
CARE
COALIZIONE
CONTRO
ANTIMICROBICO
RESISTENZA

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

ReserveX (Reserve and Listed antibiotics eXploration)

Project final report

Fanno parte della della coalizione multistakeholder CAЯe: Advanz Therapeutics, Menarini, Pfizer, Shionogi, Viatris, con la collaborazione scientifica di Società Italiana Malattie Infettive e Tropicali (SIMIT), Associazione Microbiologi Clinici Italiani (AMCLI) e CittadinanzAttiva

Il coordinamento tecnico-scientifico della coalizione CAЯe è di:

LS CUBE OUTSIDE THE BOX

IQVIA for CAЯe – March 2026

Agenda

- **Project overview**
- Reserve/Listed Fund: operations and impact
- Baseline
- Key insights from the physician survey
- Forecast
- *Appendix*

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

IQVIA has supported CAЯe in estimating the evolution of “Reserve/Listed” antibiotics in the next 3 years

Project overview | *Objectives and scope*

Objectives

- Evaluate the potential evolution of the **“Reserve/ Listed” antibiotics utilization in the new regulatory scenario**
- Predict the future uptake of the **upcoming “Reserve/Listed” antibiotics** and their **impact on public expenditure**
- Estimate the financial requirements for **2026-2027-2028**

Scope

- Assess **consumption expected evolution**, including the impact of **next launches**
- Develop a **3-year (2026-28) forecasting** of the “reserve/listed” antibiotics
- **Disseminate project results**

The project has leveraged multiple IQVIA assets and capabilities

Project overview | *Main steps*

01 Market assessment	02 Insight gathering & integration	03 Forecast development	04 Results dissemination
• Analyze in-scope antibiotic market dynamics, leveraging **IQVIA unique proprietary data assets** • **Deep dive on the regulatory context** (i.e. Innovative Medicine Fund) • In-depth analysis of currently **marketed products and pipeline**	• Collect IQVIA **internal knowledge** of the antibiotic market and healthcare context, built through projects and interactions with clients and institutions • Perform an ad-hoc **physician survey** to capture clinicians' insights and validate/inform the forecast assumptions	• Project the Reserve/Listed antibiotic **baseline** • Define the main **assumptions** for the future scenario (based on the key **evolution variables** and inputs collected in the previous steps) • Development of the most likely **forecast scenario**	• **Final Report** on **Reserve/Listed** antibiotic consumption and the **capacity** of the dedicated fund
MAIN DELIVERABLES			
• **Current market overview**	• **Insight summary and quantitative inputs** for the forecasting model	• **3-year forecast**	• **Final report**

Agenda

- Project overview
- **Reserve/Listed Fund: operations and impact**
- Baseline
- Key insights from the physician survey
- Forecast
- *Appendix*

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

The Innovative Medicine Fund includes a specific budget allocated for Reserve/Listed antibiotics

Innovative Medicine Fund | *Timeline and current Fund composition*

2017-2021

Establishment of the Innovative Medicine Fund (effective since 2017)

From 2017 to 2021, co-existence of 2 distinct funds[1]:

- **€500M** for **innovative drugs**
- **€500M** for **innovative oncology drugs**

2022-2024

Unified fund creation and progressive increase in resource allocation

- **Merger of the 2 funds** into a **single fund** with an annual allocation of **€1B**[2]
- **Introduction** of a **progressive increase in fund allocation (+100 million per year)**[3]
  - In **2023** increased from **€1.1B** to **€1.2B**
  - In **2024** further increase by **€100M**, reaching **€1.3B**

2025

Tripartite fund allocation[4]

- **€900M** dedicated to **Innovative drugs**
- **€300M** allocated to medicines with **conditional innovation status**
- **€100M** allocated to **anti-infective agents** for infections caused by multi-resistant pathogens (**Reserve/Listed**)

2026

Budget Law 2026

Partial decrease in total fund allocation[5]**, extension to all regions**

- Overall fund reduction to **€1.16B** (-140M)
- **€100M Reserve/Listed** fund preserved
- **Broader access**: now **open to all regions**, including special-status regions

Sources: 1) Legge di Bilancio 2017 (L. 232/2016); 2) Legge di Bilancio 2021 (L. 178/2020) and D.L. 73/2021, conv. L. 106/2021; 3) Legge di Bilancio 2022 (L. 234/ 2021); 4) Legge di Bilancio 2025 (L. 207/2024); 5) Legge di Bilancio 2026 (L. 199/2025)

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

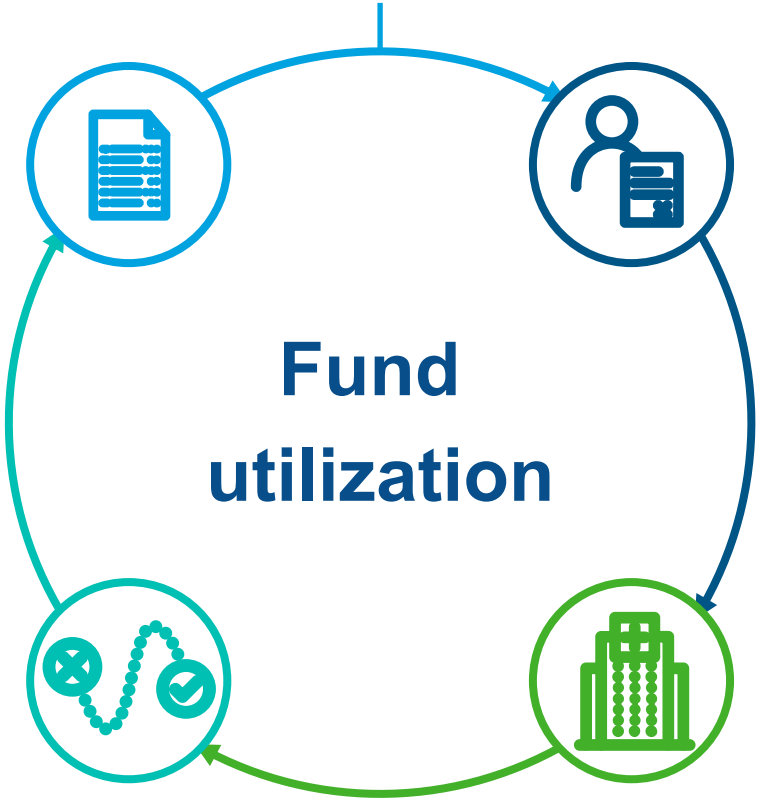
Reserve/Listed fund utilization cycle is composed of key steps required to secure reimbursement to regions for purchases

Reserve/Listed Fund | *How the fund works*

Reimbursement to Regions for Reserve drug purchases

4. Distribution[3]

AIFA assigns Fund allocations to the Regions according to **dispensations** (DF) documented in the **monitoring registry**



1. Procurement

Regions carry out **centralized purchasing** to supply Reserve medicines to pharmacies of authorized hospitals

3. Tracking[2]

Physicians must record dispensing, through the **drug delivery form (DF)** in the monitoring registry to ensure proper tracking

2. Usage[1]

Before use, **physicians** must complete the **electronic data form** (monitoring registry) on the AIFA website, in line with **eligibility** and **prescribing criteria**

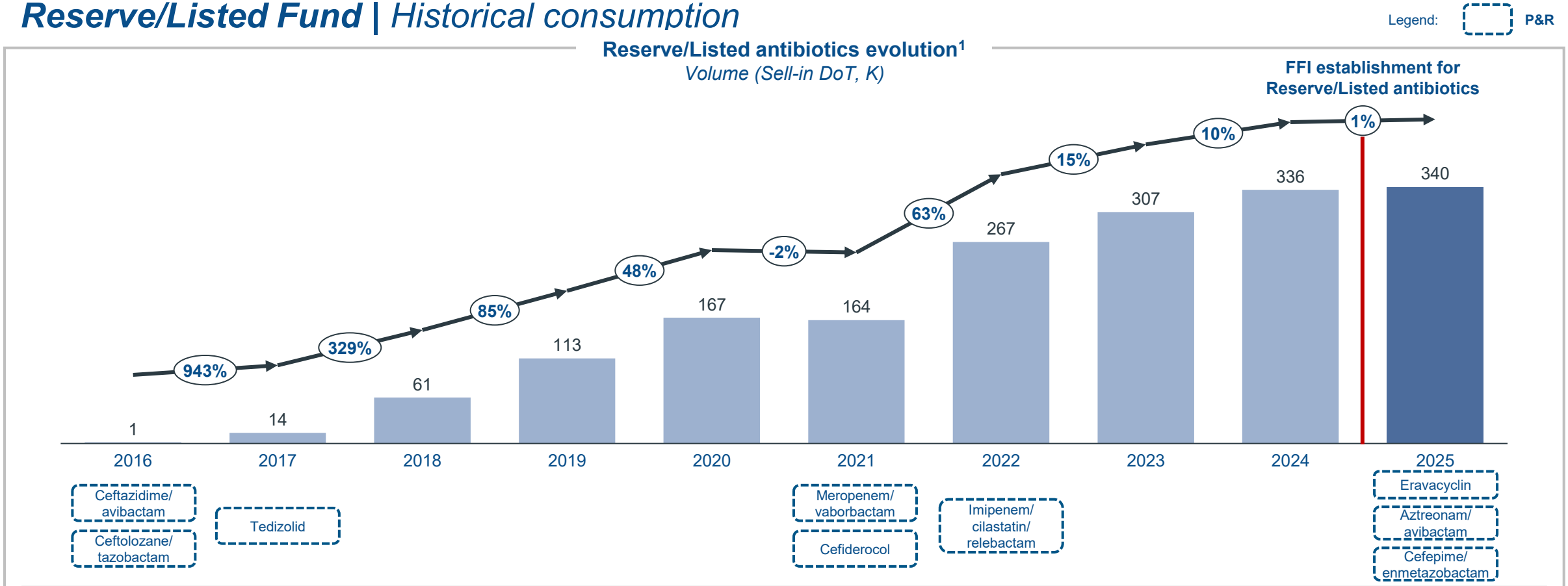
Antibiotic expenditure monitored through the "**Nuovo Sistema Informativo Sanitario (NSIS)**"

Sources: 1) Determination 06/06/25, Amendment of conditions and monitoring procedures for AIFA registries; 2) Reserve antibiotics and access to the Fund – initial guidelines for Lombardia Region; 3) Communication to the Regions on access to funds for innovative medicines, 06/06/25

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

The inclusion of Reserve/Listed antibiotics in the Fund has not led to an increase in their consumption

Reserve/Listed Fund | *Historical consumption*



- Historical consumption analysis of Reserve/Listed antibiotics shows that **previous annual growth rates were higher than the 2025 rate**, the first year after the Fund's establishment
- The historical trend indicates that the **inclusion in the Fund did not lead to increased antibiotic consumption**

