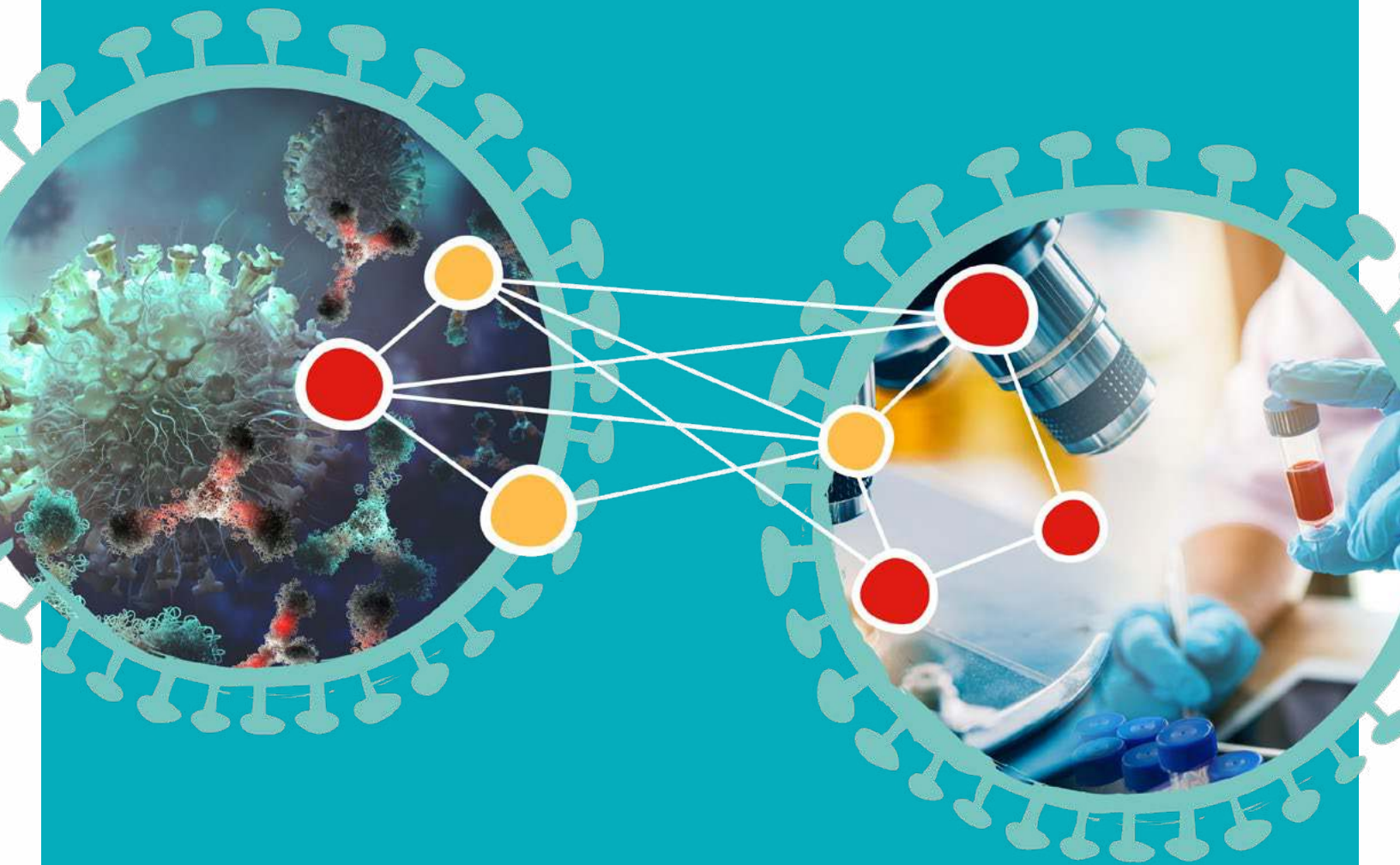


# Addressing Market Failures:

The Role of CEPI in Bridging the Innovation Gap to Prevent the Next Pandemic



# Authors

**Volta Capital** is an impact investment and development finance advisory firm. We develop market analyses and funding strategies that effectively bridge the public, private, and civil sectors to advance systemic market transformation. Whether in global health, education, agriculture, or financial inclusion, we have an extensive track record of bringing innovative financing tools and partnerships from concept to reality.



**Pandemic Action Network** drives collective action to bring an end to COVID-19 and ensure the world is better prepared for the next pandemic. With more than 130 partners around the world and growing, the Network catalyzes political action and resources, shapes evidence-based policy solutions and fosters partnerships and collaborations to pandemic-proof the planet.



**Africa Centres for Disease Control and Prevention (Africa CDC)** is a specialized technical institution of the African Union (AU) established to support public health initiatives of AU Member States and strengthen the capacity of their public health institutions to detect, prevent, control and respond quickly and effectively to disease threats.



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# Glossary

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**ACT-A**

The Access for COVID-19 Tools Accelerator

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**Africa CDC**

Africa Centres for Disease Control and Prevention

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**AMC**

Advance Market Commitment

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**BARDA**

Biomedical Advanced Research and Development Authority

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**CEPI**

Coalition for Epidemic Preparedness Innovations

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**CEPI 1.0**

CEPI's 2017-2021 strategy

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**CEPI 2.0**

CEPI's 2022-2026 strategy and \$3.5B funding target

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**COVAX**

The vaccines pillar of the ACT Accelerator

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**EID**

Emerging infectious disease

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**EUA**

Emergency Use Authorization

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**Gavi**

Global Alliance for Vaccines & Immunizations

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**HERA**

Health Emergency Preparedness and Response Authority

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**HIC**

High-income Country

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**IP**

Intellectual Property

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**LMIC**

Low- and middle-income countries

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**MNC**

Multi-national companies

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**NIAID**

National Institute of Allergy and Infectious Diseases

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**OWS**

Operation Warp Speed

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**PPR**

Pandemic preparedness and Response

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**PRND**

Poverty-related neglected disease

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**R&D**

Research and Development

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**WHO**

World Health Organization

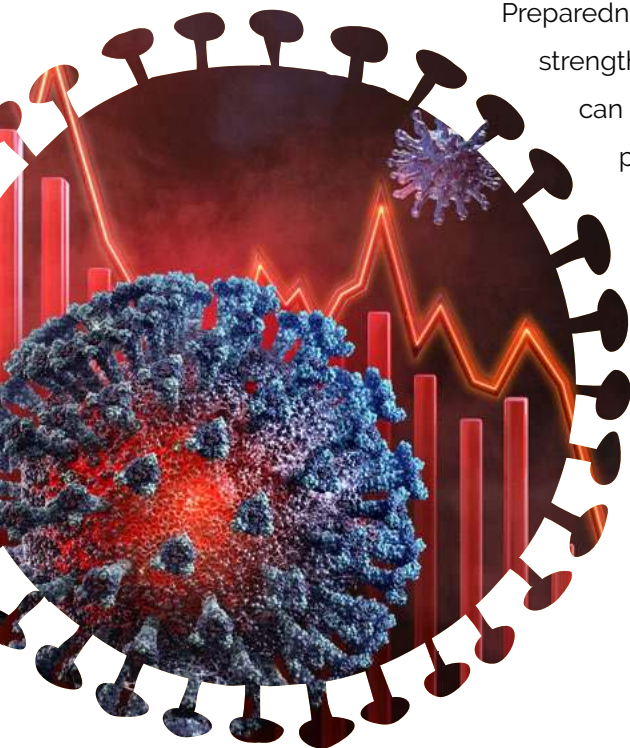
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# Executive Summary

The global response to COVID-19 has shown that the world was ill-prepared to prevent and rapidly respond to a novel pandemic threat, and it has exposed the persistent market and systems failures in global health research and development (R&D). These failures have resulted in gross inequities in global access to COVID-19 vaccines that are fueling the continued spread of the virus in many low- and middle-income countries (LMICs). As of this writing, the pandemic is far from over, yet policymakers have already begun to consider the emerging lessons from COVID-19 and a critical assessment of these market and systems failures is essential, whether the next pandemic's trajectory looks similar to COVID-19 or entirely different.

