

# Shionogi & Co, Ltd

Large R&D-based pharmaceutical company

Stock exchange: TSE • Ticker: 4507 • HQ: Osaka, Japan • Employees: 5,120

## PERFORMANCE

Shionogi performs well in its evaluated Research Areas when compared to other large R&D-based pharmaceutical companies in scope.

**R&D:** Middle-performing. Pipeline consists of eight projects for medicines and vaccines for priority pathogens. It reports plans for access for its one late-stage R&D project. No intellectual capital sharing initiatives were reported.

**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 low. It markets antibacterial and antifungal medicines mainly in Japan. It reports no strategies on how it ensures the continuous supply of its products to access countries.

**Stewardship:** Performs well. It has educational programmes with broad conflict of interest (COI) mitigation. It is active in surveillance and publicly shares results. It fully decouples sales incentives from volumes. It adapts brochures for paediatric use in Japan only.

## SALES AND OPERATIONS

**Therapeutic areas:** Diabetes; Infectious diseases; Haematology; Neurology; Pain management

**Business segment:** Prescription Drugs

**Product Categories:** Innovative medicines (including ViiV Healthcare, JV with Pfizer and GSK)

**Manufacturing & supply:** Shionogi reports having one manufacturing site that produces antibacterial APIs and/or drug products. It supplies more than 40 million defined daily doses (DDDs) of antibacterial medicines to date.

**M&A since 2018:** In July 2019, Shionogi announced that it will out-license COT-143 to the AMR Centre. COT-143 is a humanised monoclonal antibody targeting the PcrV protein of *P. aeruginosa*.

## PIPELINE for diseases in scope

**Pipeline size:** 8 projects for priority pathogens\* (6 antibacterial medicines and 2 antifungal medicines)

**Development stages:** 1 clinical project, cefiderocol, which has been submitted for EMA and FDA approval for the treatment of multidrug-resistant (MDR) Gram-negative infections, and 7 discovery/pre-clinical projects

**Novelty:** No novel clinical-stage medicine projects

**Regulatory approvals:** 0 approvals for priority pathogens

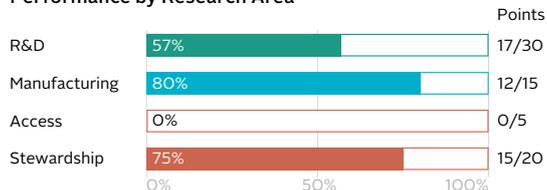
**Access plans:** Its 1 late-stage R&D project with a project-specific access plan.

**Stewardship plans:** Its 1 late-stage R&D medicine project lacks a project-specific stewardship plan.

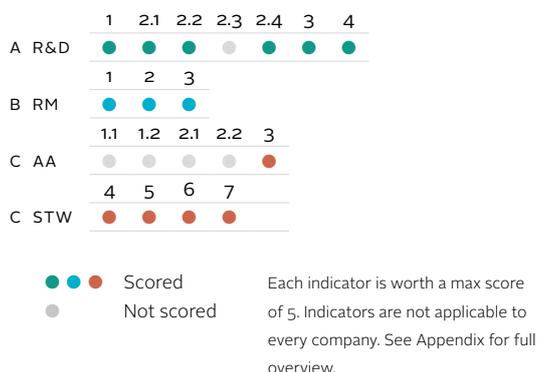
## Performance in the Benchmark



## Performance by Research Area



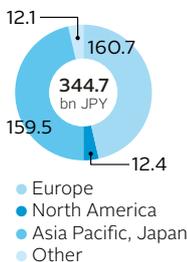
## How Shionogi was evaluated



## Revenues by product (2017-18)



## Revenues by region (2017-18)



## PORTFOLIO for diseases in scope

**Comparatively small portfolio:** At least 7 products (7 unique INNs): 7 antibacterial medicines

**Essential medicines:** 29% (2) products are on the 2019 WHO EML

**AWaRe medicines\*\*:** 2 Access group

**Anti-TB medicines\*\*:** None

## 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 Shionogi'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 SHIONOGI

**Develop access and stewardship plans for cefiderocol (Fetroja®).** Cefiderocol was approved by the FDA in November 2019. Shionogi can swiftly develop plans to ensure that cefiderocol is widely available and affordable in access countries, while appropriately used globally. As examples of access plans, the company can commit to an equitable pricing strategy and/or look for out-licensing opportunities with multiple manufacturers in low- and middle-income countries. As examples of stewardship plans, it can take steps to ensure the continuous supply of this product and/or include it into its antibacterial surveillance activities

**Follow up to public commitments and increase public disclosure on environmental risk management.** After the period of analysis, Shionogi published information, disaggregated per antibacterial product, on whether its own sites and (anonymised) suppliers met the expectations of the CAMF and discharge limits. Building on this positive step and following up on its commitments as a signatory to the Industry Roadmap for Progress on Combating AMR, Shionogi 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 supply of antibacterial medicines to access countries.** Shionogi can consider expanding supply of antibacterial medicines in its current portfolio on the 2019 WHO EML to access countries (eg. sulfamethoxazole/trimethoprim and vancomycin).

