Novartis AG

Large R&D-based pharmaceutical company • Stock exchange: SWX • Ticker: NOVN • HQ: Basel, Switzerland • Employees: 125,161

PERFORMANCE

Novartis is middle-performing in its evaluated Research Areas when compared to other large R&D-based pharmaceutical companies in scope.

R&D: Performs low. Divested its antibacterial research programmes in 2018 but maintains an adapted project pipeline including a partnership with GARDP. It publicly shares all data for discontinued projects on Pew’s SPARK platform.

Responsible Manufacturing: Performs well. Reports comprehensive environmental risk-management strategy for own sites and suppliers, but not audits to waste-treatment plants; risk assessments based on discharge limits completed at own sites and ongoing at suppliers’ sites.

Appropriate Access: Performs well. Files its relevant off-patent products for registration in access countries. Employs strong strategies to ensure continuous supply and supplies three forgotten antibiotics.

Stewardship: Middle-performing. It has educational programmes with comprehensive conflict of interest (COI) mitigation. It adapts brochures and packaging for literacy and paediatric use for one product. Sells products through tenders and does not link incentives to the sales volume. It is not involved in AMR surveillance.

SALES AND OPERATIONS

Therapeutic areas: Cardiovascular diseases; Dermatology; Immunology; Infectious diseases; Metabolic disorders; Neurology; Oncology; Ophthalmology; Respiratory diseases

Business segments: Sandoz; Novartis Oncology; Novartis Pharmaceuticals

Product categories: Generic medicines; Innovative medicines

Manufacturing & supply: Novartis reports having 24 manufacturing sites that produce antibacterial APIs and/or drug products. It reports selling its antibacterial and antifungal medicines across approximately 140 countries, 71 of which are low- and middle-income countries.

M&A since 2018: In September 2018, Novartis announced that it would divest the Sandoz US dermatology business and generic US oral solids portfolio to Aurobindo. The deal includes USD 900 million in cash and potential earn-outs of USD 100 million. In April 2019, Novartis completed the spin-off of Alcon as a separately traded company.

PIPELINE for diseases in scope

Pipeline size: 1 project for priority pathogens*

Development stages: 1 pre-clinical project

Novelty: No novel clinical-stage medicine projects

Regulatory approvals: 0 approvals for priority pathogens

Access plans: No late-stage R&D projects

Stewardship plans: No late-stage R&D projects

PORTFOLIO for diseases in scope

Comparatively large portfolio: At least 152 products (74 unique INNs): 130 antibacterial medicines; 22 antifungal medicines

Essential medicines: 43% (66) of products are on the 2019 WHO EML

AWaRe medicines**: 29 Access group; 15 Watch group

Anti-TB medicines**: 9 (incl. 2 Reserve Group)

Revenues by product (2018)

- Anti-infectives (generics) - Europe
- Other pharmaceuticals - USA
- Others - Asia, Africa, Australasia, Canada, Latin America

Revenues by region (2018)

- Canada, Latin America
- Asia, Africa, Australasia
- Europe

Performance in the Benchmark

Overall score 54% 35/65

Performance by Research Area

| R&D | 75% |
| Manufacturing | 73% |
| Access | 80% |
| Stewardship | 55% |

How Novartis was evaluated

Revenues by product (2018)

- Anti-infectives (generics)

Revenues by region (2018)

- Europe

Antibacterial (AB) vaccine
Antibacterial (AB) medicine
Antifungal (AF) medicine
AB+AF combination

The number of products is based on data from public sources, IQVIA, and data submitted by the company. It may not account for Novartis’ entire portfolio.

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.

** Listed on the 2019 WHO EML (Section 6).
OPPORTUNITIES FOR NOVARTIS

Follow up to public commitments and increase public disclosure on environmental risk management. Following up on its commitments as a signatory to the Industry Roadmap for Progress on Combating AMR, Novartis can work with stakeholders to develop a practical mechanism to publicly disclose (1) a list of its suppliers and waste-treatment plants and (2) the results of environmental audits and the levels of antibiotic discharge from its own sites and the sites of its suppliers.

Expand registration and ensure adequate supply of antibacterial medicines in more access countries. Novartis can file for registration and ensure adequate supply of antibacterial medicines on the 2019 WHO EML within its current portfolio (e.g. the forgotten antibiotics benzathine benzylpenicillin and fosfomycin) within its current portfolio in access countries.

Fully decouple sales incentives from sales volumes for all antibacterial and/or antifungal medicines not sold through tenders. Novartis sells most of its products through government and hospital tenders. In order to mitigate the risk of inappropriate use, Novartis can fully decouple sales incentives from sales volumes for its antibacterial and/or antifungal medicines not sold through tenders.