**This paper examines failures in the global health R&D ecosystem to help inform policy and funding decisions to bolster preparedness and response for emerging pandemic**

**threats.** In particular, this paper considers the unique role of the Coalition for Epidemic Preparedness Innovations (CEPI) in addressing some of these failures, its strengths and challenges in the COVID-19 response, and the role CEPI can play through its new strategy to bolster future epidemic and pandemic preparedness.







- **Longstanding and persistent market and systems failures in global health research and development (R&D), especially for vaccines against novel pathogens, have left the world at grave risk of deadly and costly pandemics.** These failures manifest differently before, during, and after a pandemic, and with each novel disease and moment in time.

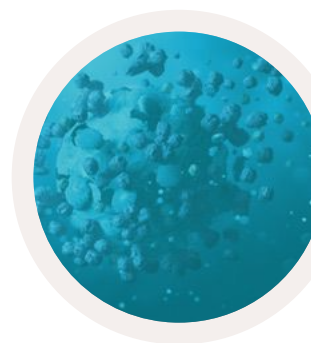
Investments, tools, and incentives to spur pandemic preparedness R&D must be robust, flexible, and nimble to match both the scale and variability of emerging infectious diseases with pandemic potential. Strong and resilient public-private partnerships and financing solutions are needed to ensure that everyone, everywhere can access the lifesaving countermeasures they need when they need them.

- **The world cannot wait for the next pandemic to bolster investments in R&D and preparedness for emerging infectious disease threats.** Governments, industry, philanthropy, multilateral, academic and research institutions, and civil society must come together to learn the lessons of COVID-19 – and ensure there is a global health R&D ecosystem that is at-the-ready to respond rapidly in the event of a fast-moving infectious disease threat from both known and unknown pathogens.

- **The Coalition for Epidemic Preparedness Innovations (CEPI) has a key role to play in a better prepared global R&D ecosystem.** CEPI was founded precisely to tackle some of these persistent market and systems failures. CEPI's role in the COVID-19 global response has propelled development of an ambitious yet achievable five-year strategy to compress vaccine development for novel pathogens to 100 days, and advance prototype vaccines for future pandemic threats. A strong R&D ecosystem that is pandemic-ready will require investments in multiple partners, *but fully resourcing CEPI is a smart place to start.*

## Market and systems failures for pandemic R&D

**Market failures for pandemic R&D fall into four categories: *market risk aversion, chronic under-investments in preparedness, equitable access, and collective action.***



### Market risk aversion

**Private industry partners cannot be expected to absorb the many and complex risks of vaccine development independently.** While private industry partners have the expertise, know-how, and resources that are critical to efficient vaccine development, their for-profit mandate is often at odds with R&D for emerging infectious diseases (EIDs) that may generate limited demand, offer time-limited markets, and/or serve only those with low ability to pay. Once an EID progresses to a global pandemic, like with COVID-19, the risk-reward calculus for industry changes, with both the rewards and the risks growing with a large global market. The ultimate severity, spread, and toll of a pandemic caused by a novel pathogen are unpredictable at the outset, which affects the appetite for risk. And the risks associated with running many stages of a carefully sequenced R&D process in parallel to speed development of countermeasures for a fast-moving pandemic can dramatically increase the cost of scientific failure.

**Incentives are required to de-risk and propel pandemic-related R&D even when there is a real and present threat.** During the early stages of the COVID-19 pandemic, the potential of a global market proved not to be attractive enough to counter the high risks to industry of engaging in R&D for new vaccines against the novel coronavirus. High-income countries (HICs), notably the United States (U.S.), invested heavily to de-risk and propel COVID-19 vaccine R&D and manufacturing—but with provisions that allowed investor countries first and primary access to resulting vaccines. In contrast, CEPI was the only entity with the mandate to invest in de-risking COVID-19 vaccine R&D with global, rather than national, access in mind. Since the next pandemic will likely present new and different bottlenecks than COVID-19, flexible and varied incentives will continue to be needed to de-risk pandemic R&D.

### Chronic underinvestment in preparedness

**Since EIDs and pandemic threats often feel like distant or future problems, both public and private actors repeatedly fail to prioritize and adequately fund them.** Vaccine R&D is traditionally a long process and requires long-term investments. It is not until EIDs become urgent epidemics or pandemics that threaten HIC markets that reactive surge funding comes, and this often dries up once the virus threat fades from the headlines. Not only does this boom-and-bust funding fail to deliver tools when needed to curb contagion at the height of an epidemic or pandemic, but it also exacerbates funding risks that pose challenges to industry engagement.

**CEPI was built to invest proactively in translational research for just-in-case vaccines for a specific set of neglected diseases and just-in-time platforms for serious EID outbreaks.**

During COVID-19, it moved quickly to accelerate development and manufacturing of new vaccines. CEPI is now working to build a wider “Disease X” vaccine portfolio to forecast and prepare for the next emerging pandemic threat and condense the vaccine development timeline to 100 days from the discovery of a novel pathogen. This work will anticipate need and release resources based on epidemiological data, rather than political or commercial considerations, to target emerging pandemic threats.

### Equitable access failures

**The dramatic inequities in global access to COVID-19 vaccines is the most glaring market failure of the current pandemic vaccine R&D system.** Before a pandemic, equity challenges stem from limited profit opportunities for neglected and emerging diseases, which means potentially life-saving vaccines do not get developed at all. When an outbreak progresses to a pandemic, vaccines may get developed, but their high-income funders drive the R&D agenda skewing both product profiles and access. Governments with the most resources are able to capture limited vaccine supply for their own citizens first, delaying access for populations in countries with fewer resources, often with fatal consequences. We are seeing this grim reality play out now with COVID-19: as of 26 July 2021, 27.2% of the world’s population had received at least one dose of a COVID-19 vaccine, but only 1.1% of those people were in low-income countries.<sup>1</sup>

**The structural inequities in the pandemic R&D ecosystem threaten the health and security of all nations—a clear case for public sector leadership and funding.** CEPI’s efforts in the COVID-19 response point to the challenges of addressing structural inequities and potential models for proactive investments with an equity lens. CEPI built a portfolio of COVID-19 vaccine investments that, while not as large in dollar value as those of some HIC funders, was well-diversified by technology, product profile, geography, and supplier. CEPI also invested in at-risk manufacturing for vaccines suitable for low-resource settings and in LMIC-based R&D to help drive global access and equity. Yet the scale of CEPI’s investments in manufacturing capacity struggled to match the size and pull of HIC country procurement funding. Although CEPI had negotiated first right-of-refusal to more than one billion doses of COVID-19 vaccines for LMICs, funding commitments had not yet been made to purchase those reserved doses, so some were bought by wealthy countries who were ready to purchase. Applying these lessons, CEPI’s new five-year strategy places equity at the center of future pandemic vaccine development efforts.