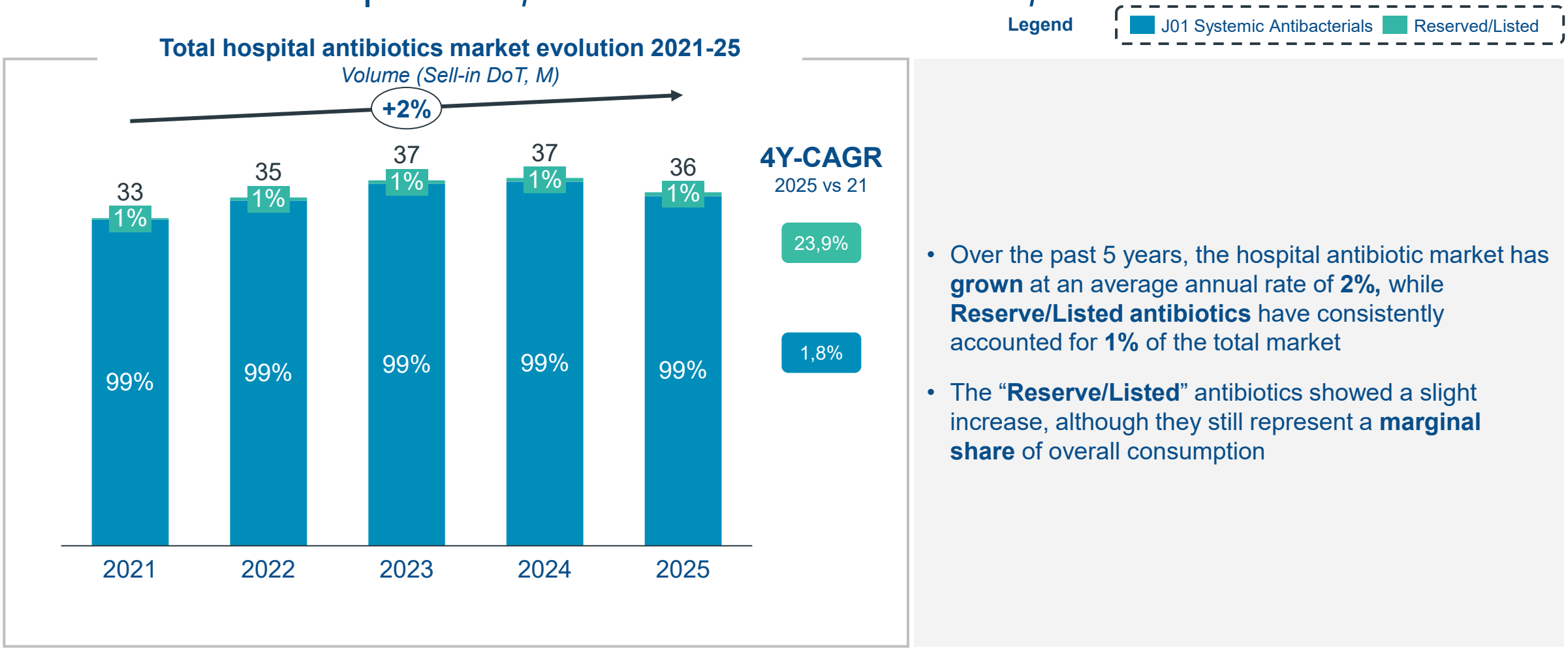
Note: 1) The represented evolution incorporates the 2025 consumption data including also the final quarter, reflecting the entry of additional Reserve/Listed antibiotics. DoT - Days of Treatment.
Source: IQVIA sales data (private clinics excluded)

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

Compared to the total hospital antibiotics consumption, Reserve/Listed account for ~1% of the market

Reserve/Listed Fund | *Total hospital antibiotics historical consumption*



- Over the past 5 years, the hospital antibiotic market has **grown** at an average annual rate of **2%,** while **Reserve/Listed antibiotics** have consistently accounted for **1%** of the total market
- The "**Reserve/Listed**" antibiotics showed a slight increase, although they still represent a **marginal share** of overall consumption

Note: DoT – Days of Treatment, CAGR – Compound Annual Growth Rate.
Source: IQVIA sales data (private clinics excluded)
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

The majority of surveyed physicians agreed that the Fund's introduction did not raise the use of Reserve/Listed antibiotics

Reserve/Listed Fund | *Perceived impact on antibiotic usage*

Physician survey

Thanks to the survey directly involving physicians who prescribe antibiotics, it was possible to assess **whether** and **to what extent** the Fund impacted Reserve/Listed antibiotic use

Specifically, for each **indication:**

- cUTI
- cIAI
- HAP & VAP
- ABSSSI
- other infections caused by Gram-negative pathogens with limited therapeutic options, or bacteremia

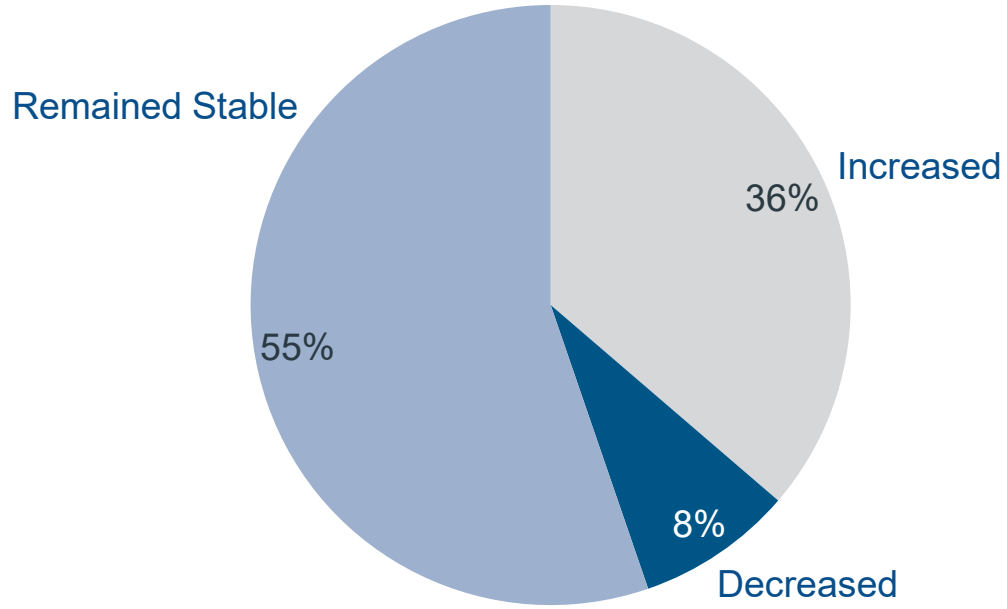
physicians were asked to consider the patients treated over the past 3 months and to indicate **whether, following the introduction of the Fund**, the number of treated patients had:

- **increased**
- **decreased**
- remained **stable**

For **more than 60% of respondents** the introduction of the Fund for Reserve/Listed antibiotics **did not lead to an increase** in the number of patients treated

Perceived impact of the Fund on the number of patients treated with Reserve/Listed antibiotics[1]

% answers by physicians

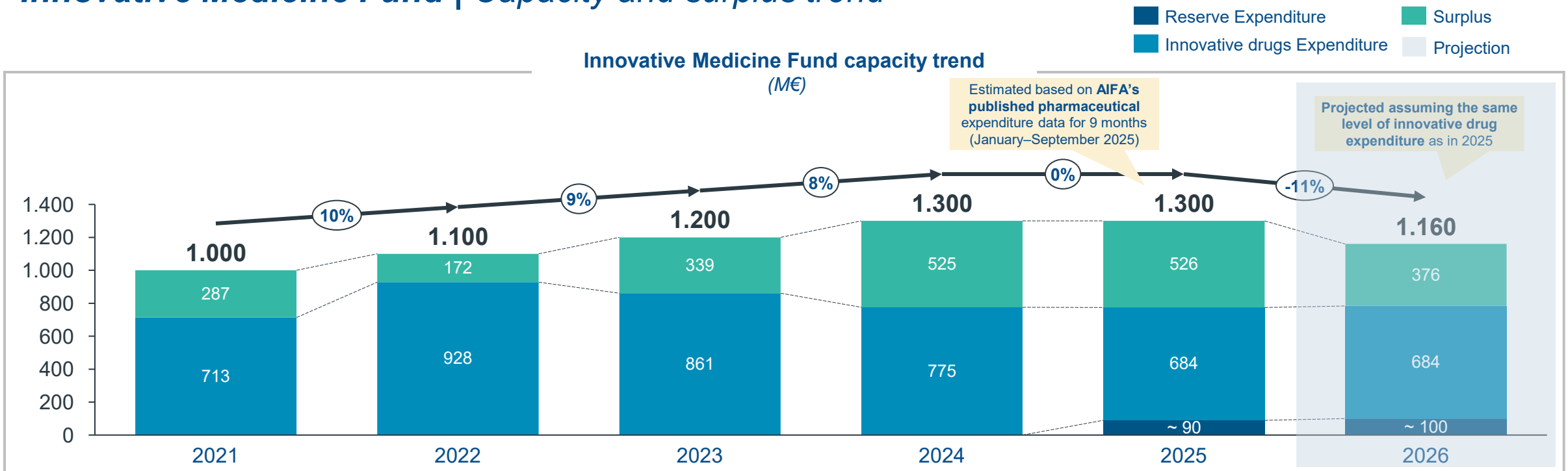


Notes: 1) You stated that in the last 3 months you have been pharmacologically treating ___ patients for complicated urinary tract infections with "Reserve/listed" antibiotics. Compared to 12 months ago, this number of patients treated with "Reserve/listed" antibiotics, thanks to their inclusion in the Fund, is ...? 1.Augmented; 2. Decreased; 3 Unchanged. Question was repeated for each indication in scope. ABSSSI – Acute Bacterial Skin and Skin Structure Infections, cIAI – Complicated Intra-Abdominal Infection, HAP – Hospital-Acquired Pneumonia, VAP – Ventilator-Associated Pneumonia, cUTI – Complicated Urinary Tract Infection, CRE – Enterobacterales carbapenem resistant

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Estimating the 2026 innovative drug expenditure based on 2025 projected data suggests a potential surplus of ~€380 million

Innovative Medicine Fund | *Capacity and surplus trend*



- From 2021 to 2025, the **IMF** grew from **€1B** to **€1.3B**. During this time, the IMF's yearly surplus increased from **€287M** to **€526M**, leading to a total surplus of roughly **€2B over five years**, averaging about **€400 million per year**
- In **2026**, the **FFI** was lowered to **€1.16B**, but if spending on innovative drugs remains at 2025 levels, a **surplus of €376M** is expected
- This surplus is due to **lower-than-anticipated expenses** on **innovative drugs** (either fully or conditionally innovative), whereas spending on Reserve antibiotics is projected to **fully utilize** the 2026 budget

Note: Surplus - unspent budget; IMF - Innovative Medicines Fund; IM - Innovative Medicines. Sources: AIFA Pharmaceutical expenditure data report 2021, 2022, 2023, 2024, Jan- Sep 2025
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

