to injunctions preventing us from selling our products and to potentially substantial damages.

Wherever possible, our products are protected by our own patents. Among other things, patents may cover the products themselves, including the product's formulation, or the processes for manufacturing a product. However, there can be no assurance that our intellectual property will protect our products or that we will be able to avoid adverse effects from the loss of intellectual property protection in the future.

In October 2018, Sandoz announced a global resolution of all intellectual property-related litigation with AbbVie concerning adalimumab. Under the terms of the agreement, AbbVie grants Sandoz a non-exclusive license to AbbVie's intellectual property relating to Humira®, beginning on certain dates in certain countries in which AbbVie has intellectual property. Sandoz will pay royalties to AbbVie for licensing its Humira® patents. AbbVie will make no

payments to Sandoz.

Alcon

Our Alcon Division, a global leader in eye care, researches, develops, manufactures, distributes and sells eye care products. Its products are sold in more than 140 countries. In 2018, the Alcon Division had consolidated net sales of USD 7.1 billion, representing 14% of total Group net sales.

To meet the needs of patients, ophthalmologists, surgeons, optometrists, opticians and physician specialists, Alcon operates with two global business franchises: Surgical and Vision Care. Each business franchise operates with specialized sales forces and marketing support.

In November 2018, Novartis announced that Alcon had filed an initial Form 20-F registration statement with the SEC in relation to the previously announced intention of Novartis to spin off our Alcon Division as an

independent, publicly traded company. An application will be made to list the shares in Alcon on SIX and the NYSE under the ticker symbol “ALC.” In addition to shareholder approval, completion of the proposed Alcon spin-off remains subject to certain conditions precedent, such as no material adverse events, receipt of necessary authorizations as well as tax rulings and opinions. If approvals are secured and conditions are met, the spin-off is expected to be completed in the first half of 2019.

Effective January 1, 2018, we transferred our over-the-counter ophthalmic products and certain surgical diagnostic products from the Innovative Medicines Division to the Alcon Division. Our prescription ophthalmic medicines business remains with the Innovative Medicines Division. In compliance with IFRS, beginning with our first-quarter 2018 results, Novartis updated its segment financial information to reflect this transfer, both for the current and prior years, to aid comparability of year-on-year results. The products of the Ophthalmic Pharmaceuticals franchise of Alcon had previously been transferred to our Innovative Medicines Division following an internal reorganization announced on January 27, 2016.

In April 2016, Alcon entered into a strategic alliance with PowerVision to develop an accommodating intraocular lens (IOL) that has the potential to change focus via a fluid-driven shape-changing technology.

In December 2018, Alcon acquired 100% of TrueVision, the manufacturer of *NGENUITY*, a 3-D visualization system that combines a high-dynamic 3-D camera, advanced high-speed image optimization, polarizing surgeon glasses, and an ultra-high-definition 4K OLED 3-D display to create a platform for digitally assisted vitreoretinal surgery to help improve visualization of the delicate tissues in the back of the eye. Alcon has distributed *NGENUITY* since February 2016 under an exclusive agreement with TrueVision.

In December 2018, Alcon acquired 100% of Tear Film Innovations, Inc., for its *iLux* Device, a therapeutic device used to treat meibomian gland dysfunction (MGD), a leading cause of dry eye.

Alcon Division products

Surgical

Our Alcon Division’s Surgical franchise is the leader in global ophthalmic surgical product sales, offering implantable products, consumables, instruments and equipment for use in surgical procedures to address cataracts, vitreoretinal conditions, refractive errors and glaucoma. We also offer service on the equipment we sell.

The Alcon Surgical portfolio includes IOLs and equipment for use in cataract procedures; equipment, instruments and devices for use in vitreoretinal surgeries; surgical equipment and diagnostic devices used in refractive surgical procedures; and devices for use in treating patients with glaucoma. Our IOL portfolio includes our *Clareon* and *AcrySof* IOL families, with options ranging from monofocal IOLs for basic cataract surgery to specialized IOLs for the correction of presbyopia and astigmatism at the time of cataract surgery; as well as the *UltraSert* and *AutonoMe* innovative IOL delivery systems. The Cataract Refractive Suite by Alcon features the *Centurion* vision system for phacoemulsification and cataract removal; the *Infiniti* vision system for phacoemulsification and cataract removal; the *LenSx* femtosecond laser used for specific steps in the cataract surgical procedure; the *LuxOR* ophthalmic microscope; the *ORA SYSTEM* technology for cataract surgery planning and intra-operative guidance during surgery; and the *Verion* imaged guided system for use during cataract surgery. The Alcon vitreoretinal portfolio includes the *NGENUITY* 3D visualization system, designed to enhance visualization of the back of the eye, and the *Constellation* vision system and associated handpieces and instruments. Our *WaveLight* devices are used for LASIK and other vision-correcting refractive procedures, including topography-guided procedures marketed under the *Contoura* brand. For glaucoma surgery, Alcon offers the *EX-PRESS* glaucoma filtration device, and formerly distributed the *CyPass* Micro-Stent. However, in August 2018, Alcon voluntarily withdrew the *CyPass* Micro-Stent from the global market based on analysis of five-year post-surgery data from the COMPASS-XT long-term safety study. In addition, Alcon provides advanced viscoelastics, surgical solutions, diagnostic ophthalmic products, surgical packs, and other disposable products for cataract and vitreoretinal surgery.

Vision Care

Our Alcon Division’s Vision Care franchise develops and markets contact lenses and ocular health products. Alcon’s broad portfolio of silicone hydrogel, daily disposable and color contact lenses includes our *Dailies, Air Optix* and *Freshlook* brands. Our *Dailies* product line includes the *Dailies Total1* lens, a first-of-its-kind water gradient contact lens that is also offered in a multifocal option for patients with presbyopia. Our *Air Optix* monthly replacement product line features silicone hydrogel contact lenses in monofocal, astigmatism-correcting and multifocal options, as well as *Air Optix* Colors and *Air Optix* plus *HydraGlyde* contact lenses. Our contact lens care solutions business

includes the *Opti-Free* line of multipurpose disinfecting solutions, as well as the *Clear Care* and *AOSEPT* Plus line of hydrogen peroxide lens care solutions. Over-the-counter ophthalmic products that have moved from our Innovative Medicines Division to the Alcon Vision Care franchise include artificial tear and related dry eye products marketed under the *Systane*, *Tears Naturale* and *Genteal* brands; *Naphcon A* and *Zaditor* eye drops for the temporary relief of ocular itching due to allergies; and vitamins for ocular health, marketed under the *ICAPS* and *Vitalux* brands. With the acquisition of Tear Film, the Alcon Vision Care portfolio also includes the *iLux* Device, a therapeutic device used to treat MGD, a leading cause of dry eye.

New products

We received a number of approvals and launched a number of products in 2018, including:

• *Systane* Complete was launched in the US and EU. This addition to the *Systane* product line offers fast hydration and lasting relief, with nano droplet technology for enhanced coverage.

• *Air Optix* plus *HydraGlyde* multifocal contact lenses launched in the US and EU. These lenses offer clear, seamless vision at all distances and combine the innovative *Air Optix* multifocal design with lasting lens surface moisture provided by the *HydraGlyde* moisture matrix.

Key marketed products

The following tables set forth certain key marketed products in our Alcon Division. While we intend to sell our marketed products throughout the world, not all products and indications are currently available in every country.

Surgical	
Cataract	*AcrySof* family of IOLs, including:
	AcrySof IQ monofocal IOLs
	AcrySof IQ Toric astigmatism-correcting IOLs
	AcrySof IQ *ReSTOR* presbyopia-correcting IOLs
	AcrySof IQ *ReSTOR* Toric presbyopia- and astigmatism-correcting IOLs
	AcrySof IQ *PanOptix* presbyopia-correcting IOLs
	AcrySof IQ *PanOptix* Toric presbyopia- and astigmatism-correcting IOLs
	AutonoMe pre-loaded IOL delivery system
	Cataract Refractive Suite by Alcon, including:
	Centurion vision system for phacoemulsification and cataract removal
	Infiniti vision system for phacoemulsification and cataract removal
	LenSx femtosecond laser used for specific steps in the cataract surgical procedure
	LuxOR ophthalmic microscope
	ORA SYSTEM technology for cataract surgery planning and intra-operative guidance during surgery
	Verion imaged-guided system for use during cataract surgery
	Clareon monofocal IOLs
	UltraSert pre-loaded IOL delivery system
Vitreoretinal	*Constellation* vision system for vitreoretinal operations
	Grieshaber surgical instruments
	NGENUITY 3D visualization system
	Purepoint laser system and probes
	Ultravit vitrectomy probes
Refractive	*WaveLight EX500* excimer laser for LASIK and other refractive correction procedures
	WaveLight FS200 femtosecond laser for refractive surgery
Glaucoma	*EX-PRESS* glaucoma filtration device

In addition, Alcon provides advanced viscoelastics, surgical solutions, surgical packs, diagnostic ophthalmics, and other disposable products for cataract and vitreoretinal surgery.

Vision Care	
Contact lenses	*Air Optix* family of silicone hydrogel contact lenses (including *Air Optix* Colors and *Air Optix* plus *HydraGlyde* lenses)
	Dailies family of daily disposable contact lenses (including *Dailies Total1* lenses)
	FreshLook family of color contact lenses
Contact lens care	*Clear Care* family of hydrogen peroxide lens care solution (*AOSEPT* Plus outside of North America)
	Opti-Free family of multipurpose disinfecting solution
Dry eye	*Genteal* family of artificial tears
	Systane family of artificial tears and related dry eye products
	Tears Naturale lubricant eye drops
	iLux Device for the treatment of MGD, a leading cause of dry eye

Allergy	*Naphcon A* for the temporary relief of ocular redness and itching due to allergies
	Zaditor for the temporary relief of ocular itching due to allergies
Vitamins	*ICAPS* and *Vitalux* families of eye vitamin products

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Principal markets

The principal markets for our Alcon Division include North America, Latin America, Japan, Asia and Europe. The following table sets forth the aggregate 2018 net sales of the Alcon Division by region:

Alcon

	2018 net sales to third parties	
	USD millions	%
Europe	1 805	25
United States	2 942	41
Asia, Africa, Australasia	1 781	25
Canada and Latin America	621	9
Total	7 149	100
Of which in Established Markets *	5 395	75
Of which in Emerging Growth Markets *	1 754	25

* Emerging Growth Markets comprise all markets other than the Established Markets of the US, Canada, Western Europe, Japan, Australia and New Zealand.

Sales of the vast majority of our Alcon Division products are not subject to material changes in seasonal demand. However, sales of certain of our Vision Care products, including those for allergies and dry eye, are subject to seasonal variation.

Research and development

Alcon has made one of the largest commitments to research and development in the eye care devices market, with proven R&D capabilities in the areas of optical design, material and surface chemistry, automation and equipment platforms. Currently, our Alcon Division research and development organization employs over 1 200 individuals dedicated to its research and development efforts, including physicians, doctors of optometry, and Ph.Ds. Alcon researchers have extensive experience in the field of ophthalmology and frequently have academic or practitioner backgrounds to complement their product development experience.

Research and development activities for Alcon's Surgical franchise are focused on expanding intraocular lens capabilities to further improve surgical and refractive outcomes, and on developing equipment and instrumentation for cataract, vitreoretinal, refractive and glaucoma surgeries, as well as new platforms for diagnostics and visualization.

The focus of the Vision Care franchise is on the research and development of new manufacturing platforms, novel contact lens materials, coatings and optical designs for various lens replacement schedules with the ultimate goal of improving patient outcomes, and novel delivery systems that safely deliver products that provide relief from symptoms of dry eye and ocular allergies.

Alcon continues to seek opportunities to collaborate with third parties on advanced technologies for various ophthalmic conditions. These include the potential to provide accommodative contact and intraocular lenses for patients living with presbyopia.

Production

The manufacture of our products is heavily regulated by governmental health authorities around the world, including the FDA. In addition to regulatory requirements, many of our products involve technically complex manufacturing processes or require a supply of highly specialized raw materials. For some products and raw materials, we may also rely on a single source of supply. The combination of these factors means that supply is never guaranteed.

Like some of our competitors, our Alcon Division faces manufacturing issues from time to time. If we or our third-party suppliers fail to comply fully with regulations, then there could be a product recall or other shutdown or disruption of our production activities. There can be no assurance that we will not experience supply interruptions for our products in the future. We have implemented a global manufacturing strategy to maximize business continuity in case of such events. However, there can be no guarantee that we will be able to successfully manage such issues if and when they arise. For additional information on Alcon production facilities, see "Item 4. Information on the Company—Item 4.D Property, plants and equipment."

Marketing and sales

Our Alcon Division conducts sales and marketing activities around the world, organized under five operating regions: Europe (including Russia)/Middle East/Africa, North America, Latin America/Caribbean, Asia and Japan. The Alcon Division's global commercial capability is organized around sales and marketing organizations dedicated to the Surgical and Vision Care franchises.

Most of our global Alcon marketing efforts are supported by advertising in trade publications and by marketing and sales representatives attending regional and national medical conferences. Marketing efforts are reinforced by targeted and timely promotional materials and direct mail to eye care practitioners in the office, hospital or surgery center setting. Technical service after the sale is provided, and an integrated customer relationship management system is in place in many markets. We also rely on direct-to-consumer marketing campaigns to promote selected products.

While our Alcon Division markets all of its products by calling on medical professionals, direct customers and distribution methods differ across business lines. Alcon Surgical products are sold directly to hospitals and ambulatory surgical centers, although Alcon sells through distributors in certain markets outside the US. In most countries, contact lenses are available only by prescription. Our contact lenses can be purchased from eye care professionals, optical chains and large retailers, subject to country regulation. Over-the-counter lens care, dry eye, allergy and ocular vitamin products can be found in major drugstore, food, mass merchandising and optical retail chains globally, subject to country regulations.

Competition

The eye care industry is highly competitive and subject to rapid technological change and evolving industry requirements and standards. Our Alcon Division competes with a number of different companies across its two franchises. Companies within this industry compete on technological leadership and innovation, quality and efficacy of their products, relationships with eye care professionals and healthcare providers, breadth and depth of product offerings, and pricing. The presence of these factors varies across our Alcon Division's product offerings. Our principal competitors also sometimes form strategic alliances and enter into co-marketing agreements in an effort to better compete.

Regulation

Most of our Surgical products and many of our Vision Care products are regulated as medical devices in the US and the EU. These jurisdictions each have risk-based classification systems that determine the type of information that must be provided to the local regulatory bodies in order to obtain the right to market a product. In the US, safety and effectiveness information for Class II and III devices must be reviewed by the FDA. Our Class II and Class III devices typically are subject to one of the following two pre-market review procedures: the Pre-Market Approval (PMA) process typically applies to Class III devices, and the Pre-Market Notification (510(k)) submission process typically applies to Class II devices. Under a PMA, the manufacturer must submit to the FDA supporting evidence sufficient to prove the safety and effectiveness of the device. Under a 510(k) submission, the manufacturer notifies the FDA that it intends to commence marketing the product, with data that establishes the product as substantially equivalent to another already-marketed Class II product.

In the EU, CE marking is required for all medical devices sold. By affixing the CE Mark, the manufacturer certifies that a product is in compliance with provisions of the EU's Medical Device Directive. Most such products are subject to a self-certification process by the manufacturer, which requires the manufacturer to confirm that the product performs to appropriate standards. This allows the manufacturer to issue a Declaration of Conformity and to notify competent authorities in the EU that the manufacturer intends to market the product. In order to comply with European regulations, our Alcon Division maintains a full Quality Assurance system and is subject to routine auditing by a certified third party (a "notified body") to ensure that this quality system is in compliance with the requirements of the EU's Medical Device Directive as well as the requirements of ISO 13485.

Many of our Vision Care dry eye and allergy products are regulated as over-the-counter pharmaceuticals in the US, and several Surgical diagnostic ophthalmic products are regulated as prescription pharmaceuticals in the US and the EU. In the US, over-the-counter pharmaceuticals that comply with the FDA over-the-counter monograph regulations may be marketed without prior FDA approval. Alcon's prescription pharmaceutical products are subject to the same regulatory approval procedures as the prescription pharmaceutical products of our Innovative Medicines Division. See "—Innovative Medicines—Regulation."

Price controls

The prices of our Surgical devices and our drugs that require a prescription are subject to reimbursement programs and price control mechanisms that vary from country to country. Due to increasing political pressure and governmental budget constraints, we expect these programs and mechanisms to remain robust – and to potentially even be strengthened. As a result, such programs and mechanisms could have a negative influence on the prices we are able to charge for our Surgical products, particularly those used in cataract and vitreoretinal surgeries.

For example, in India, the National Pharmaceutical Pricing Authority (NPPA) has imposed 75% to 85% price reductions on coronary stents (implantable medical devices intended to ensure an adequate flow of blood to the heart). The NPPA has begun to evaluate prices on other categories of medical devices, potentially including IOLs used in cataract surgeries. If the NPPA chooses to impose similar price reductions on IOLs from Alcon, this could have a negative impact on our Surgical franchise sales in India. It is also possible that regulatory agencies in other countries may consider applying similar price controls on IOLs and other Surgical products sold by Alcon.

Intellectual property

We strive to protect our investment in the research, development, manufacturing and marketing of our

products through the use of patents, trademarks, copyrights, trade secrets and other intellectual property. In general, we seek intellectual property protection under applicable laws for significant product developments in major markets. Among other things, patents may cover the products themselves, the processes for manufacturing a product, and particular uses of a product.

The protection offered by our intellectual property extends for varying periods, depending on its legal life in the various countries. The protection afforded, which may also vary from country to country, depends upon the type of intellectual property and its scope of coverage. We monitor infringements of our intellectual property and typically challenge such infringements. We also defend challenges through litigation and administrative proceedings to the validity of our intellectual property. However, because the outcomes of intellectual property challenges can be difficult to predict, there can be no assurance that we will be able to successfully protect our intellectual property rights in all cases. If we are unsuccessful in defending such challenges, we may face loss of exclusivity and increased competition in the affected territories. See generally "—Innovative Medicines—Intellectual property."

We take reasonable steps to ensure that our products do not infringe valid intellectual property rights held by others. Nevertheless, third parties may assert patent and other intellectual property rights against our products. As a result, we can become involved in significant intellectual property litigation regarding our products. If we are unsuccessful in defending these suits, we could be subject to injunctions preventing us from selling our products and to damages that may be substantial.

In addition to our patents and pending patent applications in the United States and selected non-US markets, we rely on proprietary know-how and trade secrets in our businesses and work to ensure the confidentiality of this information, including through the use of confidentiality agreements with employees and third parties. In some instances, we also acquire, or obtain licenses to, intellectual property rights that are important to our businesses from third parties.

All of our major Alcon Division products are sold under trademarks that we consider in the aggregate to be important to our Alcon Division business as a whole. We consider trademark protection to be particularly important to the protection of our investment in the sales and marketing of our Vision Care franchise. The scope and duration of trademark protection varies widely throughout the world. In some countries, trademark protection continues only as long as the mark is used. Other countries require the registration of trademarks and the payment of registration fees. Trademark registrations are generally for fixed, but renewable, terms.

We rely on copyright protection in various jurisdictions to protect the software and printed materials our business relies upon, including software used in our surgical and diagnostic equipment. The scope of copyright protection for computer software varies throughout the world, although it is generally for a fixed term that begins on the date of copyright registration.