## Collective action failures

**Global COVID-19 R&D efforts have been hampered by nationalistic responses to the pandemic.** Before COVID-19, no standing multilateral structure existed to lead and coordinate pandemic preparedness R&D. As the pandemic accelerated in the spring of 2020, the Access to COVID-19 Tools Accelerator (ACT-A) and its COVAX Vaccine Pillar were rapidly stood up to help drive a coordinated strategy across global health and development organizations, governments, scientists, industry, philanthropy, and civil society for the development and delivery of COVID-19 vaccines, therapeutics, and diagnostics. ACT-A and COVAX, with CEPI as one of the lead agencies, have played an important role in prioritizing equitable access to these lifesaving tools, yet they have also been significantly hampered in their efforts in several ways. Among the challenges: having to build new processes from scratch in the midst of a fast-moving global crisis, with a distributed leadership model across multiple international agencies; lacking upfront funding to compete with first-wave HIC vaccine procurement; facing continued financing gaps and supply bottlenecks; and confronting nationalistic policies that compete with global access. As of June 2021, COVAX had delivered just 4% of the world's vaccine doses, and only 193 million of the 2 billion doses that they had initially targeted.<sup>2</sup> These constraints have led many countries to pursue bilateral or regional deals in an attempt to accelerate vaccine access for their populations, and illustrates a significant inability of the current multilateral system to counteract strong bilateral incentives and imbalance in global resources.

## Toward a better ecosystem for pandemic preparedness and response R&D

**In light of these failures, there are growing calls to build a better prepared global R&D ecosystem to lead and accelerate the development of lifesaving innovations for emerging pandemic threats.** Key elements must include: mobilizing and sustaining significant new funding; addressing longstanding inequities in public health; engaging the private sector in global goods production; ensuring more resilient supply chains; and finding the optimal models for collective leadership and alignment. Multi-sectoral, multi-stakeholder collaboration and partnership will be essential, as will tailoring interventions to address specific market and systems failures.

**While it cannot fill all the gaps in a complex and evolving pandemic R&D landscape, CEPI can address some of the critical failures in global vaccine access.** If fully resourced, CEPI's new five-year strategy would enable it to:



- **Accelerate pandemic preparedness and counter chronic underinvestment** by investing in technologies and processes to advance a 100-day goal for pandemic vaccine development and build a library of novel vaccine technologies against emerging threats.
- **Deploy a flexible set of incentives to de-risk pandemic vaccine R&D**, attracting private industry R&D actors into the space, and coordinating closely with national governments, philanthropy and other actors who can bring additional and needed resources for risk-sharing in product development.
- **Ensure access and equity are front and center in pandemic vaccine R&D efforts** by continuing to prioritize vaccine product profiles that are appropriate for diverse and low-resource settings, linking CEPI funding to access provisions, and partnering with downstream actors to facilitate the affordable, efficient manufacture and delivery of vaccines once they are developed.
- **Partner with other global actors to build a more robust preparedness R&D ecosystem** and facilitate end-to-end vaccine development to ensure timely, affordable vaccine access for all in the face of the next deadly epidemic or pandemic.

**No single organization can independently address all the failures identified in this paper; the world needs to invest in a better equipped and better coordinated global health R&D ecosystem to be ready for the next pandemic.** In addition to fully resourcing CEPI's new strategy to accelerate pandemic vaccine R&D, world leaders should commit now to increased and sustained investments in regional and national core health security capacities, resilient supply chains, and distributed manufacturing capacity to quickly develop and deploy an array of medical countermeasures and tools. The sprint to develop COVID-19 vaccines in record time has shown that science can deliver amazing innovations. But breaking the past cycles of panic and neglect to ensure those innovations are advanced and delivered in time to save lives and protect everyone, everywhere will require strong and sustained political will, collective alignment and action, and integrated end-to-end approaches with a steadfast commitment to keep all of humanity safer from pandemics.

# Introduction

The global response to COVID-19 not only shows that the world was ill-prepared to prevent and respond to a pandemic caused by a novel respiratory pathogen, but also that there are an array of system and market failures in the global health R&D ecosystem that hamper timely, affordable, and equitable global access to lifesaving new tools and technologies.

Solving for these system and market failures and building a ready and sustainable ecosystem for R&D for pandemic preparedness will be critical to advancing global health security and preventing future infectious disease outbreaks from becoming the next deadly and costly pandemic. To do so, we must examine the failures exposed during the COVID-19 pandemic and other recent global health emergencies and the roles that various institutions played to either exacerbate or mitigate them.

Since a pandemic, by definition, affects the global population, it is easy to assume that it creates a large, lucrative market that prompts timely and effective R&D and response from market actors. It is true that with the onset of the COVID-19 pandemic certain industry players rose to the R&D challenge and advanced novel vaccines, diagnostics, and therapeutics in record time. But this view is overly simplistic and misses the myriad other challenges to investment and coordination for an effective and equitable response. Just as with poverty-related and neglected diseases (PRNDs), R&D for emerging infectious diseases (EIDs) is plagued by false dichotomies that separate obscure diseases in low- and middle-income countries (LMICs) from infectious diseases that pose direct threats to high-income countries (HICs) and the global economy; pandemic preparedness from response; emerging disease threats from realized pandemics; and R&D of new products from access to existing ones. The reality is that these are all much more interconnected.



These challenges have led to a global R&D system for pandemic threats that is largely reactive, subject to boom-and-bust funding patterns and fails to quickly develop and deploy appropriate medical countermeasures and other vital tools to all who need them in an emergency. As we have seen with COVID-19, these failures have contributed to a grossly inequitable world of vaccine haves and have-nots, allowing a deadly pathogen to spread unchecked in a majority of the world's population.

This paper seeks to

- **ANALYZE** the market and systems failures for pandemic preparedness R&D, particularly for vaccines, and examine how solving for these failures can build a more proactive, effective global health security ecosystem;
- **EXPLORE** why, despite decades of epidemiological evidence, both the public and private sectors continue to neglect EIDs as distant threats, only to ramp up to crisis mode during a health emergency and then quickly revert to the mean as the crisis wanes.

The paper specifically examines the role of the **Coalition for Epidemic Preparedness Innovations (CEPI)**, which was created in 2017 to address a long-neglected gap in vaccine development for EIDs with epidemic potential, and to build rapid response platforms for "Disease X." It explores CEPI's evolving role in advancing vaccine development and deployment for COVID-19, and its promise to sustainably address pervasive and emerging market and systems failures in the pandemic preparedness R&D ecosystem through its next five-year strategy.

Finally, the paper looks ahead to the future of the pandemic preparedness R&D ecosystem and some of the questions and challenges the world must address to build a global system that is forward-looking, nimble, sustainably resourced, politically prioritized, and equitable.

Ultimately, the COVID-19 pandemic has shown the world that there is a need for fresh thinking and new tools if we are going to prevent a devastating global health crisis like this pandemic from ever happening again. The world cannot continue to rely on market-based systems or funding mechanisms alone to direct our global health R&D priorities; COVID-19 points to the devastating impact of such dependencies. When the ecosystem was stressed during this pandemic, markets and existing structures failed to take care of humanity, particularly the most vulnerable. Now is the time to take stock of and act on lessons learned.



