

GlaxoSmithKline plc

Large R&D-based pharmaceutical company

Stock exchange: LSE • Ticker: GSK • HQ: Brentford, UK • Employees: 95,490

PERFORMANCE

GSK performs strongly in its evaluated Research Areas, and leads when compared to other large R&D-based pharmaceutical companies in scope.

R&D: Performs strongly. Pipeline consists of 27 projects for medicines and vaccines for priority pathogens. Its two clinical-stage medicines are both novel. Reports access and/or stewardship planning for most of its late-stage projects and leads in intellectual capital sharing.

Responsible Manufacturing: Performs strongly. Reports comprehensive environmental risk-management strategy for own sites and suppliers; risk assessments based on discharge limits have been completed at own sites and are ongoing at suppliers' sites.

Appropriate Access: Performs strongly. Files its on- and off-patent products for registration in access countries. Leader in strategies for continuous supply to access countries.

Stewardship: Performs well. It has educational programmes with comprehensive conflict of interest (COI) mitigation. Regressed from 2018 to now to only partially decoupling sales incentives from volumes. It shares surveillance results and adapts brochures and packaging for appropriate use.

SALES AND OPERATIONS

Therapeutic areas: Immunology; Infectious diseases; Oncology; Respiratory diseases

Business segments: Pharmaceuticals; Vaccines; Consumer Healthcare;

Product categories: Innovative medicines (including ViiV Healthcare JV with Pfizer and Shionogi); Consumer healthcare (JV with Pfizer); Vaccines

Manufacturing & supply: GSK reports having 24 manufacturing sites that produce antibacterial APIs and/or drug products. It supplies its antibacterial medicines, antibacterial vaccines and antifungal medicines across 121 countries, 71 of which are low- and middle-income countries.

M&A since 2018: None in the antibacterial and/or antifungal sectors

PIPELINE for diseases in scope

Pipeline size: 27 projects for priority pathogens* (12 antibacterial medicines; 15 antibacterial vaccines)

Development stages: 8 clinical projects, including a Phase III project for an expanded indication of its meningococcal B vaccine Bexsero® for the prevention of gonorrhoea and 10 discovery/pre-clinical projects.

Novelty: 2 novel projects, including GSK-3036656, a Phase II clinical candidate for the treatment of tuberculosis (TB) that belongs to a new chemical class of antibacterials and has a new drug target, mode of action and no known cross-resistance to other antibacterial classes

Regulatory approvals: 0 approvals for priority pathogens

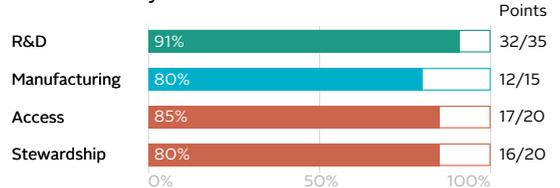
Access plans: 5 of 7 late-stage R&D projects with project-specific access plans, most commonly registration commitments and equitable pricing strategies

Stewardship plans: 2 of 2 late-stage R&D medicine projects with stewardship plans, including commitments to conduct global surveillance studies for all new antibacterials

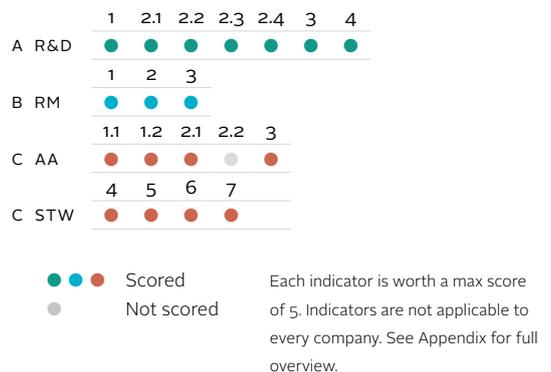
Performance in the Benchmark



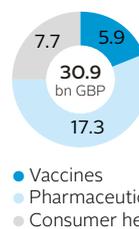
Performance by Research Area



How GSK was evaluated



Revenues by product (2018)



