

White Paper

Race for Immunity: Exploring the Evolving Landscape of the Vaccines Market

A forward-looking perspective on vaccine innovation

STEFAN LUTZMAYER, Consultant, EMEA Thought Leadership

HELENA BAYLEY, Analyst, EMEA Thought Leadership



Table of contents

Introduction	3
The life-saving power of vaccines	3
Case Study — Vaccine Track: US adult vaccination trends	7
The promising vaccine landscape	8
Deep Dive — mRNA's moment of truth	12
Outlook for the vaccines market	16
Succeeding with vaccines	18
Acknowledgements	19
References	20
About the authors	24

Introduction

The contribution of vaccines to global public health is beyond question - demonstrated by the historic near eradication of smallpox to the biggest and fastest global vaccine rollout during the COVID-19 pandemic. As we celebrate this recent victory, we also uncover the pressing need to bolster immunisation rates against vaccine-preventable diseases (VPDs) to avoid human suffering. Moreover, we must fuel vaccine innovation towards better protection and easier administration against current and future health challenges. In this pursuit, vaccine manufacturers must find their role as partners for the healthcare sector. Together, they bear the responsibility of co-creating and shaping a future-proof vaccines market that can foster sustained innovation to society.

For the scope of this white paper, we will focus on the vaccine need for high-income countries. We will explore the evolving vaccine innovative landscape, highlight recent breakthroughs, give an outlook on the vaccine market, and take a deep dive into mRNA as an emerging new vaccine platform. A second white paper will focus on vaccines as a global public health intervention and their implications particularly for low- and middle-income countries.

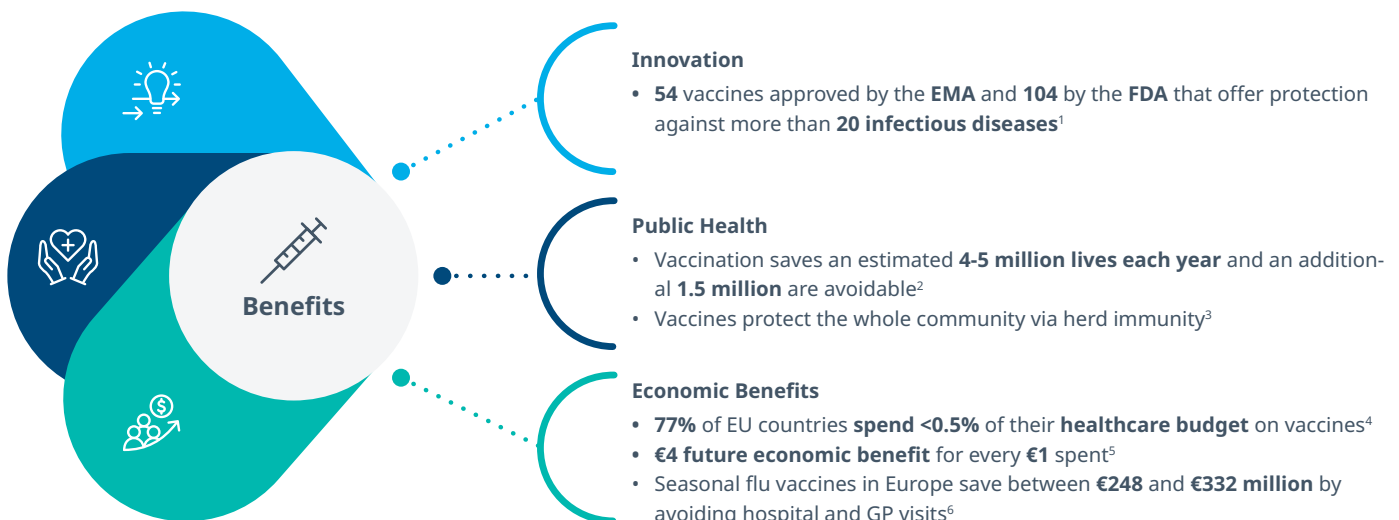
The life-saving power of vaccines

Vaccination is one of the most effective public health interventions, offering protection to all ages and saving an estimated 4-5 million lives each year¹. It helps to protect whole communities, including the unvaccinated, through herd immunity². Vaccination is also one of our most cost-effective interventions against infectious disease, with an estimated saving of €4 in future health-related costs for every €1 spent on adult immunisation³.

For example, in Europe, seasonal influenza vaccination saves between €248 and €332 million annually, and these figures would increase substantially if vaccination coverage reached the WHO target of 75% in the elderly or other at-risk population⁴. Despite the clear economic value of vaccination, and its benefits to health systems and society more generally, 77% of EU countries spend less than 0.5% of their healthcare budget on vaccines⁵.

Vaccination is also one of our most cost-effective interventions against infectious disease, with an estimated saving of €4 in future health-related costs for every €1 spent on adult immunisation

Figure 1: Vaccines — an unparalleled success story with massive benefits



Source: IQVIA EMEA Thought Leadership; (1) Vaccines for Europe, EMA, FDA; (2) WHO; (3) Desai A & Majumder M (2020). What is Herd Immunity?; (4) Faivre P et al (2021). Immunization funding across 28 European countries, Expert Rev Vaccines; (5) Conolly et al (2020). Estimating the Fiscal Consequences of National Immunization Programs; (6) Preaud E et al (2014). Annual public health and economic benefits of seasonal influenza vaccination: a European estimate

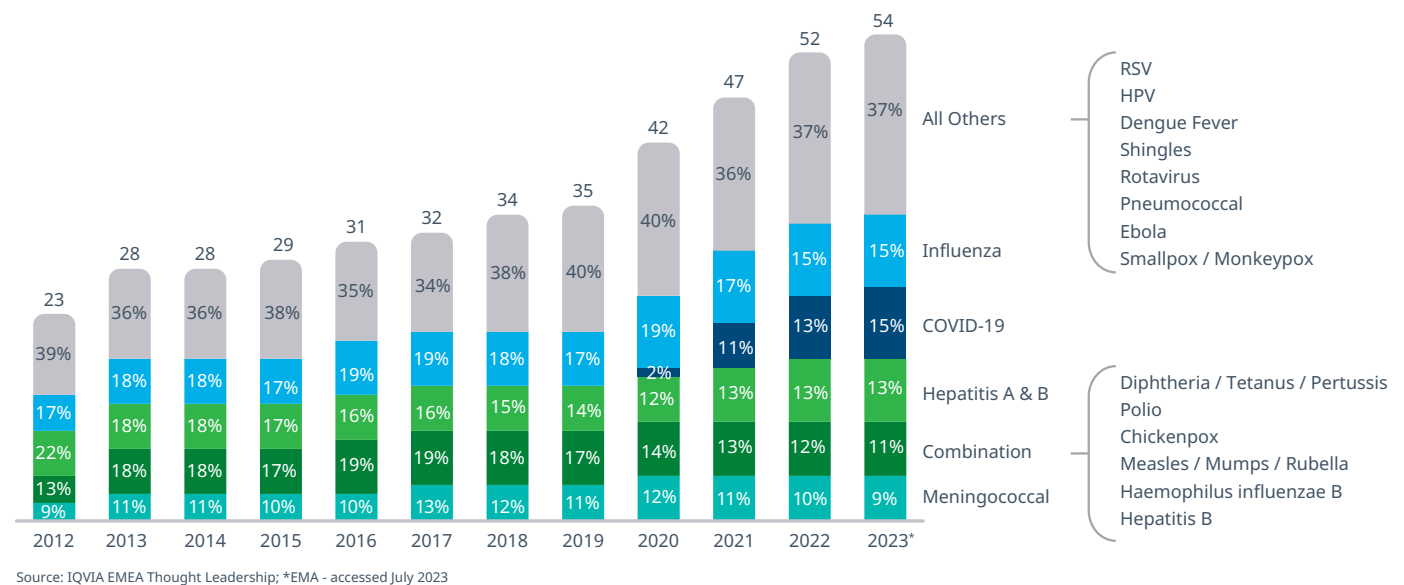
The history of vaccines is also one of innovation. Currently there are 54 vaccines approved by the EMA and 104 by the FDA that protect against more than 20 infectious diseases⁶. The number of EMA-approved vaccines has risen steadily in the last decade across many disease areas (Figure 2). Although recent approvals have been dominated by COVID-19 vaccines, innovation in other indications has continued — exemplified by the approval of the first respiratory syncytial virus (RSV) vaccines in 2023⁷.

One of the world’s most successful vaccination efforts has been against poliomyelitis — a highly infectious disease. Polio attacks the central nervous system and causes great morbidity, especially among young children, and as there is no cure, prevention is crucial. By the mid-20th century, global polio epidemics were frequent, and caused half a million people to die or become paralysed each year. In major breakthroughs, two different polio vaccines were developed during the 1950s. Immense vaccination efforts from individual

countries combined with global collaboration have led to polio being eradicated from many regions successively: for example, the Americas became polio-free in 1994, and the Western Pacific in 2000. Case numbers have continued to fall in recent decades: the WHO’s African region was certified polio-free in 2020⁸, and with just 42 cases globally each year now, worldwide eradication is within reach⁹.

However, we cannot rest on the success of the past. The polio virus is slowly evolving and is dependent on humans as hosts. There remain disease areas for which there are no vaccines available to date. In other cases, vaccines exist but access disparities, vaccine hesitancy or funding gaps prevent broad immunisation uptake. For example, polio vaccination coverage is now at its lowest since 1994, with calls for renewed vaccination campaigns¹⁰. In the section below we will explore the unmet need within vaccine-preventable diseases (VPDs) and other communicable diseases without an approved vaccine.

Figure 2: 54 EMA-approved vaccines against over 20 infectious diseases



However, we cannot rest on the success of the past. The polio virus is slowly evolving and is dependent on humans as hosts. There remain disease areas for which there are no vaccines available to date. In other cases, vaccines exist but access disparities, vaccine hesitancy or funding gaps prevent broad immunisation uptake.