4.C Organizational structure

Organizational structure

See “Item 4. Information on the Company—Item 4.A History and development of Novartis,” and “Item 4. Information on the Company—Item 4.B Business overview—Overview.”

Significant subsidiaries

See “Item 18. Financial Statements—Note 31. Principal Group subsidiaries and associated companies.”

4.D Property, plants and equipment

Our principal executive offices are located in Basel, Switzerland. Our divisions operate through a number of affiliates that have offices, research and development facilities, and production sites throughout the world.

We generally own our facilities or have entered into long-term lease arrangements for them. Some of our principal facilities are subject to mortgages and other security interests granted to secure indebtedness to certain financial institutions.

Novartis Technical Operations manages the production and supply chains of our Innovative Medicines and Sandoz Division products through a network of 64 manufacturing sites, as well as through external suppliers, and warehouse and distribution centers. Our Alcon Surgical and Vision Care manufacturing sites continue to be managed by the Alcon Division. In addition, following the transition of our over-the-counter ophthalmic products and certain surgical diagnostics products to Alcon, and the overall strategic decision to create greater operational autonomy for our Alcon Division, management of the manufacturing site in Fort Worth, Texas, was transferred back to Alcon on July 1, 2018, and our aseptic manufacturing site in Singapore was transferred to Alcon on January 1, 2019. Our Puurs, Belgium, site will remain within Novartis Technical Operations, with the exception of Alcon *Custom Pak* production and warehousing, which was transferred to Alcon on January 1, 2019. AAA manages four sites for radioligand therapies production, and certain other small sites for diagnostics and enriched water production. AveXis manages five sites for research and development, production, warehousing, its headquarters and administrative offices. Endocyte manages two sites for research and its headquarters and administrative offices.

The following table sets forth our major headquarters and most significant production, research and development, and administrative facilities. See also "—Item 4.B Business overview—Innovative Medicines—Production," "—Item 4.B Business overview—Sandoz—Production" and "—Item 4.B Business overview—Alcon—Production" for a discussion of our manufactu processes.

Major facilities

Location	Size of site (in square meters)	Major activity
Basel, Switzerland – St. Johann	724 000	Global Group headquarters, global Innovative Medicines Division headquarters, research and development, production of drug substances and drug intermediates
Kundl and Schaftenau, Austria	480 000	Production of biotechnological products, drug products and finished products, anti-infectives, active drug substances, product development
East Hanover, New Jersey	391 000	Innovative Medicines Division US headquarters, research and development
Barleben, Germany	340 000	Production of broad range of generics finished dosage forms
Fort Worth, Texas	315 200	Alcon Division US headquarters; production, research and development for Alcon Vision Care and Surgical franchises; Novartis Finance Service Center
Changshu (Suzhou), China	230 000	Technical research, development and manufacturing of drug substances and drug intermediates
Cambridge, Massachusetts	205 000	Research and development
Shanghai, China	106 500	Research and development
Ringaskiddy, Ireland	85 000	Production of drug substances and drug intermediates
Johns Creek, Georgia	84 100	Production, research and development for Alcon Vision Care franchise
Ljubljana, Slovenia	83 000	Production of broad range of finished solid and sterile dosage forms
Hyderabad, India	80 500	General administrative and development global service center
Grosswallstadt, Germany	65 200	Production, research and development for Alcon Vision Care franchise
Stein, Switzerland	64 700	Production of sterile vials, pre-filled syringes and ampoules, and of inhalation capsules, tablets and transdermals, and of active pharmaceutical ingredients
Holzkirchen, Germany	64 200	Sandoz Division global headquarters, production of oral films, transdermal delivery systems, matrix patches, product development
Grimsby, UK	64 000	Production of drug substances and drug intermediates
Menges, Slovenia	62 400	Production of drug substances and drug intermediates
Puurs, Belgium	55 000	Production for Innovative Medicines ophthalmic products and Alcon Surgical franchise
Kurtkoy, Turkey	51 700	Production of Innovative Medicines solids
Stryków, Poland	45 000	Production of broad range of bulk oral solid forms and packaging
Rudolstadt, Germany	44 000	Development and production of respiratory technologies and ophthalmics
Johor, Malaysia	43 900	Production for Alcon Vision Care franchise
Rueil-Malmaison, France	43 700	Administrative offices for Innovative Medicines and Alcon
Irvine, California	40 800	Production, research and development for Alcon Surgical franchise
Torre, Italy	40 100	Production of Innovative Medicines solids
Houston, Texas	37 400	Production for Alcon Surgical franchise
Batam, Indonesia	35 000	Production for Alcon Vision Care franchise
Huningue, France	35 000	Production of drug substances for clinical and commercial supply
Singapore	35 000	Production for Alcon Vision Care franchise and Innovative Medicines solids and biologics
Barbera, Spain	33 000	Production of tablets, capsules and inhalation products
	31 700	Production of drug substances and drug intermediates

Basel, Switzerland – Schweizerhalle		
Wehr, Germany	31 700	Production of tablets and packaging
Huntington, West Virginia	27 500	Production for Alcon Surgical franchise
Tokyo, Japan	26 000	Administrative offices for Innovative Medicines, Sandoz and Alcon
Sasayama, Japan	23 300	Packaging site for Innovative Medicines
Sinking Spring, Pennsylvania	21 800	Production for Alcon Surgical franchise
Morris Plains, New Jersey	15 600	Production for Innovative Medicines Division cell and gene therapies
Princeton, New Jersey	14 300	Sandoz Division US headquarters
Cork, Ireland	13 600	Production for Alcon Surgical franchise
Libertyville, Illinois	9 800	Production, warehouse, and administrative offices for AveXis
Targu Mures, Romania	9 070	Production of solids for Innovative Medicines and Sandoz
Schaffhausen, Switzerland	4 100	Production for Alcon Surgical franchise
La Jolla, California	3 300	Research and development, and quality control testing for AveXis
Bannockburn, Illinois	3 000	AveXis headquarters
West Lafayette, Indiana	2 000	Headquarters, research laboratory and administrative offices for Endocyte
Millburn, New Jersey	1 400	AAA primary production site for radioligand therapy
Colleretto Giacosa/Ivrea, Italy	1 200	AAA primary production site for radioligand therapy
Saint-Genis-Pouilly, France	600	AAA global headquarters

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To support the objectives of Novartis Technical Operations, we are progressing with our network transformation project, under which we are reviewing our manufacturing network to ensure it can appropriately meet the future needs of the Group. Under this transformation plan, we have made the following announcements:

• In May 2017, we announced the planned closure of one manufacturing building at each of our Basel, Switzerland, and Schweizerhalle, Switzerland, sites by 2019.

• In October 2017, we announced our plan to close commercial production operations at our Broomfield, Colorado, site, with production anticipated to conclude during 2019.

• In November 2017, we announced our plan to exit our packaging operations in Wehr, Germany, by 2022.

• In April 2018, we announced the planned closure of our Kaminoyama, Japan, site and the transfer of all packaging activities to Sasayama, Japan, by 2020.

• In May 2018, we announced an agreement with Avara Pharmaceutical Services to divest our Boucherville, Canada, plant. This divestment was completed on September 1, 2018.

• In September 2018, we announced that Aurobindo Pharma USA Inc. agreed to acquire our manufacturing facilities in Wilson, North Carolina; Hicksville, New York; and Melville, New York, as part of the divestment of the US dermatology business and generic US oral solids portfolio of our Sandoz Division. We expect this transaction to be completed during the course of 2019.

• In September 2018, we announced the acquisition of our Mahad, India, site by Olon S.p.A., which we expect to be completed in 2019.

• Also in September 2018, we announced the proposed exit of manufacturing operations in Grimsby, United Kingdom, as well as the closure of a building in Schweizerhalle, Switzerland, by 2020 and the milling and blending center in Stein, Switzerland, by 2021.

• In December 2018, we announced the transfer of the packaging and repackaging activities from our Candelaria, Mexico, site to a local contract manufacturer in 2019.

• In December 2018, we announced an offer to acquire Cell*for*Cure from LFB, including its cell and gene manufacturing facility located in Les Ulis, France. If this transaction closes as planned, Cell*for*Cure is expected to become a wholly owned Novartis manufacturing site managed by NTO. We expect this transaction to be completed during the first half of 2019.

• In December 2018, we completed the exit of our site in Turbhe, India.

In 2012, Novartis announced the construction of a new state-of-the-art production facility to produce solid dosage form medicines for the Innovative Medicines Division in Stein, Switzerland. We expect our investment in this facility to exceed USD 0.6 billion. The new facility is planned to replace an older facility. In addition, Novartis is investing in new technologies and packaging facilities for pharmaceuticals at Stein. Stein is a technological competence center for both sterile and solid dosage form drugs. Through December 31, 2018, the total amount paid and committed to be paid on this project is equivalent to approximately USD 0.6 billion.

In 2012, we announced the planned construction of a new state-of-the-art biotechnology production site in Singapore, with a planned investment of over USD 0.8 billion. The new facility will focus on drug substance manufacturing based on cell culture technology. Ground was broken in February 2013, and construction was completed in the third quarter of 2015 for phase one of the project. Phase one of this project is now operational, and we expect phase two to be operational in 2019. The facility is co-located with the pharmaceutical production site based in Tuas, Singapore. In the future, Singapore is expected to be a technological competence center for both biotechnology and pharmaceutical manufacturing at Novartis. Through December 31, 2018, the total amount paid and committed to be paid on this project is equivalent to USD 0.7 billion.

An expansion of our Alcon Division's Johns Creek, Georgia, facility was approved in 2017 to add three production lines of *Dailies Total1* contact lenses. This project is still in progress. We expect to pay a total amount of approximately USD 0.1 billion on this project. Through December 31, 2018, the total amount paid and committed to be paid on this project is approximately USD 0.1 billion.

In March 2018, the second phase of expansion of the Grosswallstadt, Germany, and Singapore facilities relating to the production of contact lenses was approved. We expect to pay a total amount of approximately USD 0.4 billion on the Grosswallstadt project and approximately USD 0.1 billion on the Singapore project, in each case for both the first and second phases of expansion. Through December 31, 2018, the total amount paid and committed to be paid on the Grosswallstadt project is equivalent to approximately USD 0.3 billion, and the total amount paid and committed to be

paid on the Singapore project is equivalent to approximately USD 0.1 billion.

In July 2018, AveXis initiated construction of a new 15 800-square-meter state-of-the-art gene therapy manufacturing facility in Durham, North Carolina. The new facility is expected to complement the existing AveXis site in Libertyville, Illinois, and allow for production of multiple gene therapy products simultaneously. The site is expected to be fully operational in 2020. We expect to pay a total amount of USD 0.2 billion. Through December 31, 2018, the total amount paid and committed to be paid on this project is approximately USD 0.1 billion.

In August 2018, Novartis Technical Operations announced its plan to establish a European cell and gene therapy hub in Stein, Switzerland. We expect our investment in this project to exceed USD 0.1 billion. Through December 31, 2018, the total amount paid and committed to be paid on this project is equivalent to USD 22 million.

In November 2018, Novartis announced the construction of a new state-of-the-art advanced integrated biologics manufacturing facility in Schaftenau, Austria. We expect our investment in this facility to exceed USD 0.2 billion. We expect phase one of this project to be operational in 2020. Through December 31, 2018, the total amount paid and committed to be paid on this project is equivalent to approximately USD 0.1 billion.

Environmental matters

We integrate core values of environmental protection into our business strategy to protect the environment, add value to the business, manage risk and enhance our reputation. For example, our Executive Committee recently endorsed new targets for environmental sustainability related to our carbon footprint, waste production and water sustainability, and we announced a virtual power purchase agreement for renewable energy.

We are subject to laws and regulations concerning the environment, safety matters, regulation of chemicals, and product safety in the countries where we manufacture and sell our products or otherwise operate our business. These requirements include regulation of the handling, manufacture, transportation, use and disposal of materials, including the discharge of pollutants into the environment. In the normal course of our business, we are exposed to risks relating to possible releases of hazardous substances into the environment that could cause environmental or property damage or personal injuries, and that could require remediation of contaminated soil and groundwater – in some cases over many years – regardless of whether the contamination was caused by us or by previous occupants of the property.

See “Item 3. Key Information—Item 3.D Risk factors—Environmental, social and governance matters may impact our business and reputation,” and “Item 3. Key Information—Item 3.D Risk factors—Environmental liabilities may adversely impact our financial results.” See also “Item 4. Information on the Company—Item 4.B Business overview—Overview—Corporate responsibility,” and “Item 18. Financial Statements—Note 19. Provisions and other non-current liabilities.”

Item 4A. Unresolved Staff Comments

Not applicable.

Item 5. Operating and Financial Review and Prospects

5.A Operating results

This operating and financial review should be read together with the Group's consolidated financial statements in this Annual Report, which have been prepared in accordance with International Financial Reporting Standards (IFRS) as published by the International Accounting Standards Board (see "Item 18. Financial Statements"). "Item 5 Operating and Financial Review and Prospects" together with the sections on compounds in development and key development projects of our divisions (see "Item 4. Information on the Company-Item 4.B Business overview") constitute the Operating and Financial Review ("Lagebericht"), as defined by the Swiss Code of Obligations.

Overview

As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. Our purpose is to reimagine medicine to improve and extend people's lives. Our vision is to be a trusted leader in changing the practice of medicine. Our strategy is to focus Novartis as a leading medicines company powered by advanced therapy platforms and data science.

The Group comprises three global operating divisions and we separately report the results of Corporate activities:

- Innovative Medicines: innovative patent protected prescription medicines
- Sandoz: generic pharmaceuticals and biosimilars
- Alcon: surgical and vision care products
- Corporate activities

The financial results of our Corporate activities include the costs of the Group headquarters and those of corporate coordination functions in major countries. In addition, Corporate includes other items of income and expense that are not attributable to specific segments such as certain revenues from intellectual property rights and certain expenses related to post employment benefits, environmental remediation liabilities, charitable activities, donations and sponsorships.

In June 2018, we announced that we plan to spin off Alcon into a separately-traded standalone company. As two distinct publicly traded companies, we believe Novartis and Alcon will be better positioned to capitalize on significant growth opportunities and focus resources on their respective businesses and strategic priorities.

Our divisions are supported by the following cross-divisional organizational units: the Novartis Institutes for BioMedical Research, Global Drug Development, Novartis Technical Operations and Novartis Business Services. The financial results of these organizational units are included in the results of the divisions for which their work is performed. As part of the planned spin-off of Alcon, efforts are being undertaken to prepare for the separation of Alcon from Novartis and to enable Alcon to operate as a standalone public company. As part of these efforts, Alcon is forming its own supporting functions and service organizations.

As part of the long-term strategy to build a leading, focused medicines company powered by advanced therapy platforms and data science, we announced and/or completed several acquisitions and divestments during 2018, 2017 and 2016. For a description of these acquisitions and divestments and other significant transactions, refer to "Item 4.A History and development of Novartis – Important Corporate developments 2016 – 2018", and "Item 18. Financial Statements – Note 2. Significant transactions" and "Note 30. Events subsequent to the December 31, 2018, consolidated balance sheet date – proposal to the Annual General Meeting of Shareholders to approve a spin-off transaction of the Alcon Division".

During 2018 and 2017 Novartis announced several new nominations to the Executive Committee of Novartis including the appointment of Vasant (Vas) Narasimhan, M.D., Global Head of Drug Development and Chief Medical Officer, as CEO of Novartis, effective February 1, 2018. For a more detailed description of these nominations please refer to "Item 4. Information on the Company – Item 4.B Business overview".

In 2018, Novartis achieved net sales of USD 51.9 billion, of which USD 13.0 billion, or 25%, came from Emerging Growth Markets, and USD 38.9 billion, or 75%, came from Established Markets. Emerging Growth Markets comprise all markets other than the Established Markets of the US, Canada, Western Europe, Japan, Australia and New Zealand.

Innovative Medicines accounted for USD 34.9 billion, or 67%, of Group net sales, and for USD 7.9 billion, or 87%, of Group operating income (excluding Corporate income and expense, net).
Sandoz accounted for USD 9.9 billion, or 19%, of Group net sales, and for USD 1.3 billion, or 15%, of Group operating income (excluding Corporate income and expense, net).
Alcon accounted for USD 7.1 billion, or 14%, of Group net sales, and an increased operating loss of USD 0.2 billion.
Effective January 1, 2018, following the internal reorganization, announced on October 24, 2017, and January 24, 2018, we transferred our over-the-counter ophthalmic products and certain surgical diagnostic products with sales in 2017 of USD 747 million (2016: USD 731 million) from the Innovative Medicines Division to the Alcon Division. Our prescription Ophthalmic medicines business remains with the Innovative Medicines Division. As

the Innovative Medicines Division will discontinue its use of the Alcon brand name, the intangible asset has been transferred from corporate to the Alcon Division. In compliance with IFRS, we updated our segment reporting to reflect this transfer, both for the current and prior years, to aid comparability of year-on-year results. This restatement had no impact on the reported financial results of the Sandoz Division or the total Group.

Opportunity and risk summary

Our financial results are affected to varying degrees by external factors. The healthcare industry is entering a phase of significant progress and change. Over the next two decades, we believe biomedical innovation will continue to accelerate – potentially spawning new treatments that could have unparalleled impact on humanity, including in areas such as cancer and heart disease. The digital revolution that is now gaining momentum in healthcare is likely to transform everything from drug research and development to how doctors diagnose and treat diseases.

These trends could help society address the changing healthcare needs of aging populations and produce better health outcomes for patients. At the same time, loss of market exclusivity and the introduction of branded and generic competitors could significantly erode sales of our innovative products. Our ability to grow depends on the success of our research and development efforts to replenish our pipeline, as well as on the commercial acceptance of our products in the markets. Increased pricing pressure could impact our ability to generate returns and invest for the future.

We have a significant global compliance program in place, but any failure to comply with local laws could lead to substantial liabilities. Our manufacturing processes are technically complex and subject to strict regulatory requirements, which introduce a greater chance for disruptions and liabilities.

Our dependence on information technology puts us at risk of information security threats and losses of personal data. We may also fail to take advantage of rapid progress in digital technologies and in the development of new business models, and third parties may enter the healthcare field and could supplant portions of our business

We carry a significant amount of goodwill and other intangible assets on our consolidated balance sheet, and may incur significant impairment charges in the future. We pay taxes in numerous countries, and tax authorities around the world have increased their scrutiny of company tax filings. In addition, tax reform initiatives by the OECD, the EU, Switzerland and the US will require us to continually assess our organizational structure against tax policy trends, could lead to an increased risk of international tax disputes and an increase in our effective tax rate, and could adversely affect our financial results.

For more details on these trends and how they could impact our results, see “—Factors affecting results of operations” starting on page 105.