Revenues by region (2018)



PORTFOLIO for diseases in scope

Mid-sized portfolio: At least 95 products (50 unique INNs): 61 antibacterial medicines; 25 antibacterial vaccines; 9 antifungal medicines

Essential medicines: 42% (40) of products are on the 2019 WHO EML

AWaRe medicines:** 17 Access group; 5 Watch group; 1 Reserve group

Anti-TB medicines:** 1

Pipeline for priority pathogens



Products on the market



The number of products is based on data from public sources, IQVIA, and data submitted by the company. It may not account for GSK's 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 GSK

Remain engaged in R&D for antibacterial medicines and vaccines. GSK is one of the few large research-based pharmaceutical companies still active in R&D for antibacterial medicines and vaccines. It is critical for the development and commercialisation of new products that large research-based pharmaceutical companies remain engaged in this space, either through acquisitions and in-licensing or through discovery.

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, GSK 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 antibacterial discharge from its own sites and the sites of its suppliers.

Expand registration and ensure adequate supply of three vaccines and two forgotten antibiotics in access countries. GSK can file for registration and ensure adequate supply of the vaccines Infanrix® Hib, Boostrix® Polio and Bexsero® and two forgotten antibiotics on the 2019 WHO EML within its current portfolio (colistin and cloxacillin) in more access countries.

Publicly share raw data from its surveillance programme SOAR. GSK can share publicly (e.g., with the AMR Register) the raw data collected for its long-term, multinational surveillance programme SOAR.

Fully decouple sales incentives from sales volumes. In order to mitigate the risk of inappropriate use of its antibacterial and antifungal medicines, GSK can change its current incentive programme for its sales agents covering antibacterial and antifungal medicines and ensure that the capped variable pay element of a sales agents' compensation will not be evaluated on the basis of volume targets.

CHANGES SINCE 2018

- Received WHO prequalification in October 2017 for its new Synflorix® 4-dose vial presentation, designed to address cold chain challenges in hot countries.
- Started supply of the Synflorix® 4-dose vial presentation in 2018 to Gavi-supported countries, which is now available in eight countries.
- Donated 150,000 units of essential medicines in 2018, incl. antibacterials via partnerships including, Amicares, Direct Relief, and IHP UK, for the humanitarian response in countries such as Guatemala, South Sudan and Syria.
- Partnered with Save the Children to reach over 220,000 children under five in 2018 with interventions including immunisation coverage.
- Changed its policy on engagement with healthcare professionals (HCPs). It now pays HCPs to speak about its innovative products for a limited period after they become available or when new data is released.
- Reverted its incentives for sales agents to partial decoupling from sales volumes at a small group level (within a country).

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT Evaluated: medicine & vaccine pipelines for priority* bacteria & fungi

A.1 Largest investment in relevant R&D
GSK reports to the Benchmark how much it invested in R&D for antibacterial medicines and vaccines in 2017 and 2018. GSK reports the largest investment in such R&D in 2017 and 2018. As a proportion of its revenues from pharmaceuticals and vaccines, these investments are above

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.

A.2.1 Largest pipeline of all companies evaluated

The company reports 27 projects targeting priority pathogens in its pipeline, all of which target bacterial pathogens, including 15 vaccine and 12 medicine projects. Out of the 27 projects, three are in discovery stage, seven are in pre-clinical

