

Otsuka Pharmaceutical Co, Ltd

This table is part of a [November 2023 report](#) that looks at what actions each company in scope of the Antimicrobial Resistance (AMR) Benchmark has taken with regards to each of the Opportunities set out in its 2021 AMR Benchmark Report Card. The full 2021 Report Card is also included in this PDF.

2021 OPPORTUNITY What was the Opportunity shared in the AMR Benchmark?	2023 UPDATE What progress has been made on this Opportunity?
<p>Expand breadth of R&D pipeline into more pathogens. Despite being the smallest of the large R&D-based companies assessed in the AMR Benchmark, Otsuka optimises its resources and has achieved remarkable expertise in tuberculosis R&D, being one of the main investors in TB R&D worldwide. Otsuka can now redirect this expertise and invest in innovative in-house R&D to target resistant pathogens for which R&D is limited, such as <i>Campylobacter spp.</i> and <i>H. pylori</i>, through acquisition or collaboration with other companies, or by joining existing public private partnerships.</p>	<p>Otsuka did not report progress on this Opportunity, referring to its current focus on tuberculosis (TB) R&D.</p>
<p>Develop an AMR-specific environmental risk-management strategy and increase public disclosure. Otsuka reports a commitment to manufacture its products in an environmentally responsible manner without specifying whether AMR is taken into account. The company can develop an AMR strategy for its own manufacturing sites, the sites of suppliers and external private waste-treatment plants, based on the guidelines of the AMR Industry Alliance, of which Otsuka is a member. This includes setting limits and quantifying discharge levels to track compliance. Moreover, Otsuka can publish information on how it manages environmental risk related to antibacterial manufacturing to curb AMR.</p>	<p>Otsuka reports that it has completed the development of an analytical method to quantify the levels of delamanid in wastewater. As a follow-up, Otsuka plans to quantify discharge levels to confirm if the existing wastewater treatment setup maintains delamanid concentration below discharge limits.</p>
<p>Ensure availability and affordability of delamanid (Delytba). Otsuka can expand the availability of delamanid (Delytba) by filing for registration in more access countries, including through its voluntary licensing agreement with Viatris, in particular in the 30 countries with the highest MDR-TB burden identified by the WHO.</p>	<p>Otsuka reports that since 2021, Delytba® is newly registered in three countries in scope of the Benchmark – Brazil, Morocco and Uzbekistan. Additionally, Otsuka has also filed for registration in four countries in scope – Malaysia, Mexico, Thailand and Vietnam. To increase affordability and accessibility, Otsuka has completed a full technology transfer for its 50mg delamanid formulation to Viatris in India. In addition, Otsuka has initiated a technology transfer of delamanid's paediatric formulation. Furthermore, Otsuka reports a commitment to ensure a continuous supply of delamanid's paediatric formulation to the Stop TB Partnership's Global Drug Facility (GDF).</p>
<p>Engage in AMR surveillance activities. Otsuka is not active in AMR surveillance activities. It can engage in AMR surveillance programmes through setting up (in-house) programmes or by funding established programmes run by research organisations. Additionally, Otsuka should publicly share raw data collected from the programme.</p>	<p>Otsuka reports plans to set up surveillance activities in at least two countries in scope. However, Otsuka does not report when these surveillance activities will commence. The company reports that future surveillance results will be submitted for publication in open access journals.</p>

Overall Performance

2020 2021

52% 57%▲

Otsuka Pharmaceutical Co, Ltd

Large R&D-based pharmaceutical company

Stock exchange: TSE • Ticker: 4578 • HQ: Tokyo, Japan • Employees: 5,657

PERFORMANCE

Otsuka performs average overall in its evaluated Research Areas compared to the other large research-based pharmaceutical companies in scope.

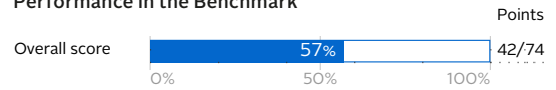
R&D: Otsuka performs well in R&D. All four projects in its pipeline are antibacterial medicines: three targeting *M. tuberculosis* and one targeting a critical and/or urgent pathogen (*P. aeruginosa*). It has one novel antituberculosis candidate in clinical development. Otsuka has two projects in late-stage development with comprehensive plans for access and stewardship.

Responsible Manufacturing: Performs low. Reports a general environmental risk-management strategy but without a specific aim to limit AMR.

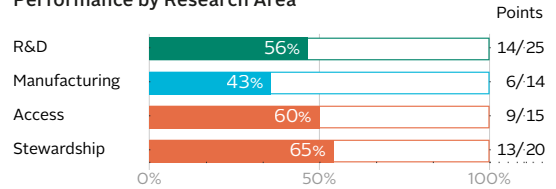
Appropriate Access: Middle-performing. Files its relevant products (on-patent medicine) for registration in access countries. Reports some strategies to expand access and ensure continuous supply of its relevant product.