Results of operations
2018 compared to 2017
Key figures

(USD millions unless indicated otherwise)	Year ended Dec 31, 2018	Year ended Dec 31, 2017	Change in USD %	Change in constant currencies %
Net sales to third parties	51 900	49 109	6	5
Other revenues	1 266	1 026	23	23
Cost of goods sold	– 18 407	– 17 175	– 7	– 6
Gross profit	34 759	32 960	5	5
Selling, general and administration	– 16 471	– 14 997	– 10	– 9
Research and development	– 9 074	– 8 972	– 1	0
Other income	1 690	1 969	– 14	– 15
Other expense	– 2 735	– 2 331	– 17	– 16
Operating income	8 169	8 629	– 5	– 5
Return on net sales (%)	15.7	17.6		
Income from associated companies	6 438	1 108	nm	nm
Interest expense	– 957	– 777	– 23	– 27
Other financial income and expense	185	39	nm	nm
Income before taxes	13 835	8 999	54	54
Taxes	– 1 221	– 1 296	6	5
Net income	12 614	7 703	64	64
Attributable to:				
Shareholders of Novartis AG	12 611	7 703	64	64
Non-controlling interests	3	0	nm	nm
Basic earnings per share (USD)	5.44	3.28	66	66
Net cash flows from operating activities	14 272	12 621	13	
Free cash flow [1]	11 717	10 428	12	

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."
nm = not meaningful

Group overview

Novartis delivered strong performance in 2018 driven by continued sales momentum from our key growth products and the successful acquisition of Advanced Accelerator Applications (AAA).

Net sales for Novartis were USD 51.9 billion, up 6% in reported terms and up 5% measured in constant currencies (cc) to remove the impact of exchange rate movements. The strong sales growth was driven by volume growth of 9 percentage points (cc), mainly driven by *Cosentyx*, AAA and four additional drugs reaching blockbuster status (*Promacta/Revolade, Tafinlar + Mekinist, Entresto* and *Xolair)*. The strong volume growth was partly offset by the negative impacts of pricing (-2 percentage points) and generic competition (-2 percentage points).

Cosentyx, our treatment for psoriasis and other autoimmune diseases, grew strongly across all indications, with sales rising 37% (+36% cc), to USD 2.8 billion. *Entresto*, our product for heart failure has now more than doubled sales reaching USD 1.0 billion.

Our treatments for certain cancer and related rare diseases continued to grow, driven by strong demand. *Promacta/Revolade*, a treatment for blood disorders, grew 35% (+35% cc) to USD 1.2 billion. *Tafinlar + Mekinist*, a combination treatment for skin and lung cancers, had sales of USD 1.2 billion, up 32% (+31% cc). *Jakavi*, a treatment for rare blood cancers, grew 26% (+24% cc) to USD 977 million. Sales of the products from AAA, including *Lutathera*, a radioligand therapy for a rare type of cancer in the pancreas or gut, amounted to USD 355 million.

By division, Innovative Medicines sales grew 8% (+8% cc). Alcon sales grew 6% (+5% cc), reflecting the second consecutive year of growth, mainly as a result of improved operations and customer relationships. Sandoz sales declined 2% (–3% cc), mainly due to lower retail generics, which was impacted by continued US industry-wide pricing pressures, partly offset by growth in Biopharmaceuticals including the continued uptake of *Rixathon* and *Erelzi* in Europe.

Operating income in 2018 was USD 8.2 billion (–5%, –5% cc), mainly due to the impacts from M&A transactions, higher restructuring and net impairment charges, and growth investments, partly offset by higher sales. Operating income margin in constant currencies decreased 1.6 percentage points; currency had a nega-

tive impact of 0.3 percentage points resulting in a net decrease of 1.9 percentage points to 15.7% of net sales.
Net income was USD 12.6 billion compared to USD 7.7 billion in the prior year, mainly benefiting from a USD 5.7 billion net gain from the divestment of our stake in the GSK consumer healthcare joint venture. Earnings per share were USD 5.44 compared to USD 3.28 in the prior year, driven by higher net income and the lower number of shares outstanding.
Free cash flow grew 12% to USD 11.7 billion compared to USD 10.4 billion in the prior year driven by higher cash flows from operating activities, which includes the receipt of a GSK sales milestone from the divested Vaccines business, partly offset by higher net investments in intangible assets.
We also present our core results, which exclude the impact of amortization, impairments, disposals, acquisitions, restructurings and other significant one-time items, to help investors understand our underlying performance.
Core operating income was USD 13.8 billion (+8%, +8% cc) driven by higher sales and gross margin, which were partly offset by growth investments, including AveXis. Core operating income margin in constant currencies increased 0.7 percentage points; currency had a negative impact of 0.3 percentage points resulting in a net increase of 0.4 percentage points to 26.6% of net sales.
Core net income was USD 11.9 billion (+5%, +5% cc), driven by growth in core operating income, which was partly offset by the discontinuation of core income from the GSK consumer healthcare joint venture from April 1, 2018.
Core earnings per share were USD 5.15 (+6%, +6% cc), driven by growth in core net income and the lower number of shares outstanding.
Net sales by segment
The following table provides an overview of net sales to third parties by segment:

(USD millions)	Year ended Dec 31, 2018	Year ended Dec 31, 2017 restated [1]	Change in USD %	Change in constant currencies %
Innovative Medicines	34 892	32 278	8	8
Sandoz	9 859	10 060	– 2	– 3
Alcon	7 149	6 771	6	5
Net sales to third parties	51 900	49 109	6	5

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.
Innovative Medicines
Following the internal reorganization announced on October 24, 2017, and January 24, 2018, that was effective January 1, 2018, we transferred our over-the-counter ophthalmic products and certain surgical diagnostic products with sales in 2017 of USD 747 million (2016: USD 731 million) from the Innovative Medicines Division to the Alcon Division. Our prescription Ophthalmic medicines business remains with the Innovative Medicines Division. In compliance with IFRS, we updated our segment reporting to reflect this transfer, both for the current and prior years, to aid comparability of year-on-year results. For details on the Innovative Medicines net sales by business franchise see also “Item 18. Financial Statement – Note 3. Segmentation of key figures 2018, 2017 and 2016.”
In addition to this, the former Immunology and Dermatology franchise was reorganized into Immunology, Hepatology and Dermatology, and certain products were transferred to Established Medicines.
Innovative Medicines Division delivered net sales of USD 34.9 billion in 2018, up 8% in reported terms and in constant currencies (cc). The Pharmaceuticals Business Unit grew 7% (cc), driven by *Cosentyx* reaching USD 2.8 billion and *Entresto* reaching USD 1.0 billion. Oncology Business Unit grew 9% (cc), driven by AAA, including *Luthathera, Promacta/Revolade* and *Tafinlar + Mekinist* both reaching USD 1.2 billion and *Jakavi* reaching USD 977 million. Volume contributed 11 percentage points to sales growth. Generic competition had a negative impact of 2 percentage points. Pricing had a negative impact of 1 percentage point.
Regionally, in the US (USD 11.9 billion, +9%), the strong performance was driven by *Cosentyx*, *Entresto*, *Promacta/Revolade* and *Lutathera*. Europe sales (USD 12.3 billion, +8% cc) were driven by *Cosentyx, Entresto* and

Jakavi. Japan sales (USD 2.4 billion, –3% cc) declined mainly due to the biennial price cut and generic competition. Emerging Growth Markets sales increased 10% (cc) to USD 8.6 billion, mainly driven by strong growth in China.
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The following table provides an overview of net sales to third parties by franchise of the Innovative Medicines Division:

(USD millions)	Year ended Dec 31, 2018	Year ended Dec 31, 2017 [1]	Change in USD %	Constant currencies change %
Total Oncology business unit	13 428	12 274	9	9
Total Pharmaceuticals business unit	21 464	20 004	7	7
Ophthalmology	4 558	4 621	– 1	– 2
Neuroscience	3 429	3 287	4	4
Immunology, Hepatology and Dermatology	3 392	2 474	37	37
Respiratory	1 767	1 617	9	8
Cardio-Metabolic	1 050	524	100	100
Established Medicines	7 268	7 481	– 3	– 3
Total Innovative Medicines	34 892	32 278	8	8

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018, and the new franchise structure of Immunology, Hepatology and Dermatology

The following table provides the top 20 Innovative Medicines Division product net sales – 2018

			US		Rest of world			Total		
Brands	Business franchise	Indication	USD m	% change USD/cc [2]	USD m	% change USD	% change cc [2]	USD m	% change USD	% change cc [2]
Gilenya	Neuroscience	Relapsing multiple sclerosis	1 765	3	1 576	7	5	3 341	5	4
Cosentyx	Immunology, Hepatology and Dermatology	Psoriasis, ankylosing spondylitis and psoriatic arthritis	1 674	31	1 163	46	44	2 837	37	36
Lucentis	Ophthalmology	Age-related macular degeneration		2	046	8	7	2 046	8	7
Tasigna	Oncology	Chronic myeloid leukemia	806	0	1 068	4	3	1 874	2	1
Sandostatin	Oncology	Carcinoid tumors and acromegaly	817	– 2	770	– 1	– 1	1 587	– 2	– 2
Gleevec/Glivec	Oncology	Chronic myeloid leukemia and GIST	440	– 30	1 121	– 15	– 16	1 561	– 20	– 20
Afinitor/Votubia	Oncology	Breast cancer/TSC	929	13	627	– 11	– 12	1 556	2	2
Galvus Group	Established Medicines	Diabetes		1	284	4	6	1 284	4	6
Promacta/Revolade	Oncology	Immune thrombocytopenic purpura	581	30	593	41	40	1 174	35	35
Tafinlar + Mekinist	Oncology	Melanoma	457	35	698	31	29	1 155	32	31
Exjade/Jadenu	Oncology	Chronic iron overload	521	1	578	6	5	1 099	4	3
Xolair [1]	Respiratory	Asthma		1	039	13	12	1 039	13	12
Entresto	Cardio-Metabolic		556	87	472	125	124	1 028	103	102

		Chronic heart failure								
Diovan Group	Established Medicines	Hypertension	84	– 3	939	8	8	1 023	7	7
Exforge Group	Established Medicines	Hypertension	19	– 32	983	5	5	1 002	4	4
Jakavi	Oncology	Myelofibrosis			977	26	24	977	26	24
Votrient	Oncology	Renal cell carcinoma	404	– 1	424	6	5	828	2	2
Ilaris	Immunology, Hepatology and Dermatology	Auto-inflammatory (CAPS, TRAPS, HIDS/MKD, FMF, SJIA, AOSD and gout)	262	34	292	42	44	554	38	39
Travoprost Group	Ophthalmology	Reduction of elevated intraocular pressure	194	– 10	323	– 13	– 13	517	– 12	– 12
Zortress/Certican	Established Medicines	Transplantation	145	12	319	12	12	464	12	12
Top 20 products total			9 654	11	17 292	10	9	26 946	10	10
Rest of portfolio			2 210	4	5 736	0	0	7 946	1	1
			11		23			34		
Total division sales			864	9	028	8	7	892	8	8

[1] Net sales reflect *Xolair* sales for all indications (e.g., including *Xolair* SAA and *Xolair* CSU, which is managed by the Immunology, Hepatology and Dermatology franchise).
[2] Constant currencies (cc) is a non-IFRS measure. For an explanation of non-IFRS measures, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

For information about the approved indications for the products described, see “Item 4. Information on the Company—Item 4.B Business overview—Innovative Medicines—Key marketed products”.

Novartis Oncology business unit

Oncology sales were USD 13.4 billion (+9% cc) driven by AAA, including Luthathera, Promacta/Revolade, Tafinlar + Mekinist and Jakavi.

Tasigna (USD 1.9 billion, +1% cc) was broadly in line with prior year across most regions.

Sandostatin (USD 1.6 billion, −2% cc) sales declined slightly, due to competitive pressure across most regions.

Gleevec/Glivec (USD 1.6 billion, −20% cc) continued to decline due to generic competition in most major markets.

Afinitor/Votubia (USD 1.6 billion, +2% cc) sales grew slightly mainly driven by the tuberous sclerosis complex (TSC) and neuroendocrine tumor (NET) indications in the US.

Promacta/Revolade (USD 1.2 billion, +35% cc) sales grew at a strong double-digit rate across all regions.

Tafinlar + Mekinist (USD 1.2 billion, +31% cc) continued strong double-digit growth due to increased demand in metastatic melanoma and NSCLC across all regions, with strong uptake in the adjuvant melanoma indication also contributing in the US and Europe.

Exjade/Jadenu (USD 1.1 billion, +3% cc) grew driven by continued uptake in Europe and Japan as well as the FCT (film-coated tablets) formulation launch in Europe.

Jakavi (USD 977 million, +24% cc) continued strong double-digit growth across all regions driven by both the myelofibrosis and polycythemia vera indications.

Votrient (USD 828 million, +2% cc) sales grew slightly driven by growth in Japan and Emerging Growth Markets partially offset by competitive pressures in the US and Europe.

Kisqali (USD 235 million, +210% cc) continues to build momentum with growth in the US and launches in several European and Emerging Growth Markets. In July 2018, the US FDA approved two new indications for *Kisqali* based on the MONALEESA 3/7 trials, also approved in Europe in December 2018.

Lutathera (USD 167 million) launch in the US is progressing well, with over 100 centers actively treating. Sales from all AAA brands (including *Lutathera* and radiopharmaceutical diagnostic products) were USD 355 million in 2018. The US FDA approved *Lutathera* in late January 2018, shortly following the acquisition of AAA. In Europe, full reimbursement for *Lutathera* has been achieved in several countries during 2018. European authorities approved *Lutathera* in late September 2017.

Kymriah sales were USD 76 million. In May, the US FDA approved *Kymriah* for a second indication – in relapsed/refractory (r/r) DLBCL. Approval of *Kymriah* was also granted by the European Commission, Health Canada and Swissmedic for the r/r pediatric and young adult ALL and r/r DLBCL indications.

Novartis Pharmaceuticals business unit

Ophthalmology

Sales in the Ophthalmology franchise were USD 4.6 billion (–2% cc), with increased sales of *Lucentis* partially offsetting the impact of generic competition for glaucoma and anti-infective portfolios mainly in the US and Europe, as well as price erosion.

Lucentis (USD 2.0 billion, +7% cc) sales delivered strong growth benefitting from the implementation of a focused global campaign and strong retina market growth.

Travoprost Group (USD 517 million, −12% cc) sales declined mainly due to generic competition in Europe and increased competition in the US.

Neuroscience

Sales in the Neuroscience franchise were USD 3.4 billion (+4% cc), mainly driven by *Gilenya*.

Gilenya (USD 3.3 billion, +4% cc) with approximately 267,000 treated patients worldwide, continued solid growth, driven by increased demand in Europe and US. *Gilenya* was approved by the FDA in May 2018 and by the European Commission in November 2018 as the first disease-modifying therapy for pediatric relapsing multiple sclerosis addressing the strong unmet clinical need of younger patients.

Aimovig received FDA approval in May 2018 and European Commission approval in July 2018 and is now available in 25 countries as the first novel treatment designed specifically for migraine prevention. *Aimovig* was successfully launched in the US and ex-US launches are now underway, including local reimbursement procedures. Additional regulatory filings are pending with other health authorities worldwide. *Aimovig* is co-commercialized with Amgen in the US, where Amgen records sales, and Novartis has exclusive commercialization rights for all territories excluding the US and Japan. More than 165,000 patients have been treated with *Aimovig* worldwide since launch.

Immunology, Hepatology and Dermatology

Sales in the Immunology, Hepatology & Dermatology franchise reached USD 3.4 billion (+37% cc), of which *Cosentyx* delivered USD 2.8 billion.

Cosentyx (USD 2.8 billion, +36% cc) delivered strong volume growth across all indications in the US and EU. In October, Novartis presented five-year data in psoriatic arthritis and ankylosing spondylitis confirming the efficacy and safety benefits of *Cosentyx*. This adds to the results of a Phase III psoriasis study reported in 2017, demonstrating that *Cosentyx* delivers high and long-lasting skin clearance in patients with moderate-to-severe plaque psoriasis, with high response rates essentially maintained from year one to year five. These scientific data are reinforcing *Cosentyx*'s unique position as a long-lasting comprehensive treatment across PsO, PsA and AS.

Ilaris (USD 554 million, +39% cc) sales were driven by strong double-digit growth across most regions driven by volume.

Respiratory

Sales in the Respiratory franchise were USD 1.8 billion (+8% cc). *Xolair* sales amounted to USD 1.0 billion and our chronic obstructive pulmonary disease (COPD) portfolio including *Onbrez Breezhaler, Seebri Breezhaler* and *Ultibro Breezhaler* achieved sales of USD 703 million (+2% cc).

Xolair (USD 1.0 billion, +12% cc) continued to grow in both indications, Severe Allergic Asthma (SAA) and in Chronic Spontaneous Urticaria (CSU, also known as CIU), a severe skin disease, driven by increasing disease

awareness. The asthma indication is managed by the Respiratory franchise which reports all *Xolair* sales.
Ultibro Breezhaler (USD 454 million, +8% cc) continued to grow driven by positive FLAME and CLAIM study results as well as the GOLD Strategy 2018 Report and further supported by the published SUNSET study results.

Cardio-Metabolic

Sales in the Cardio-Metabolic franchise were USD 1.1 billion (+100% cc).
Entresto (USD 1.0 billion, +102% cc) sales doubled year on year driven by growing adoption by physicians and strong volume in all markets (US +87%, rest of world +124% cc). New data from the landmark PIONEER-HF trial presented at AHA 2018 and published in the NEJM reconfirms the superiority of *Entresto* over enalapril as demonstrated in PARADIGM-HF.

Established Medicines

The Established Medicines franchise had sales of USD 7.3 billion (−3% cc).
Galvus Group (USD 1.3 billion, +6% cc) continues to grow driven by solid performance in Emerging Growth Markets including China.
Diovan Group (USD 1.0 billion, +7% cc) saw increased demand mainly due to the recall of generic products in many markets.
Exforge Group (USD 1.0 billion, +4% cc) saw increased sales mainly in Emerging Growth Markets.
Zortress/Certican (USD 464 million, +12% cc) sales were driven by strong double-digit growth across all regions.
Neoral/Sandimmun(e) (USD 463 million, −6% cc) declined due to generic competition and mandatory price reductions.
Voltaren/Cataflam (USD 445 million, −3% cc) declined due to generic competition.

Sandoz

Sandoz net sales in 2018 were USD 9.9 billion, down 2% in reported terms. In constant currencies, or cc, sales declined 3%, as 8 percentage points of price erosion, mainly in the US, were partially offset by volume growth of 5 percentage points. In the US, sales were USD 2.8 billion (−16%), down mainly due to continued industry-wide pricing pressure. Sales in Europe were USD 5.0 billion (+5% cc) with growth in biosimilars mainly in Germany, France, UK and Italy. Sales in Asia, Africa and Australasia were USD 1.4 billion, down 2% (cc). Sales in Canada and Latin America were USD 779 million (+8% cc). Excluding the US, net sales grew 4% (cc).

(USD millions)	Year ended Dec 31, 2018	Year ended Dec 31, 2017	Change in USD %	Constant currencies change %
Retail Generics[1]	7 880	8 409	– 6	– 7
Biopharmaceuticals	1 436	1 135	27	24
Anti-Infectives (partner label/API)	543	516	5	3
Total	9 859	10 060	– 2	– 3

[1] Of which USD 826 million (2017: USD 880 million) represents anti-infectives sold under the Sandoz name

Retail Generics

Sandoz markets active ingredients, intermediates and finished dosage forms of pharmaceuticals. The Retail Generics franchise includes products in the therapeutic areas of cardiovascular, central nervous system, dermatology, gastrointestinal and hormonal therapies, metabolism, oncology, ophthalmics, pain and respiratory, plus finished dosage forms of anti-infectives sold under the Sandoz name. Retail Generics sales in 2018 were USD 7.9 billion (–7% cc), due to the decline in the US (–22%).