Agenda

- Project overview
- Reserve/Listed Fund: operations and impact
- **Baseline**
- Key insights from the physician survey
- Forecast
- *Appendix*

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

The forecasting involved five steps using IQVIA data and physician insights from market research

Baseline definition | *Methodology*

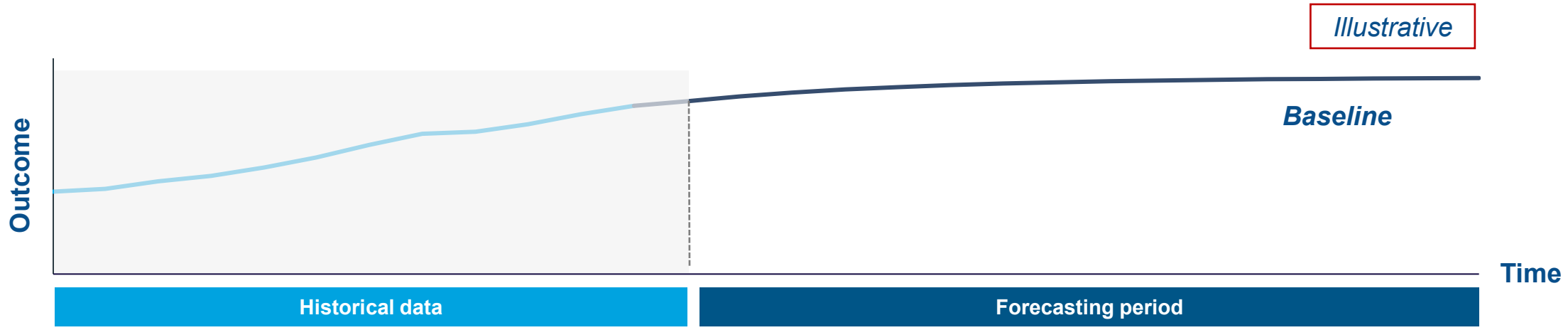
Baseline focus

1 ***Historical trend analysis*** *(in volumes)*	2 ***Conversion*** *of historical volumes* ***in patients***	3 ***Baseline projection*** *(in patients & values)*	4 *Estimation of events impact on baseline (in patients)*	5 *Forecast projections (in patients & values)*
				
• Based on the defined **reference market**, **consumption historical trends** were analyzed • Volume **split by indication** (not disclosed to companies**)** was estimated based on IQVIA internal knowledge and **market research**	• Historical volumes were converted into **# patients** by applying the **posology** per product and indication • **Market research** was leveraged to estimate the average **patient treatment recurrence rate**	• **Patient baseline** was projected in the future with an **IQVIA predictive model** • The baseline reflects the expected evolution **based solely on historical data**, without accounting future events or external drivers	• Impact of external drivers was estimated • In addition to new products (e.g. future launches and expected penetration) other key topics were explored through market research (e.g. AMR evolution and diagnostics impact)	• The patient-based forecast was converted into volumes • Volume projection considers posology and market research insights; value estimates were based on historical pricing trends
Sources/methodology:				
• *IQVIA sales DB (volumes in UMF and sales in EUR/PMP)* • *Market research (product consumption by indication)*	• *IQVIA sales DB (volumes in UMF)* • *Market research (patient treatment recurrence rate)*	• *IQVIA exponential smoothing approach*	• *IQVIA sales DB (uptake analysis)* • *Market research (assessment of external market drivers)*	• *IQVIA sales DB (past price trend)* • *Market research (assessment of external market drivers)*

The baseline was projected starting from the analysis of past performances and trends

Baseline definition | *Methodology*

- The **market baseline** represents the state of the future market and products market shares **if nothing happens interrupting historical trends.** This implies that:
  - **no events** are considered when generating the baseline
  - **historical performances** are the **only factor** influencing the baseline
- Baseline is built **through a statistical model** starting from past performances
- Baseline will be leveraged as a **basis for event-based final forecasting**



The forecast inputs originated from 3 main sources: IQVIA data, desk research on public sources, and the physician survey

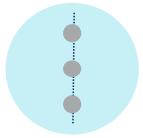
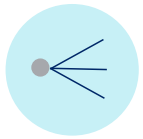
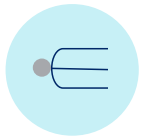
Baseline definition | *Input collection*

		IQVIA data	Public sources	Physician survey
Historical market trend	• Analysis of **historical performances** (volumes and values) of Reserve/Listed antibiotics • Assessment of **product characteristics/attributes** (e.g., indications, dosage, efficacy) • Identification of **historical market drivers** (e.g. population aging, increase in antibiotic resistance)	✓	✓	
Competitive events	• Mapping of next Reserve/Listed antibiotic **launches** (with expected P&R date) • Analysis of **price trends** for marketed Reserve/Listed antibiotics • Assessment of **level of awareness, perception and expected uptake of new entrants**	✓	✓	✓
Clinical & diagnostics trends	• **Epidemiological evolution** and use of Reserve/Listed antibiotics over the next 3 years • Current and future **adoption and impact of diagnostics** on clinical decisions and on antibiotic consumption			✓
Policy & access dynamics	• **Physicians' perception** on: − Main impacts of **innovative fund adoption** (e.g. prescribing appropriateness, purchasing and administrative processes) − Expected **changes in the next years**			✓

Historical market trend was projected through the “exponential smoothing” methodology

Baseline definition | *Methodology*

- The baseline was established using the “**exponential smoothing**” method, a statistical approach that predicts future results by calculating a **weighted average of past observations**
- This projection is defined by **three parameters**: **level, trend, and decay**

Parameter	Description	Value	
Level 	The position of the first forecast point	0%----------100%	
		Weight on historical data	*Weight on latest data point*
Level and trend are interdependent			
Trend 	The overall trend of the projections	0%----------100%	
		Weight on historical data	*Weight on latest data point*
Decay 	The dampening factor applied to the projections	0%----------100%	
		High decay (flat)	*No decay (linear)*

- A value is assigned to each parameter based on **product maturity and past trend**
- For example, **recently launched products** have a **higher value of the trend and level** parameters, so the future growth trend will be based more on latest data points
- The **decay** parameter determines the level of **smoothing over the last forecast years,** so the value is assigned according to the expected growth of the market/molecule

To set Level and Trend parameters in the baseline forecasting model, product characteristics were factored

Baseline definition | *Level & Trend parameters*

Parameter

- Level
- Trend
- Decay

Product	Main characteristics			
	Maturity *(P&R date)*	**Range of activity**[1]	**Efficacy**[1,2]	**Dosage** (n. of vials per use)[1]
Ceftazidime/ avibactam	01/2018	Multiple indications	• As effective as carbapenems for HAP/VAP and cIAI, cUTI • As effective as BAT[3] for cIAI and cUTI caused by ceftazidime-resistant gram-negative bacteria	• Same dose (1 vial) for cIAI, cUTI, HAP/VAP
Ceftolozane/ tazobactam	09/2016	Multiple indications	• Non inferior efficacy than meropenem for cIAI and HAP/VAP • Slightly higher rates of clinical success than ceftazidime/ avibactam for invasive infections due to multidrug-resistant P. aeruginosa[3]	• Single vial for cIAI and cUTI, double vial for HAP/VAP
Meropenem/ vaborbactam	03/2021	Multiple indications	• Non inferior efficacy than piperacillin and tazobactam for cUTI • More effective than BAT for CRE infections	• Same (double) vial for cIAI, cUTI and HAP/VAP
Cefiderocol	06/2021	Multiple indications	• Non inferior efficacy than meropenem for HABP/VABP • Non inferior efficacy than imipenem/cilastatin for cUTI	• Same (double) vial for cIAI and HAP/VAP
Imipenem/ cilastatin/ relebactam	05/2022	Single indication	• Non inferior efficacy than piperacillin and tazobactam for HAP/VAP	• Single vial for HAP/VAP
Tedizolid	06/2017	Single indication	• Non inferior efficacy than linezolid for ABSSSI	• Single vial for ABSSSI
Eravacycline	01/2025	Single indication	• As effective as meropenem for cIAI • Non inferior efficacy than ertapenem for cIAI	• Dosage depending on patient weight

Note: 1) Range of activity, Dosage and Efficacy sections report data on the main indications, not including secondary bacteremia and infections due to aerobic Gram-negative organisms with limited treatment options; 2) Efficacy data based on the most significant studies for the indications considered; 3) Observational study. ABSSSI – Acute Bacterial Skin and Skin Structure Infections, BAT – Best Available Therapy, CRE – Enterobacterales carbapenem resistant, cIAI – Complicated Intra-Abdominal Infection, cUTI – Complicated Urinary Tract Infection, HAP – Hospital-Acquired Pneumonia, VAP – Ventilator-Associated Pneumonia

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration) Sources: Summary of product characteristics; EMA Clinical trials recap

The “Decay” variable was determined through an analysis of historical performance and key market factors

Baseline definition | *Decay parameter*

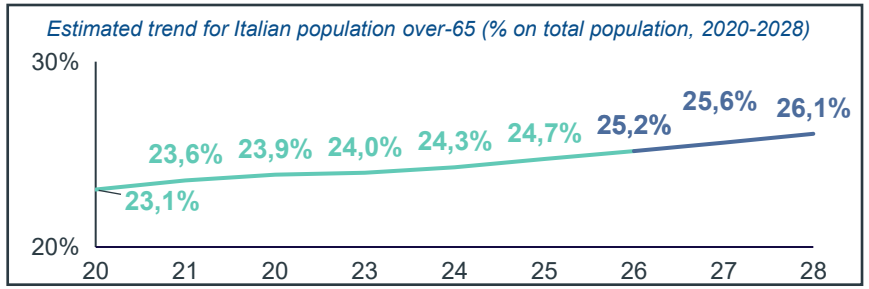
Parameter

Trend

Decay

Demographic trends[2] *(Population aging)*

- **From 2020 to 2025, the percentage of Italian population over 65 years** has increased by **+1,6%,** from **23,1%** to **24,7%**
- The trend of **continuous population aging** is projected by ISTAT also for the 2026–2028 period, reaching **26,1%** with a three-year CAGR of **+1.1%**



Antibiotic resistance evolution

- **Resistance increase** confirmed by the comparison of the **Drug Resistance Index (DRI) values in 2023 and in the previous years** for the monitored pathogens **(+3,4%)**

Pathogen (GN-)	Pathogen prevalence	2023 DRI
Escherichia coli	**34%**	**29%** *(+3% vs 2021)*
Klebsiella pneumoniae	**17%**	**48%** *(similar to 2021)*
Pseudomonas aeruginosa	**8%**	**19%** *(-4% vs 2021)*
Acinetobacter species	**4%**	**65%** *(-1% vs 2021)*