Stewardship: Middle-performing. It does not promote delamanid (Delytba®) to healthcare professionals which is its only product in scope. It is not involved in AMR surveillance programmes. It reports comprehensive conflict of interest mitigation for its educational programme. It adapts brochures for patients.

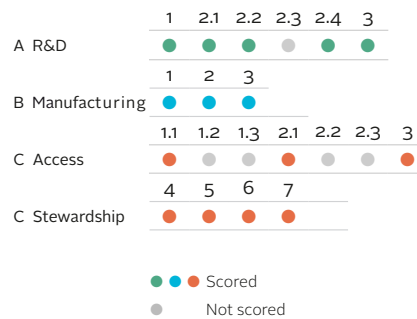
Performance in the Benchmark



Performance by Research Area



How Otsuka was evaluated



OPPORTUNITIES FOR OTSUKA

Expand breadth of R&D pipeline into more pathogens. Despite being the smallest of the large R&D-based companies assessed in the AMR Benchmark, Otsuka optimizes its resources and has achieved remarkable expertise in tuberculosis R&D, being one of the main investors in TB R&D worldwide. Otsuka can now redirect this expertise and invest in innovative in-house R&D to target resistant pathogens for which R&D is limited, such as *Campylobacter* spp. and *H. pylori*, through acquisition or collaboration with other companies, or by joining existing public private partnerships.

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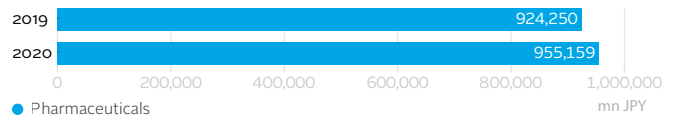
CHANGES SINCE 2020

- In February 2020, Otsuka joined the Project to Accelerate New Treatments for Tuberculosis (PAN-TB), a collaboration among philanthropic, non-profit and private sectors partners that aims to develop an investigational drug regimen capable of treating all forms of TB.
- In September 2020, the European Medicines Agency (EMA) approved the extension of Otsuka's MDR-TB treatment delamanid (Delytba®) to include children with a body weight of at least 30 kg. In July 2021, the EMA approved the use of the 25 mg dispersible tablet formulation of delamanid (Delytba®) for the treatment of pulmonary MDR-TB in adults, adolescents, children and infants with a body weight of at least 10 kg.

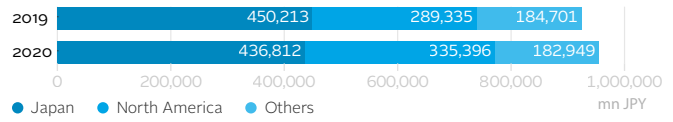
SALES AND OPERATIONS

Therapeutic areas: Cardiovascular and renal diseases, Central nervous system, Oncology, Ophthalmology, Tuberculosis
Business segments: Pharmaceuticals
Product categories: Innovative medicines
M&A since 2020: None in the antibacterial and/or antifungal sectors

Revenue by business segment



Revenue by region



PIPELINE for pathogens in scope

Pipeline size: 4 projects targeting pathogens in scope* (4 antibacterial medicines).
Development stages: 1 clinical project, OPC-167832, a Phase II candidate for the treatment of *M. tuberculosis*; and 1 preclinical project targeting *P. aeruginosa*.
Novelty: 1 novel project, OPC-167832, an antituberculosis candidate that meets all four criteria set by WHO for innovativeness.
'Critical' and/or 'urgent' pathogens: 1 project, VIS705, a preclinical therapeutic candidate, targeting *P. aeruginosa*, including MDR strains.
Regulatory approvals: 2 approvals. Marketing authorisation by the EMA was granted to the antituberculosis drug delamanid (Delytba®) for the treatment of children with a body weight of at least 30 kg. In July 2021 the EMA approved the use of the 25 mg dispersible tablet formulation of delamanid (Delytba®) for the treatment of pulmonary MDR-TB in adults, adolescents, children and infants with a body weight of at least 10 kg.

PORTFOLIO for pathogens in scope

Comparatively small portfolio: At least 1 product: 1 antibacterial medicine
On-patent medicine: 1 (delamanid)
AWaRe medicines: 0
Anti-TB medicine:** 1

Pipeline for priority pathogens



Products on the market



PERFORMANCE BY RESEARCH AREA

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

A.1 Investments in R&D

Otsuka discloses to the Benchmark its R&D investments during 2019 and 2020 in antibacterial and antifungal medicines and/or vaccines for pathogens in scope. Otsuka reports that it invested USD 34.61 mn in R&D for antibacterial medicines in 2019 and 2020. This constitutes a small proportion of its revenues compared to the other companies who reported investments to the Benchmark.