Biopharmaceuticals

The Biopharmaceuticals business comprises biosimilars, contract biologics supplied to third parties, and *Glatopa*, a generic version of Copaxone®, which treats relapsing forms of multiple sclerosis and is marketed in the US. Global sales of Biopharmaceuticals grew 24% (cc) to USD 1.4 billion driven by both Europe and the US. By region, Europe continued double-digit growth driven by *Rixathon* (rituximab) and *Erelzi* (etanercept). In the US, growth was mainly driven by *Zarxio* (now the leading filgrastim in the US market).

Anti-Infectives

Sandoz sells pharmaceutical ingredients and intermediates (mainly antibiotics) to third-party customers, as well as finished dosage forms. Anti-infectives sold to third parties for sale under their own name were USD 543 million, up 3% (cc). Total Anti-Infectives sales were USD 1.4 billion (–3% cc), and included USD 826 million sales of finished dosage forms sold under the Sandoz name.

Alcon

Sales in Alcon were restated for 2017 to reflect the product transfer between the Innovative Medicines Division and Alcon Division, announced on October 24, 2017, and January 24, 2018, that was effective as of January 1, 2018. In 2017, these sales transferred from the Innovative Medicines Division to Alcon Division amounted to USD 747 million.

Alcon net sales in 2018 were USD 7.1 billion (+6%, +5% cc), compared to USD 6.8 billion in the prior year. Alcon's results reflect the second consecutive year of net sales growth mainly as a result of improved operations and customer relationships.

(USD millions)	Year ended Dec 31, 2018	Year ended Dec 31, 2017 restated [1]	Change in USD %	Constant currencies change %
Surgical				
Consumables	2 227	2 097	6	6
Implantables	1 136	1 034	10	11
Equipment/other	636	594	7	8
Total	3 999	3 725	7	7
Vision Care				
Contact lenses	1 928	1 833	5	4
Ocular health	1 222	1 213	1	1
Total	3 150	3 046	3	3
Total net sales	7 149	6 771	6	5

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Surgical

Surgical sales were USD 4.0 billion (+7% cc), with growth across all key product categories, driven mainly by advanced technology intraocular lenses (AT-IOLs) and consumables.

Vision Care

Vision Care sales were USD 3.2 billion (+3% cc), driven by growth in contact lenses with continued double-digit growth of *Dailies Total1*.

Operating income

The following table provides an overview of operating income by segment:

(USD millions)	Year ended Dec 31, 2018	% of net sales	Year ended Dec 31, 2017 restated [1]	% of net sales	Change in USD %	Change in constant currencies %
Innovative Medicines	7 871	22.6	7 595	23.5	4	4
Sandoz	1 332	13.5	1 368	13.6	– 3	– 2
Alcon	– 194	– 2.7	– 3	0.0	nm	nm
Corporate	– 840		– 331		– 154	– 148
Operating income	8 169	15.7	8 629	17.6	– 5	– 5

nm = not meaningful

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Operating income in 2018 was USD 8.2 billion (–5%, –5% cc), mainly due to the impacts from M&A transactions, higher restructuring and net impairment charges, and growth investments, partly offset by higher sales. Operating income margin in constant currencies decreased 1.6 percentage points; negative currency impact was 0.3 percentage points, resulting in a net decrease of 1.9 percentage points to 15.7% of net sales.

Core operating income key figures1

(USD millions unless indicated otherwise)	Year ended Dec 31, 2018	Year ended Dec 31, 2017	Change in USD %	Change in constant currencies %
Core gross profit	39 418	36 578	8	7
Selling, general and administration	– 16 429	– 15 000	– 10	– 9
Research and development	– 8 681	– 8 313	– 4	– 4
Other income	596	778	– 23	– 24
Other expense	– 1 081	– 1 193	9	11
Core operating income	13 823	12 850	8	8
As % of net sales	26.6	26.2		

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

The adjustments made to operating income to arrive at core operating income amounted to USD 5.7 billion (compared to USD 4.2 billion in 2017), increasing mainly due to higher restructuring and net impairment charges.

Core operating income was USD 13.8 billion (+8%, +8% cc) driven by higher sales and gross margin, partly offset by growth investments, including AveXis. Core operating income margin in constant currencies increased by 0.7 percentage points; currency had a negative impact of 0.3 percentage points, resulting in a net increase of 0.4 percentage points to 26.6% of net sales.

The following table provides an overview of core operating income by segment:

(USD millions)	Year ended Dec 31, 2018	% of net sales	Year ended Dec 31, 2017 restated [1]	% of net sales	Change in USD %	Change in constant currencies %
Innovative Medicines	11 151	32.0	10 019	31.0	11	11
Sandoz	2 002	20.3	2 080	20.7	– 4	– 3
Alcon	1 279	17.9	1 168	17.3	10	10
Corporate	– 609		– 417		– 46	– 43
Core operating income	13 823	26.6	12 850	26.2	8	8

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Innovative Medicines

Operating income was USD 7.9 billion (+4%, +4% cc) mainly driven by higher sales, partly offset by increased growth and launch investments, and higher restructuring charges and net impairment charges. Operating income margin in constant currencies decreased 0.8 percentage points; currency had a negative impact of 0.1 percentage points, resulting in a net decrease of 0.9 percentage points to 22.6% of net sales.

Core adjustments amounted to USD 3.3 billion, including USD 2.2 billion of amortization of intangible assets. Prior year core adjustments were USD 2.4 billion. Core adjustments increased compared to prior year mainly due to higher restructuring and net impairment charges. Core operating income was USD 11.2 billion (+11%, +11% cc) mainly driven by strong sales growth and gross margin expansion, partly offset by higher growth investments. Core operating income margin in constant currencies increased by 1.0 percentage points; currency had a negligible impact, resulting in a net increase of 1.0 percentage points to 32.0% of net sales.

Core gross margin as a percentage of net sales increased by 0.9 percentage points (cc). Core R&D expenses decreased by 0.8 percentage points (cc). Core SG&A expenses increased by 0.7 percentage points (cc) due to launch investments

and AveXis and AAA acquisitions. Core Other Income and Expense, net, was in line with prior year.

Sandoz

Operating income was USD 1.3 billion (–3%, –2% cc) mainly driven by impairment charges related to the Sandoz US dermatology business and generic US oral solids portfolio and lower sales partly offset by continued gross margin expansion and lower amortization. Operating income margin was broadly in line with prior year.

Core adjustments amounted to USD 670 million, including USD 363 million of amortization. Prior year core adjustments were USD 712 million. Core adjustments declined compared to prior year driven by net changes in legal provisions and lower amortization partially offset by impairment charges related to the Sandoz US dermatology business and generic US oral solids portfolio. Core operating income was USD 2.0 billion (–4%, –3% cc), mainly due to the sales decline, ex-US M&S investments, partially offset by continued core gross margin expansion. Core operating income margin decreased by 0.1 percentage points, currency had a negative impact

of 0.3 percentage points, resulting in a net decrease of 0.4 percentage points to 20.3% of net sales.

Core gross margin as a percentage of net sales increased by 2.4 percentage points (cc), mainly driven by productivity gains and favorable product and geographic mix. Core R&D expenses increased by 0.4 percentage points (cc). Core SG&A expenses increased by 2.2 percentage points (cc), mainly due to higher M&S investments in key ex-US markets. Core Other Income and Expense increased the margin by 0.1 percentage points (cc).

Alcon

Operating loss was USD 194 million for the full year, compared to a loss of USD 3 million in prior year, as higher sales were more than offset by the voluntary withdrawal of *CyPass* (USD 0.3 billion) and higher investments in growth drivers. Operating income margin in constant currencies decreased 2.5 percentage points; currency had a negative impact of 0.2 percentage points, resulting in a net decrease of 2.7 percentage points to negative 2.7% of net sales.

Core adjustments increased to USD 1.5 billion compared to USD 1.2 billion in the prior year, primarily due to the voluntary withdrawal of *CyPass*. Core operating income was USD 1.3 billion (+10%, +10% cc) as higher sales and improved gross margin were partly offset investments in growth drivers. Core operating income margin in constant currencies increased by 0.8 percentage points; currency had a negative impact of 0.2 percentage points, resulting in a net increase of 0.6 percentage points to 17.9% of net sales.

Core gross margin as a percentage of net sales increased by 1.4 percentage points (cc). Core R&D expenses decreased 0.2 percentage points (cc). Core SG&A expenses increased by 0.9 percentage points (cc) reflecting higher growth and operational investments. Core Other Income and Expense increased the margin by 0.1 percentage points (cc).

Corporate income and expense, net

Corporate income and expense, which includes the cost of Group management and central services, amounted to an expense of USD 840 million in 2018 compared to USD 331 million in prior year. The increase in net expense compared to prior year was mainly due to lower contributions from the Novartis Venture Fund, lower income from retained vaccines intellectual property, higher NBS restructuring costs and an income from a sales milestone in the prior year related to the Vaccines divestment.

Research and development of Innovative Medicines Division

The following table provides an overview of the reported and core research and development expense of the Innovative Medicines Division:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2018	Year ended Dec 31, 2017 restated [1]	Change in USD %	Change in constant currencies %
Research and exploratory development	– 2 770	– 2 729	– 2	– 1
Confirmatory development	– 4 905	– 4 886	0	0
Total Innovative Medicines Division research and development expense	– 7 675	– 7 615	– 1	0
As % of Innovative Medicines net sales to third parties	22.0	23.6		
Core research and exploratory development[2]	– 2 665	– 2 603	– 2	– 2
Core confirmatory development[2]	– 4 675	– 4 431	– 6	– 5
Total core Innovative Medicines Division research and development expense	– 7 340	– 7 034	– 4	– 4
As % of Innovative Medicines net sales to third parties	21.0	21.8		

[1] 2017 figures are restated to reflect the product transfers between divisions that was effective as of January 1, 2018, and in addition for certain amounts that were reclassified from research and exploratory development to confirmatory development for comparative purposes.

[2] Core excludes impairments, amortization and certain other items. For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

Innovative Medicines Division research and exploratory development expense increased by 2% (–1% cc) to USD 2.8 billion in 2018, and confirmatory development expense amounted to USD 4.9 billion, broadly in line with prior year. This was mainly due to higher pipeline investments, including AveXis, which were offset by lower net impairment charges (mainly prior-year RLX030) and productivity.

Total core research and development expense in the Innovative Medicines Division as a percentage of sales decreased by 0.8 percentage points in constant currencies mainly driven by continued resource allocation and productivity efforts, and the higher net sales. The impact from currency exchange rates was negligible, yielding a net decrease of 0.8 percentage points to 21.0% of net sales.

Non-operating income and expense

The following table provides an overview of non-operating income and expense:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2018	Year ended Dec 31, 2017	Change in USD %	Change in constant currencies %
Operating income	8 169	8 629	– 5	– 5
Income from associated companies	6 438	1 108	nm	nm
Interest expense	– 957	– 777	– 23	– 27
Other financial income and expense	185	39	nm	nm
Income before taxes	13 835	8 999	54	54
Taxes	– 1 221	– 1 296	6	5
Net income	12 614	7 703	64	64
Basic EPS (USD)	5.44	3.28	66	66

nm = not meaningful

Income from associated companies

Income from associated companies increased to USD 6.4 billion from USD 1.1 billion in prior year, an increase of USD 5.3 billion. This increase was mainly due to the pre-tax gain of USD 5.8 billion recognized on the divestment of the 36.5% stake in the GSK consumer healthcare joint venture. Excluding this divestment gain, income from associated companies amounted to USD 648 million compared to USD 1.1 billion in prior year.

The share of income from Roche was USD 526 million compared to USD 456 million in prior year. The higher estimated income for Roche of USD 130 million in 2018, was partly offset by the net impacts from a negative prior year adjustment of USD 125 million recognized in 2018, compared to a negative prior year adjustment of USD 67 million recognized in 2017. The share of income from the GSK consumer healthcare joint venture decreased by USD 509 million compared to prior year, due to the discontinuation of the recognition of income from April 1, 2018 (see “Item 18. Financial Statements—Note 2. Significant transactions”).

Interest expense and other financial income and expense

Interest expense was USD 957 million compared to USD 777 million in prior year, an increase of USD 180 million due to higher interest expense of USD 134 million relating to the level of outstanding debt, and higher interest expense of USD 46 million on discounting of long term liabilities.

Other financial income and expense amounted to an income of USD 185 million compared to an income of USD 39 million in prior year, mainly due to higher interest income of USD 294 million compared to USD 110 million in prior year, partly offset by higher currency losses of USD 65 million compared to currency losses of USD 58 million in prior year and higher other financial expenses, net of USD 44 million compared to USD 13 million in prior year.

Taxes

The tax rate in 2018 was 8.8% compared to 14.4% in prior year, due to the impact on taxes of the divestment of the 36.5% stake in the GSK consumer healthcare joint venture. Excluding the impact of the divestment, the tax rate in 2018 would have been 14.4% in line with the 14.4% in prior year, as the benefit from favorable profit mix was offset by the impact from the discontinuation of the recognition of the income from associated companies related to the GSK consumer healthcare joint venture from April 1, 2018 (see “Item 18. Financial Statements—Note 2. Significant transactions”).

Net income

Net income was USD 12.6 billion, compared to USD 7.7 billion in prior year, mainly benefiting from a USD 5.7 billion net gain from the divestment of our stake in the GSK consumer healthcare joint venture, in the second quarter of 2018.

EPS

Basic earnings per share (EPS) in 2018 was USD 5.44, compared to USD 3.28 in the prior year, driven by higher net income and lower number of shares outstanding.

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Core non-operating income and expense[1]

The following table provides an overview of core non-operating income and expense:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2018	Year ended Dec 31, 2017	Change in USD %	Change in constant currencies %
Core operating income	13 823	12 850	8	8
Core income from associated companies	1 113	1 335	– 17	– 17
Core interest expense	– 957	– 777	– 23	– 27
Core other financial income and expense	185	39	nm	nm
Core income before taxes	14 164	13 447	5	5
Core taxes	– 2 226	– 2 056	– 8	– 8
Core net income	11 938	11 391	5	5
Core basic EPS (USD)	5.15	4.86	6	6

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

nm = not meaningful

Core income from associated companies

Core income from associated companies amounted to USD 1.1 billion compared to USD 1.3 billion in prior year. The core income contribution from Roche amounted to USD 970 million compared to USD 832 million in prior year, an increase of USD 138 million, mainly due to the higher estimated contribution from core income. The share of core income from GSK consumer healthcare joint venture decreased by USD 338 million compared to prior year, due to the discontinuation of core income from April 1, 2018 (see “Item 18. Financial Statements—Note 2. Significant transactions”).

Core interest expense and other financial income and expense

Core interest expense was USD 957 million compared to USD 777 million in prior year. Core other financial income and expense amounted to a net income of USD 185 million, compared to USD 39 million in 2017.

Core taxes

The core tax rate (core taxes as a percentage of core pre-tax income) increased to 15.7% from 15.3% in the prior year.

Core net income

Core net income was USD 11.9 billion (+5%, +5% cc) driven by growth in core operating income, partly offset by the discontinuation of core income from the GSK consumer healthcare joint venture from April 1, 2018.

Core EPS

Core earnings per share were USD 5.15 (+6%, +6% cc), driven by growth in core net income and the lower number of shares outstanding.

2017 compared to 2016
Key figures

(USD millions unless indicated otherwise)	Year ended Dec 31, 2017	Year ended Dec 31, 2016	Change in USD %	Change in constant currencies %
Net sales to third parties	49 109	48 518	1	2
Other revenues	1 026	918	12	11
Cost of goods sold	– 17 175	– 17 520	2	2
Gross profit	32 960	31 916	3	4
Selling, general and administration	– 14 997	– 14 192	– 6	– 7
Research and development	– 8 972	– 9 039	1	1
Other income	1 969	1 927	2	1
Other expense	– 2 331	– 2 344	1	0
Operating income	8 629	8 268	4	7
Return on net sales (%)	17.6	17.0		
Income from associated companies	1 108	703	58	58
Interest expense	– 777	– 707	– 10	– 12
Other financial income and expense	39	– 447	nm	nm
Income before taxes	8 999	7 817	15	12
Taxes	– 1 296	– 1 119	– 16	– 13
Net income	7 703	6 698	15	12
Attributable to:				
Shareholders of Novartis AG	7 703	6 712	15	12
Non-controlling interests	0	– 14	nm	nm
Basic earnings per share (USD)	3.28	2.82	16	14
Net cash flows from operating activities	12 621	11 475	10	
Free cash flow [1]	10 428	9 455	10	

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."
nm = not meaningful
Group overview
Novartis had solid performance in 2017, as strong sales of our growth drivers – including *Cosentyx* (secukinumab), *Entresto* (sacubitril/valsartan) and other recently launched products – continued to offset the impact of generic competition for our cancer treatment *Gleevec/Glivec*, which lost patent protection in the US and Europe during 2016. Our results underscore the breadth and strength of our product portfolio and highlight our success at steering through the patent expiration of one of our biggest selling drugs.
Our divisions had varied results. Sales increased in the Innovative Medicines Division, and the Alcon eye care division returned to growth in 2017. Sandoz Division sales declined, as the effects of increased price competition in the US more than offset growth in the rest of the world.
Net sales in 2017 for Novartis were USD 49.1 billion, up 1% in reported terms and up 2% measured in constant currencies (cc) to remove the impact of exchange rate movements. Sales volumes increased 7%, as growth drivers – such as *Cosentyx* (USD 2.1 billion; +84%, +82% cc), *Entresto* (USD 507 million; +198%, +195% cc), *Promacta/Revolade* (USD 867 million; +37%, +37% cc), and *Tafinlar + Mekinist* (USD 873 million; +30%, +29% cc) – more than offset the impact of patent expirations for *Gleevec/Glivec* (USD 1.9 billion; –42%, –41% cc).
The impact of currency exchange headwinds eased in 2017 compared to what we have seen for several years, particularly in 2015 when currency fluctuations had a negative 10% impact on sales. To help investors assess the impact of exchange rates on our performance, we continue to also indicate growth rates in constant currencies.

Operating income in 2017 was USD 8.6 billion (+4%, +7% cc), mainly driven by higher sales, productivity improvements and lower amortization, which were partly offset by generic competition and higher marketing investments to support product launches.

Net income in 2017 was USD 7.7 billion (+15%, +12% cc), benefiting from growth in operating income and higher income from our stake in GSK Consumer Healthcare Holdings Ltd.

Basic earnings per share were USD 3.28 (+16%, +14% cc), benefiting from higher net income and our share buyback program.

Free cash flow rose 10% to USD 10.4 billion, driven mainly by improved cash flow from operating activities.

Net sales by segment

The following table provides an overview of net sales to third parties by segment:

(USD millions)	Year ended Dec 31, 2017 restated [1]	Year ended Dec 31, 2016 restated [1]	Change in USD %	Change in constant currencies %
Innovative Medicines	32 278	31 831	1	2
Sandoz	10 060	10 144	– 1	– 2
Alcon	6 771	6 543	3	4
Net sales to third parties	49 109	48 518	1	2

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Innovative Medicines

Following changes to the divisional structure of Novartis effective January 1, 2018, the sales and results of Innovative Medicines in 2017 and 2016 were restated and exclude the sales of the over-the-counter ophthalmic products and certain surgical diagnostic products, which were transferred to the Alcon Division. In 2017, these sales amounted to USD 747 million, and in 2016, they amounted to USD 731 million. In both years, they were reported under the Ophthalmology franchise.