**1**

# Setting the Scene





## 1A. Actors in the Pandemic R&D Ecosystem and Their Roles in the COVID-19 Response

The actors in the pandemic R&D ecosystem, much like other areas of health R&D, broadly fall into four categories: **academia/scientific institutions, government, private industry, and multilateral institutions**. Under optimal conditions, these actors play largely complementary roles to take a product successfully through the entire product lifecycle, from basic research to clinical trials to regulatory review and to manufacturing and distribution.



**Academia/Scientific Institutions**



**Government**



**Private Industry**



**Multilateral Institutions**

Academic and other scientific institutions take on basic research, exploring new and existing pathogens and novel platforms and innovations for medical countermeasures. Governments tend to fund basic research and development of enabling technologies, and step in to provide “push” and “pull” incentives like grants or advanced market commitments to encourage private industry to translate basic research into new tools and technologies. In some instances, governments build fit-for-purpose entities to accelerate the development of medical countermeasures, with specialized funding and incentive mechanisms to work expeditiously with partners across sectors. Private industry tends to lead on product development and manufacturing, using its end-to-end product development capabilities to take a medical countermeasure from proof-of-concept to commercial product. Because R&D is expensive, and industry typically recuperates these upfront investments through sales, if there is not a strong or lucrative market, government incentives are often needed to spur the private sector to action. Multilateral institutions help with global coordination and alignment, and also play a role in global distribution and access to vaccines, therapeutics, and diagnostics.

An explanation of different types of private sector and public sector actors is available in Annex 1 and 2 respectively, detailing their market roles, incentive structures, and capabilities.



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## Academia/Scientific Institutions

Decades of funding for global health and EID R&D laid the groundwork for the rapid development of vaccines, therapeutics, and diagnostics for COVID-19. For example, research into SARS and MERS (two other coronaviruses), virus spike proteins, and mRNA<sup>3</sup> and viral vector vaccine platforms provided a strong foundation for the first-to-market COVID-19 vaccines. This type of basic research is often conducted by academic and research institutions and often supported by federal funding.



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## Government

When COVID-19 was recognized as a serious global threat, many governments—particularly in high-income countries—stepped in with emergency funding to propel development of vaccines, therapeutics, and diagnostics. This surge funding was used both to accelerate R&D and product development, as well as spur manufacturing and procurement of novel countermeasures to drive industry and other stakeholder engagement.

A notable catalyst to COVID-19 vaccine development was the United States' Operation Warp Speed (OWS),<sup>4</sup> which launched on May 15, 2020 with \$18 billion to accelerate the development, manufacturing, and distribution of COVID-19 vaccines. Additional funding and support was also provided through the U.S. Biological Advanced Research and Development Authority (BARDA), a specialized U.S. agency that supports the advanced development of medical countermeasures against naturally occurring health threats, including EIDs, and uses unique contracting and incentive mechanisms to build sustained partnerships with developers to bridge the so-called “valley of death” between basic and clinical research to advance products to market.<sup>5</sup> Funds from OWS supported significant “push” funding to entice major pharmaceutical companies to prioritize the COVID-19 vaccine space and “pull” incentives through guaranteed purchases for the U.S. population, and supported vaccine development by Johnson & Johnson, Oxford/Astra Zeneca, Moderna, Novavax, Merck, Sanofi, and GlaxoSmithKline (GSK). This funding helped de-risk private sector participation in the vaccine market, which often carries turbulent and unpredictable profits, and de-risked manufacturing of vaccine doses (for domestic consumption) before they received regulatory approval. Likewise, the German government supported the biotechnology firm BioNTech with \$445 million,<sup>6</sup> enabling the firm to partner with Pfizer to advance a successful mRNA vaccine.




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## Private Industry

Private industry is not monolithic, and in general can be separated into several distinct categories: smaller biotechnology firms, large pharmaceutical companies, and developing country-based firms.

Smaller biotechnology firms are often financed by venture capital and built to tackle new R&D challenges, which often entails significant risk-taking. These actors were some of the first industry movers in COVID-19 countermeasures, with companies like BioNTech, Moderna, and CureVac acting early to develop prototype vaccines and technologies against COVID-19. When COVID-19 became more recognized as a pandemic threat, large pharmaceutical companies started to get engaged. This included partnerships between “big pharma” and smaller biotechnology companies to advance a new technology (e.g., Pfizer and BioNTech partnership), as well as exploring their portfolios to see what could be leveraged for COVID-19 (e.g., Johnson & Johnson applying its viral vector vaccine research to develop a COVID-19 vaccine). Most large pharmaceutical companies waited for government funding to de-risk engagement before entering the COVID-19 vaccine space.<sup>7</sup> Meanwhile, firms in developing countries, like the Serum Institute in India, have pledged to manufacture COVID-19 vaccines at the scale and price point needed to reach the world’s poor, and have received public funding to support this objective. They have been unable to fully deliver on this promise to date, however, given these manufacturers are largely reliant on inputs and technology transfer from HICs, internal production capacity has struggled, and the huge surge in virus cases in India caused the government to restrict vaccine exports, making them unable to meet their production promises to other developing countries to date.<sup>8</sup>




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## Multilateral Institutions

### COALITION FOR EPIDEMIC PREPAREDNESS INNOVATION (CEPI)

CEPI was founded in 2017 to advance the development of vaccines for a select set of emerging infectious diseases with epidemic potential. Created as a result of lessons learned during the 2014 Ebola outbreak in West Africa—where there was no vaccine ready to deploy—CEPI was designed to focus where most industry and government players do not: shepherding vaccine technologies for emerging infectious diseases with epidemic potential through the “valley of death” from the lab to the market, and funding R&D phases from enabling science, preclinical studies, through Phase 1-3 of



development.<sup>9</sup> Importantly and uniquely, CEPI was set-up with global needs and global access front-of-mind, and since its founding has required vaccines produced with its support to be accessible first and foremost to low-resource settings—not just high-income settings that can self-finance R&D. It also requires equitable access provisions in all contracts with industry partners.

CEPI was a key first mover on the COVID-19 vaccine front, however, the organization was not originally structured or resourced to advance R&D for vaccines to combat pandemic threats—with broader and different market and geo-political dynamics than epidemic threats. In 2019 its R&D investments totaled \$103.8 million, largely supported by bilateral donor and philanthropic funding.<sup>10</sup> Despite these capacity and funding limitations, when COVID-19 emerged, CEPI quickly identified gaps and pivoted to play new and leading roles in the global response. Within three weeks of the publication of the genome sequence for COVID-19 (at the end of January 2020), CEPI initiated vaccine development investments with CureVac, Inovio and The University of Queensland, and Moderna, investing \$44 million. In addition to funding translational R&D for a diverse portfolio of COVID-19 vaccine technologies, CEPI also stepped out from its original mandate to support another critical gap in the global system: funding more than \$500 million for “at-risk” manufacturing of vaccine candidates to accelerate vaccine production.

Yet while CEPI was an important early mover in COVID-19 vaccine R&D, the scale and relative flexibility of U.S. and other HIC government investments dwarfed resources available through CEPI’s globally-pooled funding mechanism at the outset of the pandemic. This resulted in more of the larger industry players partnering with those HIC governments, the rapid development of mRNA vaccines with a product profile less suited to low-resource settings, and the ability of the U.S. and other high-income-country financiers to get first rights to supply through advanced market commitments and purchase agreements used to incentivize industry to action.