Pathogen (GN+)	Pathogen prevalence	2023 DRI
Staphylococcus aureus	**18%**	**26%** *(+10% vs 2021)*
Streptococcus pneumoniae	**2%**	**22%** *(+9% vs 2022)*
Enterococcus faecalis	**10%**	**11%** *(-2% vs 2022)*
Enterococcus faecium	**7%**	**62%** *(+16% vs 2021)*

Note: 1) 3Y CAGR MAT 9/2022- MAT 9/2025 due to the global recall in 2021. GN- – Gram negative, GN+ – Gram positive. Sources: IQVIA sales data (private clinics excluded); ISTAT; AIFA
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

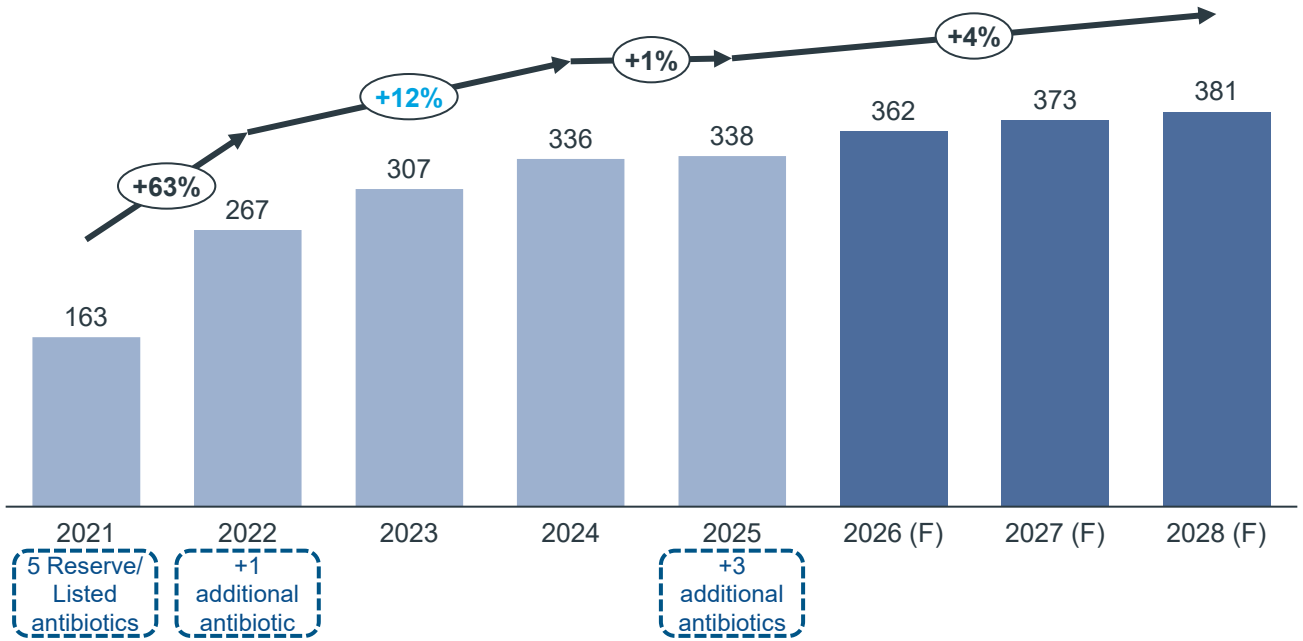
The use of current Reserve/Listed antibiotics is expected to increase in the coming years, but more slowly than before

Baseline | *Volume projection*

Legend: P&R

Reserve/Listed antibiotics evolution

Volume (Sell-in DoT, K)



	CAGR 21-25	CAGR 22-25	CAGR 25-28 (F)
Market growth	20,0%	8,2%	4,0%

- Over the **past 5 years**, the Reserve/Listed consumption has **grown 2-digit annually**
- The exceptional growth recorded between 2021 and **2022** was driven by the **stock-out of ceftolozane/ tazobactam** (due to a global recall) in 2021 and by the launches of **meropenem/vaborbactam** and **cefiderocol**
- **Imipenem/cilastatin/relebactam** launched in **May 2022,** while **eravacycline** gained reimbursement in **January 2025**
- In the next 5 years **the market is expected to grow, but at moderate rates** – similarly to the **last 4 quarters,** since:
  - The **high CAGR in recent** years has been driven **by product launches**
  - **Future growth** will be driven by **the uptake of the products being launched**

Note: DoT - Days of Treatment.

Sources: IQVIA sales data (private clinics excluded); AIFA; Gazzetta Ufficiale. Baseline projections do not consider impacts of recent and future launches and LoE

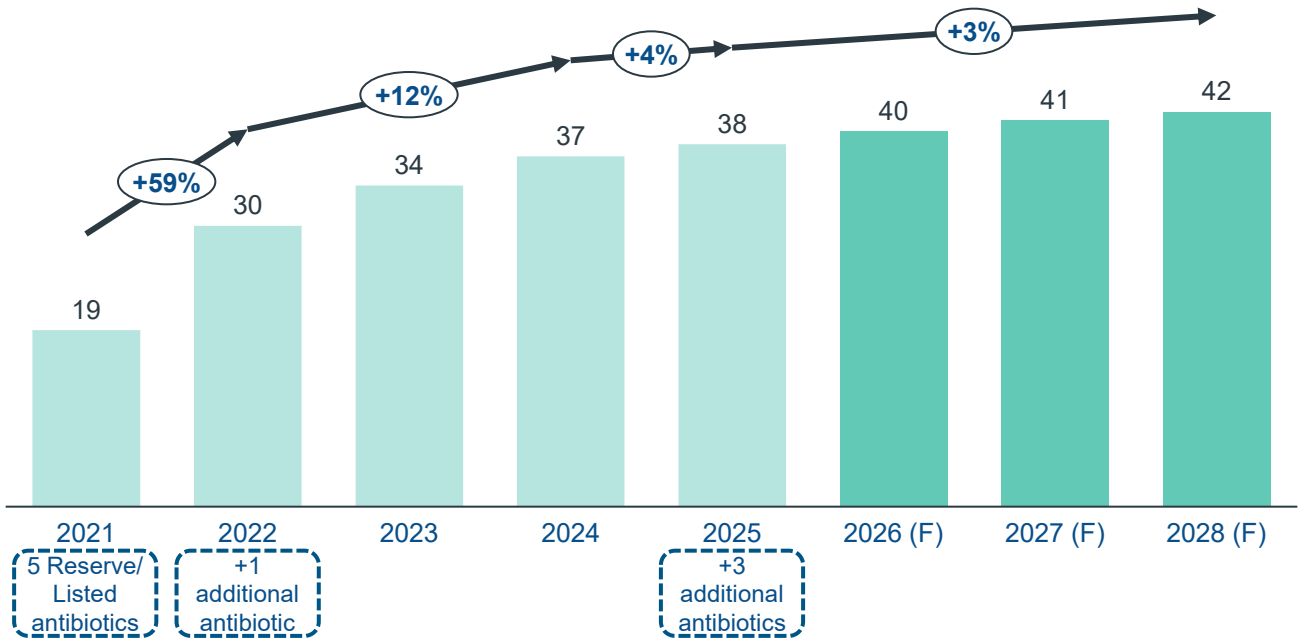
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

The number of patients treated with Reserve/Listed antibiotics is expected to increase by 3%/yr over the next 3 years

Baseline | *Patients projection*

Legend: P&R

Reserve/Listed antibiotics evolution
(# of patients, K)



	CAGR 21-25	CAGR 22-25	CAGR 25-28 (F)
Patient population growth	21,5%	9,5%	3,1%

- The baseline projection **does not take into account** the **market entry of aztreonam/avibactam** and **cefepime/enmetazobactam**, **nor** the future launch of **cefepime/zidebactam** (lefamulin and cefepime/ taniborbactam are considered marginal also in the final forecast, as their entry is expected at the end of 2028)
- **The loss of exclusivity** of ceftazidime/avibactam expected in 2028 is also **not considered** in the baseline
- The expected **patient growth in the baseline** by 2028 is about **one-third** of what was observed over the past three years: **+3.1%** vs **+9.5%**

Notes: CAGR – Compound Annual Growth Rate.
Source: IQVIA sales data (private clinics excluded). Baseline projections do not consider impacts of recent and future launches and LoE
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Without considering new launches and LoE, the Reserve/Listed antibiotics would reach a total value of €113 M in 2028

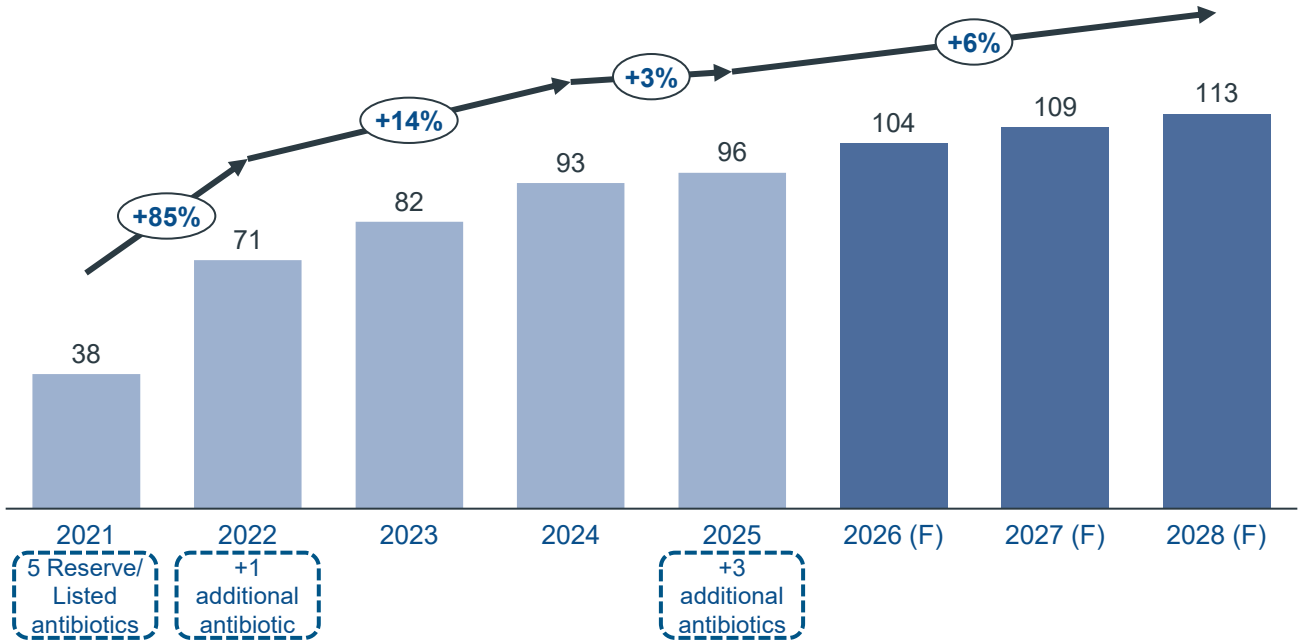
Baseline | *Value projection*

Legend: P&R

Reserve/Listed antibiotics evolution

Value (Sell-in € PMP, M)