In addition to this, the former Immunology and Dermatology franchise was reorganized into Immunology, Hepatology and Dermatology, and certain products were transferred to Established Medicines. For details on the Innovative Medicines net sales by business franchise, see also “Item 18. Financial Statements—Note 3. Segmentation of key figures 2018, 2017 and 2016.”

Innovative Medicines Division sales in 2017 were USD 32.3 billion, up 1% in reported terms. In constant currencies (cc), sales grew 2%. An 8% increase in volume more than offset the impact of generic competition (−5 percentage points) and price declines (−1 percentage point). Products contributing to sales growth included *Cosentyx, Entresto, Promacta/Revolade, Tafinlar + Mekinist,* and *Jakavi.*

Regionally, sales performance was mixed. In the US, sales rose 2% to USD 10.9 billion, overcoming the impact of generic competition, mainly for *Gleevec*. Sales in Europe were USD 11.1 billion, up 1% in reported terms and in line with the prior year in constant currencies, as growth drivers offset the impact of patent loss for *Gleevec/Glivec*. Sales rose 3% (+7% cc) in Emerging Growth Markets to USD 8.1 billion. Sales in Japan were USD 2.4 billion, a decline of 4% in reported terms and in line with the prior year in constant currencies.

The following table provides an overview of net sales to third parties by franchise of the Innovative Medicines Division:

(USD millions)	Year ended Dec 31, 2017 [1]	Year ended Dec 31, 2016 [1]	Change in USD %	Constant currencies change %
Total Oncology business unit	12 274	12 790	– 4	– 3
Total Pharmaceutical business unit	20 004	19 041	5	6
Ophthalmology	4 621	4 733	– 2	– 2
Neuroscience	3 287	3 233	2	2
Immunology, Hepatology and Dermatology	2 474	1 412	75	74
Respiratory	1 617	1 521	6	8
Cardio-Metabolic	524	184	185	182
Established Medicines	7 481	7 958	– 6	– 4
Total Innovative Medicines	32 278	31 831	1	2

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018, and the new franchise structure of Immunology, Hepatology and Dermatology

The following table provides the Top 20 Innovative Medicines Division product net sales—2017

			US		Rest of world			Total		
Brands	Business franchise	Indication	USD m	% change USD/cc [3]	USD m	% change USD	% change cc [3]	USD m	% change USD	% change cc [3]
Gilenya	Neuroscience	Relapsing multiple sclerosis	1 709	2	1 476	4	3	3 185	2	2
Cosentyx	Immunology, Hepatology and Dermatology	Psoriasis, ankylosing spondylitis and psoriatic arthritis	1 275	67	796	119	115	2 071	84	82
Gleevec/Glivec	Oncology	Chronic myeloid leukemia and GIST	627	– 48	1 316	– 38	– 37	1 943	– 42	– 41
Lucentis	Ophthalmology	Age-related macular degeneration			1 888	3	4	1 888	3	4
Tasigna	Oncology	Chronic myeloid leukemia	810	12	1 031	1	6	1 841	6	9
Sandostatin	Oncology	Carcinoid tumors and acromegaly	832	– 2	780	– 2	1	1 612	– 2	– 1
Afinitor/Votubia	Oncology	Breast cancer/TSC	819	6	706	– 5	– 3	1 525	1	2
Galvus Group	Cardio-Metabolic	Diabetes			1 233	3	5	1 233	3	5
Exjade/Jadenu	Oncology	Chronic iron overload	515	15	544	7	8	1 059	11	11
Exforge Group	Established Medicines	Hypertension	28	180	932	2	2	960	4	4
Diovan Group	Established Medicines	Hypertension	87	– 41	870	– 6	– 4	957	– 11	– 9
Xolair [1]	Respiratory	Asthma			920	10	11	920	10	11
Tafinlar + Mekinist	Oncology	Melanoma	339	14	534	43	41	873	30	29
Promacta/Revolade	Oncology	Immune thrombocytopenic purpura	446	44	421	30	31	867	37	37
Votrient	Oncology	Renal cell carcinoma	407	14	401	8	7	808	11	10
Jakavi	Oncology	Myelofibrosis			777	34	32	777	34	32
Travoprost Group	Ophthalmology	Reduction of elevated intraocular pressure	216	2	373	– 9	– 9	589	– 5	– 5
Entresto	Cardio-Metabolic	Chronic heart failure	297	161	210	275	262	507	198	195
Neoral/Sandimmun(e)	Immunology, Hepatology and Dermatology	Transplantation	38	– 7	450	– 5	– 4	488	– 5	– 4
Voltaren/Cataflam	Established Medicines	Inflammation/pain			465	– 11	– 4	465	– 11	– 4
Top 20 products total			8 445	6	16 123	2	3	24 568	4	4

Rest of portfolio[2]	2 412	– 11	5 298	– 2	0	7 710	– 5	– 4
Total division sales[2]	10 857	2	21 421	1	2	32 278	1	2

[1] Net sales reflect *Xolair* sales for all indications (e.g. including *Xolair* SAA and *Xolair* CSU, which are managed by the Immunology, Hepatology and Dermatology franchise).

[2] Restated to reflect the product transfers between the Innovative Medicines and Alcon Divisions that was effective as of January 1, 2018

[3] Constant currencies (cc) is a non-IFRS measure. For an explanation of non-IFRS measures, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

For information about the approved indications for the products described below, see “Item 4. Information on the Company—Item 4.B Business overview—Innovative Medicines—Key marketed products.”

Novartis Oncology business unit

Oncology sales in 2017 were USD 12.3 billion (−3% cc), as strong performance of existing products and the launch of new products, including *Kisqali, Rydapt* and *Kymriah*, helped to partially offset the effects of generic competition on *Gleevec/Glivec*. Significant gains on key hematology products, such as *Tasigna*, *Promacta/Revolade* and *Jakavi*, were complemented by *Tafinlar + Mekinist*, which was approved for advanced non-small cell lung cancer in addition to the existing use in melanoma.

Gleevec/Glivec (USD 1.9 billion, −41% cc) continued to decline this year, driven by generic competition primarily across Europe and the US.

Tasigna (USD 1.8 billion, +9% cc) continued to grow this year, primarily in the US and Emerging Growth Markets, despite some impact of generic imatinib in Europe for patients with previously untreated Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia.

Sandostatin (USD 1.6 billion, −1% cc) declined slightly this year, driven by increased competitive pressure primarily in the US and Japan, which was partially offset by growth in Latin America and Emerging Growth Markets.

Afinitor/Votubia (USD 1.5 billion, +2% cc) grew slightly this year as the neuroendocrine tumors and tuberous sclerosis complex indications compensated for competitive pressure in the breast cancer and renal cell carcinoma indications.

Exjade/Jadenu (USD 1.1 billion, +11% cc) sales growth was primarily driven by solid growth in the US in addition to continued uptake of the film-coated tablet formulation in Europe.

Tafinlar + Mekinist (USD 873 million, +29% cc) sales growth was primarily driven by combination uptake across Europe in addition to launch uptake in the US for the non-small cell lung cancer indication.
Promacta/Revolade (USD 867 million, +37% cc) continued to deliver solid double-digit growth across all regions.
Votrient (USD 808 million, +10% cc) worldwide growth was driven primarily by the advanced renal cell carcinoma indication both in the US and in Emerging Growth Markets, specifically China and Asia-Pacific countries.
Jakavi (USD 777 million, +32% cc) delivered strong double-digit growth across all regions, driven by continued momentum in the myelofibrosis indication in addition to reimbursement and launch uptake in the polycythemia vera indication across Europe.

Novartis Pharmaceuticals business unit

Ophthalmology

Sales in the Ophthalmology franchise were restated for 2017 and 2016 to reflect the product transfers between the Innovative Medicines and Alcon Divisions, announced on October 24, 2017, and January 24, 2018, that was effective January 1, 2018.
Total sales for 2017 amounted to USD 4.6 billion (–2% cc), with increased sales of *Lucentis* helping to partially offset the impact of generic competition.
Lucentis (USD 1.9 billion, +4% cc) sales continued to grow, driven by market expansion in Europe, Japan and Emerging Growth Markets, and reimbursement listing in China for neovascular age-related macular degeneration.
Travoprost Group (USD 589 million, –5% cc) sales declined mainly due to loss of exclusivity in Europe.

Neuroscience

Neuroscience franchise sales in 2017 were USD 3.3 billion (+2% cc), driven by increased sales for *Gilenya* (USD 3.2 billion, +2% cc) which continued to grow across regions, mainly driven by volume.

Immunology, Hepatology and Dermatology

Sales in 2017 in the Immunology, Hepatology and Dermatology franchise reached USD 2.5 billion (+74% cc).
Cosentyx saw continued strong growth across all indications, particularly in the US and Europe, reaching USD 2.1 billion (+82% cc). *Ilaris* also continued to deliver strong gains (+42% cc).

Respiratory

Respiratory franchise sales in 2017 were USD 1.6 billion (+8% cc). Our chronic obstructive pulmonary disease (COPD) portfolio – including *Onbrez Breezhaler*, *Seebri Breezhaler* and *Ultibro Breezhaler*– achieved sales of USD 674 million (+5% cc). Sales of *Xolair*, for moderate-to-severe or severe, persistent asthma, as well as for chronic hives, reached USD 920 million (+11% cc) and showed balanced growth across all regions.

Cardio-Metabolic

Sales for the franchise in 2017 were USD 524 million (+182% cc). *Entresto*– which has been launched in nearly 60 countries and used to treat more than 420 000 heart failure patients worldwide – continued to grow, and sales reached USD 507 million (+195% cc). *Entresto* performance was driven by growing adoption by physicians in the US and EU, and continued market access improvement.

Established Medicines

The Established Medicines franchise had sales in 2017 of USD 7.5 billion (–4% cc). Increased sales of *Galvus* Group and *Exforge* Group were more than offset by declines for products such as *Diovan* Group, *Neoral/Sandimmun(e)* and *Exelon/Exelon* Patch (–14% cc) due to generic competition.
Galvus Group (USD 1.2 billion, +5% cc) continued to grow, driven by solid performance in Japan and Emerging Growth Markets.
Exforge Group (USD 960 million, +4% cc) grew despite ongoing generic competition in the US and Japan, and new generic competition in Europe in 2017. Growth was driven by Emerging Growth Markets.
Diovan Group (USD 957 million, –9% cc) saw sales decline due to loss of exclusivity including in the US, EU and Japan, while sales continued to grow in China and some Emerging Growth Markets.
Neoral/Sandimmun(e) (USD 488 million, –4% cc) sales declined slightly due to generic competition and mandatory price reductions, mainly in Europe and Japan.
Voltaren/Cataflam (USD 465 million, –4% cc) sales were impacted by increased generic competition.

Sandoz

Sandoz net sales in 2017 were USD 10.1 billion, down 1% in reported terms. In constant currencies, or cc, sales declined 2%. A 6 percentage-point increase in volume was more than offset by the negative 8 percentage-point effect

of price erosion. Sales rose +4% (cc) in Europe to USD 4.6 billion. In the US, where we continue to see customer consolidation and greater competition, sales were USD 3.3 billion (−12%), mainly due to increased industrywide pressure on prices in generics. Sales in Asia, Africa and Australasia were USD 1.4 billion, up 1% in constant currencies.

(USD millions)	Year ended Dec 31, 2017	Year ended Dec 31, 2016	Change in USD %	Constant currencies change %
Retail Generics[1]	8 409	8 623	– 2	– 3
Biopharmaceuticals	1 135	1 002	13	12
Anti-Infectives (partner label/API)	516	519	– 1	– 2
Total	10 060	10 144	– 1	– 2

[1] Of which USD 880 million (2016: USD 860 million) represents Anti-infectives sold under Sandoz name

Retail Generics

Sandoz markets active ingredients, intermediates, and finished dosage forms of pharmaceuticals. The Retail Generics franchise includes products in the therapeutic areas of cardiovascular, central nervous system, dermatology, gastrointestinal and hormonal therapies, metabolism, oncology, ophthalmics, pain and respiratory, plus finished dosage forms of anti-infectives sold under the Sandoz name. Franchise sales in 2017 were USD 8.4 billion, down 3% (cc). Declines in the US (−14%) more than offset increased sales in the rest of the world (+3% cc).

Biopharmaceuticals

The Biopharmaceuticals business comprises biosimilars; contract biologics supplied to third parties; and a generic version of Copaxone® 20 mg, *Glatopa*, which treats relapsing forms of multiple sclerosis and is marketed in the US. Global sales in 2017 of Biopharmaceuticals grew 12% (cc) to USD 1.1 billion, driven by *Zarxio* (filgrastim), *Binocrit* (epoetin alfa), and the launch of *Rixathon* (rituximab) and *Erelzi* (etanercept) in several European countries.

Anti-Infectives

Sandoz sells pharmaceutical ingredients and intermediates (mainly antibiotics) to third-party customers, as well as finished dosage forms. Anti-infectives sold to third parties for sale under their own name were USD 516 million, down 2% (cc) due to the discontinuation of some low-margin products. Total Anti-Infectives sales in 2017 were USD 1.4 billion, in line with the prior year in constant currencies, and included sales of finished dosage forms sold under the Sandoz name of USD 880 million, up 2% (cc).

Alcon

Sales in Alcon were restated for 2017 and 2018 to reflect the product transfer between the Innovative Medicines Division and Alcon Division, announced on October 24, 2017, and January 24, 2018, that was effective as of January 1, 2018. In 2017, these sales transferred from the Innovative Medicines Division to Alcon Division amounted to USD 747 million and in 2016 USD 731 million.

Alcon continued to implement its growth plan in 2017, with a focus on strengthening customer relationships, improving operations, and accelerating innovation and sales. In the US, Alcon launched the *AcrySof* IQ *ReSTOR* +2.5 D Multifocal Toric intraocular lens (IOL) with ACTIVEFOCUS optical design, which aims to improve distance vision in cataract patients with astigmatism. Other product launches in 2017 include the *CyPass* Micro-Stent in the EU to treat glaucoma. Alcon also received European approval for the *Clareon* IOL with *AutonoMe* pre-loaded delivery system, the first and only automated, disposable IOL delivery system for cataract surgery.

(USD millions)	Year ended Dec 31, 2017 restated [1]	Year ended Dec 31, 2016 restated [1]	Change in USD %	Constant currencies change %
Surgical				
Consumables	2 097	2 007	4	5
Implantables	1 034	1 007	3	4
Equipment/other	594	565	5	5
Total	3 725	3 579	4	5
Vision Care				
Contact lenses	1 833	1 762	4	4
Ocular health	1 213	1 202	1	0
Total	3 046	2 964	3	2
Total net sales	6 771	6 543	3	4

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Surgical

Surgical sales in 2017 grew 5% (cc) to USD 3.7 billion, mainly driven by the by the consumables portfolio (+5% cc), particularly for cataract and vitreoretinal surgery. Implantables grew 4% (cc) as strong performance of new products,

including the UltraSert pre-loaded IOL delivery system, the *AcrySof* IQ *PanOptix* trifocal IOL and *AcrySof* IT *ReSTOR* +2.5D Toric IOL , was partly offset by declines in monofocal IOLs which continued to face competitive pressures. Sales of equipment grew 5% (cc), mainly driven by sales of vitreoretinal equipment.

Vision Care

Vision Care sales in 2017 grew 2% (cc) to USD 3.0 billion driven by contact lens sales (+4% cc). Contact lens sales growth was driven by continued double-digit growth of *Dailies Total1*, the world's first and only water gradient lens, and was partly offset by declines in reusable lenses as the market continues to shift to daily disposable lenses. Ocular health sales remained broadly in line with the prior year (0% cc), as dry eye growth was offset by a decline in contact lens care product sales impacted by the continued market shift to daily disposable lenses.

Operating income

The following table provides an overview of operating income by segment:

(USD millions)	Year ended Dec 31, 2017 restated [1]	% of net sales	Year ended Dec 31, 2016 restated [1]	% of net sales	Change in USD %	Change in constant currencies %
Innovative Medicines	7 595	23.5	7 255	22.8	5	7
Sandoz	1 368	13.6	1 445	14.2	– 5	– 7
Alcon	– 3	0.0	39	0.6	nm	nm
Corporate	– 331		– 471		30	27
Operating income	8 629	17.6	8 268	17.0	4	7

nm = not meaningful

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Operating income in 2017 was USD 8.6 billion (+4%, +7% cc), as growth drivers, productivity, lower amortization, and a gain from the achievement of a sales milestone related to the 2015 Vaccines divestment to GSK more than offset generic erosion. Operating income margin in constant currencies increased 0.8 percentage points compared to the prior year; currency had a negative impact of 0.2 percentage points, resulting in an increase of 0.6 percentage points to 17.6% of net sales.

Core operating income key figures1

(USD millions unless indicated otherwise)	Year ended Dec 31, 2017	Year ended Dec 31, 2016	Change in USD %	Change in constant currencies %
Core gross profit	36 578	35 806	2	3
Selling, general and administration	– 15 000	– 14 111	– 6	– 6
Research and development	– 8 313	– 8 402	1	1
Other income	778	753	3	2
Other expense	– 1 193	– 1 059	– 13	– 13
Core operating income	12 850	12 987	– 1	0
As % of net sales	26.2	26.8		

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

The adjustments made to operating income to arrive at core operating income in 2017 amounted to USD 4.2 billion (2016: USD 4.7 billion), less than in the prior year due to lower amortization and a gain from the achievement of a sales milestone related to the 2015 Vaccines divestment to GSK.

Core operating income in 2017 was USD 12.9 billion (−1%, 0% cc). Core operating income margin in constant currencies decreased 0.3 percentage points, mainly due to generic competition for *Gleevec/Glivec*, and higher launch investments, which were partially offset by expanded gross margin and productivity improvements. Currency exchange rates had an additional negative impact of 0.3 percentage points, yielding a net decrease of 0.6 percentage points to 26.2% of net sales.

The following table provides an overview of core operating income by segment:

(USD millions)	Year ended	% of	Year ended	% of	Change in USD	Change in constant currencies

	Dec 31, 2017 restated [1]	net sales	Dec 31, 2016 restated [1]	net sales	%	%
Innovative Medicines	10 019	31.0	10 054	31.6	0	2
Sandoz	2 080	20.7	2 071	20.4	0	– 1
Alcon	1 168	17.3	1 150	17.6	2	5
Corporate	– 417		– 288		– 45	– 53
Core operating income	12 850	26.2	12 987	26.8	– 1	0

[1] Restated to reflect the product transfers between divisions that was effective as of January 1, 2018.

Innovative Medicines

Operating income in 2017 was USD 7.6 billion (+5%, +7% cc), mainly driven by higher sales, productivity improvements and lower amortization, which offset the impact of generic competition and investments in growth drivers.

Core operating income, which excludes certain items, in 2017 was USD 10.0 billion (0%, +2% cc). Core operating income margin decreased 0.2 percentage points in constant currencies, and fluctuations in exchange rates had a further negative impact of 0.4 percentage points, resulting in a net decrease of 0.6 percentage points to 31.0% of net sales.

Sandoz

Operating income in 2017 was USD 1.4 billion (−5%, −7% cc), down mainly due to pressure on prices in the US, investments in marketing and sales in key markets outside the US, and higher manufacturing restructuring charges. These negative impacts were partly offset by favorable changes in product mix.