### ACCESS FOR COVID-19 TOOLS ACCELERATOR (ACT-A)

While CEPI mobilized to help accelerate vaccine R&D for the COVID-19 pandemic, it quickly became clear that there no single entity charged with global leadership and mandate to develop and deliver the array of innovations necessary to support the global response. On April 24, 2020, the Access for COVID-19 Tools Accelerator (ACT-A) launched, bringing together a coalition of governments, scientists, businesses, civil society, philanthropists, and global health organizations (i.e., the [Bill & Melinda Gates Foundation](#), [CEPI](#), [FIND](#), [Gavi](#), [The Global Fund](#), [Unitaid](#), [Wellcome](#), [WHO](#), [World Bank](#), [UNICEF](#), and [PAHO](#)) to support the development and equitable distribution of the tests, treatments and vaccines to control and end the COVID-19 pandemic.



The vaccines pillar of ACT-A, led by GAVI, CEPI, and WHO and known as COVAX, was established to accelerate the global supply and equitable access to COVID-19 vaccines for every country in the world. Notably, all participating countries in COVAX have equal access to COVID-19 vaccines through the facility at fair prices. Ninety-two LMIC economies are eligible to access vaccines through the COVAX Advance Market Commitment (AMC) facility, and as of June 2021,<sup>11</sup> more than 44 countries contribute as donors. ACT-A has served as an important expression of global solidarity, commitment to equity, and multilateral cooperation in the fight against COVID-19;<sup>12</sup> however, it has also faced several constraints which have limited its impact to date. These limitations include: a distributed leadership and execution model, bureaucratic hurdles, limited ambition in terms of target setting, underfunding as well as funding competition among the pillars and participating agencies. These challenges are discussed later in this paper.

## 1B. System Failures in the Pandemic R&D ecosystem

**COVID-19 has exposed longstanding weaknesses in the pandemic preparedness and response R&D ecosystem.** There is a clear need to recognize these market and systems failures and take steps to remedy them. Specifically, four key system-level failures are evident: i) market risk aversion, ii) chronic underinvestment in R&D for pandemic preparedness, iii) equitable access failures, and iv) multilateral collective action failures.

These failures are fundamentally different *before* a pandemic than *during* a pandemic.

Before a global pandemic, PRNDs and EIDs with epidemic and pandemic potential typically suffer from lack of global attention and funding, leaving vaccines for those diseases languishing in the R&D pipeline. Private industry and private capital lack incentives to invest, prompting the public sector to step in and de-risk. Yet government often responds based on political self-interest rather than epidemiological need, in some cases acting too late and in other cases overreacting to outbreaks with surge funding that gets pulled once the panic abates, perversely exacerbating future market risk aversion. This volatile approach to investing in EID and pandemic threats as distant, time-limited problems, or problems that primarily impact LMIC regions, is shortsighted because it fails to continually scan for and invest in emerging, novel epidemiological threats and support promising research in countermeasures through to completion.

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**Systems failures** are failures across the entire network of pandemic preparedness and response R&D actors, and the norms, incentives, and processes by which they interact. Systems failures are driven by a series of underlying interdependent failures and inefficiencies including market failures, collective action failures, coordination failures, and failures of equitable access. While each of these terms have various connotations depending on the context, we define each below as they are used in the context of this paper.

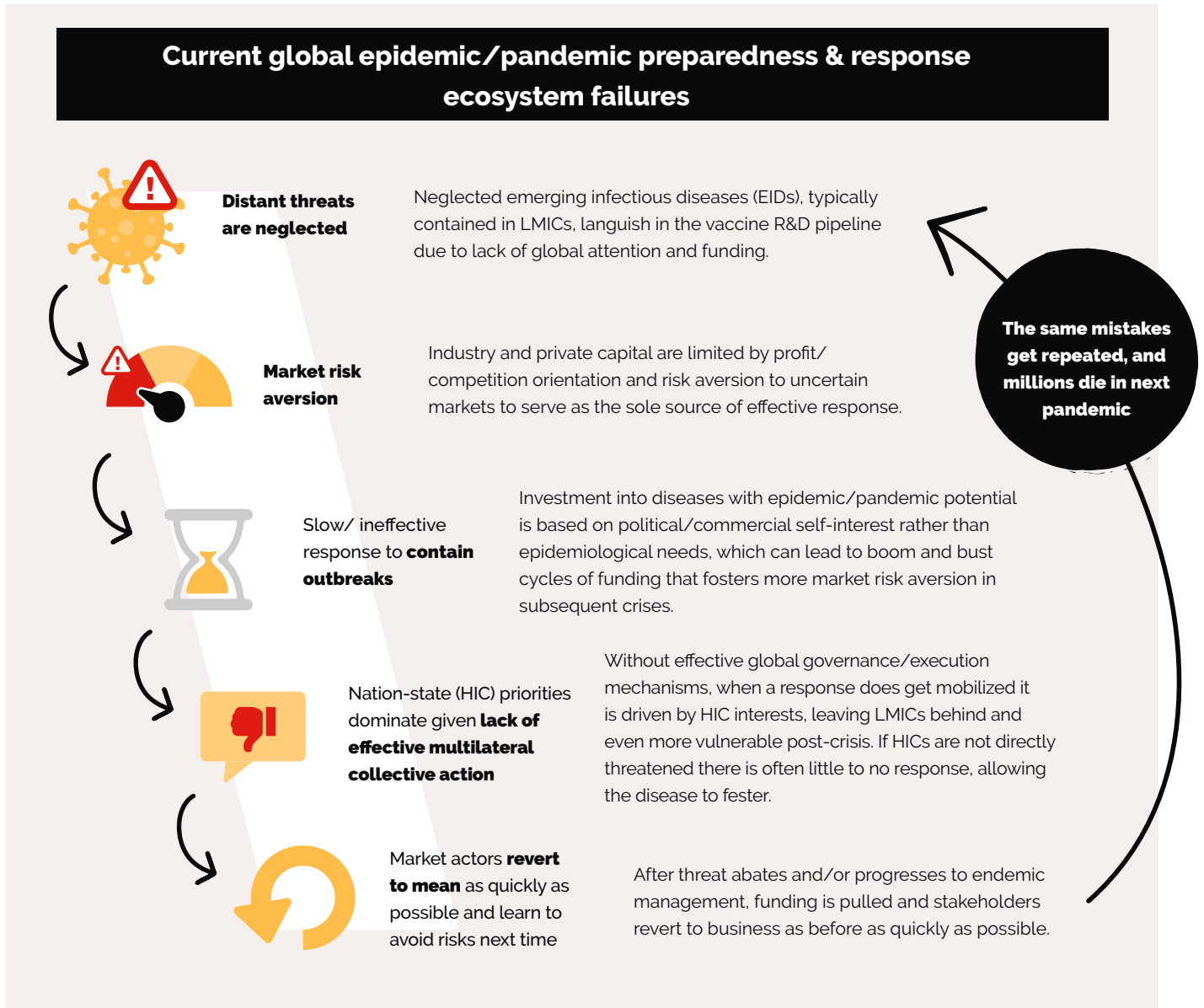


In a **market failure**, individual incentives for rational behavior do not lead to rational outcomes for the group, meaning that each actor in a system makes decisions best for themselves which perversely leads to inefficient or inequitable outcomes for the larger group. Markets, particularly the vaccine markets of interest here, are made up of both private and public sector actors, and market failures can result from the behaviors of either sector as well as the interaction between the two.