**Publicly share raw data from its four surveillance programmes in Japan.** Shionogi can share publicly (e.g., with the AMR Register) the raw data collected for its surveillance programme in Japan, such as SIDERO-WT and the Shionogi Japanese Surveillance Studies Programme.

## CHANGES SINCE 2018

- Received FDA approval in November 2019 for cefiderocol (Fetroja®) for the treatment of complicated urinary tract infections.
- Received, in March 2018, a CARB-X award of USD 4.7 million to support development of a new beta-lactam antibacterial medicine targeting carbapenem-resistant *Enterobacteriaceae* (CRE) infections.
- Published its AMR-specific environmental risk-management strategy for antibacterial manufacturing in its EHS report.
- Extended its AMR-specific environmental risk-management strategy to suppliers and assesses whether their antibacterial discharge levels are below limits during audits.

## PERFORMANCE BY RESEARCH AREA

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

#### A.1 Highest investments in relevant R&D, as proportion of pharmaceutical revenues

Shionogi reports that it invested USD 133 million in R&D for antibacterial and antifungal medicines in 2017 and 2018. As a proportion of its revenues from pharmaceuticals, these investments are the highest compared to investments in such R&D made by other large research-based

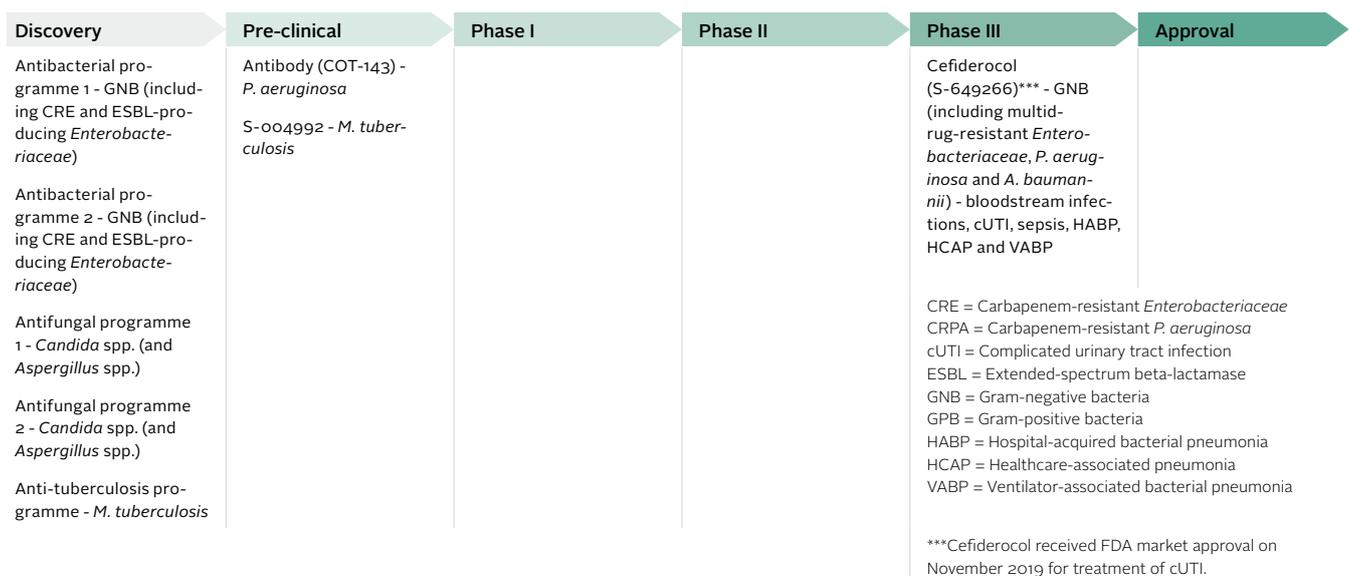
pharmaceutical companies evaluated in the Benchmark. Shionogi does not invest in vaccine development.

#### A.2.1 Mid-sized pipeline compare to peers

Among the large research-based pharmaceutical companies evaluated, this pipeline is mid-sized. Shionogi reports eight projects targeting priority pathogens in its pipeline. It is one of the two

large research-based pharmaceutical companies within the scope of the Benchmark to have both antibacterial and antifungal projects (all medicine projects). The company's projects are mostly in discovery stage or pre-clinical development (7 out of 8), with one project, cefiderocol, that has been submitted for market approval by the EMA and FDA.

#### Pipeline targeting priority pathogens: 8 As at 16 October 2019



\* 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.

**A.2.2 No clinical-stage novel projects**

Shionogi's clinical-stage medicine pipeline for priority pathogens consists of one new R&D project. It does not currently include candidates that are considered novel. However, Shionogi has applied for EMA and FDA market approval for cefiderocol, a siderophore cephalosporin antibacterial for the treatment of multi-drug resistant infections caused by Gram-negative bacteria as well as complicated urinary tract infections and hospital-acquired and ventilator-associated pneumonia.