Pipeline targeting priority pathogens: 27*** As at 16 October 2019

Discovery	Pre-clinical	Phase I	Phase II	Phase III	Approval
Intracellular active series - <i>M. tuberculosis</i>	FimH - <i>E. coli</i> (CRE and ESBL-producing <i>Enterobacteriaceae</i>)		Gepotidacin† - <i>N. gonorrhoeae</i> , <i>Enterobacteriaceae</i> (CRE and ESBL-producing <i>Enterobacteriaceae</i>) - Bacterial infections (including gonorrhoea) - Novel	♦ <i>N. gonorrhoeae</i> vaccine - Adaptation (additional indication of meningococcal group B vaccine Bexsero®)	
Gram negative antibacterial program (CRE, ESBL, MDR <i>Enterobacteriaceae</i> & <i>P. aeruginosa</i>)	Sanfetrinem cilexetil - <i>M. tuberculosis</i>		GSK-070 (GSK-3036656) - <i>M. tuberculosis</i> - Novel	♦ = Vaccine	
Whole cell hit-to-lead programme - <i>M. tuberculosis</i>	♦ <i>C. difficile</i> vaccine†		♦ <i>Shigella</i> monovalent GMMA- and biconjugate-based vaccines	COPD = Chronic obstructive pulmonary disease	
KasA - <i>M. tuberculosis</i>	♦ Invasive non-typhoidal <i>Salmonella</i> (iNTS; bivalent GMMA) vaccine - <i>S. enterica</i> Typhimurium & Enteritidis		♦ <i>Shigella</i> multivalent biconjugate vaccine (Phase I/II)	CRE = Carbapenem-resistant <i>Enterobacteriaceae</i>	
	Tuberculosis Chol-dep-GSK'286 - <i>M. tuberculosis</i>		♦ Tuberculosis prophylactic vaccine - <i>M. tuberculosis</i>	ESBL = Extended-spectrum beta-lactamase	
			♦ GSK-3277511A - non-typeable <i>H. influenzae</i> (NTHi) and <i>M. catarrhalis</i> (Mcat) multi-antigen vaccine adjuvanted with ASo1E - COPD	GMMA = Generalized modules for membrane antigens	
				MDR = Multidrug-resistant	

* 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.

*** Includes 11 projects not shown in the figure: 6 projects provided to the Benchmark on the basis of confidentiality; 3 projects with undisclosed stages of development (2 tuberculosis medicines and 1 other antibacterial medicine); and 2 adapted R&D projects in technical lifecycle (heat-stable and cold-stable formulations of GSK's *S. pneumoniae* (Synflorix®) vaccine)

† After the period of analysis, the project has moved to Phase I.

‡ After the period of analysis, the project has moved to Phase III.

development, eight are in clinical development and two are technical lifecycle projects. The stages of development for seven projects were provided on the basis of confidentiality.

A.2.2 Two late-stage novel projects

GSK's clinical-stage medicine pipeline for priority pathogens consists entirely of new R&D projects. GSK has two late-stage antibacterial medicine projects that are considered novel. The two projects are: GSK-3036656, for TB, which meets all four criteria set by WHO for innovativeness; and gepotidacin, for bacterial infections caused by *Enterobacteriaceae* and *N. gonorrhoeae*, which belongs to a new chemical class, has a new mode of action and no cross resistance to existing antibacterials.

A.2.3 Largest vaccine pipeline

GSK reports 15 vaccine projects in its pipeline. It is by far the largest vaccine pipeline from the five companies evaluated for this indicator. It includes 12 new and 3 adapted projects. One is in discovery; six are in pre-clinical development; and six are in clinical development. It includes vaccines being developed to prevent bacterial infections from Shigella and Salmonella. GSK is also developing, in collaboration with the International Aids Vaccine Initiative (IAVI), a

prophylactic vaccine against TB that is currently in Phase II.

A.2.4 Seven candidates targeting critical and/or urgent priorities

GSK's clinical pipeline includes an antibacterial medicine candidate in Phase II (gepotidacin) that targets *N. gonorrhoeae* and CRE, and a vaccine candidate in Phase III targeting *N. gonorrhoeae*. GSK also has four candidates in its pre-clinical pipeline targeting either a 'critical' pathogen as defined by WHO and/or an 'urgent' pathogen as defined by the US Centers for Disease Control and Prevention (CDC).