Also relevant to pandemic preparedness and response efforts are **collective action and coordination failures**, which occur when actors have the opportunity to achieve mutual welfare gains by working together but fail to do so. Collective action failures are used in this paper to refer particularly to instances when there is a lack of leadership and mechanisms to solve a problem shared by multiple parties globally, such as the lack of a central decision-making or funding body. Coordination failures refer to actors operating in independent siloes, which disrupts the integrated “end-to-end” intervention approach needed for successful vaccine research, development, production, and delivery. Any of these failures can lead to equity failures, whereby a key product or service (i.e., a life-saving vaccine) is inaccessible to certain populations only because of where they are from or how much money they have.

**Figure 1:**

## Chronic Cycles of Complacency and Panic in Global PPR Ecosystem



When the COVID-19 pandemic struck, its extreme impacts on health and the economy galvanized unprecedented global action from many quarters. However, once a disease progresses to a widespread pandemic, there are new and different sets of failures, many of which remain unsolved. On the one hand, the private sector jumped into the market, investing billions to bring multiple effective vaccines to market in record time, often through remarkable inter-firm collaborations from an otherwise highly competitive industry. However, these investments were not automatic: despite

the promise of a large market for countermeasures, private sector engagement was still de-risked and aided by large-scale public sector response efforts, such as through OWS, BARDA, and CEPI as described above.

Global coordination gaps and bottlenecks were also exposed, requiring rapid creation of a new multilateral response mechanism, ACT-A, to accelerate development, production, and equitable access to COVID-19 tests, treatments, and vaccines. While global collaboration through ACT-A is unprecedented and the coordination mechanism was stood up quickly, the fact that no global structure previously existed with a clear mandate or leadership to propel this work, as well as the entity's relative lack of defined central leadership, funding, purchasing power and ambition, highlights a significant collective action failure.

Additional failures linking supply chain, manufacturing, and access bottlenecks uniquely emerge in a pandemic situation as the world works to rapidly progress from R&D, to end product, to delivered product for all populations—an urgent priority with an urgent timeline during a pandemic, but one that will span a much longer time period in a non-emergency situation.

The COVID-19 pandemic is far from over, and an accelerated global effort to distribute and deliver vaccines is urgently required. At the same time, these failures demand an urgent review of the R&D ecosystem for pathogens with epidemic or pandemic potential, given their growing number and frequency. Epidemics and pandemics are not one-size-fits-all, and each event creates unique market dynamics, with different gaps and bottlenecks, that may be impossible to predict or guarantee at the outset. Accordingly, any future system will need to be forward-looking and nimble—because while we can outline a myriad of potential systems and market failures, how, when, and if they manifest will change according to disease, geography, timing and other circumstances.





**2**

# **Exploring System Failures in Pandemic R&D and the Role of CEPI**

The following sections detail deeper analysis of each of the key systems failures in the pandemic R&D ecosystem and how CEPI can serve to address them, namely: i) market risk aversion; ii) chronic underinvestment in R&D for pandemic preparedness; iii) equitable access failures; and iv) multilateral collective action failures.

## 2A. Market risk aversion

### Vaccine R&D and delivery risks in pandemic and non-pandemic situations

Risk is inherent in any health R&D undertaking—there is always the risk of scientific failure and that a product may not prove safe or effective. However, understanding system-level failures related to risk appetite in the pandemic preparedness and response R&D ecosystem requires an appreciation for many specific types and degrees of risk, as well as which actors are willing and able to absorb those risks.

**Even under normal conditions, vaccine development is costly and time-intensive, with a relatively weak risk/reward proposition compared to other business lines of medical R&D.** In general, vaccine development from discovery to licensure can cost billions of dollars and take over a decade to complete, with an average 94% chance of failure.<sup>13</sup> Under non-pandemic circumstances, commercial R&D actors take a deliberate sequenced approach across each stage of the vaccine development process in order to manage risk by investing incrementally as each milestone is achieved. Taking fundamental risks like these comes with the expectation of proportionate reward. However, additional risks related to demand and profitability for vaccines for health emergencies pose yet more uncertainty and risk that frequently tip the scales against private sector engagement.



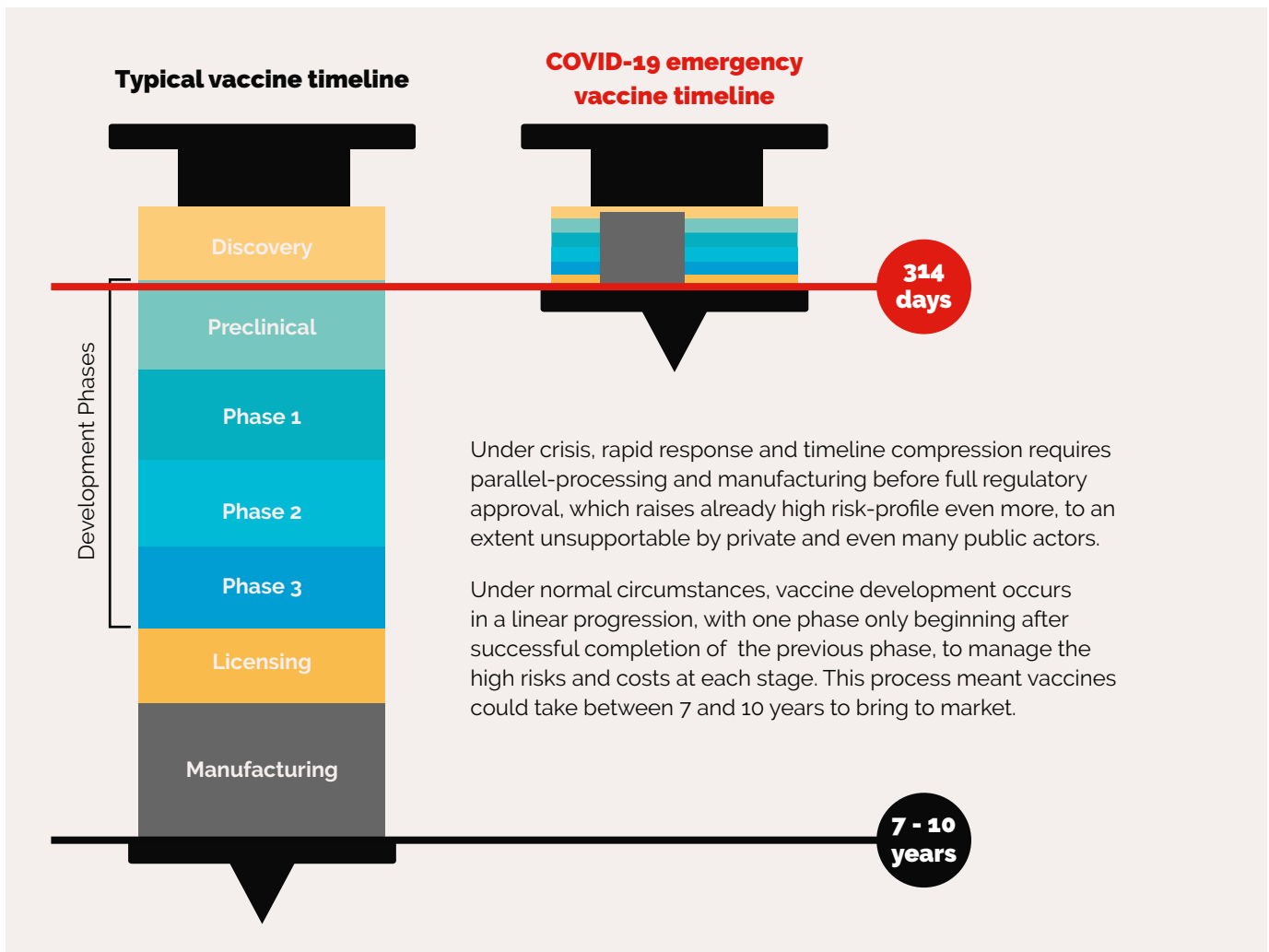
**Low profit potential:** If a particular vaccine will primarily be used by populations located in resource-poor countries there will be low ability to pay, even if demand and volume is high, dampening the profit motive, and prompting reduction or elimination of less profitable products.