VAT included



	CAGR 21-25	CAGR 22-25	CAGR 25-28 (F)
Market growth	25,7%	10,6%	5,5%

- Over the **last five years**, the market has expanded at similar rates in both volume and value, with annual growth of **27%** and **26%**, respectively
- Given that **price negotiations have not occurred** recently, the **baseline value forecast** (derived from sales volumes) remains **unchanged** for the **forecast period** (2026–2028)
- The **slightly greater increase in value** compared to volume **(5.5% vs 4.5%)** results from the anticipated rise in consumption of **products priced above the market average**

Note: PMP - Average purchase price calculated based on the sell-in data recorded by the hospital pharmacies (VAT included), CAGR – Compound Annual Growth Rate.
Sources: IQVIA sales data (private clinics excluded); Gazzetta Ufficiale. Baseline projections do not consider impacts of recent and future launches and LoE
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Agenda

- Project overview
- Reserve/Listed Fund: operations and impact
- Baseline
- **Key insights from the physician survey**
- Forecast
- *Appendix*

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

The physician survey examined several topics to inform or confirm the forecast assumptions

Physician survey | *Main topics*

Methodology & sample	**120 interviews** in selected centers covering **~80% of consumptions of Reserve/Listed antibiotics** against MDR infections. **CAWI** (Computer Aided Web Interview) interviews lasting an average of **20 minutes**
Involved physicians	**Infectious Disease specialists** and **other physicians** who can prescribe Reserve/Listed antibiotics and work in the departments that mostly use this category of antibiotics (e.g. Intensive care and Pulmonology)

Treatment & clinical behavior

- Number of **currently treated patients** with Reserve/Listed antibiotics, and **split by indication**
- Average current and future **treatment duration** by indication and product

Epidemiology & infection trends

- Quantification of **eligible patients** to Reserve/Listed antibiotics
- **Incidence evolution by indication** for patients eligible to Reserve/Listed antibiotics
- Current antibiotics **resistance rate** and next years estimated **evolution**

Diagnostics & decision-making

- Current **adoption rate of rapid tests** and **automated panels**
- **Impact** of rapid test and **automated panels** results **on treatment decision**
- Expected **future adoption** of rapid test **and impact** on treatment algorithm

Access dynamics

- Clinicians' perception of the **impact that access to the Fund has on the current use of Reserve/Listed antibiotics**
- Clinicians' views on **how the Fund may influence their future use**

Expected use of Reserve/Listed antibiotics

- Key drivers of current Reserve/Listed **antibiotics choice**
- Level of **awareness and perception of new** antibiotics
- **Expected uptake** of new entrants by indication

Note: MDR – Multi-drug resistant
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Physician survey key findings

01

Patient management and current use of Reserve/Listed antibiotics

- Physicians report a **consistent and organized method** for managing severe bacterial infections and assessing new Reserve/Listed antibiotics throughout the sample
- In the past quarter, physicians reported to have treated an average of **32 patients with severe bacterial infections with Reserve/Listed antibiotics**, with **HAP and VAP** being the most commonly addressed conditions, followed by **cUTIs**
- Across the patients treated with different therapies, the **CRE is the pathogen with the highest prevalence**

02

Factors influencing antibiotic selection and treatment duration

- When selecting an antibiotic, physicians **primarily focus on efficacy** while also considering the **patient's overall clinical condition, known resistance patterns, infection location, and the safety and tolerability** of the treatment
- The typical **duration of treatment** with these newer antibiotics ranges from **8 to 10 days**, though this varies depending on the infection type, with **HAP and VAP generally requiring longer courses**

03

Awareness, interest, and willingness to use new and potential Reserve/Listed antibiotics

- There is a high level of **awareness** and **recognizability** regarding antibiotics that have more recently gained access to the fund
- Physicians demonstrate also **strong interest in future use** of potential Reserve/Listed antibiotics with expected launch between 2026 and 2028
- Overall, a significant share of physician has **intention** and **interest in prescribing** recently introduced and upcoming Reserve/Listed antibiotics

Notes: cUTI – complicated urinary tract infection, HAP – Hospital-acquired pneumonia, VAP – Ventilator associated pneumonia.
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Over the past 3 months, each specialist treated an average of 32 patients with severe bacterial infections with Reserve/Listed antibiotics. The most frequently treated conditions - accounting for 1/3 patients - were HAP and VAP, followed by cUTIs

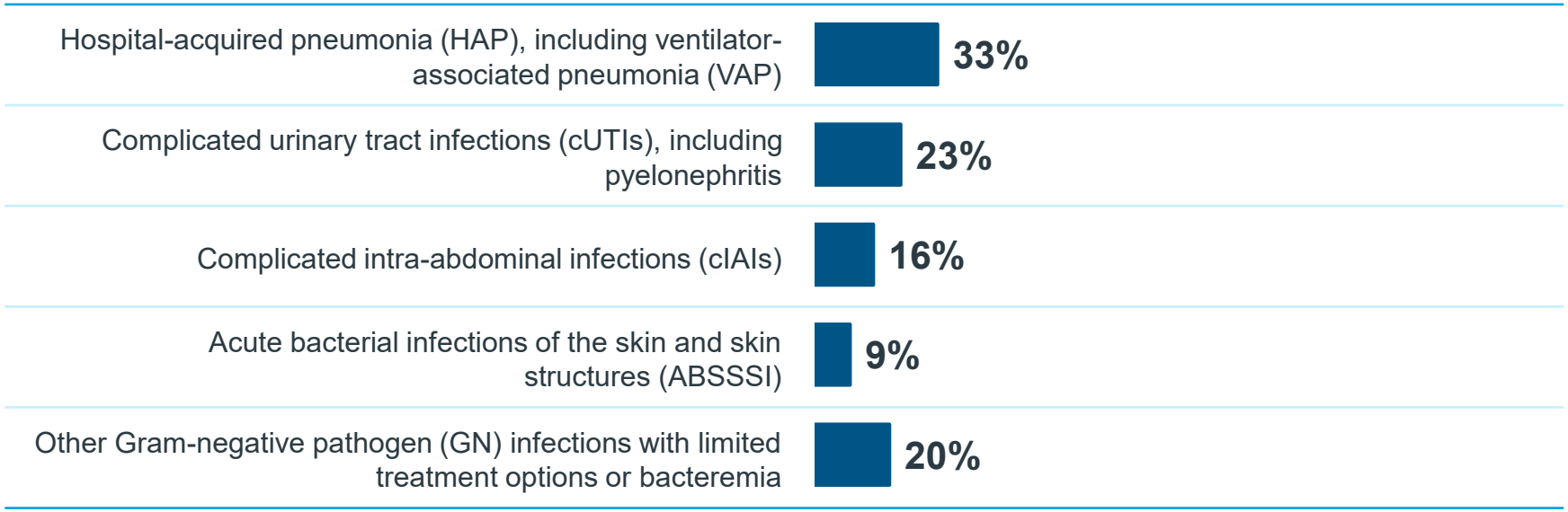
Patients treated with “Reserve/listed" antibiotics & target pathology

AVG. **32**

PATIENTS TREATED WITH "RESERVE/LISTED" ANTIBIOTICS IN THE LAST 3 MONTHS FROM EACH RESPONDENT

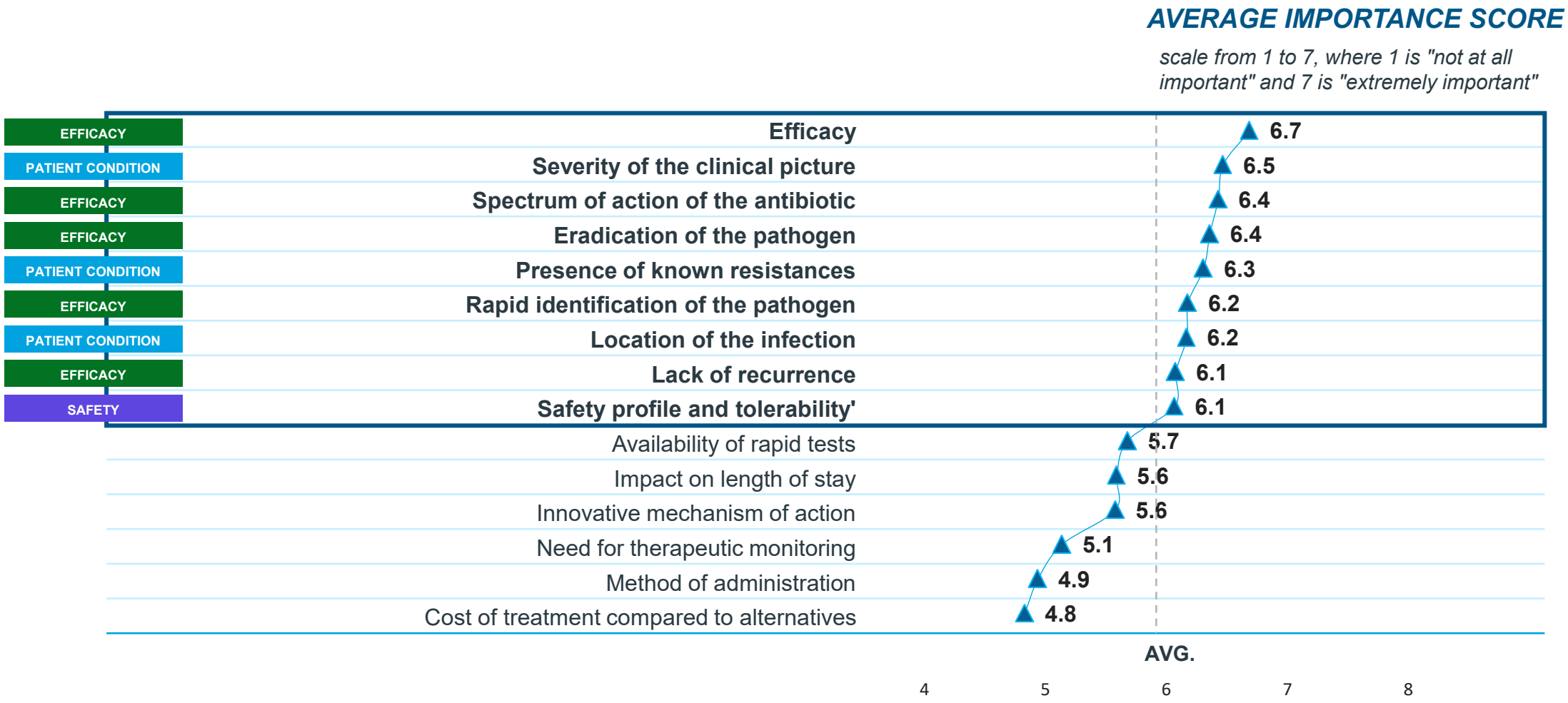
100%

TYPE OF INFECTION



The primary factor in choosing an antibiotic treatment is its efficacy. Additionally, the patient's overall health - including clinical symptoms, known resistances and infection location - is considered. Lastly, medication safety and tolerability are crucial in making the final decision