Unmet need and challenges

The burden of infectious diseases is greatest among the very young and the very old, due to an increased susceptibility to infection and a greater likelihood of serious illness¹¹. Between 2020-2050, the number of people aged 60 years and above is expected to double, to 2.1 billion, and the number of people older than 80 years will triple¹². The pandemic has also exacerbated the issue of vaccine hesitancy, identified by the WHO in 2019 as a top-10 threat to global health. Factors driving hesitancy are complex and include resource strain, side effect concerns, and lack of trust, impacting vaccination rates across demographics, posing significant concerns¹³.

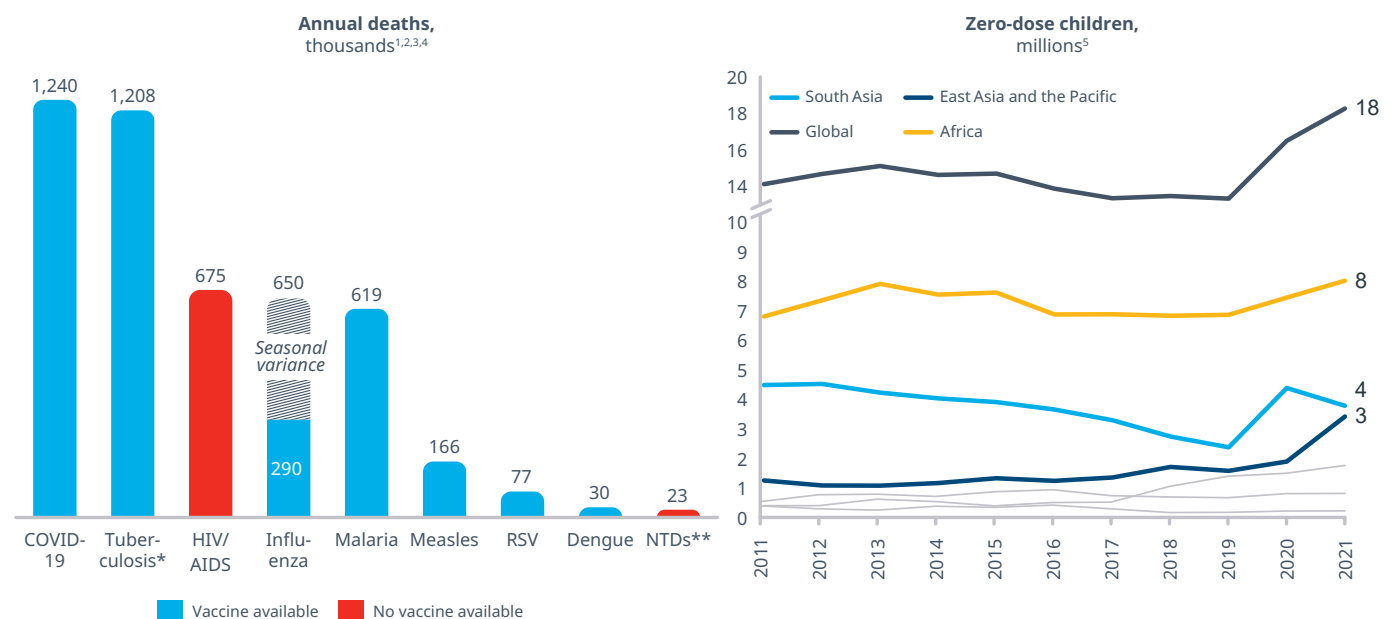
There are vaccines available for the diseases with highest global burden, as illustrated in Figure 3, except for HIV. Developing an HIV vaccine is challenging due to its rapid mutation, immune evasion, and weak immunogenicity of its envelope¹⁴. Among the diseases without approved vaccines are many neglected

The pandemic has also exacerbated the issue of vaccine hesitancy, identified by the WHO in 2019 as a top-10 threat to global health.

tropical diseases (NTDs), which represent an area of significant unmet need. Of these, the biggest killer is schistosomiasis, for which vaccine candidates have so far had little success, rarely reaching clinical trials¹⁵. Recent progress has been made with some NTDs though, such as dengue, which infects 100-400 million people each year but now has approved vaccines.

Significant unmet needs persist within VPDs (Figure 3 left panel). COVID-19 and tuberculosis each claimed over 1.2 million lives. In the case of tuberculosis, the current Bacille Calmette-Guérin (BCG) vaccine offers only partial protection limited to children, leaving adolescents and adults vulnerable, compounded by antibiotic resistance. Influenza, despite having had vaccines available for 60+ years, causes 290,000 to 650,000 deaths annually. Low vaccine rates among the elderly and strain-matching issues contribute to the toll. Measles vaccination also falls short; while 85% start the regimen, just 64% complete their second dose but three doses are recommended¹⁶. Malaria took 619,000 lives in 2021, prompting WHO to endorse the first widespread malaria vaccine, which has shown positive outcomes in Kenya's immunisation programme and reducing paediatric hospital admissions¹⁷.

Figure 3: Unmet need for a selection of VPDs and other communicable diseases



*Available BCG vaccine offers only limited protection amongst adolescents and adults.

**Includes the NTDs in the burden of disease analysis in the WHO's 2023 global report on NTDs, apart from those which have a human or animal vaccine available.

Source: IQVIA EMEA Thought Leadership; EMA — accessed July 2023; (1) WHO — Global Health Estimates: leading causes of death; (2) RSV and Influenza data taken from Lancet Infect Dis 2018; (3) WHO Malaria Fact Sheet, 2021; (4) Our World in Data for COVID19; (5) WHO/UNICEF Estimates of National Immunisation Coverage, 2021 revision

Vaccines play a crucial role in addressing antimicrobial resistance (AMR), a pressing global crisis affecting both high-income countries (HICs) and low- and middle-income countries (LMICs)^{18,8}. In 2019, 1.2 million deaths globally each year were estimated to be attributable to drug-resistant diseases, and this figure is projected to rise to 10 million deaths per year by 2050^{19,20}. Excessive, inappropriate use of antibiotics against viral infections and incomplete courses of antibiotics are linked to the increase seen in AMR, and as a result the EU has set a goal to reduce antibiotic consumption by 20% in 2030²¹. IQVIA analyses showed that Germany reduced its antibiotics prescriptions in the last ten years²². Prophylactic vaccines not only protect against bacterial infections and prevent AMR development; they also protect against viral infections, and therefore aid in reducing the inappropriate prescription of antibiotics. A modelling study suggested that vaccines could avoid 500,000 AMR-associated deaths every year²³.

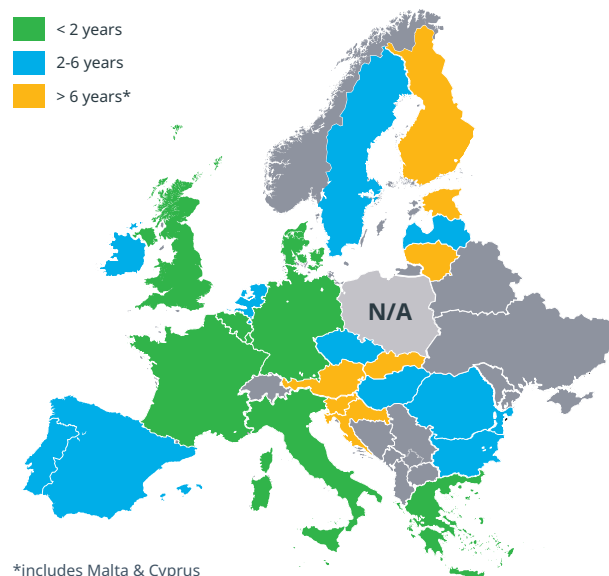
Prophylactic vaccines not only protect against bacterial infections and prevent AMR development; they also protect against viral infections, and therefore aid in reducing the inappropriate prescription of antibiotics.

Contrasting vaccination challenges across the globe

There are major differences between the vaccination needs of HICs and LMICs. In LMICs, paediatric vaccination remains the pressing priority; despite progress in recent decades, this is now slowing and even going backwards²⁴. Globally, there are millions of zero-dose children — meaning they have not received a first dose of a diphtheria/tetanus/pertussis-containing vaccine (Figure 3 right panel)²⁵ — and alarmingly, the numbers have spiked since the start of the COVID-19 pandemic. This indicates that there are many children who are not engaging with a health system at all. These zero-dose children live in the poorest and most marginalised communities²⁶, and furthermore, almost half of them are in Africa. This is a major public health concern, especially given that 40% of the world's children (under 18 years old) will live in Africa by 2050²⁷.

Figure 4: Access to vaccines varies by country

Time from marketing authorisation to access, median time, EU27 + UK, 2021



*includes Malta & Cyprus

Source: Vaccine market access pathways in the EU27 and the United Kingdom analysis and recommendations for improvements

In HICs, where paediatric vaccination coverage is good, focus is needed on increasing vaccination uptake by adults, especially in the context of an ageing population. Adult immunisation rates were decreased by 12% between 2020 and 2022 according to IQVIA audit data²⁸. Population access to vaccines also varies significantly by country — further compounding the issue (Figure 4). The research conducted on behalf of Vaccines Europe mentioned budget limitations, lack of transparency around decision-making and complexity of vaccine market access pathways as key barriers for rapid access²⁹. Indeed, adult vaccination spend as a share of total pharmaceutical expenditure in selected countries was low and varied between 0.1% and 1.7% in Spain and Germany respectively. Vaccine Track was developed by GSK in collaboration with IQVIA and aims to address the lack of data transparency around vaccination data to support stakeholders to make data-driven decisions (see case study below for further details).

In HICs, where paediatric vaccination coverage is good, focus is needed on increasing vaccination uptake by adults, especially in the context of an ageing population.

Case Study — Vaccine Track: US adult vaccination trends

Situation

The pandemic highlighted the importance of vaccines and health data in the fight against infectious diseases. Adult immunisation rates in the US were low even before the pandemic which led to resurgence of vaccine-preventable diseases. In 2019, the CDC reported 1,274 measles cases amongst mostly unvaccinated people across 31 US states. Publicly available data on routine immunisation is limited and can lag by a year or more. Understanding changes in adult vaccination trends as they happen will be crucial in supporting public health efforts to improve vaccination rates back to pre-pandemic levels and beyond.