A.3 Eight intellectual capital sharing initiatives

Its eight relevant initiatives include its collaboration with WIPO Research consortium, providing UC Berkeley researchers with a library of molecules with activity against *M. tuberculosis*. In addition, GSK is part of the TB Drug Accelerator Programme, a consortium of research institutions and pharmaceutical companies that aims to develop new treatments for TB. A third TB-related initiative includes the GSK TB Compounds Data Set, where the company has published a list of molecule leads with activity against TB. Further, GSK created its Tres Cantos

Open Lab Foundation in 2010, a not-for-profit research centre where external researchers can use the centre's facilities (e.g., animal models) to test its molecules.

A.4 Commits to systematically developing access plans in Phase III

GSK has seven late-stage R&D projects targeting priority pathogens. It reports having project-specific access plans for five of these projects. The company has committed to developing access plans for all of its projects when they reach Phase III. GSK reports that it has developed an equitable pricing strategy framework for LMICs that applies across its portfolio and business units. Its access plans include equitable pricing strategies, registration filings, non-exclusive licensing and supply chain commitments. Furthermore, it commits to registering successful products in those countries where it is running clinical trials. It also commits to not enforce patents in Least Developed Countries (LDCs) or Low Income Countries (LICs) if it is seeking to license that same product in Lower Middle Income Countries. The company reports it is committed to conducting global surveillance studies for all its new antibacterials to enable appropriate use and support stewardship.

B RESPONSIBLE MANUFACTURING Evaluated: antibacterials manufacturing (APIs and drug products)

B.1 Comprehensive environmental risk-management for own sites and suppliers

GSK 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 three years. 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. It reports using a mass balance approach to assess whether discharge levels meet these limits and also reports employing direct sampling and analytical testing to validate or refine this approach. GSK expects third-party suppliers of antibacterial APIs and drug products to follow the same standards, including limits. It reports conducting a questionnaire-based AMR assessment of all suppliers and on-site audits with a risk-based frequency. Suppliers have been requested to provide antibacterial mass balance assessments to GSK and, if these exceed PNEC limits, to

develop appropriate corrective action plans. GSK expects external private waste-treatment plants to comply with its environmental standards and guidelines and reports auditing them on the basis of risk. The company does not report monitoring discharge levels of wastewater plants.

B.2 Publicly discloses some information on environmental risk management

GSK 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 GSK. GSK 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

GSK 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. It reports auditing its suppliers at its 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 GSK's own sites or any subsidiaries.¶

C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS

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

C.1.1 Filed to register six of nine relevant on-patent products¶ in 10+ access countries

GSK is one of the leaders when it comes to filing on-patent products for registration. It files its products in 16.6 access countries on aver-

age. Overall, 67% of its relevant on-patent products (of nine vaccines) are filed in 10+ access countries. Its most widely filed relevant product is the vaccine Synflorix®, used to prevent diseases such as pneumonia and meningitis, filed in 51 countries.

C.1.2 Filed to register its relevant off-patent products in 12.8 access countries on average

GSK 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 anti-

§ 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.

bacterials) for registration in access countries. Its most widely filed product in this analysis is amoxicillin/clavulanic acid (Augmentin™), used for conditions including pneumonia and skin infections. GSK has filed its version of this product in 54 countries. Amoxicillin/clavulanic acid is followed by ceftazidime and trimethoprim/sulfamethoxazole, filed by GSK for registration in 28 and 18 access countries, respectively.

C.2.1 Takes socioeconomic factors into account when setting prices for on-patent products

When setting prices for on-patent products, GSK takes socioeconomic factors into account. Nine vaccines were included for analysis. For the public sector, GSK uses a seven-tiered pricing strategy based on Gross National Income (GNI). For the private sector, its pricing tiers are based on a country's Human Development Index (HDI). For two vaccines, it applies tiered pricing strategies in 40 and 23 access countries respectively.

In LDCs, GSK has set a ceiling price for the private sector per vaccine.