A.2.1 Pipeline targets mainly *M. tuberculosis*

The company reports four projects targeting

pathogens in scope. All of them are medicines targeting bacterial pathogens: three are antituberculosis agents and the remaining one targets *P. aeruginosa*. Out of the four projects, one is in preclinical stage, one in Phase II, delamanid (Delytba®) for paediatric patients received marketing approval during the period of analysis and the adult indication remains in Phase IV.

A.2.2 Small innovative pipeline

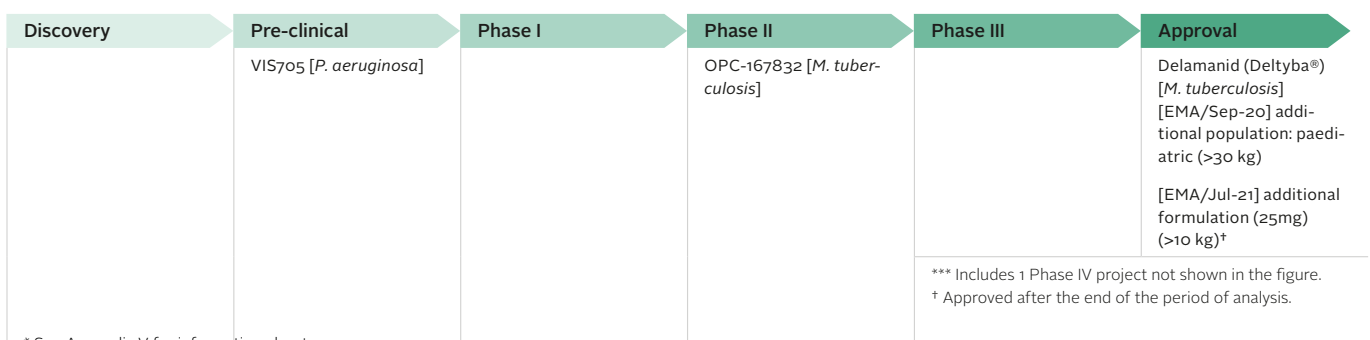
Otsuka's clinical-stage medicine pipeline consists of both innovative and adaptive R&D projects. Otsuka has one antituberculosis medicine candidate which meets all four WHO's innovativeness criteria: OPC-167832. In September 2020, EMA approved the extension of Otsuka's MDR-TB treatment delamanid (Delytba®) to include children with a body weight of at least 30 kg. In July 2021, the EMA approved the use of the 25 mg dispersible tablet formulation of delamanid (Delytba®) for the treatment of pulmonary MDR-TB in adults, adolescents, children and infants with a body weight of at least 10 kg.

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A.2.3 Not active in vaccine development

Otsuka is not active in vaccine development targeting

Pipeline targeting priority pathogens: 4*** As at 24 September 2021



* See Appendix V for information about eligibility for R&D projects and Appendix VII for eligibility criteria of products.

** Listed on the 2019 WHO EML.

*** Includes 1 Phase IV project not shown in the figure.
 † Approved after the end of the period of analysis.

getting pathogens in scope.

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

Otsuka has one medicine candidate in its R&D pipeline targeting pathogens defined as 'critical' by WHO's list of priority pathogens and/or characterised as 'urgent' threats by the US Centers for Disease Control and Prevention (CDC). VIS705 is in preclinical development and targets *P. aeruginosa*, including MDR strains.

A.3 Comprehensive planning for access and stewardship

Otsuka has two medicine projects in late-stage development. For its project OPC-167832, in Phase II, Otsuka has committed itself contractually to a comprehensive access strategy as stipulated by the Bill & Melinda Gates Foundation. Otsuka also reports plans to engage in surveillance and monitoring of the emergence of resistance to this new antituberculosis candidate.

For the paediatric indication of the antituberculosis drug delamanid (Delytba®) for which marketing authorisation by the EMA was granted in September 2020 for children above 30 kg and on July 2021 for children above 10 kg, Otsuka also has comprehensive strategies to

ensure its appropriate use, as well as availability and affordability in access countries†.

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

B.1 No AMR-specific environmental risk management strategy

Otsuka's general environmental strategy includes a commitment to manufacture its products in an environmentally responsible manner but without a specific aim to limit AMR. Its strategy also does not include any actions specific to delamanid (Delytba®), the only antibacterial produced at its manufacturing sites, in both its API and drug product forms.