Solution

Vaccine Track is a comprehensive platform developed by GSK and IQVIA for use by public health officials, industry leaders and medical professionals to strengthen vaccination data transparency, raise awareness and publicly share vaccination trends to aid improvements in routine adult vaccinations to create healthier communities across the US. Vaccine Track sources information from IQVIA claims and longitudinal prescription data of adults 19+ and is updated on a quarterly basis.

Results

Data from Vaccine Track revealed sustained decline of recommended adult immunisations, excluding flu vaccinations, across the US during the pandemic, especially in minority populations:

- National trends for adults aged 19 and older continue to remain below pre-pandemic 2019 baselines with an average decrease of 18% through 2021 in overall claims for recommended vaccines, excluding influenza
- Average monthly overall claims data through 2021 for recommended vaccines (excluding influenza) were 12-42% below by payer compared to a 2019 baseline
- For Medicare, analysis found more than a 30% reduction in overall claims for recommended vaccines among Black and Hispanic populations between 2019 and 2021. This highlights the significant potential impact on disparities in immunisation rates in Medicare due to the pandemic
- At the state level, as of December 2021 nearly half of the states in the US were facing greater than 30% reductions in overall claims for recommended vaccines from 2019 pre-pandemic levels

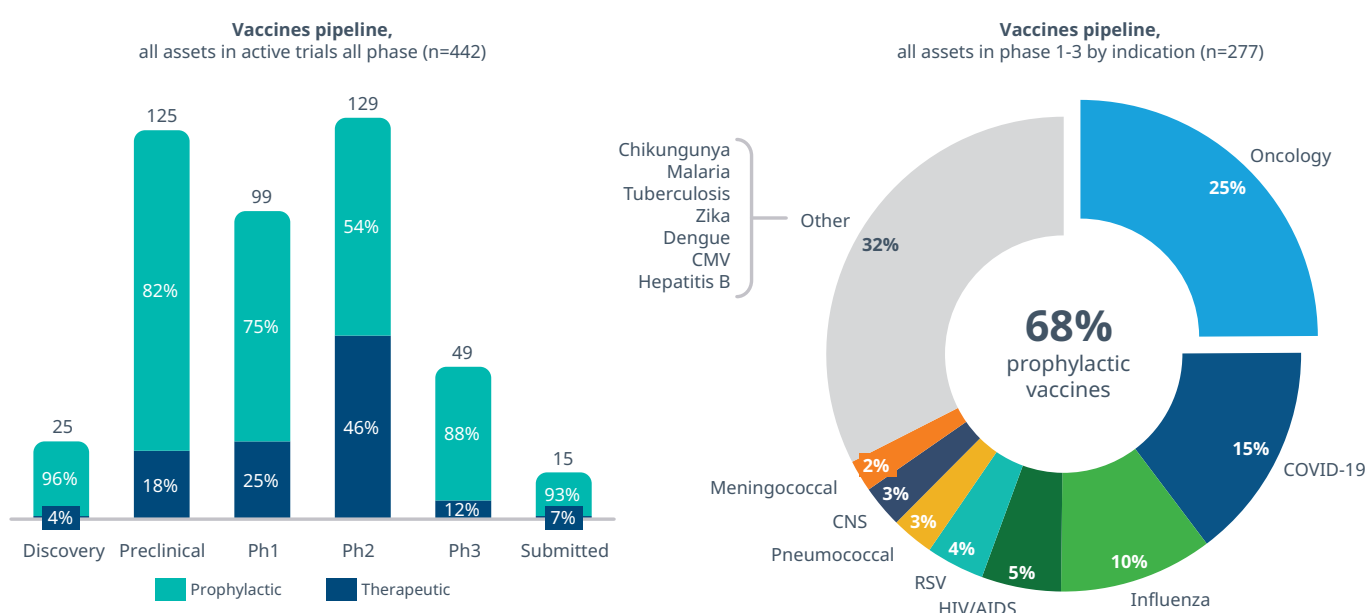
These findings must guide future decision making for targeted interventions, emphasising the need to address barriers to access and communication, and to tailor strategies for improving immunisation rates among marginalised communities. The utilisation of Vaccine Track can serve as a powerful tool for the public health community to work towards the common goal to bolster vaccination rates to prevent disease and death.

The promising vaccine landscape

The COVID-19 pandemic and the race to develop an effective vaccine led to an increased number of vaccine clinical trials. Between 2017 and 2022, vaccine clinical trials expanded by 14% and in 2022, accounted for 7% of the overall industry pipeline (Figure 5)^{30,31}. The clinical-stage R&D pipeline was split 2:1 between prophylactic and therapeutic vaccines.

COVID-19, influenza, HIV/AIDS and RSV were the leading indications among prophylactic vaccines. The industry is deeply committed to developing vaccines for areas currently lacking available options, with approximately 33% of the prophylactic vaccine clinical R&D pipeline dedicated to addressing underserved areas. Therapeutic vaccines were mainly developed in oncology and are based on mRNA technology (Figure 5) - a topic that will be discussed in more detail in a separate deep-dive section.

Figure 5: Global vaccine R&D pipeline



Abbreviations: CMV — Cytomegalovirus; CNS — Central nervous system diseases; RSV — respiratory syncytial virus; HIV — human immunodeficiency virus; Source: IQVIA EMEA Thought Leadership; IQVIA Pipeline Link, April 2023

RSV, the quest for a tuberculosis vaccine 2.0, tackling tropical diseases and AMR

Climate change, antimicrobial resistance, and pandemic readiness challenges underscore the necessity for new and improved vaccines. The recent FDA and EMA approvals of RSV vaccines marked a significant breakthrough, following years of unsuccessful clinical trials^{32,33}. While most experience cold-like symptoms from an RSV infection, it can be fatal for immunocompromised, older adults, and infants. Early RSV vaccine progress was halted when inactivated candidates rendered children more susceptible to the virus, leading to hospitalisations and deaths in 80% of cases³⁴. In 2010, a breakthrough

was achieved as scientists generated neutralising antibodies against RSV, paving the way for the development of prophylactic vaccines³⁵. GSK's AREXVY and Pfizer's ABRYVVO received regulatory approval for individuals aged 60 and older in 2023³⁶. Furthermore, both the EMA and FDA approved ABRYVVO for immunising pregnant mothers to confer passive immunity to infants during their first six months after birth^{37,38}. Moderna has sought market authorisation for its mRNA-1345 RSV candidate on both sides of the Atlantic and Australia³⁹. Additionally, Sanofi and AstraZeneca's FDA- and EMA-approved long-lasting monoclonal antibody, nirsevimab, offers protection against hospitalisation for new-borns and infants⁴⁰.



Tuberculosis (TB) BCG vaccines have been available for a century, but the infection remains a serious threat that kills 1.2 million people globally each year (Figure 3), with the disease killing 1,200 people every day in India alone⁴¹. To better understand the disease burden, an IQVIA study funded by the Bill and Melinda Gates Foundation revealed even more TB infections than previously thought⁴². AMR further exacerbates the situation⁴³. BCG vaccines only protect younger children. Moreover, TB can return in 10% of people after being dormant for decades⁴⁴. New strategies and vaccines must be deployed to reach the WHO's ambitious target to reduce 90% of TB deaths by 2030⁴⁵. The M72:AS01E recombinant protein vaccine showed 50% efficacy against reinfection and could prevent 76 million TB cases and 8.5 million deaths⁴⁶.

In the last decade, significant progress has been made on tackling vaccine development for NTDs. Unfortunately, the COVID-19 pandemic caused major disruptions. 2020/2021 saw several outbreaks of dengue, leishmaniasis, scabies and chikungunya⁴⁷. For the latter a vaccine could be within reach. Valneva's VLA1533 vaccine candidate provoked a strong antibody response in 99% of healthy volunteers⁴⁸. The live-attenuated vaccine must now be tested in areas where the virus is endemic.

AMR is a major public health threat, with just six pathogens accounting for over 73% of global AMR deaths in 2019⁴⁹. Vaccines prevent the primary infection and therefore the use of antibiotics. In 2000, the introduction of a conjugate pneumococcal vaccine for infants in the US was highly effective and saw a decline of 57% in diseases

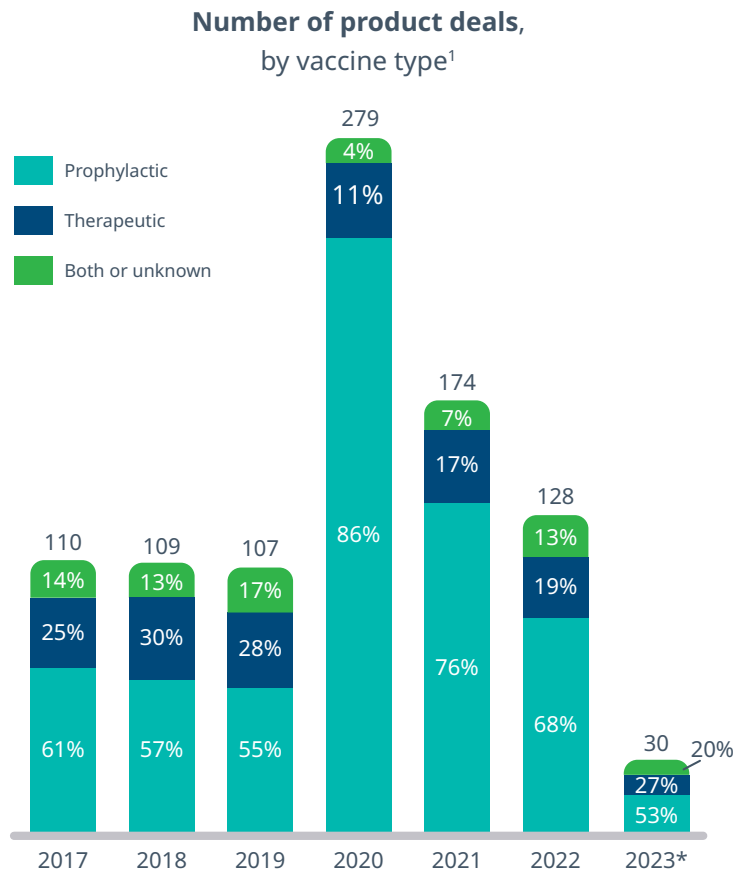
caused by penicillin-resistant strains in four years⁵⁰. The industry is invested and determined to address AMR, with vaccines being developed against e.g., *Escherichia coli*, *Staphylococcus aureus* and *Clostridium difficile* which are also on the WHO's Priority Pathogen list^{51,52}.