Engage in surveillance activities. Novartis is one of the only two large research-based pharmaceutical companies not active in surveillance activities. Novartis can engage in surveillance programmes and share publicly (e.g., through the AMR Register) the raw data from these programmes.

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT

A.1 Below average investments in relevant R&D, as proportion of pharmaceutical revenues

Novartis reports to the Benchmark how much it invested in R&D for antibacterial medicines in 2017 and 2018. As a proportion of its revenues from pharmaceuticals, these investments are below average compared to investments in such R&D made by other large research-based pharmaceutical companies evaluated in the Benchmark. The Benchmark is not able to publish further information, as the details were provided on the basis of confidentiality. Novartis is not involved in vaccines R&D.

A.2 Novelty of pipeline

A.2.2 Novelty of pipeline

Novartis is not eligible for this indicator as it does not have any R&D candidates in clinical development.

A.2.3 Vaccines in the pipeline

Novartis is not eligible for this indicator as it is not active in vaccine development targeting priority pathogens.

A.2.4 One candidate targeting critical and/or urgent priorities

Novartis has one candidate targeting pathogens considered critical and/or urgent R&D priorities for limiting AMR, as identified by WHO and/or the US Centers for Disease Control and Prevention (CDC). Further details were provided on the basis of confidentiality.

A.3 One intellectual capital sharing initiative

Novartis shares data on the Pew Charitable Trusts’ open-access Shared Platform for Antibiotic Research and Knowledge (SPARK). Through this platform, Novartis shares the results of susceptibility tests and target enzyme potency data (IC50) for discontinued projects so that they can be used under a non-exclusive, royalty-free, sublicensable and transferable licence by research organisations. Novartis and GARDP partnered in September 2018 to improve and adapt existing generic antibacterial formulations and dosing regimens for newborns and children, specifically to develop heat-stable paediatric formulations against leading childhood diseases in lower-income countries.

A.4 Access and stewardship planning

Novartis is not eligible for this indicator as it has no projects in late-stage clinical development. Companies are expected to have plans in place for pipeline projects in Phase II and beyond.

Pipeline targeting priority pathogens: 1 As at 16 October 2019

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval**</th>
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<tr>
<td></td>
<td>Adapted R&amp;D project with confidential details</td>
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** Clofazimine (Lamprene®), originally approved for the treatment of leprosy, is currently under review for WHO prequalification for tuberculosis. A Phase Ib/II trial for this additional indication was prematurely terminated by the company before the period of analysis. Novartis reports a commitment to make this tuberculosis project available with affordable pricing.

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.
B RESPONSIBLE MANUFACTURING

Evaluated: antibacterials manufacturing (APIs and drug products)

B.1 Comprehensive environmental risk-management for own sites and suppliers; limited oversight of waste-treatment plants

Novartis reports a comprehensive strategy to minimise the environmental impact of wastewaters and solid waste from antibacterial manufacturing at its sites, with an aim to limit AMR. This includes audits every 2–4 years, depending on risk. The company reports setting discharge limits for all antibacterials manufactured at its sites, based on PNECs to limit AMR (or more stringent PNECs), as published by the AMR Industry Alliance. Novartis uses these PNECs to conduct risk assessments applying a mass balance approach, complemented by direct sampling and analytical testing, where needed.

Novartis expects third-party suppliers of antibacterial APIs and drug products to follow the same standards, including limits. The company reports that suppliers are audited based on risk, typically every three years. Review of antibacterial discharges has now been incorporated in the audit protocol, to be monitored in future audits. Novartis expects external private waste-treatment plants to comply with its environmental standards, but does not audit them. It does not report monitoring discharge levels of wastewater plants.

B.2 Publicly discloses some information on environmental risk management

Novartis publishes some components of its environmental risk-management strategy. Further, it is a member of the AMR Industry Alliance, which publishes a list of recommended antibacterial discharge targets. The underlying methodology was summarised in an open-access journal article co-authored by Alliance members including Novartis. Novartis does not publish: (1) the results of environmental audits, whether conducted at its own sites, the sites of suppliers or external private waste-treatment plants; (2) a list of these suppliers and waste-treatment plants; or (3) the levels of antibacterial discharge from its own sites.

B.3 Has system to maintain production quality for own and suppliers’ sites: no requests for official corrective action

Novartis reports having a system to maintain high-quality antibacterial production, consistent with international GMP standards. This includes risk-based internal audits and tracking of corrective and preventive actions. The company reports requiring suppliers to abide by regulatory and company quality standards, as specified, e.g., in quality agreements and the Novartis Supplier Code. It reports auditing its suppliers as its own sites and having the same expectations in terms of corrective action implementation. The Benchmark found no requests for official corrective action from the FDA or EMA related to non-conformities with cGMP at Novartis’ own sites or any subsidiaries.*

C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS

Evaluated: access activities relating to antibacterial & antifungal medicines & vaccines in 102 access countries†

C.1 Registration of on-patent products

Novartis was not eligible for this indicator as it does not have on-patent antibacterial or antifungal medicines or vaccines in its portfolio.