Core operating income, which excludes certain items, in 2017 was USD 2.1 billion (0%, −1% cc). Core operating income margin in constant currencies increased 0.1 percentage points, and an additional 0.2 percentage point increase from exchange rates yielded a result of 20.7% of net sales.

Alcon

Operating loss in 2017 was USD 3 million, compared to an operating income of USD 39 million the year before, as higher sales were offset by continued investment in the division's growth plan and charges related to business development activities.

Core operating income, which excludes certain items, in 2017 was USD 1.2 billion (+2%, +5% cc). Core operating income margin in constant currencies increased by 0.2 percentage points, offset by negative currency impact of 0.5 percentage points, yielding a net decrease of 0.3 percentage points to 17.3% of net sales.

Corporate income and expense, net

Corporate income and expense, which includes the cost of Group management and central services, amounted to a net expense of USD 331 million (+30%, +27% cc) in 2017, compared to a net expense of USD 471 million in the prior year. The favorable decrease in expense was mainly due to a gain from the achievement of a sales milestone related to the 2015 Vaccines divestment to GSK, partly offset by lower gains from divestment in real estate and lower contributions from the captive insurance companies.

Research and development of Innovative Medicines Division

The following table provides an overview of the reported and core research and development expense of the Innovative Medicines Division:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2017 restated [1]	Year ended Dec 31, 2016 restated [1]	Change in USD %	Change in constant currencies %
Research and exploratory development	– 2 729	– 2 720	0	0
Confirmatory development	– 4 886	– 4 976	2	2
Total Innovative Medicines Division research and development expense	– 7 615	– 7 696	1	1
As % of Innovative Medicines net sales to third parties	23.6	24.2		
Core research and exploratory development[2]	– 2 603	– 2 618	1	1
Core confirmatory development[2]	– 4 431	– 4 482	1	1
Total core Innovative Medicines Division research and development expense	– 7 034	– 7 100	1	1
As % of Innovative Medicines net sales to third parties	21.8	22.3		

[1] 2017 and 2016 figures are restated to reflect the product transfers between divisions that was effective as of January 1, 2018, and in addition for certain amounts that were reclassified from research and exploratory development to confirmatory development for comparative purposes.

[2] Core excludes impairments, amortization and certain other items. For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

Innovative Medicines Division research and exploratory development expense amounted to USD 2.7 billion in 2017, in line with the prior year. Confirmatory development expense decreased by 2% (+2% cc) to USD 4.9 billion, compared to USD 5.0 billion in 2016, driven by resource allocation and continued productivity efforts, including the benefit of the creation of the Novartis Global Drug Development (GDD) organization.

Total core research and development expense in the Innovative Medicines Division as a percentage of sales decreased by 0.7 percentage points in constant currencies, mainly due to resource allocation and continued productivity efforts. Currency exchange rates had a negative impact of 0.2 percentage points, yielding a net decrease of 0.5 percentage points to 21.8% of net sales.

Non-operating income and expense

The following table provides an overview of non-operating income and expense:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2017	Year ended Dec 31, 2016	Change in USD %	Change in constant currencies %
Operating income	8 629	8 268	4	7
Income from associated companies	1 108	703	58	58
Interest expense	– 777	– 707	– 10	– 12
Other financial income and expense	39	– 447	nm	nm
Income before taxes	8 999	7 817	15	12
Taxes	– 1 296	– 1 119	– 16	– 13
Net income	7 703	6 698	15	12
Total basic EPS (USD)	3.28	2.82	16	14

nm = not meaningful

Income from associated companies

Income from associated companies in 2017 increased to USD 1.1 billion, compared to USD 703 million in the prior year. The increase was due to higher income recognized from our investment in GSK Consumer Healthcare Holdings Ltd. (GSK Consumer Healthcare).

The estimated income from our investment in GSK Consumer Healthcare in 2017 amounted to USD 629 million, compared to USD 234 million in 2016. The increase is due to improved operational results of USD 89 million; an estimate of a one-time deferred tax income of USD 237 million, arising from a change in a Swiss cantonal statutory tax rate; and a positive prior-year adjustment of USD 47 million based on the actual audited results for 2016, compared to a negative prior-year adjustment of USD 22 million recognized in 2016 for 2015.

The estimated income from our investment in Roche in 2017 amounted to USD 456 million (2016: USD 464 million). This reflected our estimated share of income for 2017 of USD 523 million (2016: USD 532 million), offset by the negative prior-year adjustment of USD 67 million, based on actual 2016 results (2016: negative prior-year adjustment of USD 68 million, based on actual 2015 results).

Interest expense and other financial income and expense

Interest expense in 2017 increased to USD 777 million from USD 707 million in the prior year due to higher outstanding debt.

Other financial income and expense amounted to an income of USD 39 million, compared to an expense of USD 447 million in the prior year, mainly on account of exceptional charges related to Venezuela of USD 305 million in 2016, as well as higher currency losses in 2016.

Taxes

The tax rate in 2017 increased to 14.4% from 14.3% in the prior year. On December 22, 2017, the US enacted tax reform legislation (Tax Cuts and Jobs Act), which – among other provisions – reduced the US corporate tax rate from 35% to 21%, effective January 1, 2018. This required a revaluation of the deferred tax assets and liabilities, and a portion of current tax payables to the newly enacted tax rate at the date of enactment, which resulted in a net tax expense of USD 61 million (0.7%). In addition, a change in a Swiss cantonal statutory tax rate resulted in a one-time income from our share in GSK Consumer Healthcare, the impact of which decreased the tax rate by 0.4%. Excluding the impact of these rate changes, the reported tax rate for 2017 would have been 14.1%, compared to 14.3% in the prior year.

Net income

Net income in 2017 was USD 7.7 billion (+15%, +12% cc), benefiting from growth in operating income and higher income from our stake in GSK Consumer Healthcare Holdings Ltd. The prior year also included the exceptional charges related to Venezuela.

EPS

Basic earnings per share in 2017 were USD 3.28 (+16%, +14% cc), up more than net income in constant currencies, benefiting from our share buyback program.

Core non-operating income and expense1

The following table provides an overview of core non-operating income and expense:

(USD millions unless indicated otherwise)	Year ended Dec 31, 2017	Year ended Dec 31, 2016	Change in USD %	Change in constant currencies %
Core operating income	12 850	12 987	– 1	0
Core income from associated companies	1 335	1 134	18	18
Core interest expense	– 777	– 707	– 10	– 12
Core other financial income and expense	39	– 99	nm	nm
Core income before taxes	13 447	13 315	1	2
Core taxes	– 2 056	– 2 001	– 3	– 4
Core net income	11 391	11 314	1	2
Core basic EPS (USD)	4.86	4.75	2	3

[1] For an explanation of non-IFRS measures and reconciliation tables, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

nm = not meaningful

Core income from associated companies

Core income from associated companies in 2017 increased to USD 1.3 billion from USD 1.1 billion in the prior-year period. The core income contribution from GSK Consumer Healthcare Holdings Ltd. increased to USD 479 million in 2017 from USD 369 million in the prior-year period, and the core income contribution from Roche increased to USD 832 million from USD 760 million.

Core interest expense and other financial income and expense

Core other financial income and expense in 2017 amounted to an income, net of USD 39 million, compared to an expense, net of USD 99 million in 2016, mainly on account of lower currency losses. In the prior year, the exceptional charges of USD 0.3 billion related to Venezuela were excluded from the 2016 core other financial expense.

Core taxes

The core tax rate in 2017 (core taxes as a percentage of core pre-tax income) increased to 15.3% from 15.0% in the prior year.

Core net income

Core net income in 2017 was USD 11.4 billion (+1%, +2% cc), benefiting from higher core income from associated companies.

Core EPS

Core earnings per share in 2017 were USD 4.86 (+2%, +3% cc), reflecting the benefit of our share buyback program.

Factors affecting comparability of year-on-year results of operations

Significant transactions in 2018, 2017, 2016 and significant pending transactions

The comparability of the year-on-year results of our operations for the total Group can be significantly affected by acquisitions and divestments. As part of the long-term strategy to focus Novartis as a leading medicines company, we announced and/or completed several acquisitions and divestments during 2018, 2017 and 2016.

A detailed description of the significant transactions of 2018, 2017, 2016 and significant pending transactions can be found in “Item 4.A History and development of Novartis – Important Corporate developments 2016 – 2018”, and “Item 18. Financial Statements—Note 2 Significant transactions”.

Critical accounting policies and estimates

Our significant accounting policies are set out in "Item 18. Financial Statements—Note 1. Significant accounting policies," which are prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB).

Given the uncertainties inherent in our business activities, we must make certain estimates and assumptions that require difficult, subjective and complex judgments. Because of uncertainties inherent in such judgments, actual outcomes and results may differ from our assumptions and estimates, which could materially affect the Group's consolidated financial statements. Application of the following accounting policies requires certain assumptions and estimates that have the potential for the most significant impact on our consolidated financial statements.

New accounting pronouncements

Novartis implemented IFRS 9 Financial Instruments as of January 1, 2018, which substantially changes the classification and measurement of financial instruments. The new standard requires impairments to be based on a forward-looking model, changes the approach to hedging financial exposures and related documentation, changes the recognition of certain fair value changes, and amends disclosures requirements.

Novartis implemented the new standard IFRS 15 Revenue from Contracts with Customers as of January 1, 2018. The new standard amends revenue recognition requirements and establishes principles for reporting information about the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers. The standard replaces IAS 18 Revenue and IAS 11 Construction contracts and related interpretations.

The Group applied the modified retrospective method upon adoption of IFRS 9 and IFRS 15 on January 1, 2018. This method requires the recognition of the cumulative effect of initially applying IFRS 9 and IFRS 15 to retained earnings and not to restate prior years. As a result, the critical accounting policies related to revenue and trade receivables described below are applicable to the preparation of the 2018 consolidated financial statements. The accounting policies for revenue and trade receivables that are applicable to the preparation of the 2017 and 2016 consolidated financial statements are described in Note 1; see "Item 18. Financial Statements—Note 1. Significant accounting policies."

Deductions from revenues

As is typical in the pharmaceutical industry, our gross sales are subject to various deductions, which are primarily composed of rebates and discounts to retail customers, government agencies, wholesalers, health insurance companies and managed healthcare organizations. These deductions represent estimates of the related obligations, requiring the use of judgment when estimating the effect of these sales deductions on gross sales for a reporting period. These adjustments are deducted from gross sales to arrive at net sales.

The following summarizes the nature of some of these deductions and how the deduction is estimated. After recording these, net sales represent our best estimate of the cash that we expect to ultimately collect. The US market has the most complex arrangements related to revenue deductions.

United States-specific healthcare plans and program rebates

The United States Medicaid Drug Rebate Program is administered by state governments, using state and federal funds to provide assistance to certain vulnerable and needy individuals and families. Calculating the rebates to be paid related to this program involves interpreting relevant regulations, which are subject to challenge or change in interpretative guidance by government authorities. Provisions for estimating Medicaid rebates are calculated using a combination of historical experience, product and population growth, product pricing, and the mix of contracts and specific terms in the individual state agreements.

The United States Federal Medicare Program, which funds healthcare benefits to individuals age 65 and older, and to people with certain disabilities, provides prescription drug benefits under the Part D section of the program. This benefit is provided and administered through private prescription drug plans. Provisions for estimating Medicare Part D rebates are calculated based on the terms of individual plan agreements, product sales and population growth, product pricing, and the mix of contracts.

We offer rebates to key managed healthcare and private plans in an effort to sustain and increase the market share of our products, and to ensure patient access to our products. These programs provide a rebate after the plans have demonstrated they have met all terms and conditions set forth in their contract with us.

These rebates are estimated based on the terms of individual agreements, historical experience, product pricing, and projected product growth rates, and are recorded as a deduction from revenue at the time, the related revenues are recorded.

These provisions are adjusted based on established processes and experiences from filing data with individual states and plans. There is often a time lag of several months between the recording of the revenue deductions and the final accounting for them.

Non-United States-specific healthcare plans and program rebates

In certain countries other than the US, we provide rebates to governments and other entities. These rebates are often mandated by laws or government regulations.

In several countries, we enter into innovative pay- for- performance arrangements with certain healthcare providers. Under these agreements, we may be required to make refunds to the healthcare providers or to provide additional medicines free of charge if anticipated treat-

ment outcomes do not meet predefined targets. Potential refunds or the delivery of additional medicines at no cost are estimated and recorded as a deduction from revenue at the time the related revenues are recorded. Estimates are based on historical experience and clinical data. In cases where historical experience and clinical data are not sufficient for a reliable estimation of the outcome, revenue recognition is deferred until such history is available.

In addition, we offer global patient assistance programs.

There is often a time lag of several months between us recording the revenue deductions and our final accounting for them.

Non-healthcare plans and program rebates, returns and other deductions

We offer rebates to purchasing organizations and other direct and indirect customers to sustain and increase market share and to ensure patient access to our products. Since rebates are contractually agreed upon, the related provisions are estimated based on the terms of the individual agreements, historical experience, and projected product sales growth rates.

Chargebacks occur where our subsidiaries have arrangements with indirect customers to sell products at prices that are lower than the price charged to wholesalers. A chargeback represents the difference between the invoice price to the wholesaler and the indirect customer's contract price. We account for vendor chargebacks by reducing revenue by the estimate of chargebacks attributable to a sales transaction. Provisions for estimated chargebacks are calculated using a combination of factors, such as historical experience, product growth rates, product pricing, level of inventory in the distribution channel and the terms of individual agreements.

When we sell a product providing a customer the right to return it, we record a provision for estimated sales returns based on our sales return policy and historical return rates. Other factors considered include actual product recalls, expected marketplace changes, the remaining shelf life of the product, and the expected entry of generic products. In 2018, sales returns amounted to approximately 1% of gross product sales. If sufficient experience is not available, sales are only recorded based on evidence of product consumption or when the right of return has expired.

We enter into distribution service agreements with major wholesalers, which provide a financial disincentive for the wholesalers to purchase product quantities in excess of current customer demand. Where possible, we adjust shipping patterns for our products to maintain wholesalers' inventory levels consistent with underlying patient demand.

We offer cash discounts to customers to encourage prompt payment. Cash discounts are estimated and accrued at the time of invoicing and are deducted from revenue.

Following a decrease in the price of a product, we generally grant customers a "shelf stock adjustment" for their existing inventory for the relevant product. Provisions for shelf stock adjustments, which are primarily relevant within the Sandoz Division, are determined at the time of the price decline or at the point of sale, if the impact of a price decline on the products sold can be reasonably estimated based on the customer's inventory levels of the relevant product.

Other sales discounts, such as consumer coupons and co-pay discount cards, are offered in some markets. The estimated amounts of these discounts are recorded at the time of sale or when the coupons are issued, and are estimated utilizing historical experience and the specific terms for each program. If a discount for a probable future transaction is offered as part of a sales transaction, then an appropriate portion of revenue is deferred to cover this estimated obligation.

We adjust provisions for revenue deductions periodically to reflect actual experience. To evaluate the adequacy of provision balances, we use internal and external estimates of the inventory in transit, the level of inventory in the distribution and retail channels, actual claims data received, and the time lag for processing rebate claims. External data sources include reports from wholesalers and third-party market data purchased by Novartis.

For the table showing the worldwide extent of our revenue deductions provisions and related payment experiences for the Group see "Item 18. Financial Statements – Note 21 Provisions and other current liabilities".

Gross-to-net sales reconciliation

The table below shows the gross to net sales reconciliation for our Innovative Medicines Division:

	Income statement charge			
	Charged through revenue deduction provisions USD millions	Charged directly without being recorded in revenue deduction provisions USD millions	Total USD millions	In % of gross sales
2018				
Innovative Medicines gross sales subject to deductions			47 785	100.0
US-specific healthcare plans and program rebates	– 3 921		– 3 921	– 8.2
Non-US-specific healthcare plans and program rebates	– 2 108	– 1 032	– 3 140	– 6.6
Non-healthcare plans and program-related rebates, returns and other deductions	– 3 157	– 2 675	– 5 832	– 12.2
Total Innovative Medicines gross-to-net sales adjustments	– 9 186	– 3 707	– 12 893	– 27.0
Innovative Medicines net sales 2018			34 892	73.0
2017[1]				
Innovative Medicines gross sales subject to deductions			43 127	100.0
US-specific healthcare plans and program rebates	– 3 303		– 3 303	– 7.7
Non-US-specific healthcare plans and program rebates	– 1 712	– 940	– 2 652	– 6.1
Non-healthcare plans and program-related rebates, returns and other deductions	– 2 652	– 2 242	– 4 894	– 11.4
Total Innovative Medicines gross-to-net sales adjustments	– 7 667	– 3 182	– 10 849	– 25.2
Innovative Medicines net sales 2017			32 278	74.8
2016[1]				
Innovative Medicines gross sales subject to deductions			41 798	100.0
US-specific healthcare plans and program rebates	– 3 051		– 3 051	– 7.3
Non-US-specific healthcare plans and program rebates	– 1 341	– 873	– 2 214	– 5.3
Non-healthcare plans and program-related rebates, returns and other deductions	– 2 696	– 2 006	– 4 702	– 11.2
Total Innovative Medicines gross-to-net sales adjustments	– 7 088	– 2 879	– 9 967	– 23.8
Innovative Medicines net sales 2016			31 831	76.2

[1] Restated to reflect the product transfers between divisions, that was effective as of January 1, 2018

Surgical equipment revenue

Surgical equipment may be sold together with other products and services under a single contract. Revenues are recognized upon satisfaction of each of the performance obligations in the contract and the consideration is allocated based on the standalone selling price of each performance obligation.

For surgical equipment, in addition to cash and installment sales, revenue is recognized under finance and operating lease arrangements. Arrangements in which Novartis transfers substantially all the risks and rewards incidental to ownership to the customer are treated as finance lease arrangements. Revenue from finance lease arrangements is recognized at amounts equal to the fair values of the equipment, which approximate the present values of the minimum lease payments under the arrangements. As interest rates embedded in lease arrangements are

approximately market rates, revenue under finance lease arrangements is comparable to revenue for outright sales. Finance income for arrangements in excess of twelve months is deferred and subsequently recognized based on a pattern that approximates the use of the effective interest method. It is recorded in “Other income.” Operating lease revenue for equipment rentals is recognized on a straight line basis over the lease term.

Impairment of goodwill, intangible assets and property, plant and equipment

We review long-lived intangible assets and property, plant and equipment for impairment whenever events or changes in circumstance indicate that the asset’s balance sheet carrying amount may not be recoverable. Goodwill, the Alcon brand name and other currently not amortized intangible assets are reviewed for impairment at least annually.

An asset is generally considered impaired when its balance sheet carrying amount exceeds its estimated recoverable amount, which is defined as the higher of its fair value less costs of disposal and its value in use. Usually, Novartis adopts the fair value less costs of disposal method for its impairment evaluation. In most cases, no directly observable market inputs are available to measure the fair value less costs of disposal. Therefore, an estimate of fair value less costs of disposal is derived indirectly and is based on net present value techniques utilizing post-tax cash flows and discount rates. In the

limited cases where the value in use method is applied, net present value techniques are utilized using pre-tax cash flows and discount rates.