Future vaccine innovation

The COVID-19 pandemic spurred pharma's appetite to engage in vaccine product deals. The total number of deals spiked in 2020/21, having remained stable between 2017 and 2019 (Figure 6 left panel). As expected, 25% of deals concerned assets to fight the pandemic⁵³. Established vaccine players entered the hype around RNA as a novel platform with, for example, Sanofi acquiring Translate Bio for \$3.2 billion in 2021⁵⁴. The two largest vaccine deals by value in 2022 focused on next-generation RNA technology (Figure 6 right panel). Given the industry's continued interest in RNA breakthrough innovation and the success of the COVID-19 mRNA vaccines, we will further elaborate on the future of the platform against both communicable and non-communicable diseases in a deep dive section below.

*The industry is invested and determined to address AMR, with vaccines being developed against e.g., *Escherichia coli*, *Staphylococcus aureus* and *Clostridium difficile* which are also on the WHO's Priority Pathogen list.*

Figure 6: Vaccine deal activity



Top vaccine deals by value, 2022 until July 2023

Year	Total Deal Value	Companies	Deal Driver
2022	\$4.5 billion	CSL Seqirus, Arcturus Therapeutics	Self-amplifying mRNA vaccine technology
2022	\$3.7 billion	MSD, Orna Therapeutics	Circular RNA therapies
2022	\$3.3 billion	GSK, Affinivax	Pneumococcal vaccine candidate

Source: IQVIA EMEA Thought Leadership; IQVIA Pharma Deals *July 2023; (1) Therapeutic defined as deals that mentioned non-infectious disease areas

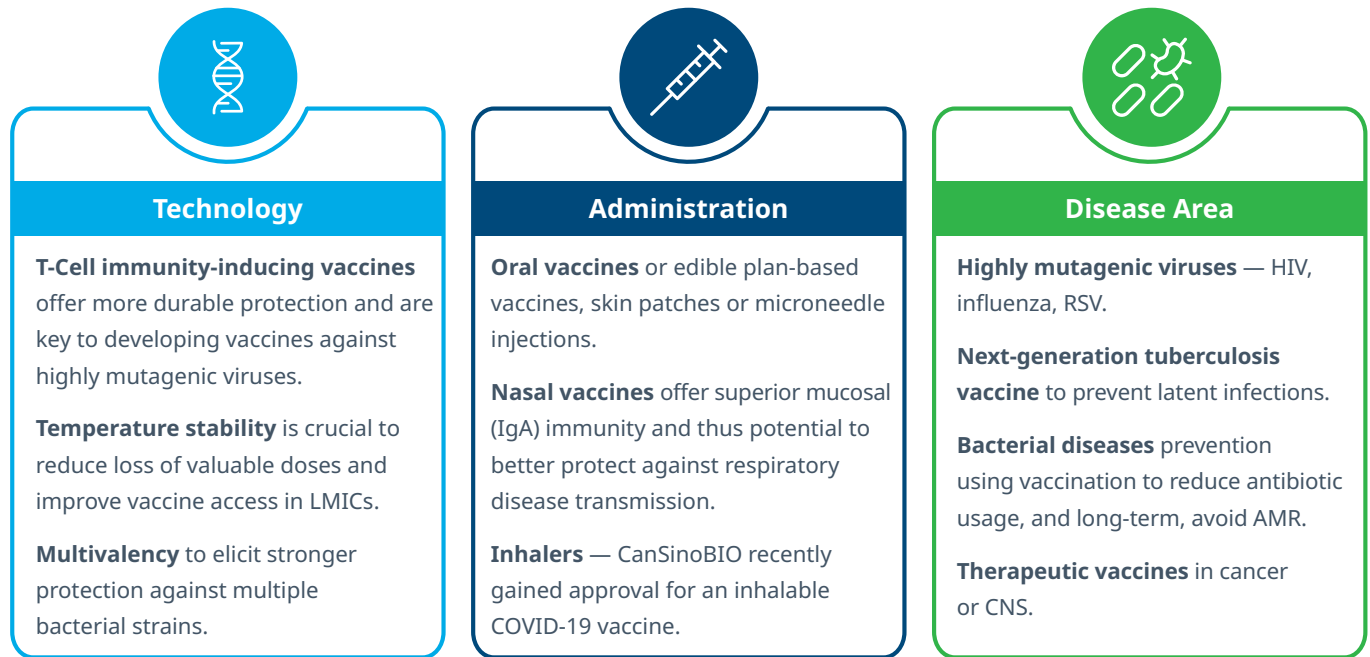
Future vaccine innovation must look beyond improving efficacy. Clearly efficacy is crucial but other parameters for future vaccines are equally important, e.g., eliciting stronger, longer-lasting immunity to avoid regular booster doses and universal vaccines against a family of viruses or against multiple bacterial strains. GSK’s acquisition of Affinivax at \$3.3 billion is a case in point. The deal included a 24-valent phase 2 asset against pneumococcal infection using the company’s proprietary MAPS technology which stimulates stronger and longer-lasting protection⁵⁵. This would be a viable alternative to the current 13-valent vaccines and addresses the emergence of new strains.

Currently available vaccines all work by triggering an immune response within the body. Historically, a lot of focus was on the ability of a vaccine to induce antibody production or a humoral immune response. Antibody titres are often used as a surrogate efficacy measure for regulatory submissions⁵⁶. Several vaccine platforms including protein-, vector- and nucleic acid-based systems can also induce an additional longer-lasting layer of protection — cellular immunity mediated via

T-cells⁵⁷. The SARS-CoV-2 Omicron variant evaded the humoral response, but our bodies’ acquired cellular immunity still protected against severe diseases⁵⁸. Inducing a strong T-cell-mediated immunity is also considered crucial for the development of a future HIV vaccine as the retrovirus is infamous for rapidly mutating its surface molecules. Duration of protection and efficacy are key target product profile features to guide vaccine development. Hence, delivering both a strong humoral and cellular immune response will be paramount in future vaccine development.

Future vaccine innovation must look beyond improving efficacy. Clearly efficacy is crucial but other parameters for future vaccines are equally important, e.g., eliciting stronger, longer-lasting immunity to avoid regular booster doses and universal vaccines against a family of viruses or against multiple bacterial strains.

Figure 7: Vaccine innovation



Source: IQVIA EMEA Thought Leadership

A previous IQVIA publication has outlined the challenges around cold-chain logistics for vaccines particularly affecting LMICs⁵⁹. Up to 50% of global vaccine doses were wasted due to temperature excursions⁶⁰. The WHO, Médecins Sans Frontières and CEPI all stated the need for temperature-stable vaccines to improve access and ensure future pandemic preparedness^{61,62,63}. Stablepharma has developed a stable version of a tetanus/diphtheria (Td) vaccine. The Td vaccine was fully recoverable after 7–10-month storage at 45°C⁶⁴. Moreover, local vaccine manufacturing in LMICs reduces transportation times and can improve access to life-saving vaccines in underserved areas.

Most vaccines are administered as intramuscular injections. However, pathogens enter our bodies through mucous membranes, e.g., in the nose. Strengthening this first line of defence might seem an obvious approach but getting there is not easy. Historically, nasal vaccines suffered from poor uptake via the mucosal tissue. Hartwell et al. developed a strategy to promote antigen uptake and drive broad protection⁶⁵. Although early in development, nasal administration could become an alternative strategy to prevent initial infections of respiratory diseases. Heterologous immunisations with non-mucosal and mucosal vaccines might offer improved protection. Moreover, the needle-free design enables fast rollout and offers an alternative for people with needle phobia.



The WHO, Médecins Sans Frontières and CEPI all stated the need for temperature-stable vaccines to improve access and ensure future pandemic preparedness.

Deep Dive — mRNA's moment of truth

The approval of COVID-19 mRNA vaccines from BioNTech/Pfizer and Moderna marked a pivotal moment, not just for pandemic response but for the entire vaccine industry. RNA's rapid computational design and synthesis in cell-free systems offer huge advantages over other platforms⁶⁶. The success of mRNA technology was validated by real-world efficacy, safety, and scalability demonstrated by the COVID-19 vaccines, which received emergency use authorisation a mere seven months after the initial clinical trial dosing, following over 50 years of research⁶⁷. In the EU, 887 million COVID-19 vaccine doses were administered by July 2023, with 90% being mRNA-based, saving over a million lives according to the WHO⁶⁸. Pioneers like BioNTech, Moderna, and CureVac have led the way, with partnerships forming, such as Pfizer collaborating with BioNTech and GSK with CureVac. Sanofi's entry was facilitated by acquisitions^{69,70}.

BioNTech and Moderna have been transformed by the enormous revenues generated from their COVID-19 vaccine business and established pharmaceutical companies have placed their bets on the technology. However, the story on mRNA outside of COVID-19 vaccines has not been written yet and it remains to be seen whether that success can be repeated.