Drivers considered when choosing an antibiotic therapy



Agenda

- Project overview
- Reserve/Listed Fund: operations and impact
- Baseline
- Key insights from the physician survey
- **Forecast**
- *Appendix*

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

The forecasting process was divided into 5 steps, combining IQVIA data and physician insights with a structured predicting methodology

Forecast | *Methodology*

Forecast focus

1 *Historical trend analysis (in volumes)*	2 *Conversion of historical volumes in patients*	3 *Baseline projection (in patients & values)*	4 ***Estimation of events impact on baseline*** *(in patients)*	5 ***Forecast projections*** *(in patients & values)*
				
• Based on the defined reference market, consumption historical trends were analyzed • Volume split by indication (not disclosed to companies) was estimated based on IQVIA internal knowledge and market research	• Historical volumes were converted into # patients by applying the posology per product and indication • Market research was leveraged to estimate the average patient treatment recurrence rate	• Patient baseline was projected in the future with an IQVIA predictive model • The baseline reflects the expected evolution based solely on historical data, without accounting future events or external drivers	• **Impact of external drivers** was estimated • In addition to **competition** (e.g. future launches and expected penetration) **other key topics** were explored through market research (e.g. AMR evolution and diagnostics impact)	• The **patient-based** forecast was converted into **volumes** • **Volume projection** consider posology and market research insights; **value estimates** were based on historical pricing trends
Sources/methodology: • *IQVIA sales DB (volumes in UMF and sales in EUR/PMP)* • *Market research (product consumption by indication)*	• IQVIA sales DB (volumes in UMF) • Market research (patient treatment recurrence rate)	• *IQVIA exponential smoothing approach*	• *IQVIA sales DB (uptake analysis)* • *Market research (assessment of external market drivers)*	• *IQVIA sales DB (past price trend)* • *Market research (assessment of external market drivers)*

The forecast inputs originated from 3 main sources: IQVIA data, desk research on public sources, and the physician survey

Forecast | *Input collection*

		IQVIA data	Public sources	Physician Survey
Historical market trend	• Analysis of **historical performances** (volumes and values) of Reserve/Listed antibiotics • Assessment of **product characteristics/attributes** (e.g., indications, dosage, efficacy) • Identification of **historical market drivers** (e.g. population aging, increase in antibiotic resistance)	✓	✓	
Competitive events	• Mapping of next Reserve/Listed antibiotic **launches** (with expected P&R date) • Analysis of **price trends** for marketed Reserve/Listed antibiotics • Assessment of **level of awareness, perception and expected uptake of new entrants**	✓	✓	✓
Clinical & diagnostics trends	• **Epidemiological evolution** and use of Reserve/Listed antibiotics over the next 3 years • Current and future **adoption and impact of diagnostics** on clinical decisions and on antibiotic consumption			✓
Policy & access dynamics	• **Physicians' perception** on: − Main impacts of **innovative fund adoption** (e.g. prescribing appropriateness, purchasing and administrative processes) − Expected **changes in the next years**			✓

In-scope products include AIFA-designated last-resort antibiotics for MDR infections with access to the 100M € Fund…

Forecast | *In-scope products (1/2)*

Already included in the baseline

Molecule	Reimbursed indications and main uses				
	Aerobic GNB inf.[1]	*HAP/VAP*	*cUTI*	*cIAI*	*ABSSSI*
Cefiderocol	✓	✓	-	✓	-
Imipenem/cilastatin/relebactam	✓	✓	-	-	-
Tedizolid	-	-	-	-	✓
Meropenem/vaborbactam	✓	✓	✓	✓	-
Eravacycline	-	-	-	✓	-
Ceftazidime/avibactam (Patent expiry in 2028)	✓	✓	✓	✓	-
Ceftolozane/tazobactam	-	✓	✓	✓	-
Cefepime/enmetazobactam	-	✓	✓	-	-
Aztreonam/avibactam	✓	✓	✓	✓	-

Notes: 1) Gram-negative bacteria infections with limited therapeutic options, excluding those explicitly stated. ABSSSI – Acute bacterial skin and skin structure infections, cIAI – complicated intra-abdominal infection, cUTI – complicated urinary tract infection, HAP – Hospital-acquired pneumonia, MDR – Multi-drug resistant, VAP – Ventilator associated pneumonia. Source: desk research on public websites
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

…and possible future molecules that could be included in the Reserve/Listed Fund during the forecast period (26-28)

Forecast | *In-scope products (2/2)*

Legend: First indication expected | Indication expected later

New launches selection

Selection of new antibiotics expected to launch in 2026-28 that would meet the eligibility criteria for the Fund

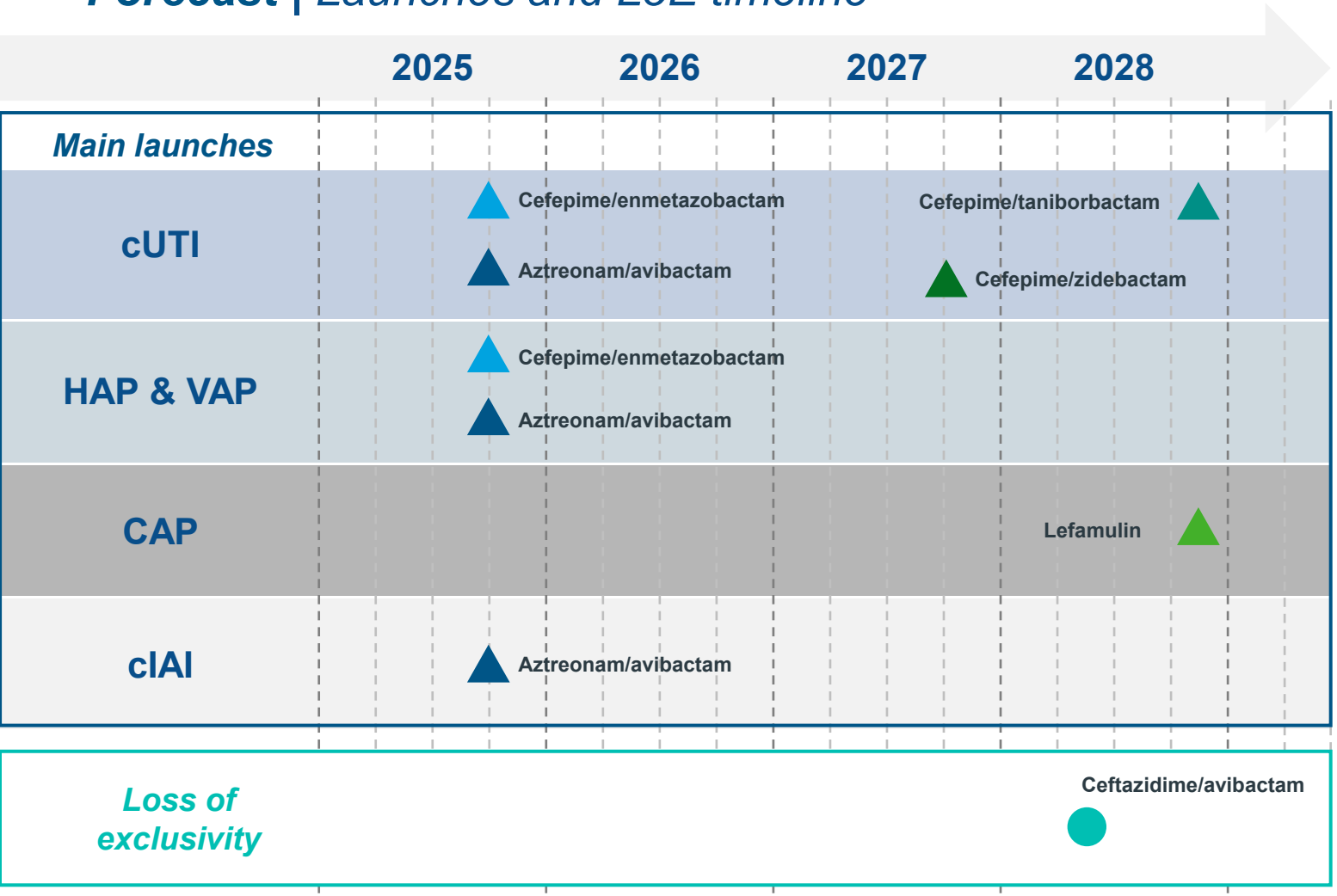
Molecule	Regulatory status	Expected indications					Expected launch year[1]
		Target pathogens[3]	*HAP/ VAP*	*CAP*	*cUTI*	*cIAI*	
Cefepime/ zidebactam	• Phase 3 completed for cUTI • NDA submitted to FDA in Oct '25 • MA application submitted to EMA in January 2026	**CRAB, CRPA, CRE**	-	-	✓	-	***2027***
Lefamulin	• EMA MA granted in July 2020 • Classified as a Reserve antibiotic • Currently in Cnn in Italy	**OPP**	-	✓	-	-	***Late 2028***
Cefepime/ taniborbactam	• Phase 3 completed for cUTI but MA application to EMA not yet submitted • FDA rejected NDA due to incomplete documentation	**CRE CRPA**	✓	-	✓	✓	***Late 2028***

Note: 1) Forecast based on the average timelines for decision-making by EMA (≥12 months) and AIFA (≥12 months). MA – Market Authorization, NDA – New Drug Application, OPP – Other Priority Pathogens (MRSA e Macrolide-resistant Streptococcus pneumoniae), CRAB – Carbapenem-Resistant Acinetobacter baumannii, CRPA – Carbapenem-Resistant Pseudomonas aeruginosa, CRE – Carbapenem-Resistant Enterobacterales. Sources: Clinical trial.gov, Company report, WHO

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Main events in the forecasting period will be the launch of 3 new antibiotics and the LoE of ceftazidime/avibactam

Forecast | *Launches and LoE timeline*



- **Cefepime/enmetazobactam**: beta-lactam/beta-lactamase inhibitor (BL/BLI) combination for the treatment of **cUTI and HAP&VAP** caused by resistant Gram-negative bacteria
- **Aztreonam/avibactam**: antibiotic combination approved to treat **HAP & VAP**, **cUTI**, **cIAI**, and infections due to aerobic Gram-negative organisms in adult patients with limited treatment options
- **Cefepime/zidebactam**: combination of a 4th generation cephalosporin (cefepime) and a novel β-lactam enhancer (zidebactam) designed to combat **MDR Gram-negative bacteria**
- **Lefamulin**: approved for the treatment of **CAP** in adults when the use of antibacterial agents commonly recommended for the initial treatment of CAP is not considered appropriate or when these agents have proven ineffective. It was assigned **class C(nn)** by AIFA in October 2020
- **Cefepime/taniborbactam**: beta-lactam/beta-lactamase inhibitor (BL/BLI) combination under development for the treatment of **cUTIs** caused by Gram-negative bacteria