C.2 Filed to register its relevant off-patent products§ in 11.8 access countries on average

Novartis is one of the leaders when it comes to filing relevant off-patent products for registration, it has filed 89% of its relevant products (8/9 antibacterial and antifungal medicines) for registration in access countries. Its most widely filed product in this analysis is the antibacterial medicine azithromycin, used for conditions including respiratory and skin infections. Novartis has filed its version of this product in 43 access countries. Azithromycin is followed by the antifungal fluconazole and the antibacterial medicine cefazidime, filed by Novartis for registration in 28 and 17 access countries, respectively.

C.2.1 Pricing strategies for on-patent products

Novartis was not eligible for this indicator, as it does not have on-patent antibacterial or antifungal medicines or vaccines in its portfolio.

C.2.2 Pricing strategies for off-patent products

Companies were not scored for this indicator as the available data was insufficient for a comparative analysis. Novartis, through Sandoz (its generic division), reports that it participates in tenders with hospitals, governments, NGOs and organizations including UNICEF, WHO and MSF. It states that it views this approach as helping to reach more patients in low-income countries, at a lower price point than via retail channels. Novartis also reports that, aside of tenders, it takes socioeconomic factors into account, such as the level of inequality and disease burden, when setting prices for new off-patent antibacterial and antifungal medicines.

C.3 Many strategies to ensure the continuous supply of relevant products

Novartis’ performance is one of the strongest of the companies evaluated when it comes to taking steps to ensure the continuous supply of its relevant products to access countries. It uses 12 to 36-month forecasting and shares data with stakeholders through weekly operational meetings. To help ensure the supply of ingredients, Novartis applies a dual-sourcing strategy and its Novartis Emergency Management (NEM) and Supply Chain Management teams are trained to respond immediately to any supply shortage. Safety stocks are buffered by keeping an optimum inventory at each point of supply. To mitigate against falsified medicines reaching the supply chain, Novartis has several strategies including an anti-counterfeiting programme, a risk-management database, in-house forensic capabilities and security features embedded on secondary packaging. Novartis also supplies the three forgotten antibiotics∥ tobramycin, cefepime and cefpodoxime to access countries.

* Including only wholly-owned direct subsidiaries of the company. More information in Appendix I.
† 102 low- and middle-income countries where better access to medicine is most needed. See Appendix VI.
∥ See Appendix VII.
A set of older off-patent antibacterials that are not always marketed or available, due to economic reasons, lack of awareness and lack of demand but are still considered effective as a treatment for bacterial infections. See Appendix VII for citation.

### C.4 Broad strategy to mitigate COI for all educational programmes

The Benchmark analysed the top five AMR-related educational programmes for healthcare professionals (HCPs) from Novartis. Novartis reports broad COI mitigation for all five programmes. Three programmes have all three COI mitigation strategies looked for by the Benchmark: (1) content is developed independently from its marketing department; (2) a pledge not to provide financial or material incentives to participants; and (3) it does not use branded materials. However, for one programme, it was unclear whether content was developed independently from its marketing department; and for the remaining programme, it was unclear whether financial or material incentives are provided to participants. After the period of analysis, the company stated that for both programmes content is developed independently from its marketing department and no financial or material incentives are given.

### C.5 Adapts sales practices to address appropriate use

Novartis engages in practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines via its sales practices. Novartis does not disclose marketing practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines. It is, however, one of the two companies evaluated to report that it sells a significant portion of its antibacterial and/or antifungal medicines through tenders and does not link employees’ incentives to the sales volume of these tenders.

### C.6 Makes multiple adaptations to brochures and/or packaging to facilitate appropriate use

Novartis adapts brochures to facilitate the appropriate use by patients of relevant products: namely the antibacterials benzathine benzylpenicillin and amoxicillin/clavulanic acid. These adaptations take account of literacy and paediatric use. Novartis has created brochures for benzathine benzylpenicillin in collaboration with the Pan-African Society of Cardiology for patients who may not be able to read. Novartis also created paediatric guidance for amoxicillin/clavulanic acid that focuses on correct dosing for children.

### C.7 No involvement in AMR surveillance programmes or consumption data sharing

Novartis does not report any involvement in AMR surveillance programmes and it does not report making antibacterial and/or antifungal consumption data available to national governments or other public health authorities.