Innovation landscape

Excluding COVID-19, the mRNA vaccine pipeline contains 67 assets: 78% for prophylactic vaccines against infectious diseases and 22% for therapeutic cancer vaccines (Figure 8). While the concept of cancer vaccines has been pursued for years, recent advancements in mRNA technology, sequencing, and bioinformatics have revitalised the field. This involves identifying patient-specific or shared tumour antigens, manufacturing, and administration. Both approaches, which take 6-8 weeks, are being tested, often combined with checkpoint inhibitors. Moderna's mRNA-4157/V940

combined with pembrolizumab showed a 44% improvement in melanoma patients' recurrence-free survival⁷¹. Encouragingly, a pivotal phase 3 study was initiated for adjuvant treatment of high-risk melanoma⁷². BioNTech's personalised cancer vaccines combined with chemotherapy and atezolizumab resulted in around 50% of pancreas cancer-resected patients remaining cancer-free after 18 months⁷³. However, these are still early days; long-term follow-ups and large randomised control trials are needed to confirm these results.

Vaccine companies are actively investigating mRNA in other infectious disease areas including influenza, RSV, HIV/AIDS and tropical diseases. Excitingly, 33% of candidates are against diseases without currently approved vaccines. Congenital cytomegalovirus (CMV) infection is the leading cause of birth defects including vision problems and hearing loss in the United States⁷⁴. The virus is highly prevalent in the public and can stay dormant for many years⁷⁵. Moderna aims to be first-to-market with its investigative vaccine candidate mRNA-1647. In the ongoing pivotal phase 3 study, the company is planning to enrol up to 6,900 healthy women of childbearing age⁷⁶.

Epstein-Barr Virus (EBV), present in around 90% of adults worldwide, is often harmless but can cause mononucleosis, and is linked to cancer and autoimmune diseases⁷⁷. While EBV vaccine development has seen little interest in the past, a significant study published in Science in June 2022, revealing a 32-fold multiple sclerosis (MS) risk increase after EBV infection, changed the public perception. Moderna currently has two EBV vaccine candidates in the clinics.

However, challenges include clinical trial recruitment due to the virus high prevalence and deciding endpoints: infection prevention or MS prevention through long-term studies.

Effectiveness of seasonal influenza vaccines is highly variable between 10 and 60%⁷⁹. The flexibility and shorter lead times with mRNA make it uniquely suitable to develop better vaccines. Unsurprisingly, mRNA companies have entered the arena, and influenza is the largest infectious disease area targeted. First clinical study readouts showed mixed results. An interim analysis of Moderna's mRNA-1010 phase 3 trial did not meet the statistical threshold to declare success⁸⁰.

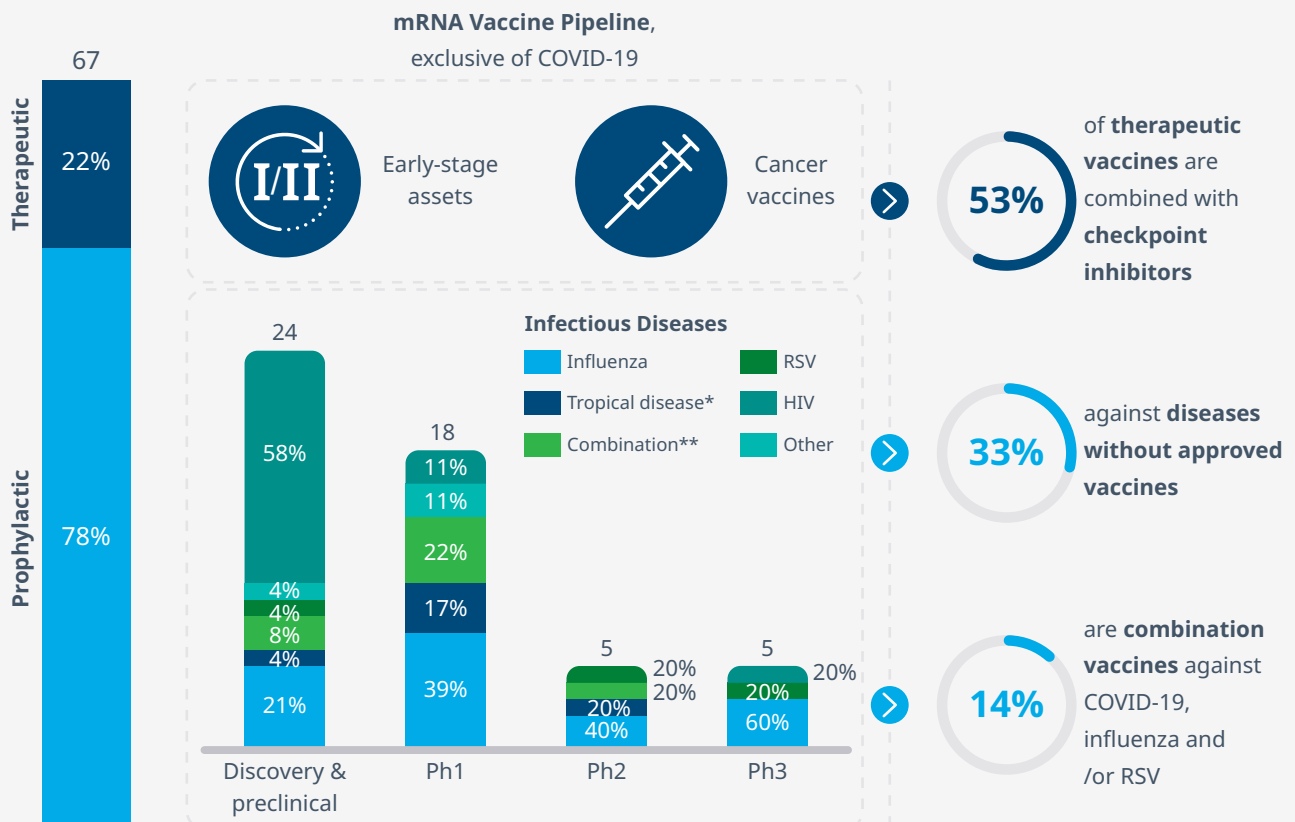
Meanwhile, Pfizer/BioNTech released preliminary data showing substantial induction of a cellular immune response⁸¹. GSK/CureVac and Sanofi/Translate Bio each have mRNA-based influenza vaccines in early development but have not presented any data yet. Targeting non-mutagenic

or conserved areas of the influenza virus is a promising alternative to seasonal updates. Such universal vaccines could lead to broader protection against current and future strains⁸².

In the 2022/23 cold season, healthcare systems faced a triple epidemic of influenza, RSV, and COVID-19.

While SARS-CoV-2's seasonality is unclear, regulators might advise a vaccination schedule akin to influenza, necessitating three vaccinations in quick succession for vulnerable individuals. Combination vaccines protecting against all three respiratory viruses would be ideal, with 14% of mRNA prophylactic pipeline focusing on such combinations.

Figure 8: The mRNA vaccines R&D pipeline



Source: IQVIA EMEA Thought Leadership; IQVIA Pipeline Link, April 2023;

*Tropical diseases include Malaria, Zika, Nipah, Lassa and Rabies;

** Covid-19 + influenza, Covid-19 + influenza + RSV, Influenza + RSV and others

The way forward

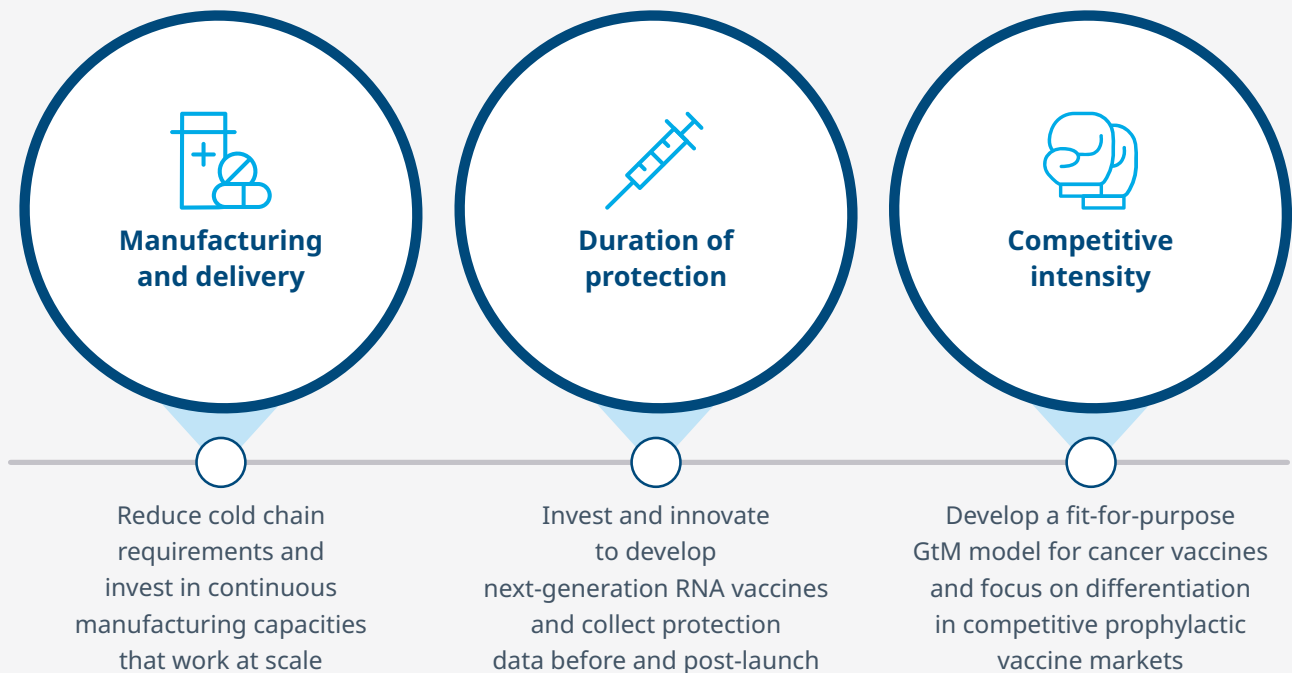
mRNA has the potential to disrupt established markets like influenza and could pioneer first-to-market opportunities in latent viral infections like CMV and EBV. Moreover, personalised cancer could expand their scope outside infectious diseases. To do so, some significant challenges must be addressed for mRNA to reach its full commercial potential:

mRNA has the potential to disrupt established markets like influenza and could pioneer first-to-market opportunities in latent viral infections like CMV and EBV.