Source: IQVIA analysis on Company reports, clinicaltrials.gov, AIFA
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Legend: New launch LoE

The forecast relies on 4 main factors: AMR evolution, uptake of diagnostics, new therapies adoption and changes in eligibility

Forecast | *Key variables impacting future trends*

1. Antibiotic resistance

- **Projected evolution** of **AMR** over the **next 3 years**, by **indication** and by individual **pathogen**
- Allows the baseline to be adjusted according to an **epidemiological factor**, specifically the evolution of antibiotic resistance (AMR)

2. Adoption of rapid tests and automated panels

- **Current and future usage level of diagnostics** in Reserve/Listed antibiotics prescription and **its impact** on treatment duration

3. New therapies adoption

- The impact of the following events has been evaluated:
  - **Expected launches** during the forecast period
  - The possible partial **erosion by newly launched products** of the share held by longer-standing antibiotics

4. Exclusion from the Fund due to LoE

- **Loss of exclusivity** (LoE) of a Reserve/Listed product in **Q2 2028, ending its eligibility** to access the Fund

Physician Survey reference:

*For each infection type, physicians were asked to **assess the current level of pathogen resistance to antibiotics** and the **expected evolution***

*Physicians rated, through a Likert scale[1], the impact of rapid diagnostic testing on **antibiotic resistance, Reserve/Listed antibiotic use and average treatment duration***

*Physicians were requested to report their **awareness** of the new products, the **timeframe** in which they **would begin prescribing them** upon release and **readiness to utilize** them*

Note: 1) Assessment tool used in questionnaires to measure opinions, perceptions, or attitudes. LoE - Loss of Exclusivity
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

The majority of factors (3 out of 4) could potentially contribute to an increase in future Reserve/Listed antibiotic usage

Forecast | *Key variables and impact*

Legend: High ●●● Low ●○○ Positive effect + Negative effect -

	Impact[1]
Antibiotic resistance • For each pathogen, physicians were asked to assess the **current level of resistance to antibiotics** and the **expected evolution over the next 3 years** • This driver is expected to **expand the Reserve/Listed antibiotic usage**	+ ○ ○
Adoption of rapid tests and automated panels • Physicians rated, through a Likert scale[1], the impact of rapid diagnostic testing on **antibiotic resistance, Reserve/Listed antibiotic use** and **average treatment duration**	+ ○ ○
New launches • To evaluate the **effects of upcoming launches** and more accurately predict their anticipated usage, physicians were requested to report their **awareness level** of the products, the timeframe in which they **would begin prescribing them** upon release, and their **readiness to utilize** them	+ + ○
Share changes and ceftazidime/avibactam Loss of Exclusivity (LoE) • **Upcoming new products** are expected to gain patient shares from antibiotics currently covered by the Fund • With **ceftazidime/avibactam LoE** in 2028, the expenditure presently assigned to this antibiotic will **cease to be reimbursed by the Fund** and could partially be **reallocated** among the antibiotics still included in the Fund	- - ○

Note: 1) Relative evaluation based on survey results; 2) Assessment tool used in questionnaires to measure opinions, perceptions, or attitudes. LoE - Loss of Exclusivity

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

CARe COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

For next launches, whose prices are not known yet, forecasted values have been based on current average price

Forecast | *Pricing assumptions*

	Product	P&R[1]
Already marketed	Cefiderocol	06/2021
	Imipenem/ cilastatin/ relebactam	05/2022
	Tedizolid	06/2016
	Meropenem/ vaborbactam	03/2021
	Eravacycline	01/2025
	Ceftazidime/ avibactam	01/2018
	Ceftolozane/ tazobactam	09/2016
	Cefepime/ enmetazobactam	09/2025
	Aztreonam/ avibactam	09/2025
Future launches	Cefepime/ zidebactam	Q3 2027
	Lefamulin	Q4 2028
	Cefepime/ taniborbactam	Q4 2028

Initial price assumption

PMP (IQVIA weighted average price)

- **Average purchase price currently** paid by hospital pharmacies

AVERAGE PURCHASE PRICE

- **Estimated** based on **average Reserve/Listed price**

Price growth assumption

STABLE PRICE

- **No price changes** identified in PMP historical data
- For 2026–2028 period, **constant prices assumed**

Note: 1) For products already marketed, P&R date is taken from the AIFA Official Gazette. For future launches, the date refers to the expected launch date. PMP - Average purchase price calculated based on the sell-in data recorded by the hospital pharmacies (VAT included)

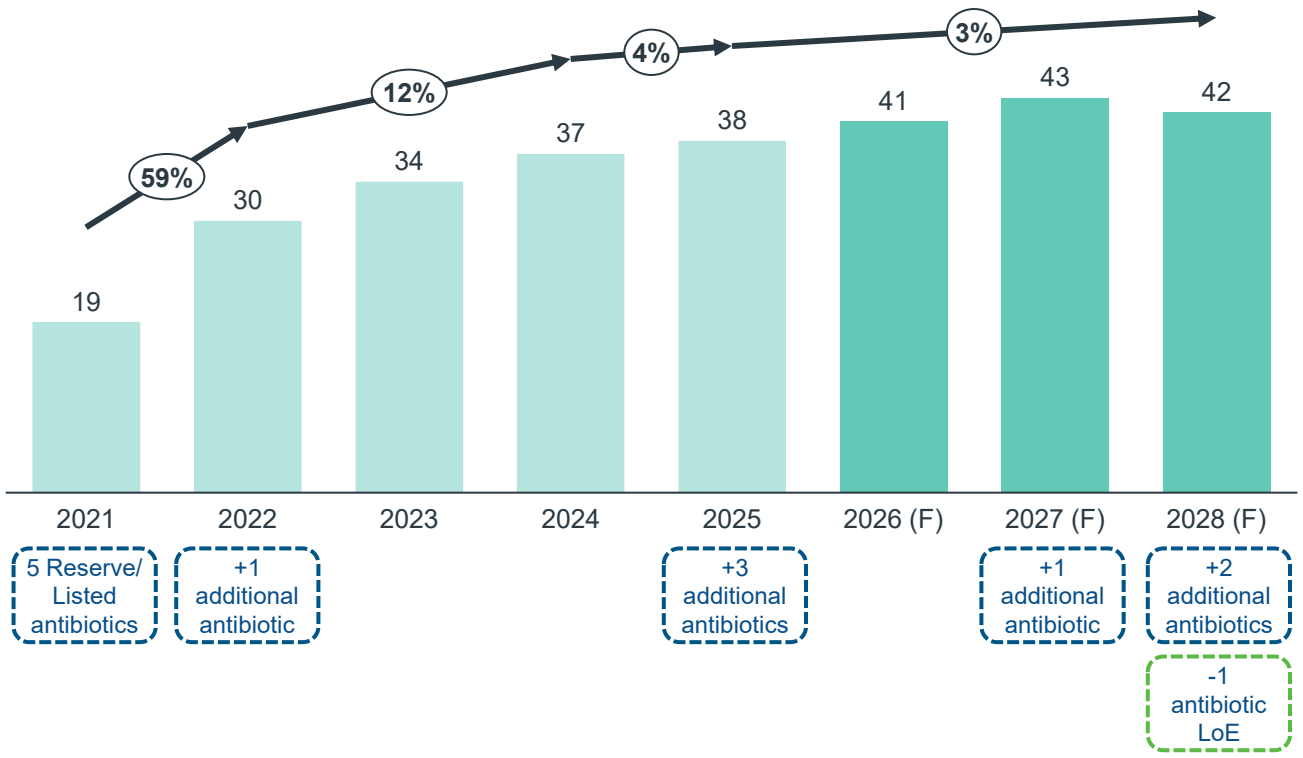
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

The projected number of patients treated with antibiotics with access to Reserve/Listed Fund will reach ~42k in 2028

Forecast | *Estimated patients*

Legend: P&R LoE

Reserve/Listed antibiotics[1] evolution
(# of patients, K)



- The estimated patient population during the forecast period is projected to be around **41k in 2026**, **43k in 2027**, and **42k in 2028**, with a **CAGR** of **+3%** from 2025 to 2028
- Growth between 2026 and 2028 is driven by factors such as the **increasing impact of antimicrobial resistance**, **diagnostic advancements**, the **possible addition of new antibiotics to the Fund**, and **more personalized patient treatments**
- The **plateau seen between 2027 and 2028** is primarily due to the **exclusion from the Fund for one** of the Reserve/Listed antibiotics, resulting from **loss of exclusivity**

Notes: 1) The perimeter of the analysis includes only the products with access (or potential access) to the Reserve/Listed antibiotics fund during the considered period
CAGR - Compound Annual Growth Rate, LoE – Loss of Exclusivity

IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

According to the exercise, the €100M budget assigned to Reserve/Listed antibiotics could no longer be adequate

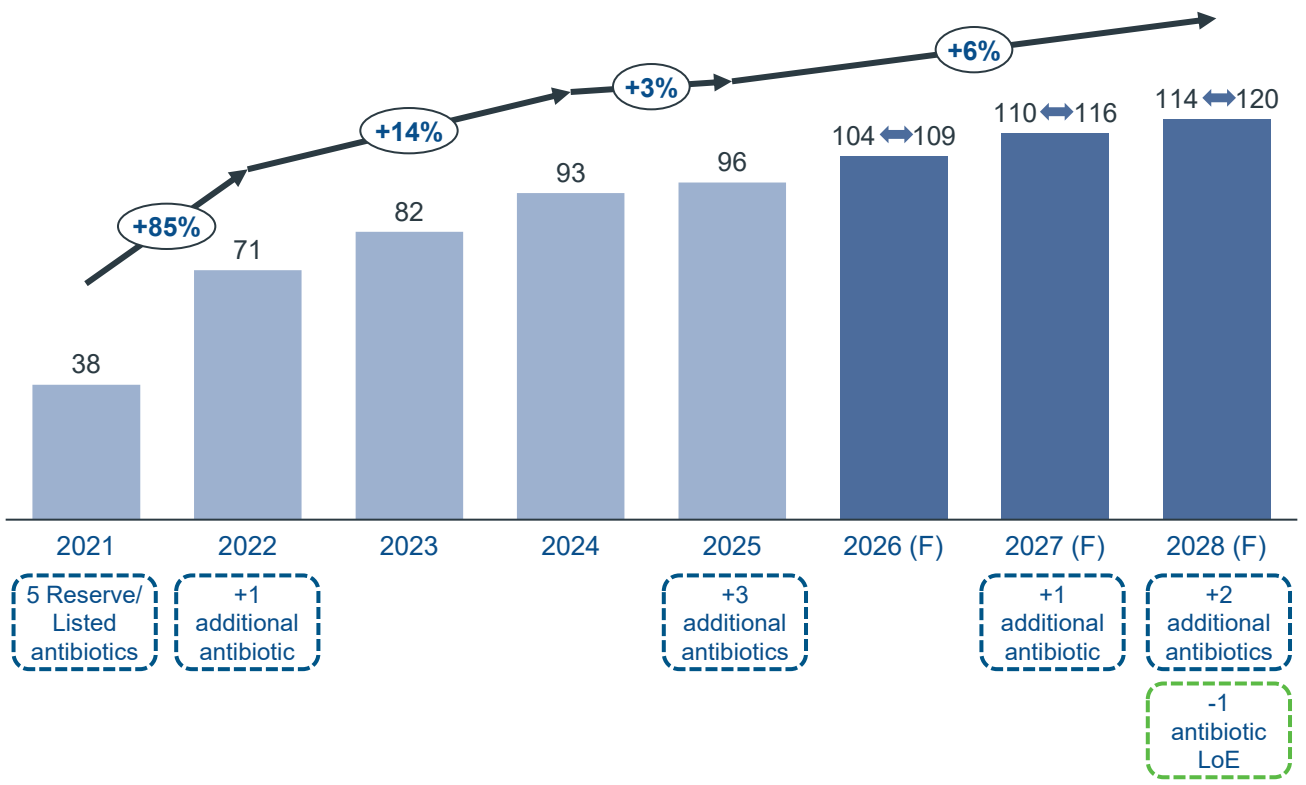
Forecast | *Value projection*

Legend: P&R LoE

Reserve/Listed antibiotics evolution

Value (Sell-in € PMP, M)