Fair value reflects estimates of assumptions that market participants would be expected to use when pricing the asset and, for this purpose, management considers the range of economic conditions that are expected to exist over the remaining useful life of the asset. The estimates used in calculating net present values are highly sensitive and depend on assumptions specific to the nature of the Group's activities with regard to:

• The amount and timing of projected cash flows
• The behavior of competitors (launch of competing products, marketing initiatives, etc.)
• The probability of obtaining regulatory approvals
• Future tax rates
• The appropriate royalty rate for the Alcon brand name
• The appropriate terminal growth rate
• The appropriate discount rate

Due to the above factors and those further described in "Item 18. Financial Statements—Note 1. Significant accounting policies – Impairment of goodwill and intangible assets", actual cash flows and values could vary significantly from forecasted future cash flows and related values derived using discounting techniques.

The recoverable amount of the grouping of cash-generating units to which goodwill and indefinite life intangible assets are allocated is based on fair value less costs of disposal. The valuations are derived from applying discounted future cash flows based on key assumptions, including the terminal growth rate and discount rate. For additional information, see "Item 18. Financial Statements – Note 1. Significant accounting policies – Impairment of goodwill and intangible assets and Note 10. Goodwill and intangible assets."

In 2018, intangible asset impairment charges of USD 1.2 billion were recognized, of which USD 592 million was recorded in the Innovative Medicines Division, USD 249 million was recorded in the Sandoz Division, and USD 391 million was recorded in the Alcon Division.

In 2017, intangible asset impairment charges of USD 709 million were recognized, of which USD 591 million was recorded in the Innovative Medicines Division, USD 61 million was recorded in the Sandoz Division, and USD 57 million was recorded in the Alcon Division.

In 2016, intangible asset impairment charges of USD 591 million were recognized, of which USD 522 million was recorded in the Innovative Medicines Division, USD 65 million was recorded in the Sandoz Division, and USD 4 million was recorded in the Alcon Division.

In 2018, 2017 and in 2016, there were no reversals of prior-year impairment charges.

Goodwill and other intangible assets represent a significant part of our consolidated balance sheet, primarily due to acquisitions. Although no significant additional impairments are currently anticipated, impairment evaluation could lead to material impairment charges in the future. For more information, see "Item 18. Financial Statements—Note 10. Goodwill and intangible assets."

Additionally, net impairment charges for property, plant and equipment during 2018 amounted to USD 304 million (2017: USD 157 million; 2016: USD 102 million).

Impairment of associated companies accounted for at equity

Novartis considers investments in associated companies for impairment evaluation whenever objective evidence indicates the net investment may be impaired, including when a quoted share price indicates a fair value less than the per share balance sheet carrying value for the investment.

If the recoverable amount of the investment is estimated to be lower than the balance sheet carrying amount, an impairment charge is recognized for the difference in the consolidated income statement under "Income from associated companies."

Trade receivables

Trade receivables are initially recognized at their invoiced amounts, including any related sales taxes less adjustments for estimated revenue deductions such as rebates, chargebacks and cash discounts.

From January 1, 2018, with the adoption of IFRS 9 Financial Instruments, provisions for expected credit losses are established using an expected credit loss model (ECL). The provisions are based on a forward-looking ECL, which includes possible default events on the trade receivables over the entire holding period of the trade receivable. These provisions represent the difference between the trade receivable's carrying amount in the consolidated balance sheet

and the estimated collectible amount. Charges for doubtful trade receivables are recorded as marketing and selling costs recognized in the consolidated income statement within “Selling, General & Administration” expenses.
Trade receivable balances include sales to drug wholesalers, retailers, private health systems, government agencies, managed care providers, pharmacy benefit managers and government-supported healthcare systems. Novartis continues to monitor sovereign debt issues and economic conditions in Greece, Italy, Portugal, Spain, Brazil, Russia, Saudi Arabia, Turkey, Argentina, and other countries, and evaluates trade receivables in these countries for potential collection risks. Substantially all of the trade receivables overdue from Greece, Portugal, Spain, Brazil, Argentina and Saudi Arabia are due directly from local governments or from government-funded entities. Deteriorating credit and economic conditions as well as other factors in these countries have resulted in – and may continue to result in – an increase in the average length of time that it takes to collect these trade receivables, and may require the Group to re-evaluate the estimated collectable amount of these trade receivables in future periods.
Contingent consideration
In a business combination or divestment of a business, it is necessary to recognize contingent future payments to previous owners representing contractually defined potential amounts as a liability or asset. Usually for Novartis, these are linked to milestone or royalty pay-

ments related to certain assets and are recognized as a financial liability or financial asset at their fair value, which is then remeasured at each subsequent reporting date. These estimations typically depend on factors such as technical milestones or market performance, and are adjusted for the probability of their likelihood of payment and, if material, are appropriately discounted to reflect the impact of time.

Changes in the fair value of contingent consideration liabilities in subsequent periods are recognized in the consolidated income statement in “Cost of goods sold” for currently marketed products and in “Research and development” for In-Process Research and Development (IPR&D). Changes in contingent consideration assets are recognized in “Other income” or “Other expense,” depending on its nature.

The effect of unwinding the discount over time is recognized for contingent liabilities in “Interest expense” and for contingent assets are recorded as interest income recognized in the consolidated income statement within “other financial income and expense”.

Retirement and other post-employment benefit plans

We sponsor pension and other post-employment benefit plans in various forms that cover a significant portion of our current and former associates. For post-employment plans with defined benefit obligations, we are required to make significant assumptions and estimates about future events in calculating the expense and the present value of the liability related to these plans. These include assumptions about the interest rates we apply to estimate future defined benefit obligations and net periodic pension expense, as well as rates of future pension increases. In addition, our actuarial consultants provide our management with historical statistical information, such as withdrawal and mortality rates in connection with these estimates.

Assumptions and estimates used by the Group may differ materially from the actual results we experience due to changing market and economic conditions, higher or lower withdrawal rates, and longer or shorter life spans of participants, among other factors. For example, in 2018, a decrease in the interest rate we apply in determining the present value of the defined benefit obligations of one-quarter of 1% would have increased our year-end defined benefit pension obligation for plans in Switzerland, the United States, the United Kingdom, Germany and Japan, which represent 94% of the Group total defined benefit pension obligation, by approximately USD 0.8 billion. Similarly, if the 2018 interest rate had been one-quarter of 1 percentage point lower than actually assumed, the net periodic pension cost for pension plans in these countries, which represent about 86% of the Group’s total net periodic pension cost for pension plans, would have increased by approximately USD 26 million. Depending on events, such differences could have a material effect on our total equity. For more information on obligations under retirement and other post-employment benefit plans and underlying actuarial assumptions, see “Item 18. Financial Statements—Note 24. Post-employment benefits for associates.”

Provisions and contingencies

A number of Group companies are involved in various government investigations and legal proceedings (intellectual property, sales and marketing practices, product liability, commercial, employment and wrongful discharge, environmental claims, etc.) arising out of the normal conduct of their businesses. For more information, see “Item 18. Financial Statements—Note 19. Provisions and other non-current liabilities” and “Item 18. Financial Statements—Note 27. Commitments and contingencies.”

We record provisions for legal proceedings when it is probable that a liability has been incurred and the amount can be reliably estimated. These provisions are adjusted periodically as assessments change or additional information becomes available. For significant product liability cases, the provision is actuarially determined based on factors such as past experience, amount and number of claims reported, and estimates of claims incurred but not yet reported. Provisions are recorded for environmental remediation costs when expenditure on remedial work is probable and the cost can be reliably estimated. Remediation costs are provided for under “Non-current liabilities” in the Group’s consolidated balance sheet.

Provisions relating to estimated future expenditure for liabilities do not usually reflect any insurance or other claims or recoveries, since these are only recognized as assets when the amount is reasonably estimable and collection is virtually certain.

Research and development

Internal research and development costs are fully charged to the consolidated income statement in the period in which they are incurred. We consider that regulatory and other uncertainties inherent in the development of new products preclude the capitalization of internal development expenses as an intangible asset usually until marketing approval

from the regulatory authority is obtained in a relevant major market, such as for the United States, the European Union, Switzerland or Japan.

Healthcare contributions

In many countries, our subsidiaries are required to make contributions to the countries' healthcare costs as part of programs other than the ones mentioned above under deductions from revenues. The amounts to be paid depend on various criteria such as the subsidiary's market share or sales volume compared to certain targets. Considerable judgment is required in estimating these contributions, as not all data is available when the estimates need to be made. The largest of these healthcare contributions relates to the US Healthcare Reform fee, which was introduced in 2011. This fee is an annual levy to be paid by US pharmaceutical companies, including various Novartis subsidiaries, based on each company's prior-year qualifying sales as a percentage of the prior year's government-funded program sales. This pharmaceutical fee levy is recognized in "Other expense."

Taxes

We prepare and file our tax returns based on an interpretation of tax laws and regulations, and we record estimates based on these judgments and interpretations. Our tax returns are subject to examination by the competent taxing authorities, which may result in an assessment being made, requiring payments of additional tax, interest or penalties. Since Novartis uses its intellectual property globally to deliver goods and services, the transfer prices within the Group as well as arrangements between subsidiaries to finance research and development and other activities may be challenged by the national tax authorities in any of the jurisdictions in which Novartis operates. Therefore, inherent uncertainties exist in our estimates of our tax positions, but we believe that our estimated amounts for current and deferred tax assets or liabilities, including any amounts related to any uncertain tax positions, are appropriate based on currently known facts and circumstances.

Internal control over financial reporting

The Group's management has assessed the effectiveness of internal control over financial reporting. The Group's independent statutory auditor also issued an opinion on the effectiveness of internal control over financial reporting. Both the Group's management and its external auditors concluded that the Group maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018.

Factors affecting results of operations

Transformational changes fueling demand

Accelerating biomedical innovation

We are seeing an explosion of innovation in medical science. Better understanding of the molecular mechanisms of disease, coupled with new types of therapies, promises to yield powerful new medicines for patients. The trend toward patient-specific precision treatments will likely accelerate.

Further advances in molecular biology, which has been a mainstay of research for decades, is expected to continue to yield results. In addition, new molecular techniques, such as gene editing, personalized cell therapies and harnessing the cell's own waste disposal system, could open new treatment opportunities – including ones that go beyond what has been possible using today's drugs.

The advent of digital technologies as therapeutic aids is also starting to alter the conventional notion of medical treatment. For instance, mobile applications that aim to treat substance abuse and help diabetics manage their disease have received clearance from the FDA. Combining traditional medicines with digital technology that helps patients follow healthy behaviors holds great promise for improving the quality of care as well as treatment outcomes for patients.

Transforming how doctors diagnose and treat diseases

Although the digital revolution has been relatively slow to arrive in healthcare, it is gaining momentum and will likely bring radical change in the coming years.

A growing proliferation of sensor technology is helping researchers and doctors gather increasing amounts of information about patients' health and how they respond to treatment. Care providers are starting to mine healthcare data using a combination of statistical methods and artificial intelligence to flag emerging medical problems and help physicians diagnose and treat patients.

Patients, armed with greater access to their own medical data, will likely play a more active role in preventing diseases and managing their own care when they become ill. The role of physicians and other care providers will likely also evolve as they help educate patients on treatment options and steer patients toward the most effective choices.

Transforming drug research and development

Digital technology may also increasingly improve the efficiency and effectiveness of researching and developing potential new therapies. The marriage of data and artificial intelligence could enable complex biological simulations that complement human scientific ingenuity. Such tools are already being considered by the FDA as replacements for preclinical animal studies to assess toxicity in potential new medicines. In 2017, for example, the FDA announced a collaboration with Emulate, Inc. to evaluate the company's "organs-on-chips" technology – part of a system that recreates the physiology of human tissues and organs, and is designed to predict human responses to diseases with greater precision than animal-based testing. As digital tools become more widespread, they may be able to shorten research times and improve the likelihood that experimental drugs will prove safe and effective.

This surge in medical innovation will likely occur in an increasingly diverse and fragmented research environment, with new advances coming from a variety of sources – sometimes unexpected ones. Molecular biology may intersect

with other disciplines, from engineering to computer science, to advance the practice of medicine. And we expect there will be greater diversity in funding for research. Already we see governments, companies and venture capitalists increasingly supporting academic researchers' efforts to advance promising experimental therapies.

All of these factors are contributing to greater competition at the forefront of innovation in medical science. One upshot is that medicines will likely be held to a higher standard of efficacy in the future.

Aging populations

While accelerating medical innovation could help tame some of the devastating diseases that still plague humanity, other trends in society pose significant challenges. Rapidly aging populations continue to put pressure on health systems around the world.

People are living longer and the worldwide elderly population continues to grow at a rapid pace. The number of people in the world aged 60 or over will reach nearly 2.1 billion by 2050, according to projections by the United Nations, up from less than 1 billion today. Aging populations, in addition to rapid urbanization and changing lifestyles in the developing world, are contributing to increased prevalence of chronic ailments such as heart disease and cancer. At the same time, many countries are working to expand access to healthcare. For example, China has expanded reimbursement of some medicines.

These factors are driving higher healthcare spending, which is expected to grow at an annual rate of 4.3% between 2015 and 2020, reaching a total of USD 8.7 trillion worldwide, projects the Economist Intelligence Unit. By 2020, about half of that spending is expected to go toward treating the three leading causes of death worldwide: cardiovascular disease, cancer and respiratory disease.

To keep costs in check, governments and health insurers are already employing a variety of tactics, including increasing the use of generics and biosimilars, imposing price cuts, and limiting access to some innovative therapies. The pharmaceutical industry is also playing a role, exploring new pricing models and delivering innovative new treatments that maximize benefits for patients.

Better health outcomes for patients

In pursuit of greater efficiency and effectiveness, some healthcare systems are also expediting the transition from a system based on fees for services toward one based on reimbursement for specific health outcomes in patients. As the transition accelerates, we expect health systems will increasingly find ways to discourage the use of medical treatments that bring little or no value for patients or healthcare systems. In parallel, they will likely place greater value on treatments that delay the progression of disease or that help avoid events requiring expensive acute care, such as heart attacks.

With people living longer and retirement ages rising, we also anticipate countries and health systems will put greater emphasis on keeping people fit and productive later in life. And we think there will be growing emphasis on maintaining quality of life as people age, with less focus on extending life by a few more months.

We think the trends driving changes in healthcare will bring new opportunities for Novartis, as well as new challenges. And we believe the changes now underway in our industry raise the importance of delivering true innovation that produces better health outcomes for patients and health systems, with greater efficiency.

Increasingly challenging business environment

Loss of exclusivity for patented products

Pharmaceutical companies routinely face generic competition when their products lose patent or other intellectual property protection, and Novartis is no exception. Major products of our Innovative Medicines Division, as well as certain products of our Alcon and Sandoz Divisions, are protected by patent or other intellectual property rights, allowing us to exclusively market those products. The loss of exclusivity has had, and will continue to have, an adverse effect on our results. In 2018, the total impact of generic competition on our net sales amounted to approximately USD 1 billion.

Some of our best selling products face or are expected to face considerable competition due to the expiration of patent or other intellectual property protection. For example, our former top selling products *Gleevec*/*Glivec*, *Diovan* and *Exforge* all face continued and increasing generic competition in major markets. which will continue. Patent protection for our *Sandostatin* products has expired and there is a risk that generic competition for *Sandostatin LAR* may arise in the future. Looking forward, intellectual property protecting a number of our major products will expire at various times in the coming years, raising the likelihood of further generic competition. Among our products expected to begin losing intellectual property protection in key countries during the coming years are *Gilenya*, our everolimus products (*Afinitor*/*Votubia* and *Certican*/*Zortress*), *Exjade*/*Jadenu* and *Lucentis*.

To counter the impact of patent expirations, we continuously invest in R&D to rejuvenate our portfolio. For example, in 2018, we invested 17% of total net sales in R&D. One measure of the output of our efforts is the performance of our growth drivers, including *Cosentyx, Entresto, Kymriah* and *Kisqali*, and the Sandoz biosimilars. Novartis also has a number of late stage product candidates in its pipeline with the potential to come to market in the next few years.

Novartis plans to launch three potentially significant products in 2019, AVXS-101, BAF312 and RTH258 (brolucizumab).

Commercial success of key products

Our ability to maintain and grow our business and to replace revenue and income lost to generic and other competitors depends in part on our commercial success, particularly with respect to our key growth driver products, which we consider to be an indicator of our ability to renew our portfolio. The commercial success of these products could be impacted at any time by a number of factors, including new competitors, changes in doctors' prescribing habits, pricing pressure, manufacturing issues, and loss of intellectual property protection. In addition, our revenue could be significantly impacted by the timing and rate of commercial acceptance of new products.

All of our businesses face intense competition from new products and scientific advances from competitors. Physicians, patients and payers may choose competitor products instead of ours if they perceive them to be better in terms of efficacy, safety, cost or convenience.

For example, our US Sandoz business has suffered significant declines in sales and profits in recent years due, at least in part, to increased competition for its products. There can be no certainty that Sandoz US sales will recover in the coming years. In any event, such competition and the costs of our efforts to improve the business's performance, as well as other factors, can be expected to affect the business, financial condition or results of operations of this organization, at least in the near term. In addition, despite the devotion of significant resources to our efforts to improve the performance of Sandoz US, and our agreement to sell the Sandoz US dermatology business and generic US oral solids portfolio to Aurobindo Pharma USA Inc., our efforts may ultimately prove insufficient. Should our efforts fail to accomplish their goals, or fail to do so in a timely manner, it could have a material adverse impact on our business, financial condition or results of operations beyond the near term, as well.

Ability to deliver new products

Our ability to grow depends not only on the commercial success of our marketed products, but also on the success of our R&D activities in identifying and developing new treatments that address unmet medical needs, are accepted by patients and physicians, and are reimbursed by payers.

Developing new healthcare products and bringing them to market is a costly, lengthy and uncertain process. R&D for a new product in our Innovative Medicines Division can take 15 years or more, from discovery to commercial launch. With time limits on intellectual property protections, the longer it takes to develop a product, the less time we may have to recoup our costs. During each stage of development, there is a significant risk that we will encounter obstacles. They may cause a delay or add substantial expense, limit the potential for commercial success, or force us to abandon a product in which we have invested substantial amounts of time and money.

In addition, as healthcare costs continue to rise, governments and payers around the world are increasingly focused on health outcomes, rewarding new products that represent truly breakthrough innovation versus those that offer an incremental benefit over other products in the same therapeutic class. This has led to requests for more clinical trial data than has been required in the past, the inclusion of significantly higher numbers of patients in clinical trials, and more detailed analyses of the trials. As a result, despite significant efforts by health authorities such as the FDA to accelerate the development of new drugs, the already lengthy and expensive process of obtaining regulatory approvals and reimbursement for pharmaceutical products has become even more challenging.

Our Sandoz Division faces similar challenges, particularly in the development of biosimilars. While Sandoz was a pioneer in introducing biosimilars to the European market in 2006, and was the first company to win approval for a biosimilar under the new regulatory pathway in the United States in 2015, many countries still lack fully developed regulatory frameworks for the development, approval and marketing of biosimilars. Further delays in establishing regulatory frameworks, or any other difficulties that may arise in the development or marketing of biosimilars, could put at risk the significant investments that Sandoz has made, and will continue to make, in this area.