Manufacturing and delivery

To meet the stringent temperature demands of mRNA vaccines, global storage facilities expanded their ultra-low temperature freezer capacities. Going forward, companies want to (1) reduce cold chain requirements and (2) pursue temperature-stable formulations. Pfizer/BioNTech are exploring freeze-drying and Moderna and CureVac work on fridge-stable versions^{83,84}. Furthermore, mRNA is a complex and more expensive technology compared to traditional approaches that required storage and shipment between facilities. Investments in continuous manufacturing capacity that work at scale are needed to stay competitive against more cost-efficient vaccines. Once established, the same process can be used for any mRNA-based product⁸⁵.

Figure 9: mRNA — the way forward



Source: IQVIA EMEA Thought Leadership

Duration of protection

Protection from getting infected by SARS-CoV-2 waned quickly after primary immunisation with an mRNA vaccine⁸⁶. Immunity is restored by booster doses but drops again by 60% after one month. According to GSK, AREXVY offers protection against RSV infections for two seasons whilst Moderna's efficacy holds up for six months. Self-amplifying RNA (saRNA) can replicate itself for 20 to 26 days; thus potentially inducing longer-lasting immunity at a lower dose⁸⁷. Circular RNA is another RNA alternative that offers similar advantages to saRNA. Duration of protection (DoP) is particularly relevant for payers as they want vaccinations to be cost-effective. Gathering sufficient DoP data prior to launch and/or collect RWE post-launch will be important to address payer concerns.

Competitive intensity

mRNA vaccines must compete against lower-cost established products like influenza vaccines. Gaining market share will be challenging, especially without superior efficacy or duration of protection data. A changed and faster strain-to-distribution timeline by the WHO could give mRNA an edge. To justify premium pricing, mRNA developers must highlight benefits like simplified dosing schedules and combination vaccines that offer health system and patient benefits.

Personalised cancer vaccines moreover require a streamlined process from tumour biopsy to target discovery and small-batch manufacturing — an expensive endeavour limited to specialised hospitals or centres. If they achieve regulatory approval, personalised cancer vaccines will launch in an increasingly unforgiving and highly competitive oncology market. Moderna and BioNTech must build oncology market capabilities from scratch, focusing on differentiation and shared value with health systems. Patient outcomes and health system readiness will be key considerations alongside efficacy and safety data.

mRNA has not disrupted the vaccines market. However, it has broadened the scope of the vaccine world. Therapeutic vaccines have long been an aspiration of the industry that could soon become reality. Next-generation prophylactic mRNA vaccines approaches could overcome challenges around stability and duration of protection. As the mRNA technology matures and more clinical data is gathered, its potential to improve cancer treatment and protect against public health threats remains incredibly promising.

mRNA has not disrupted the vaccines market. However, it has broadened the scope of the vaccine world.



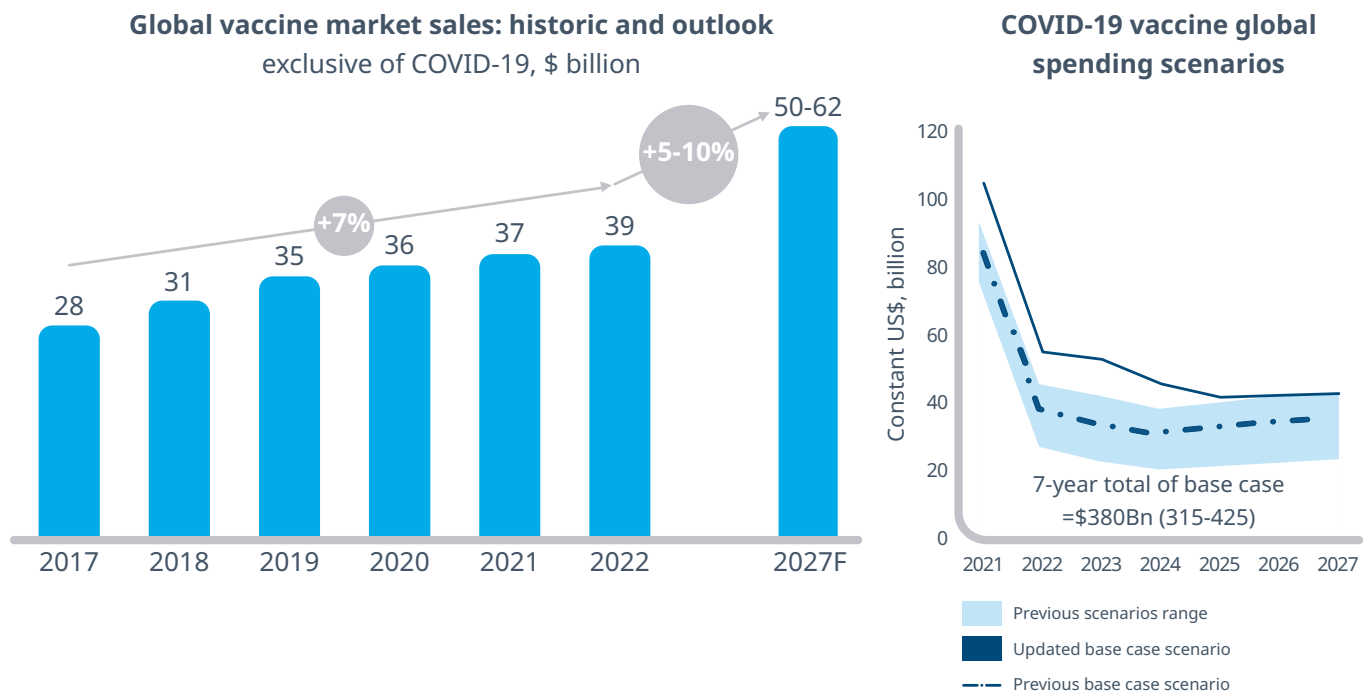
Outlook for the vaccines market

The global vaccines market — exclusive of COVID-19 — has reached \$39 billion in 2022, growing at a 7% CAGR between 2017-22. Vaccines protecting against human papilloma virus (HPV) and varicella-zoster virus (VZV) in high-income markets have driven historic growth. Adult immunisation campaigns and new vaccine launches will drive future growth. We expect the market to grow at a future 5-year CAGR (2022-2027) between 5-10% with the vaccines market to reach \$50-62 billion globally by 2027 (Figure 10 left panel). COVID-19 vaccine spending exceeded \$50 billion in

2022 and cumulative 7-year spending until 2027 is expected to reach between \$315 and \$425 billion globally (Figure 10 right panel)⁸⁸.

Collecting vaccine volume information is challenging. The WHO is one of the most comprehensive sources available with data gathered directly from the member states. According to its global vaccine market report 2022, the 2021 vaccine market supplied 16 billion doses in total, including COVID-19 vaccines, and 5.3 billion doses without. Higher seasonal influenza vaccine usage drove volume growth in high-income markets. Reduced childhood immunisations in LMICs led to a reduction of paediatric vaccine volume by 14% compared to 2019⁸⁹.

Figure 10: Global Vaccine market size



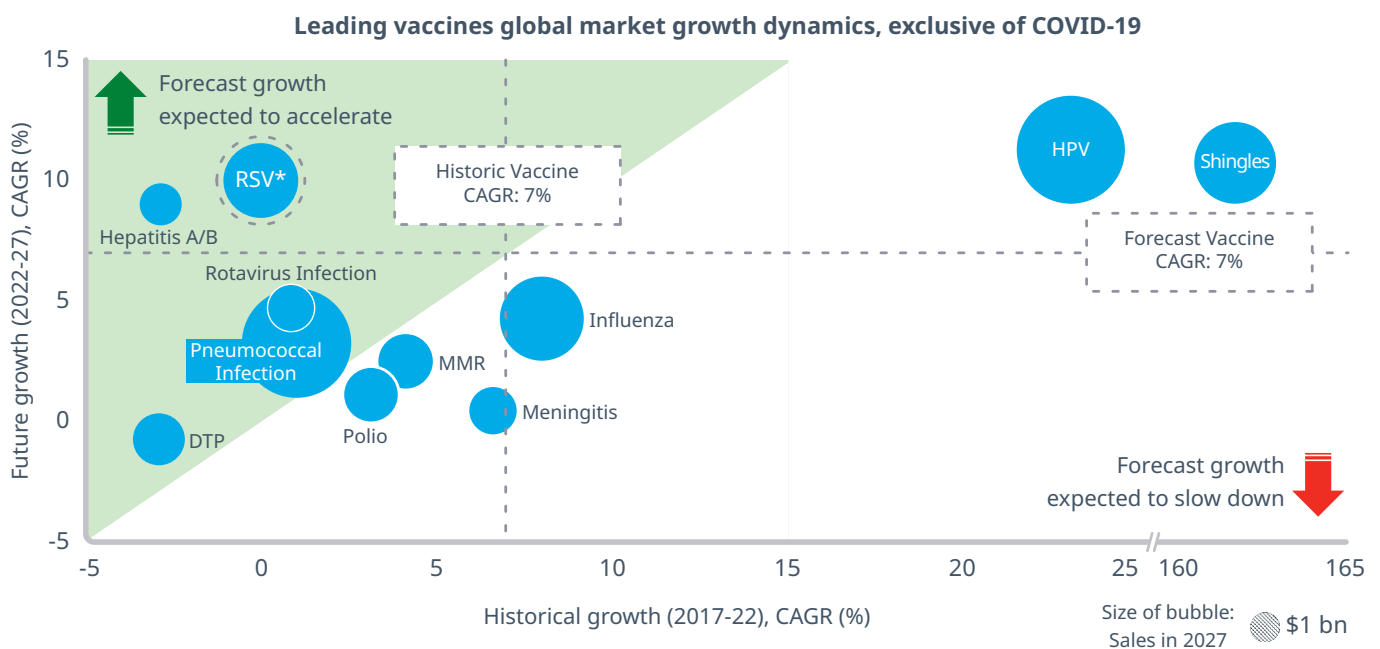
Source: IQVIA Analytics Link, July 2023; IQVIA Global Use of Medicines Outlook to 2027

The vaccines markets for HPV and shingles are expected to grow at a 10% 5-year CAGR until 2027 — the market expansion is driven by immunisation campaigns in adolescents and older adults respectively. Influenza vaccines are expected to grow around 5% in the next five years as seasonal respiratory infections are projected to be higher⁷⁸.