**A.2.3 Vaccines in the pipeline**

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

**A.2.4 Four candidates targeting critical and/or urgent priorities**

Shionogi's clinical pipeline includes the medicine cefiderocol, active against Carbapenem-resistant *A. baumannii* (CRAB), Carbapenem-resistant *P. aeruginosa* (CRPA) and CRE. It has been submitted for first marketing authorisation to both the FDA and EMA. Shionogi also has three further candidates in its discovery and pre-clinical pipeline 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).

**A.3 No intellectual capital sharing practices**

The company does not report any intellectual capital sharing initiatives.

**A.4 Access plan for its late-stage R&D project targeting a priority pathogen**

Shionogi has one such R&D project. It reports to run a global compassionate use programme for cefiderocol. Shionogi has affiliate companies in a limited number of countries and is also currently seeking partners to help increase access. It reports a commitment to discuss stewardship strategies with the access country governments.

**B RESPONSIBLE MANUFACTURING** Evaluated: antibacterials manufacturing (APIs and drug products)**B.1 Comprehensive environmental risk-management for own sites and suppliers**

Shionogi 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 five 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 or the EMA. It reports using analytical testing to validate its antibacterial deactivation procedure and having plans to develop a monitoring system in the near future.

Shionogi expects third-party suppliers of antibacterial APIs and drug products to follow the same standards, including limits. Audits are set to take place at least every five years and suppliers have been requested to provide information to Shionogi on whether their discharges are below the PNECs or, where PNECs are not available, below EMA environmental emission stand-

ards. The company reports that on-site audits have been conducted for all Japanese-based suppliers and corrective actions requested when their antibacterial discharge levels were found to be above the limits. Shionogi also expects external private waste-treatment plants to comply with its environmental standards and guidelines and reports auditing them once a year. All solid waste and wastewater sent to these plants is set to be incinerated.

**B.2 Publicly discloses some information on environmental risk management**

Shionogi 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. Shionogi 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. After the period of analysis,

Shionogi published, in its 2019 EHS report, some information on how its strategy and individual discharge limits are being implemented at its own and suppliers' sites.

**B.3 Has system to maintain production quality for own and suppliers' sites; no requests for official corrective action**

Shionogi 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 actions. The company reports requiring suppliers to abide by regulatory and company quality standards, as specified in quality agreements. It reports auditing its suppliers as 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 Shionogi'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 - C.2 Registration and pricing**

Shionogi was not eligible for this indicator as it does not have relevant on-patent§ or off-patent marketed products in its portfolio for which it has the global rights to market or distribute. It reports that the patent on its antibacterial medicine doripenem (Doribax®, Finibax®) has expired and has been licenced out to Takeda for markets other than Japan, Taiwan and Korea. Shionogi also reports that it has marketing rights for the antibacterial cefiderocol and that it currently runs a global compassionate use programme.

**C.3 No measures to ensure continuous supply of products**

Shionogi does not take steps to ensure continuous supply of antibacterial medicines 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.

## C APPROPRIATE ACCESS & STEWARDSHIP – STEWARDSHIP

Evaluated: stewardship activities relating to antibacterial & antifungal medicines globally

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

The Benchmark analysed three AMR-related educational programmes for healthcare professionals (HCPs) from Shionogi. Shionogi reports broad COI mitigation for all three programmes. Two 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 the remaining programme, it is unclear whether financial or material incentives are provided to participants. After the period of analysis, the company stated that no payments were given to participants.

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

Shionogi engages in practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines, both via its mar-

keting practices and sales remuneration. At least some of Shionogi's marketing materials reflect emerging resistance trends and include guidelines for HCPs to raise awareness of AMR and address appropriate use: namely for the antibacterials doripenem (Finibax®) and flomoxef (Flumarin®). Shionogi is the only large-research-based pharmaceutical company evaluated that reports fully decoupling incentives for sales agents from sales volumes to help prevent the inappropriate use of its antibacterials.

### C.6 Adapts brochures to facilitate appropriate use; takes account of paediatric needs

Shionogi adapts brochures in Japan to facilitate the appropriate use by patients of relevant products: namely for its antibacterial cefcapene pivoxil (Flomox®). This adaptation takes account of paediatric use. Shionogi has created a brochure that is easy to understand thanks to simple illustrations. The brochure is tailored to the treatment of children to improve paediatric use.

### C.7 Active in multiple AMR surveillance programmes; openly publishes results

Shionogi runs four long-term AMR surveillance programmes. The number of pathogens (species) tested in these programmes varies from ten to 16. One of the programmes, SIDERO-WT, focuses on resistance against Gram-negative bacteria in 13 countries and is repeated every year. The other three programmes focus on antibacterial drug susceptibility in Japan. For example, the Shionogi Japanese Surveillance Studies Programme has run since 1992 and tests 43 antimicrobials. Only the results of these four programmes are shared through peer-reviewed open-access journal articles. Shionogi does not report making antibacterial and/or antifungal consumption data available to national governments or other public health authorities.