Our Alcon Division faces medical device development and approval processes that are often similarly difficult. As part of its growth plan, Alcon has taken steps to accelerate innovation. It has started to see the results of its efforts, with the approval and launch of intraocular lens innovations in recent years, including *Clareon* and *PanOptix* IOLs, *AutonoMe* and *Ultrasert* IOL delivery systems, and, *ReSTOR* Toric IOL with *ACTIVEFOCUS* optical design, as well as a multifocal version of *Dailies Total1*. But there is no certainty that Alcon will continue to be successful in these efforts, and if it is not, there could be a material adverse effect on the success of the Alcon Division, and on the Group as a whole.

In spite of our significant investments, there can be no guarantee that our R&D activities will produce commercially viable new products that will enable us to grow our business and replace revenue and income lost to competition.

Pricing and reimbursement

Around the world, governments and payers continue to struggle with rising healthcare costs as aging populations contribute to increased prevalence of chronic diseases. There have also been examples of significant controversies about prices for pharmaceuticals that some politicians and members of the public have considered excessive. These factors have intensified the pressures we face regarding the prices we charge for our drugs, and our ability to establish satisfactory rates of reimbursement for our products by governments, insurers and other payers.

We expect scrutiny to continue in 2019, and the following years, as governments and insurers around the world strive to reduce healthcare costs through steps such as restricting access to higher priced new medicines, increasing coinsurance or copays owed by patients for medicines, increasing the use of generics, and imposing price cuts. In this environment, we believe it is more important than ever to demonstrate the value that true innovation brings to the

healthcare system.

To manage these pressures, we are investing in real world data and analytics to provide additional evidence of the health benefits of our products, exploring new technologies and patient management services, and partnering with payers to develop and scale outcomes based commercial models. For example, we are working with customers on flexible pricing approaches where we are fully compensated only if a drug succeeds in meeting certain performance targets.

Business practices

In recent years, there has been a trend of increasing government investigations and litigation against companies operating in our industry, including in the United States and other countries. We are obligated to comply with the laws of all countries in which we operate, as well as any new requirements that may be imposed upon us. In addition, governments and regulatory authorities worldwide

are also increasingly challenging practices previously considered to be legal and compliant. But beyond legal requirements, we strive to meet evolving public expectations for ethical behavior. We have a significant global compliance program in place, and we devote substantial time and resources to efforts to ensure that our business is conducted in a legal and publicly acceptable manner. Despite these efforts, any failure to comply with the law could lead to substantial liabilities that may not be covered by insurance and could affect our business and reputation. Responding to these challenges and new regulations is costly. Investigations and litigation may affect our reputation, create a risk of potential exclusion from government reimbursement programs in the United States and other countries, and potentially lead to large damage payments and agreements intended to regulate company behavior. This is why we continued to strengthen the Integrity & Compliance function in 2018. The function is headed by our Chief Ethics, Risk and Compliance Officer, who reports directly to the CEO of Novartis.

Investors and Novartis are increasingly focused on Environmental, Social and Governance (ESG) issues. Novartis has made strides to transform culture and return more to society in 2018, which are two of the key priorities of our new CEO. We continue our journey to rebuild trust with society and for all our new medicines, we will systematically integrate access strategies in how we research, develop and deliver globally and we are developing innovative treatments for under-treated diseases, including SEG101 in sickle cell disease.

Supply continuity

The production of pharmaceutical products and medical devices can be highly complex, and any manufacturing issue compromising supply or quality could have serious consequences for the health of patients. For this reason, there are strict regulatory requirements surrounding our manufacturing processes, which, in addition to our own quality standards, introduce a greater chance for disruptions and liabilities. Any significant failure by us or our third party suppliers to comply with these requirements or the health authorities' expectations may cause us to shut down the production facilities or production lines. Alternately, we may be forced to shut them down by a government health authority.

Beyond regulatory requirements, many of our products involve technically sophisticated manufacturing processes or require specialized raw materials. For example, we manufacture and sell a number of sterile products, biologic products and products involving advanced therapy platforms, such as CAR-T therapies, gene therapy and radioligand therapy, all of which are particularly complex and involve highly specialized manufacturing technologies. As a result, even slight deviations at any point in their production process may lead to production failures or recalls.

Given the complexity of our manufacturing processes, we have worked for several years to adopt a single high quality standard across the company. We believe these efforts are having an impact. The results of inspections by regulatory agencies in 2018 were consistent with the year before. Out of a total of 192 inspections, all but two (99%) were without major findings.

IT security, data integrity and data privacy

We are heavily dependent on critical, complex and interdependent information technology systems, including Internet based systems, to support our business processes.

The size, age and complexity of our information technology systems make them potentially vulnerable to external and internal security threats, outages, misplaced or lost data, programming or human errors, or other similar events. Although we have devoted and continue to devote significant resources and management attention to cybersecurity, information management and business continuity efforts, like many companies, we have experienced certain of these events and expect to continue to experience them in the future, as the external and internal information security threat continues to grow. We believe that the information security incidents we have experienced to date have yet to result in significant disruptions to our operations, and have not had a significant adverse effect on our results of operations, or on third parties. However, we may not be able to prevent future outages, security incidents or other breaches in our systems from having a material adverse effect on our business, financial condition, results of operation or reputation.

In addition, our routine business operations increasingly involve our gathering personal information (including sensitive personal information) about patients, vendors, customers, employees, collaborators and others, through the use of information technologies such as the Internet, social media, mobile technologies, and technology based medical devices. Breaches of our systems or those of our third party contractors, or other failures to protect such information, could expose such people's personal data to unauthorized persons. Any event involving the substantial loss of personal data could give rise to significant potential liability, reputational harm, damaged relationships with business partners and potentially substantial monetary penalties under laws enacted or being enacted around the world. Such events

could also lead to restrictions on our ability to transfer personal data across country borders.

Transformational technologies and business models

Rapid progress in digital technologies and in the development of new business models is substantially transforming numerous industries around the world, while sometimes quickly rendering established businesses uncompetitive or obsolete. To take advantage of these opportunities, Novartis has embarked upon a digital transformation strategy, with the goal of making Novartis an industry leader in leveraging advanced analytics and other new technologies. This includes the 2018 launch of *reSET* the first digital therapeutic for substance abuse disorder. At the same time, there is a risk that other companies with specialized expertise or business models may enter the healthcare field, potentially disrupting our relationships with patients, healthcare professionals, customers, distributors and suppliers, with unknown potential consequences for us.

If we should fail to succeed in our efforts at a digital transformation of our company, then there is a risk that we may fail to create the innovative new products, tools or techniques that such technologies may make possi-

ble, or may fail to create them as quickly and efficiently as such technologies may enable. We may also lose opportunities to engage with our stakeholders and to profit from improved business processes, and may lose the resources devoted to these efforts to transform our business. At the same time, should third parties successfully enter the healthcare field with disruptive new technologies or business models, then we potentially may see our business supplanted in whole or in part by these new entrants.

Intangible assets and goodwill

We carry a significant amount of goodwill and other intangible assets on our consolidated balance sheet, primarily due to acquisitions, including the acquisition of Alcon and the oncology assets acquired from GSK. As a result, we may incur significant impairment charges if the fair value of intangible assets and groupings of cash generating units containing goodwill are less than their carrying value on the Group's consolidated balance sheet at any point in time. We regularly review our long lived intangible and tangible assets for impairment. In 2018, for example, we recorded intangible asset impairment charges of USD 1.2 billion, including USD 0.4 billion write-down of *Votrient*, USD 0.3 billion for the net charges from the voluntary withdrawal of *CyPass* and USD 0.2 billion related to the write-down of the goodwill and the currently marketed products related to the sale of the Sandoz US portfolio to Aurobindo Pharma USA Inc. Impairment testing may lead to additional impairment charges in the future. Any significant impairment charges could have a material adverse effect on our results of operations and financial condition.

Tax

Our multinational operations are taxed under the laws of the countries and other jurisdictions in which we operate. However, the integrated nature of our worldwide operations can produce conflicting claims from revenue authorities in different countries as to the profits to be taxed in the individual countries, including potential disputes relating to the prices our subsidiaries charge one another for intercompany transactions, known as transfer pricing. The majority of the jurisdictions in which we operate have double tax treaties with other foreign jurisdictions, which provide a framework for mitigating the impact of double taxation on our revenues and capital gains. However, mechanisms developed to resolve such conflicting claims are largely untried, and can be expected to be very lengthy.

In recent years, tax authorities around the world, including in the EU, Switzerland and the US, have increased their scrutiny of company tax filings, and have become more rigid in exercising any discretion they may have, and numerous changes in tax laws and rules have been enacted or proposed. The current tax regime of Switzerland is under international pressure and efforts are underway in Switzerland to transform its corporate tax laws and regulations. The outcome of these efforts remains subject to change and could end up in a materially different form from what is currently proposed, or could be administered or implemented in a manner different from our expectations.

As a result, such tax reform efforts, including with respect to tax base or rate, transfer pricing, intercompany dividends, cross border transactions, controlled corporations, and limitations on tax relief allowed on the interest on intercompany debt, will require us to continually assess our organizational structure against tax policy trends, and could lead to an increased risk of international tax disputes and an increase in our effective tax rate, and could adversely affect our financial results.

Approach to risk management

See "Item 6. Directors, Senior Management and Employees—Item 6.C Board Practices—Our Board of Directors—Information and control systems of the Board vis-à-vis management—Risk management" and "Item 18. Financial Statements—Note 28. Financial instruments—additional disclosures."

Non-IFRS measures as defined by Novartis

Novartis uses certain non-IFRS metrics when measuring performance, especially when measuring current-year results against prior periods, including core results, constant currencies, free cash flow and net debt.

Despite the use of these measures by management in setting goals and measuring the Group's performance, these are non-IFRS measures that have no standardized meaning prescribed by IFRS. As a result, such measures have limits in their usefulness to investors.

Because of their non-standardized definitions, the non-IFRS measures (unlike IFRS measures) may not be comparable to the calculation of similar measures of other companies. These non-IFRS measures are presented solely to permit investors to more fully understand how the Group's management assesses underlying performance. These non-IFRS measures are not, and should not be viewed as, a substitute for IFRS measures.

As an internal measure of Group performance, these non-IFRS measures have limitations, and the Group's performance management process is not solely restricted to these metrics.

Core results

The Group's core results – including core operating income, core net income and core earnings per share – exclude fully the amortization and impairment charges of intangible assets, except software, net gains and losses on fund investments and equity securities valued at fair value through profit and loss, and certain acquisition-related items. The following items that exceed a threshold of USD 25 million are also excluded: integration- and divestment-related income and expenses;

divestment gains and losses; restructuring charges/releases and related items; legal-related items; impairments of property, plant and equipment, and financial assets; as well as income and expense items that management deems exceptional and that are or are expected to accumulate within the year to be over a USD 25 million threshold.

Novartis believes that investor understanding of the Group's performance is enhanced by disclosing core measures of performance because, since they exclude items that can vary significantly from year to year, the core measures enable better comparison of business performance across years. For this same reason, Novartis uses these core measures in addition to IFRS and other measures as important factors in assessing the Group's performance.

The following are examples of how these core measures are utilized:

• In addition to monthly reports containing financial information prepared under IFRS, senior management receives a monthly analysis incorporating these core measures.

• Annual budgets are prepared for both IFRS and core measures.

A limitation of the core measures is that they provide a view of the Group's operations without including all events during a period, such as the effects of an acquisition, divestments, or amortization/impairments of purchased intangible assets and restructurings.

Constant currencies

Changes in the relative values of non-US currencies to the US dollar can affect the Group's financial results and financial position. To provide additional information that may be useful to investors, including changes in sales volume, we present information about our net sales and various values relating to operating and net income that are adjusted for such foreign currency effects.

Constant currency calculations have the goal of eliminating two exchange rate effects so that an estimate can be made of underlying changes in the consolidated income statement excluding the impact of fluctuations in exchange rates:

• The impact of translating the income statements of consolidated entities from their non-US dollar functional currencies to US dollars

• The impact of exchange rate movements on the major transactions of consolidated entities performed in currencies other than their functional currency

We calculate constant currency measures by translating the current year's foreign currency values for sales and other income statement items into US dollars, using the average exchange rates from the prior year and comparing them to the prior-year values in US dollars.

We use these constant currency measures in evaluating the Group's performance, since they may assist us in evaluating our ongoing performance from year to year. However, in performing our evaluation, we also consider equivalent measures of performance that are not affected by changes in the relative value of currencies.

Free cash flow

Free cash flow is presented as additional information because management believes it is a useful supplemental indicator of the Group's ability to operate without reliance on additional borrowing or use of existing cash. Free cash flow is a measure of the net cash generated that is available for debt repayment and investment in strategic opportunities, and for returning to shareholders. Free cash flow is a non-IFRS measure, which means it should not be interpreted as a measure determined under IFRS. Free cash flow is not intended to be a substitute measure for net cash flows from operating activities as determined under IFRS.

Novartis defines free cash flow as net cash flows from operating activities and cash flows associated with the purchase or sale of property, plant and equipment, as well as intangible, other non-current and financial assets, excluding marketable securities. Cash flows in connection with the acquisition or divestment of subsidiaries, associated companies and non-controlling interests in subsidiaries are not taken into account to determine free cash flow.

Net debt

Net debt is presented as additional information because management believes it is a useful supplemental indicator of the Group's ability to pay dividends, to meet financial commitments, and to invest in new strategic opportunities, including strengthening its balance sheet. Net debt is a non-IFRS measure, which means it should not be interpreted as a measure determined under IFRS.

Novartis defines net debt as current and non-current financial debt less cash and cash equivalents, current investments and derivative financial instruments.

Novartis Cash Value Added

Novartis Cash Value Added (NCVA) is a metric that is based on what the Company assesses to be its cash flow return less a capital charge on gross operating assets. NCVA is used as the primary internal financial measure for determining payouts under the Long-Term Performance Plan introduced in 2014. More information on NCVA is presented as part of the Compensation Report; see “Item 6. Directors, Senior Management and Employees—Item 6.B Compensation.”

Additional information

EBITDA

Novartis defines earnings before interest, tax, depreciation and amortization (EBITDA) as operating income, excluding depreciation of property, plant and equipment (including any related impairment charges) and amortization of intangible assets (including any related impairment charges).

(USD millions)	2018	2017	2016
Operating income	8 169	8 629	8 268
Depreciation of property, plant and equipment	1 717	1 520	1 489
Amortization of intangible assets	3 639	3 690	3 861
Impairments of property, plant and equipment, and intangible assets	1 536	866	693
EBITDA	15 061	14 705	14 311

Enterprise value

Enterprise value represents the total amount that shareholders and debt holders have invested in Novartis, less the Group’s liquidity.

(USD millions unless indicated otherwise)	Dec 31, 2018	Dec 31, 2017	Dec 31, 2016
Market capitalization	196 950	195 541	172 048
Non-controlling interests	78	59	59
Financial debts and derivatives	32 148	28 532	23 802
Liquidity	– 15 964	– 9 485	– 7 777
Enterprise value	213 212	214 647	188 132
Enterprise value/EBITDA	14	15	13

2018 and 2017 reconciliation from IFRS results to core results

(USD millions unless indicated otherwise)	Innovative Medicines 2018	Innovative Medicines 2017 restated [1]	Sandoz 2018	Sandoz 2017	Alcon 2018	Alcon 2017 restated [1]	Corporate 2018	Corporate 2017	Group 2018	Group 2017
IFRS operating income	7 871	7 595	1 332	1 368	– 194	– 3	– 840	– 331	8 169	8 629
Amortization of intangible assets	2 158	2 119	363	454	1 007	1 025			3 528	3 598
Impairments										
Intangible assets	592	591	249	61	391	57			1 232	709
Property, plant and equipment related to the Group-wide rationalization of manufacturing sites	170	7	63	60					233	67
Other property, plant and equipment	65	77		13					65	90
Financial assets [2]						29		197		226
Total impairment charges	827	675	312	134	391	86		197	1 530	1 092
Acquisition or divestment of businesses and related items										
- Income		– 2					– 21	– 115	– 21	– 117
- Expense	126	32					29	130	155	162
Total acquisition or divestment of businesses and related items, net	126	30					8	15	134	45
Other items										
Divestment gains	– 482	– 368	– 78				– 56		– 616	– 368
Financial assets - fair value adjustments [2]	– 107				– 18		113		– 12	
Restructuring and related items										
- Income	– 25	– 53	– 12	– 7	– 4	– 4	– 2	– 1	– 43	– 65
- Expense	665	268	179	134	45	34	133	29	1 022	465
Legal-related items										
- Income	– 1	– 21	– 63						– 64	– 21
- Expense	36	35	90		28	61			154	96
Additional income	– 73	– 534	– 171	– 3	– 66	– 51	– 19	– 372	– 329	– 960
Additional expense	156	273	50		90	20	54	46	350	339
Total other items	169	– 400	– 5	124	75	60	223	– 298	462	– 514
Total adjustments	3 280	2 424	670	712	1 473	1 171	231	– 86	5 654	4 221
Core operating income	11 151	10 019	2 002	2 080	1 279	1 168	– 609	– 417	13 823	12 850
as % of net sales	32.0%	31.0%	20.3%	20.7%	17.9%	17.3%			26.6%	26.2%
Income from associated companies	1	– 1	5	23			6 432	1 086	6 438	1 108
Core adjustments to income from associated companies, net of tax		1					– 5 325	226	– 5 325	227
Interest expense									– 957	– 777
									185	39

Other financial income and expense		
Taxes, adjusted for above items (core taxes)	– 2 226	– 2 056
Core net income	11 938	11 391
Core net income attributable to shareholders of Novartis AG	11 935	11 391
Core basic EPS (USD) [3]	5.15	4.86

[1] Restated to reflect the product transfers between Innovative Medicines and Alcon that was effective as of January 1, 2018

[2] For financial instruments accounted for as fair value through profit and loss, as of January 1, 2018, unrealized gains/losses on financial assets are shown under "Financial assets - fair value adjustments", due to the change in IFRS 9 (see Note 1).

[3] Earnings per share (EPS) is calculated on the amount of net income attributable to shareholders of Novartis AG.

2017 and 2016 reconciliation from IFRS results to core results

(USD millions unless indicated otherwise)	Innovative Medicines		Sandoz		Alcon		Corporate		Group	
	2017 restated [1]	2016 restated [1]	2017	2016	2017 restated [1]	2016 restated [1]	2017	2016	2017	2016
IFRS operating income	7 595	7 255	1 368	1 445	– 3	39	– 331	– 471	8 629	8 268
Amortization of intangible assets	2 119	2 316	454	460	1 025	1 025			3 598	3 801
Impairments										
Intangible assets	591	522	61	65	57	4			709	591
Property, plant and equipment related to the Group-wide rationalization of manufacturing sites	7	1	60	– 7					67	– 6
Other property, plant and equipment	77	76	13	8					90	84
Financial assets		18			29		197	99	226	117
Total impairment charges	675	617	134	66	86	4	197	99	1 092	786
Acquisition or divestment of businesses and related items										
- Income	– 2	– 68					– 115	– 229	– 117	– 297
- Expense	32	41					130	223	162	264
Total acquisition or divestment of businesses and related items, net	30	– 27					15	– 6	45	– 33
Other items										
Divestment gains	– 368	– 608		– 6				– 48	– 368	– 662
Restructuring and related items										
- Income	– 53	– 41	– 7	– 23	– 4	– 4	– 1	– 5	– 65	– 73
- Expense	268	413	134	123	34	38	29	65	465	639
Legal-related items										