**Unpredictable demand:** Disease trajectory can be difficult to predict, such that by the time billions of dollars have been sunk into R&D, the disease threat may have already diminished, dampening demand and causing companies to “miss the market”, or face volatile earnings, which is also a strong disincentive for private industry.



**Fragmented demand:** Even if total vaccine demand is high and profitable across many small countries, aggregating this demand by negotiating multiple country-by-country procurement contracts and navigating national regulatory requirements, import/export terms, and liability coverage, represent significant costs and risks. While this could create a combined large and lucrative market, industry can prefer easier routes to profit, including foregoing a large global market for smaller, national ones."

**Figure 2:**  
Vaccine Development and Production Phases



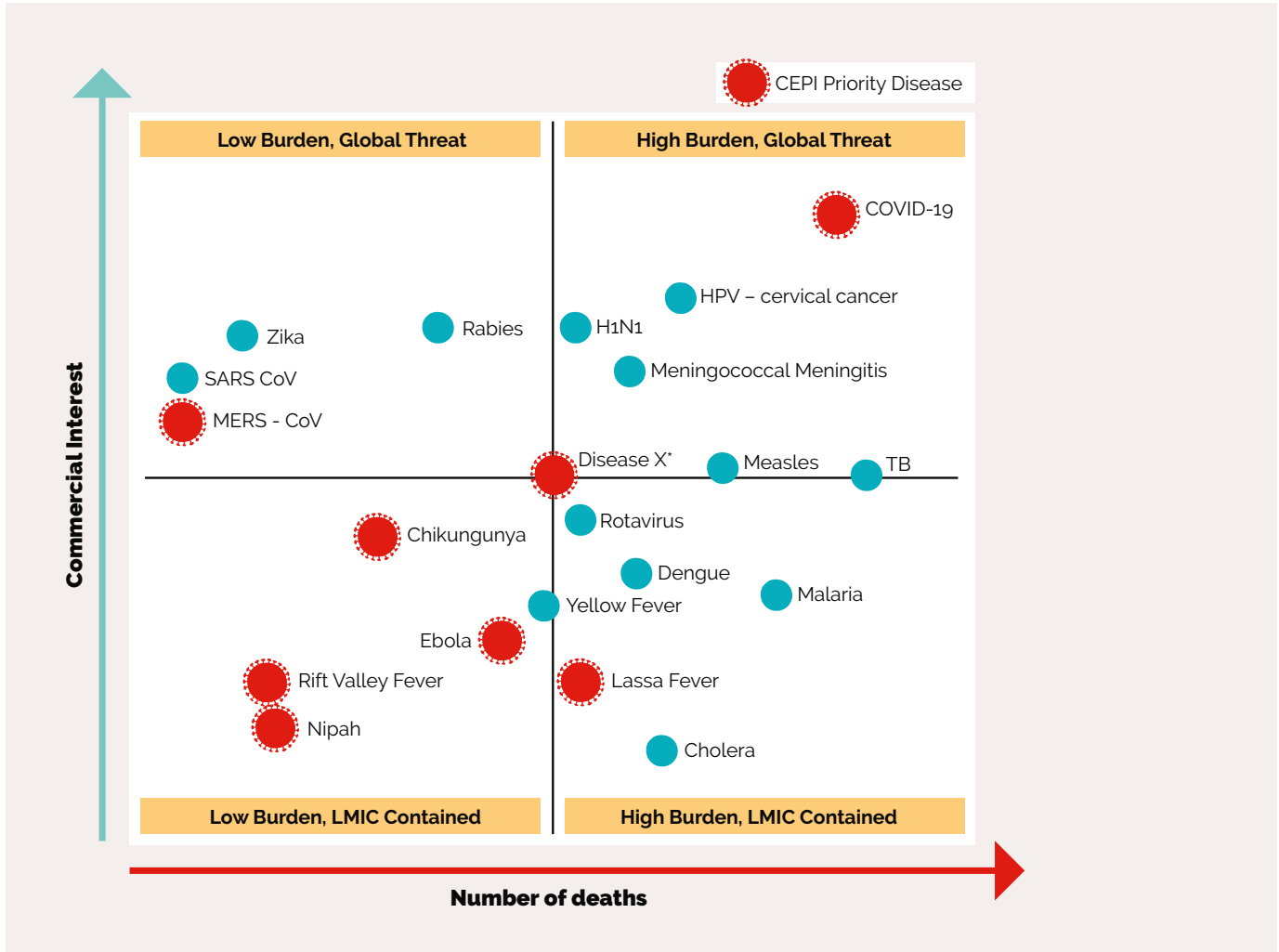
**In a global health emergency, the need for speed requires developers to reconfigure and parallel track traditional, carefully sequenced investments, which exacerbates already high risks.** For example, whereas costly manufacturing investment is typically withheld until a product has successfully achieved regulatory approval and licensure, in the case of COVID-19, rapidly scaling production of vaccines called for large investments in commercial-scale manufacturing capacity (millions and billions of doses) *before* full regulatory approval/licensure. As outlined in Figure 2, the 314-day period it took to develop a COVID-19 vaccine represents an unprecedented compression of normal vaccine development timelines. While costly in any situation, if vaccines proved ineffective or unsafe, at-risk investments in manufacturing could create huge and expensive losses.

**In the COVID-19 response, funding for “at-risk” manufacturing and advance purchase of vaccines created and exacerbated market gaps and failures.** While some HICs and large pharmaceutical companies did invest heavily in R&D and manufacturing, this structure tipped the access scale towards those who put in capital and already had R&D platforms capable of addressing COVID-19. As such, HICs who financed R&D and at-risk manufacturing were able to reserve all or most of the production for their own citizens instead of prioritizing a global pool of vaccines to be distributed based on global need. CEPI and philanthropic organizations like the Bill & Melinda Gates Foundation stepped in to partially fill the gap in at-risk manufacturing for global populations, but this was juxtaposed against HIC manufacturing investments, and coupled with the time it took to develop and fundraise for a fit-for-purpose, global, and equitable structure for COVID-19 vaccine procurement through the COVAX Advanced Market Commitment, global access to vaccines was significantly slowed.