C.2.2 Pricing strategies for off-patent products

Companies were not scored in this indicator as the available data was insufficient for a comparative analysis. GSK does report several pricing strategies for its off-patent antibacterial or antifungal medicines and vaccines. It states that its prices are driven by a country's relative wealth and the level of affordability. GSK offers discounts and participates in tenders addressing specific populations within a given country. It has a tiered pricing policy for its vaccines, for which it has supply contracts with MSF and UNICEF. These pricing strategies are applied in all access countries.

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

GSK leads in its approach to ensure the contin-

uous supply of its relevant products to access countries. It discloses multiple strategies to achieve this aim. It uses three-year forecasts and long-term demand projections that look up to ten years ahead. It focuses these initially on those countries expected to demand the highest volumes. GSK uses dual sourcing for APIs for its critical products and maintains and monitors safety stocks. It works with various partners, including the Tanzanian and Nigerian Ministries of Health, in its mVaccination programme to improve immunisation coverage. GSK is a member of International Federation of Pharmaceutical Manufacturers and Associations' (IFPMA) 'Fight the Fakes' campaign, which aims to mitigate against falsified medicine reaching the supply chain, as do its use of security features, tamper evident packaging, track-and-trace coding, auditing of warehouses and reviews of areas of potential fraudulent activity. GSK also supplies one forgotten antibiotic# (cloxacillin) to Pakistan and Zambia.

C APPROPRIATE ACCESS & STEWARDSHIP – STEWARDSHIP

Evaluated: stewardship activities relating to antibacterial & antifungal medicines globally

C.4 Comprehensive strategy to mitigate COI for all educational programmes

The Benchmark analysed the top five AMR-related educational programmes for HCPs from GSK. GSK reports comprehensive 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 (as a company-wide policy); (2) a pledge not to provide financial or material incentives to participants; and (3) a policy of not using branded materials. The remaining two programmes are also accredited by an independent body that evaluates potential COI.

C.5 Adapts marketing materials and sales practices to address appropriate use

GSK engages in practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines, both via its marketing practices and sales remuneration. At least some of GSK's marketing materials reflect emerging resistance trends and include guidelines for

HCPs to raise awareness of AMR and address appropriate use: namely, it includes SOAR surveillance data in marketing materials for antibacterials amoxicillin/clavulanic acid (Augmentin™) and cefuroxime (Zinnat®). GSK reports that it partly decouples incentives for sales agents from sales volumes to help prevent the inappropriate use of its antibacterial and/or antifungal medicines.

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

GSK adapts brochures and packaging to facilitate the appropriate use by patients of relevant products: namely its antibacterial amoxicillin/clavulanic acid (Augmentin™). These adaptations take account of language, adherence to treatment, literacy and the environment. GSK has translated a Patient Knowledge Card into English, French and Portuguese. This card highlights information that aims to improve adherence to treatment. GSK uses an artificial intelligence-enabled chatbot to educate patients on

the appropriate use of antibacterials in a low-literacy format by using graphics. Further, GSK has created blister packaging with a specific lidding foil that is sensitive to moisture for high humidity environments.

C.7 Active in one AMR surveillance programme; openly publishes results; shares consumption data

GSK runs one long-term AMR surveillance programme. The Survey of Antibiotic Resistance (SOAR) is a multinational programme focused on community-acquired respiratory-tract infections in more than 30 countries and runs periodically. It only shares its results through peer-reviewed open-access journal articles. GSK reports that it shares consumption data on colistin periodically with the Pharmaceuticals and Medical Devices Agency in Japan.

DIAGNOSTICS, ANIMAL HEALTH & AGRICULTURE

Activities in this area are not scored by the Benchmark. This information is provided given the importance of diagnostics, animal health and agriculture on the topic of AMR.

While GSK does not have its own diagnostics division, the company reports that it works with third parties to complement AMR product development with diagnostic tests whenever possible, and publicly advocates the need for rapid, accurate diagnostics to further support the appropriate use of all antibacterials.

It has a public policy in place which states that the company will not license its new antibacterials for any agricultural use.

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.