VAT included



- **Pricing assumptions** are based on the **use of PMP** (IQVIA weighted average purchase price paid by hospital pharmacies) for antibiotics currently on the market, and on the **average purchase price** of products presently included in the Reserve/Listed Fund for expected future launches
- **Revenues** from Reserve/Listed antibiotics within the Fund are projected to reach **€104-109M in 2026**, **€110-116M in 2027** and **€114-120M in 2028** (VAT included), reflecting a **+6% CAGR from 2025 to 2028**
- While the **number of patients is anticipated to remain stable between 2027 and 2028**, total value is expected to grow due to **increased use of newer molecule**

Note: PMP - Average purchase price calculated based on the sell-in data recorded by the hospital pharmacies (VAT included). The forecast ranges for the years 2026, 2027, and 2028 incorporate the estimated result with a +5% variation margin.
CAGR - Compound Annual Growth Rate
Sources: IQVIA sales data (private clinics excluded); Gazzetta Ufficiale.
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Agenda

- Project overview
- Reserve/Listed Fund: operations and impact
- Baseline
- Key insights from the physician survey
- Forecast
- ***Appendix***

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

ReserveX (Reserve and Listed antibiotics eXploration)

APPENDIX – Physician survey additional data

Fanno parte della della coalizione multistakeholder CAЯe: Advanz Therapeutics, Menarini, Pfizer, Shionogi, Viatris, con la collaborazione scientifica di Società Italiana Malattie Infettive e Tropicali (SIMIT), Associazione Microbiologi Clinici Italiani (AMCLI) e CittadinanzAttiva

Il coordinamento tecnico-scientifico della coalizione CAЯe è di:

LS CUBE OUTSIDE THE BOX

IQVIA for CAЯe – March 2026

Physician profile

Geographic Area

NORTH WEST	20%
NORTH EAST	13%
CENTER	28%
SOUTH&ISLANDS	38%

100%

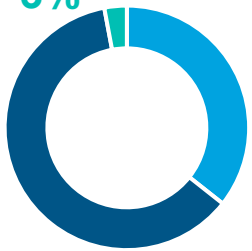
defines and manages, in person ora with a team, the antibiotic therapy for patients with severe bacterial infections

Physician role

Level I manager	60%
Highly specialized manager	15%
Director of complex structure / level II manager	13%
Simple facility manager	13%

Patient management

The patients I manage belong to different hospitals
3%



The patients I manage belong to different departments
62%

I only manage patients from my department
36%

Physician specialization

Infectious disease specialist	80%
Internal medicine specialist	8%
Onco-hematologist	5%
Pulmonologist	7%

Treatment typically lasts 8 to 10 days. The length of therapy mainly depends on the infection type; for instance, treatments for HAP and VAP generally need somewhat extended durations

Therapy duration

AVERAGE THERAPY DURATION

HOW MANY DAYS does a treatment with the following drugs last on average

	cUTI	cIAI	HAP & VAP	ABSSSI	Other infections with GN pathogens
Cefiderocol	-	9,6	10,1	-	9,2
Ceftazidime/avibactam	8,5	9,8	10,1	-	9,1
Ceftolozane/tazobactam	8,2	9,9	9,9	-	-
Eravacycline	-	9,4	-	-	-
Imipenem/cilastatin/relebactam	-	-	9,5	-	9,3
Meropenem/vaborbactam	8,4	10,0	10,0	-	9,2
Tedizolid	-	-	-	8,6	-
Cefepime/enmetazobactam	7,8	-	9,1	-	8,6
Aztreonam/avibactam	7,8	10,0	9,3	-	8,7

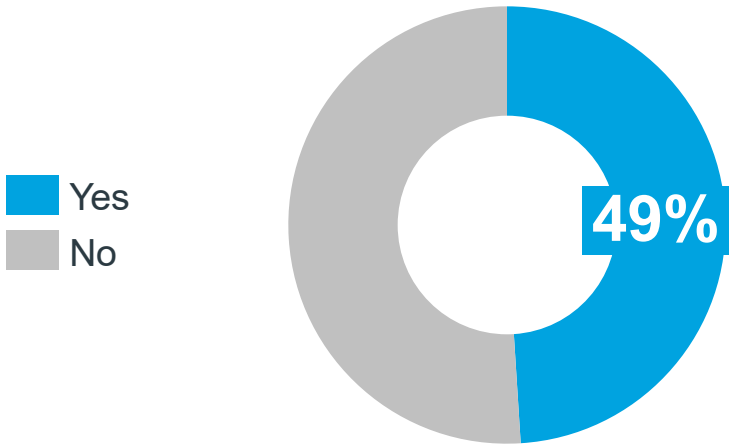
IQVIA for LS3 | ReserveX (Reserve and Listed antibiotics eXploration)

Currently almost on half of the patients treated with Reserved/listed antibiotics are performed rapid test, while in 59% of patients are performed automated panels

Test - current adoption rate

RAPID TEST ADOPTION RATE

% of patients treated with reserved/listed antibiotics with RAPID TEST performed

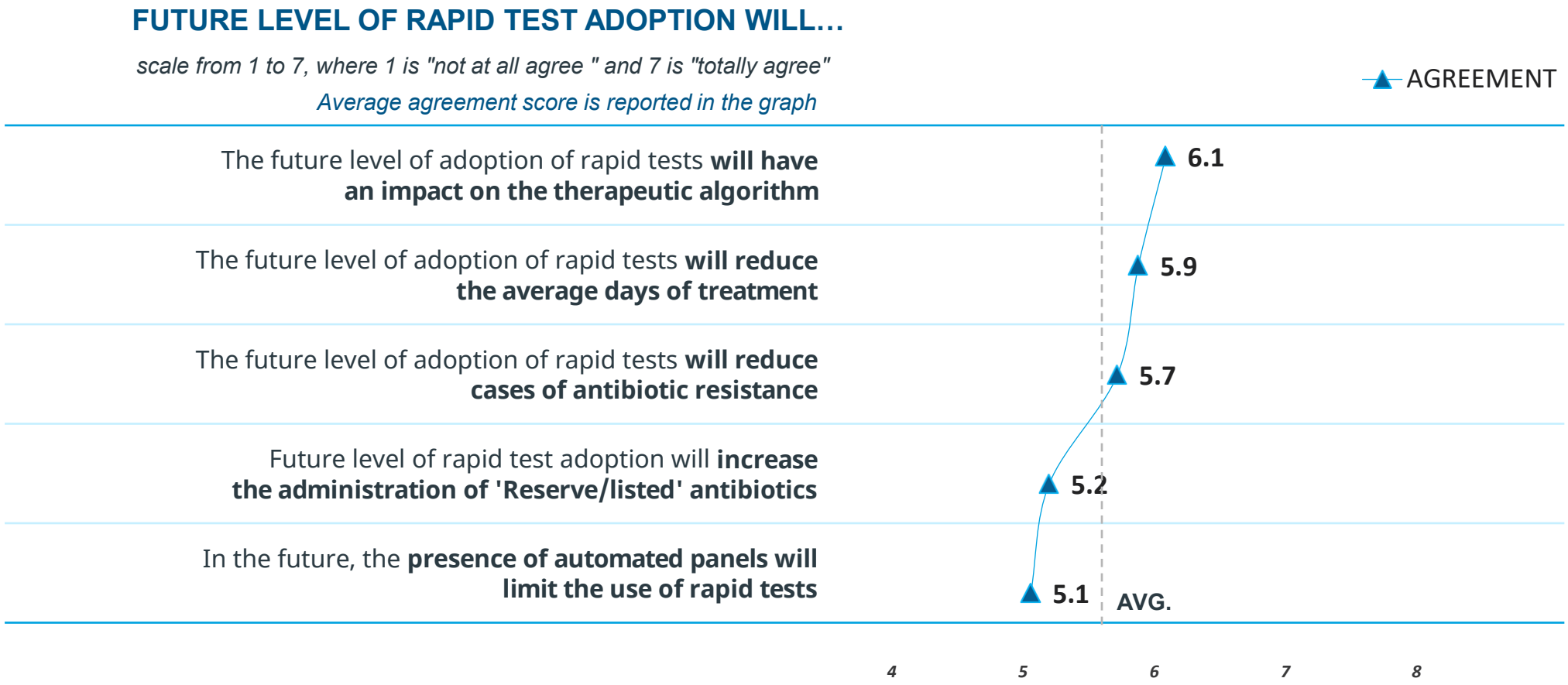


AUTOMATED PANEL ADOPTION RATE

% of patients treated with reserved/listed antibiotic tested using AUTOMATED PANELS

Physicians largely agree that increasing the adoption of rapid tests will influence the therapeutic algorithm and help reduce the average duration of treatment

Future impact of rapid tests for the diagnosis and use of antibiotics



COALIZIONE CONTRO ANTIMICROBICO RESISTENZA

THANK YOU!

Fanno parte della della coalizione multistakeholder CAЯe: Advanz Therapeutics, Menarini, Pfizer, Shionogi, Viatris, con la collaborazione scientifica di Società Italiana Malattie Infettive e Tropicali (SIMIT), Associazione Microbiologi Clinici Italiani (AMCLI) e CittadinanzAttiva

Il coordinamento tecnico-scientifico della coalizione CAЯe è di:

LS CUBE OUTSIDE THE BOX

IQVIA for CAЯe – March 2026