Otsuka does not report making any requirements in this regard to the third-party drug product manufacturer contracted for an intermediate step in delamanid production.

There is also limited information on the requirements Otsuka makes of external private waste-treatment plants, in terms of strategy, audits and discharge limits and levels. It reports these plants are audited every three years but audit parameters are not related to AMR. It also reports wastewater is treated on-site and external private and public wastewater treatment plants are not used.

B.2 Publicly discloses some information on environmental risk management

Otsuka publishes some components of its environmental risk-management strategy, without specific references to AMR. It is a member of the AMR Industry Alliance, which publishes a list of recommended antibacterial discharge targets. Otsuka does not publish: (1) the results of environmental audits, whether conducted at its own sites, the sites of suppliers or external private and public waste-treatment plants; (2) a list of these suppliers and plants; or (3) the levels of antibacterial discharge from its own or suppliers' sites.

B.3 System in place to maintain production quality for own and suppliers' sites; no requests for official corrective action

Otsuka reports that its own sites and suppliers have a system to maintain high-quality antibacterial production consistent with international GMP standards. This includes periodic risk-based audits and tracking of corrective and preventive actions. Otsuka reports it does not have any

subsuppliers of antibacterials. The Benchmark found no requests for official corrective action from the FDA or EMA related to non-conformities with cGMP at Otsuka's own sites or any subsidiaries.

C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS

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

Otsuka is not eligible for indicators: C.1.2, C.1.3, C.2.2 and C.2.3. For more information, see Appendix VII.

C.1.1 Filed to register its on-patent medicine in 9 access countries

Otsuka has an average performance, filing its one on-patent medicine for registration in nine access countries. The medicine is the anti-tuberculosis medicine, delamanid (Delytba®).

C.2.1 Some strategies to expand access to its on-patent medicine

Otsuka has an average performance. It aims to expand access to its one on-patent medicine in access countries through a voluntary licensing agreement and a partnership. It partners with the Global Drug Facility - Stop TB Partnership to provide delamanid at a global access price

of USD 1,700 for a 6-month treatment course. Otsuka has a voluntary licensing agreement with Viatrix and R-Pharm to accelerate access to delamanid (Delytba®) in high TB burden countries. Otsuka and Viatrix have entered into a technology transfer agreement, to produce and distribute a lower-cost generic version of delamanid (Delytba®). Otsuka provides evidence of patient reach and geographic reach for its reported approaches. It estimates that at least 24,700 treatment courses were distributed in 2020. Delamanid (Delytba®) is available in all 30 WHO high-burden countries for MDR-TB.

C.3 Some strategies to ensure continuous supply

Otsuka has an average performance, with strategies reported in all four areas assessed. Otsuka ensures accurate demand planning and

data sharing by conducting long-term planning and S&OP planning. Otsuka mitigates against shortage risks by keeping a 1.5-year average buffer stock in the countries where delamanid (Delytba®) has a marketing authorisation. It conducts annual inventory checks and external audits of its stocks. Otsuka conducts a technology transfer to allow Viatrix to manufacture, package, and distribute delamanid (Delytba®) in a set of access countries. To mitigate against substandard and falsified products, Otsuka uses security features such as serialisation, GS1 barcodes and GDSN traceability. Delamanid (Delytba®) has a unique packaging process including alu-alu blisters, tamper-proof seals, and unique identifier codes.

† 102 low- and middle-income countries where better access to medicine is most needed.

C APPROPRIATE ACCESS & STEWARDSHIP – STEWARDSHIP

Evaluated: stewardship activities relating to antibacterial & antifungal medicines globally

C.4 Comprehensive COI mitigation strategies in place for its educational programme

Otsuka performs strongly in conflict of interest (COI) mitigation for the one AMR-related educational programme for HCPs assessed by the Benchmark. The programme has 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.

C.5 Does not promote its antibacterial medicine

Otsuka performs strongly in sales practices as it does not promote its product in scope. It does not deploy any sales agents to promote delamanid (Delyba®) to healthcare professionals, because treatment is only available in specialised centres under tightly controlled conditions. Since Otsuka does not develop or use marketing materials for delamanid (Delyba®) to promote it to

healthcare professionals, the company is not eligible to be assessed on marketing materials.

C.6 Makes one type of brochure and/or packaging adaptation to facilitate appropriate use by patients

Otsuka adapts brochures to facilitate the appropriate use of delamanid (Delyba®) by patients. Otsuka is middle-performing in this measure, taking account of language. It has translated its Educational Risk Minimisation Materials into English, French, Spanish and Russian, which are distributed through the Global Drug Facility.

C.7 No involvement in AMR surveillance programmes

Otsuka is the only large R&D-based company that does not report any involvement in AMR surveillance programmes.