RSV vaccines were approved in 2023 and will be available in time for the cold season later this year. IQVIA analysts expect the market to reach between \$4.5 to \$7.5 billion by 2027 (Figure 11).

The forecast assumes immunisation rates similar to those of influenza at a premium price. Adult RSV vaccines will contribute most sales compared to maternal ones. Clinical trial success in areas of high unmet need including CMV or tropical diseases could see rapid sales growth over the next five years but due to large uncertainties were not included in the forecast.

Figure 11: Leading vaccines global market growth dynamics



Source: IQVIA Analytics Link, July 2023;

*no historic and future CAGR available; HPV — Human Papilloma Virus; DTP — Diphtheria, Tetanus & Pertussis; MMR — Mumps, Measles & Rubella; RSV — respiratory syncytial virus

Succeeding with vaccines

The COVID-19 pandemic reinforced the power of vaccines, the importance of innovation with the rise of mRNA and how crucial high vaccine uptake was to avoid human suffering. COVID-19 was not the first and will not be the last pandemic. An ageing society, high vaccine hesitancy in high-income countries, climate change, AMR and health system crises will make vaccination an even more important public health imperative.

The global vaccine market landscape is inherently complex. Regulatory, market access and

commercialisation dynamics vary greatly across regions and sometimes even within countries. The phenomenon of vaccine nationalism led to an uneven global distribution of vaccines, with certain countries like China opting to prioritise their domestically developed products over western mRNA vaccines. Moreover, there are differences depending on the vaccine type — adult or paediatric — and whether a public, private or hybrid commercialisation model is required.

For the scope of this white paper, which is focused on achieving commercial success in high-income markets, we have outlined five critical priorities below:

Figure 12: How to succeed with vaccines



Source IQVIA EMEA Thought Leadership, IQVIA Consulting expertise

- 1. Shape the policy:** Engage with stakeholders in the healthcare system to prioritise and invest in immunisation as a public health priority. Formalisation of horizon scanning to screen for innovation can provide an opportunity for the industry to formally interact with the authorities. Ensure adequate funding for a low-threshold provision of vaccines to a broad part of the population. Ultimately, embed vaccination as a foundation for population health management.
- 2. Build a vaccine GtM model:** Navigate the complex national vaccine environments and devise a fit-for-purpose go-to-market model that engages with all stakeholders across the relevant private/public, paediatric/adult and tendering landscape. Consumers are more aware about vaccines, and their preferences for e.g. a platform must be considered.
- 3. Put evidence front and centre:** The vaccine value proposition must show safety, cost effectiveness and sufficient public health benefits amongst others. Supplementing RCT data with RWE studies enables the quantification of these benefits and allows the translation from efficacy to effectiveness, hence providing both positive patient and health system outcomes data.
- 4. Improve vaccine delivery:** Make vaccines accessible and expand to additional care settings including pharmacies. Ease of access and convenience is

crucial for pandemic preparedness and routine immunisations. Digital solutions that remind people based on their vaccination history, risk factors and age can further aid in increasing immunisation rates.

- 5. Activate patients:** Address vaccine hesitancy and raise media and public awareness of vaccine benefits. E.g., run campaigns to show the positive impact of vaccines on society instead of focusing on vulnerable populations. Encourage, support, and incentivise HCPs to discuss vaccinations during regular consultations.

The future of vaccines holds immense promise fuelled by our continuously evolving and expanding arsenal of vaccine platforms. Moreover, we must learn from the lessons of the COVID-19 pandemic and acting on those will be important to foster a healthy vaccines market that can sustain innovation while addressing public health needs. Vaccine companies can and must play a central role in this endeavour.

We must learn from the lessons of the COVID-19 pandemic and acting on those will be important to foster a healthy vaccines market that can sustain innovation while addressing public health needs. Vaccine companies can and must play a central role in this endeavour.

Acknowledgements

The authors would like to gratefully acknowledge the contributions to this report by Henrike Resemann, Filip Hechtermans, Philippe Salphati, Paul Turner, Kevin O'Brian, Hammit Mistry, Richard Mee, Ruggero Rossi and Richard Bergström who provided valuable meaningful insights.

References

1. https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_1
2. <https://jamanetwork.com/journals/jama/article-abstract/2772168>
3. <https://www.mdpi.com/2076-393X/8/3/495>
4. <https://pubmed.ncbi.nlm.nih.gov/25103091/>
5. <https://www.tandfonline.com/doi/full/10.1080/14760584.2021.1905257>
6. Vaccines for Europe, EMA, FDA
7. <https://www.ema.europa.eu/en/news/first-rsv-vaccine-protect-infants-6-months-age-older-adults>
8. <https://www.who.int/news-room/spotlight/history-of-vaccination/history-of-polio-vaccination>
9. <https://ourworldindata.org/vaccine-preventable-diseases>
10. <https://www.paho.org/en/stories/history-polio-eradication-re-emergence>
11. <https://www.tandfonline.com/doi/full/10.1080/07853890.2017.1417632>
12. <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>
13. <https://pharmaphorum.com/sales-marketing/pandemic-caused-vaccine-confidence-fall-even-further>
14. <https://www.nature.com/articles/nm0598supp-495.pdf>
15. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8879820/>
16. <https://ourworldindata.org/vaccine-preventable-diseases>
17. <https://www.who.int/news-room/feature-stories/detail/beyond-the-numbers--the-real-world-impact-of-the-malaria-vaccine-in-kenya>
18. <https://www.nature.com/articles/s41579-020-00506-3>
19. <https://www.who.int/publications/i/item/no-time-to-wait-securing-the-future-from-drug-resistant-infections>
20. <https://www.ox.ac.uk/news/2022-01-20-estimated-12-million-people-died-2019-antibiotic-resistant-bacterial-infections>
21. EU, EU. (2023). Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach
22. The COVID-19 Pandemic Enhanced the Decade-Long Trend of the Decreasing Utilization of Antibiotics, IQVIA
23. <https://www.gavi.org/vaccineswork/vaccines-could-prevent-half-million-deaths-linked-drug-resistance-year>
24. <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1004166>
25. <https://data.unicef.org/resources/zero-dose-the-children-missing-out-on-life-saving-vaccines/>
26. <https://www.unicef.org/media/108161/file/SOWC-2023-full-report-English.pdf>
27. https://www.unicef.org/media/48686/file/Generation_2030_Africa_2.0-ENG.pdf
28. IQVA, Trends in global adult vaccination: Impact of COVID-19
29. Laigle V, Postma MJ, Pavlovic M, Cadeddu C, Beck E, Kapusniak A, Toumi M. Vaccine market access pathways in the EU27 and the United Kingdom - analysis and recommendations for improvements. *Vaccine*. 2021 Sep 15;39(39):5706-5718. doi: 10.1016/j.vaccine.2021.07.040. Epub 2021 Aug 14. PMID: 34404557.
30. IQVIA Global Trends in R&D: Overview through 2022
31. IQVIA Pipeline Link, July 2023
32. <https://www.reuters.com/business/healthcare-pharmaceuticals/gsk-rsv-vaccine-first-get-eu-regulators-nod-2023-04-26/>

33. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-respiratory-syncytial-virus-rsv-vaccine>
34. <https://www.scientificamerican.com/article/rsv-vaccines-are-finally-here-after-decades-of-false-starts/>
35. <https://www.nature.com/articles/nsmb.1723>
36. EMA, FDA
37. <https://www.ema.europa.eu/en/news/first-rsv-vaccine-protect-infants-6-months-age-older-adults>
38. <https://www.fiercepharma.com/pharma/pfizers-abrysvo-becomes-first-maternal-rsv-shot-protect-newborns>
39. <https://investors.modernatx.com/news/news-details/2023/Moderna-Announces-Global-Regulatory-Submissions-For-Its-Respiratory-Syncytial-Virus-RSV-Vaccine-MRNA-1345/default.aspx>
40. EMA, FDA
41. <https://www.who.int/publications/i/item/9789241565714>
42. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(16\)30259-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)30259-6/fulltext)
43. WHO Global Tuberculosis Report 2020. (2020).
44. Houben, R. M., and Dodd, P. J. (2016). The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling.
45. <https://www.who.int/teams/global-tuberculosis-programme/the-end-tb-strategy>
46. <https://www.telegraph.co.uk/global-health/science-and-disease/gamechanging-tuberculosis-vaccine-could-save-85-million/>
47. Global report on neglected tropical diseases 2023, WHO
48. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(23\)00641-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00641-4/fulltext)
49. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis
50. Kyaw MH, Lynfield R, Schaffner W, Craig AS, Hadler J, Reingold A, Thomas AR, Harrison LH, Bennett NM, Farley MM, Facklam RR, Jorgensen JH, Besser J, Zell ER, Schuchat A, Whitney CG; Active Bacterial Core Surveillance of the Emerging Infections Program Network. Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *N Engl J Med*. 2006 Apr 6;354(14):1455-63. doi: 10.1056/NEJMoa051642. Erratum in: *N Engl J Med*. 2006 Aug 10;355(6):638. PMID: 16598044.
51. IQVIA Pipeline Link
52. <https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed>
53. IQVIA Pharma Deals, Review of 2021
54. <https://www.sanofi.com/en/media-room/press-releases/2021/2021-08-03-05-00-00-2273307>
55. <https://www.gsk.com/en-gb/media/press-releases/gsk-completes-acquisition-of-affinivax-inc/>
56. IQVIA Consulting Expertise
57. Ura T, Takeuchi M, Kawagoe T, Mizuki N, Okuda K, Shimada M. Current Vaccine Platforms in Enhancing T-Cell Response. *Vaccines (Basel)*. 2022 Aug 21;10(8):1367. doi: 10.3390/vaccines10081367. PMID: 36016254; PMCID: PMC9413345.
58. Wherry EJ, Barouch DH. T cell immunity to COVID-19 vaccines. *Science*. 2022 Aug 19;377(6608):821-822. doi: 10.1126/science.add2897. Epub 2022 Aug 18. PMID: 35981045.
59. IQVIA White Paper: Pharma's frozen assets
60. WHO
61. <https://www.who.int/publications/m/item/who-guidelines-on-stability-testing-of-active-pharmaceutical-ingredients-and-finished-pharmaceutical-products>

62. <https://www.msf.org/heat-stable-vaccines-urgently-needed-reach-one-five-children-missed-immunisation-worldwide>
63. https://cepi.net/get_involved/cfps/?learn-more-7106=38
64. de la Torre Arrieta J, Briceño D, de Castro IG, Roser B. A thermostable tetanus/diphtheria (Td) vaccine in the StablevaX™ pre-filled delivery system. *Vaccine*. 2023 May 22;41(22):3413-3421. doi: 10.1016/j.vaccine.2023.04.039. Epub 2023 Apr 28. PMID: 37121799.
65. Hartwell BL, Melo MB, Xiao P, Lemnios AA, Li N, Chang JYH, Yu J, Gebre MS, Chang A, Maiorino L, Carter C, Moyer TJ, Dalvie NC, Rodriguez-Aponte SA, Rodrigues KA, Silva M, Suh H, Adams J, Fontenot J, Love JC, Barouch DH, Villinger F, Ruprecht RM, Irvine DJ. Intranasal vaccination with lipid-conjugated immunogens promotes antigen transmucosal uptake to drive mucosal and systemic immunity. *Sci Transl Med*. 2022
66. Yoo-Ah Kim, Kambiz Mousavi, Amirali Yazdi, Magda Zwierzyna, Marco Cardinali, Dillion Fox, Thomas Peel, Jeff Coller, Kunal Aggarwal, Giulietta Maruggi, Computational design of mRNA vaccines, *Vaccine*, 2023
67. IQVIA Institute Report “Lessons Learned from COVID-19 Vaccine Trials”
68. Our world in data & WHO
69. <https://www.curevac.com/en/curevac-and-gsk-bivalent-second-generation-mrna-vaccine-candidate-shown-to-be-highly-effective-against-sars-cov-2-variants-in-preclinical-study/>
70. <https://www.sanofi.com/en/media-room/press-releases/2021/2021-04-09-17-45-00-2207664>
71. <https://investors.modernatx.com/news/news-details/2022/Moderna-and-Merck-Announce-mRNA-4157V940-an-Investigational-Personalized-mRNA-Cancer-Vaccine-in-Combination-with-KEYTRUDAR-pembrolizumab-Met-Primary-Efficacy-Endpoint-in-Phase-2b-KEYNOTE-942-Trial/default.aspx>
72. <https://investors.modernatx.com/news/news-details/2022/Moderna-and-Merck-Announce-mRNA-4157V940-an-Investigational-Personalized-mRNA-Cancer-Vaccine-in-Combination-with-KEYTRUDAR-pembrolizumab-Met-Primary-Efficacy-Endpoint-in-Phase-2b-KEYNOTE-942-Trial/default.aspx>
73. Rojas LA, Sethna Z, Soares KC, Olcese C, Pang N, Patterson E, Lihm J, Ceglia N, Guasp P, Chu A, Yu R, Chandra AK, Waters T, Ruan J, Amisaki M, Zebboudj A, Odgerel Z, Payne G, Derhovanessian E, Müller F, Rhee I, Yadav M, Dobrin A, Sadelain M, Łuksza M, Cohen N, Tang L, Basturk O, Gönen M, Katz S, Do RK, Epstein AS, Momtaz P, Park W, Sugarman R, Varghese AM, Won E, Desai A, Wei AC, D’Angelica MI, Kingham TP, Mellman I, Merghoub T, Wolchok JD, Sahin U, Türeci Ö, Greenbaum BD, Jarnagin WR, Drebin J, O’Reilly EM, Balachandran VP. Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. *Nature*. 2023
74. <https://www.ncbi.nlm.nih.gov/books/NBK582519/>
75. Naing ZW, Scott GM, Shand A, Hamilton ST, van Zuylen WJ, Basha J, Hall B, Craig ME, Rawlinson WD. Congenital cytomegalovirus infection in pregnancy: a review of prevalence, clinical features, diagnosis and prevention. *Aust N Z J Obstet Gynaecol*. 2016 Feb;56(1):9-18. doi: 10.1111/ajo.12408. Epub 2015 Sep 22. PMID: 26391432.
76. Moderna company presentation
77. Young LS, Rickinson AB. Epstein-Barr virus: 40 years on. *Nat Rev Cancer*. 2004 Oct;4(10):757-68. doi: 10.1038/nrc1452. PMID: 15510157.
78. Kjetil Bjornevik et al. ,Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis. *Science* 375,296-301(2022).DOI:10.1126/science.abj8222

79. Erbeiding EJ, Post D, Stemmy E, Roberts PC, Augustine AD, Ferguson S, Paules CI, Graham BS, Fauci AS. 2018. A universal influenza vaccine: the strategic plan for the National Institute of Allergy and Infectious Diseases. *J Infect Dis* 218(3):347–354
80. <https://www.fiercebiotech.com/biotech/modernas-mrna-flu-shot-continues-struggle-prove-its-worth-phase-3-trials>
81. https://s28.q4cdn.com/781576035/files/doc_financials/2022/q2/Q2-2022-Earnings-Charts-FINAL.pdf
82. mRNA, the beginning of a new influenza vaccine game
83. <https://www.clinicaltrials.gov/study/NCT04816669>
84. <https://www.nationalgeographic.com/science/article/future-covid-19-vaccines-might-not-have-to-be-kept-so-cold>
85. <https://www.nytimes.com/interactive/2021/health/pfizer-coronavirus-vaccine.html>
86. Menegale F, Manica M, Zardini A, et al. Evaluation of Waning of SARS-CoV-2 Vaccine-Induced Immunity: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2023;6(5):e2310650. doi:10.1001/jamanetworkopen.2023.10650
87. <https://www.forbes.com/sites/williamhaseltine/2022/10/06/supercharging-mrna-vaccines-with-self-amplifying-rna-technology/>
88. IQVIA Global Use of Medicines Outlook to 2027
89. WHO, Global vaccine market report 2022

About the authors



STEFAN LUTZMAYER
Consultant, EMEA Thought
Leadership, IQVIA

Stefan Lutzmayer has over 8 years of experience working in academia and life sciences. He joined the thought leadership team in June 2021 where he creates novel materials on emerging next-generation biotherapeutic platforms like the microbiome or gene-editing, new developments across therapeutic areas including central nervous diseases or cardiometabolic diseases as well as cold chain pharmaceuticals.

Stefan is considered a subject matter expert in these areas. He frequently engages with senior client stakeholders, speaks at conferences, and supports consulting projects.

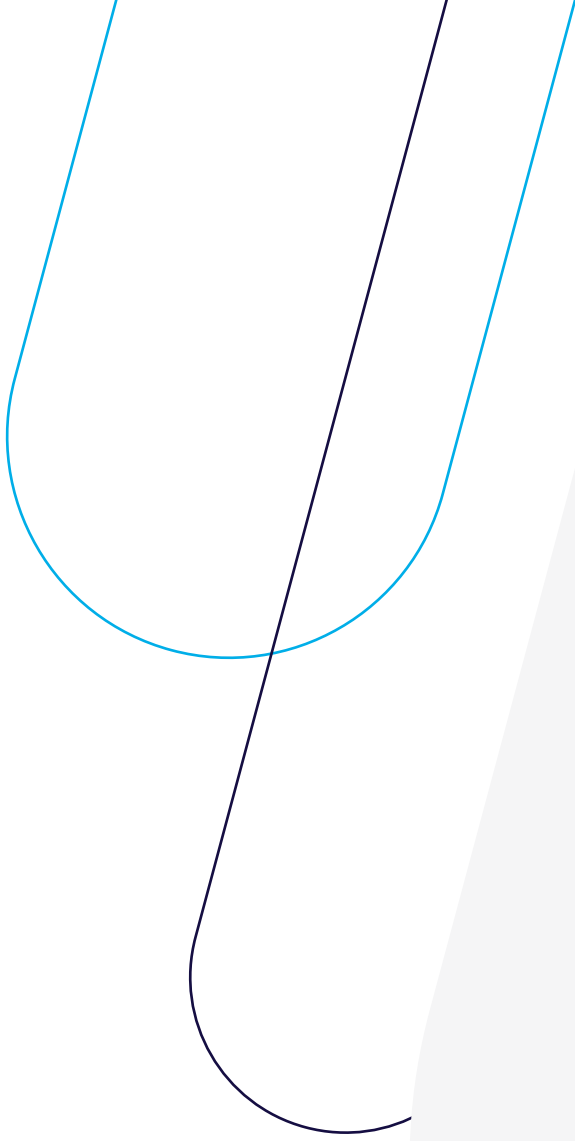
Stefan has prior experience working as an IT consultant advising healthcare and life sciences clients. He holds a PhD degree from the University of Vienna, is trained in molecular biology and data analysis and has published multiple peer-reviewed articles in internationally-renown journals.



HELENA BAYLEY
Analyst, EMEA Thought
Leadership, IQVIA

Helena joined IQVIA in May 2023, and she currently works across several areas that the team covers. Helena also interned with the Thought Leadership team two years ago, where her projects included co-authoring a white paper on haematological cancers, and analysing trends in head-to-head trials in auto-immune indications.

Since her internship, Helena has completed her degree in Physics at the University of Oxford, specialising in Biophysics in her Master's year there.



CONTACT US
iqvia.com