**The COVID-19 experience should imprint some key lessons to mitigate future threats from market or manufacturing risks.** However, the world also needs to avoid the trap of believing that the next pandemic will play out in the same way as the current one and that the bottlenecks and gaps will be the same. In the next pandemic, the vaccine science may prove far more complex, costly and time-intensive—echoing the longstanding efforts to develop effective vaccines for HIV, malaria, and tuberculosis, whose complex and mutating virus and parasite structures continue to challenge vaccine science. mRNA and other current technology might not be appropriate for the next pandemic threat, requiring new and different technology platforms. Manufacturing and procurement bottlenecks might look different or become secondary to scientific challenges.

**Each different pandemic threat presents different market dynamics for private sector R&D actors to consider.** Ideally, disease burden and epidemiological considerations alone would drive private sector investment in vaccine development, but as noted above a variety of other factors—heavily weighted toward risk appetite—affect commercial interest, along a complex spectrum (see Figure 3).

**Figure 3:**  
Spectrum of Disease Market Characteristics<sup>14</sup>



This variability and unpredictability of each new epidemic or pandemic threat calls both for flexible funding for innovation across a broad range of tools and technologies as well as for sustainable, flexible funding approaches that can be forward-looking and mitigate risk in whatever form it manifests.

## Responses to market risk aversion challenges

**COVID-19 and previous pandemics and epidemics show that disease trajectory is inherently unpredictable and presents different market dynamics with different risks, failures, and gaps.**

Individual R&D actors will have different risk tolerance, with different appetites for incentives based on their portfolio strategy, existing resources, risk-adjusted profit & loss projections, previous experience,

perceived shareholder risk tolerability, C-suite interest level, and other variables. To counter this variability, a wide range of risk-sharing tools is needed to tailor the right incentives to the right actors at the right time.

**Public-sector actors in governments and multilateral organizations can leverage a variety of tools to reduce risk by subsidizing costs or guaranteeing revenue for private actors.** Subsidies to help defray the costs, and therefore risks, of vaccine R&D and manufacturing activities represent “push” funding that motivates firms to innovate and engage. Incentives that “pull” innovators and the private sector into the market work by guaranteeing price, volume, and/or revenues for a successfully developed product where market demand risk is high. These include advance purchase contracts/agreements with specific companies to purchase a specific product they provide, at a negotiated volume and price (e.g., OWS, the European Union Advance Purchase Agreements, and the initial phases of COVAX), and Advance Market Commitments, commitments to purchase a yet undeveloped vaccine that meets certain pre-set product specifications, disbursed to whichever supplier can eventually deliver.

**There remains ongoing debate on how to balance push v. pull incentives to make the most effective use of limited or constrained public sector resources;** these points are summarized in Annex 3.<sup>15</sup> Ultimately, a financing strategy that makes best use of public funding requires the ability to deploy combinations of push and pull levers that respond to changing market dynamics and recognize risk-taking across a spectrum rather than push-only or pull-only.

**COVID-19 has also demonstrated that market uncertainty and technical risk is often so high for a private sector developer at the outset of a pandemic that R&D push funding is vital to get research underway and candidates into the pipeline quickly.** Traditional pull mechanisms alone may be insufficient if they only make commitments for successfully developed and delivered products, forcing the developer to absorb all the risk. At the same time, some form of a demand guarantee has been shown to be needed as additional incentive and to stimulate ongoing R&D risk-taking by the private sector.

**Because a pandemic affects the entire world—and therefore requires expedited access to vaccines and other tools for everyone, everywhere—publicly-funded incentives must be balanced with conditions that ensure the global public interests are served.** This can be a delicate balance to strike: too much conditionality may slow or stop negotiations with developers seeking more flexible financing, which might pose unaffordable delays in an emergency; on the other hand, too little conditionality risks over-subsidizing the private sector (or accusations thereof) and supporting products that have limited global applicability or fail to reach the most vulnerable equally, which is the situation the world is experiencing 18 months into the COVID-19 pandemic.

Indeed, during COVID-19 it has been perceived that in the urgent response by governments with deep pockets, for-profit companies benefited excessively from multiple sources of public subsidy combining R&D push funding incentives, purchase guarantee pull incentives, and “at-risk” down payments to reserve manufacturing capacity—all with very few conditions attached to ensure global access and equity.<sup>16</sup>

Yet this only tells one side of a more complex story, where the high risks and losses of many previous R&D failures borne by industry, the high opportunity cost of more profitable business opportunities available to industry actors, and the parallel investments of private capital are often not acknowledged alongside the size and scale of public sector investments. As even some public health actors like the Africa CDC recognize, fiscal discipline and the requirement for a strong return on investment are the very factors that allowed private industry to gain the decades of expertise and experience that enabled their rapid development of COVID-19 vaccines. Nonetheless, if the public sector is going to help share these costs and risks, the benefits/rewards must also be fairly shared between private and public needs and expectations. This is especially true in a pandemic situation where vaccines and other tools are a necessary global public good, lest the disease continue to spread in some parts of the world. This calls for careful consideration, and perhaps amplification, of conditions and protections aligned with public financing to develop products and ensure equitable access, such as the right to direct supply to specific populations, conditions around pricing, or conditions around intellectual property and data sharing.

## CEPI's role in addressing market risk aversion

**Given these multiple and varying risk considerations, there is clearly no one-size-fits-all approach to designing the right set of incentives and risk-sharing terms.** Each disease market presents unique bottlenecks and risks, calling for incentives and funding with enough flexibility to meet new challenges and engage developers effectively. A prepositioned global platform to deploy such funding and incentives, such as CEPI, can help with the forethought and speed needed to drive action and engage partners to counter emerging epidemics and pandemics before they explode into crises.

**During COVID-19, the high risk of developing a vaccine in an emergency outweighed the potential global market for many industry actors.** As a result, HICs, notably the U.S., invested heavily to de-risk COVID-19 vaccine R&D—but with provisions that allowed investor countries first and primary access to resulting vaccines. In contrast, CEPI was the only multilateral entity investing to de-risk vaccine R&D/manufacturing at scale with global interests—and specifically the needs of low-resource settings in mind.

**CEPI's core funding tools are “push” funding in the form of grant and loan agreements that incentivize innovators through lowering their cost and risk of engaging in EID vaccine R&D.**

Depending on the particular stage of development and gap to be filled, CEPI's funding can be used for:

- Enabling science and earlier-stage development activities such as preclinical studies, clinical trials, regulatory planning and R&D-scale production (thousands of doses)
- Ramping up manufacturing to supply larger amounts of vaccine
- Securing large-scale manufacturing capacity to produce national/global supply (hundreds of millions and billions of doses), including funding the transfer of proprietary technology to manufacturing partners for scaling and having a geographically distributed footprint

**CEPI's funding of upstream R&D activities is meant to complement pull funding from downstream actors who would procure and distribute developed vaccines to global populations.**

This complementarity is evident in the structure of the COVAX Advanced Market Commitment (AMC), which serves as an explicit mechanism for CEPI to coordinate its funding for COVID-19 vaccine R&D with downstream procurement actors like GAVI. Through this partnership, push and pull incentives are combined with the goal of developing and delivering vaccines that are affordable and appropriate for low-resource settings.

**CEPI's upstream funding comes with conditions designed to serve its core public interest and equitable access mandate.**

These conditions are individually negotiated for each partnership and contract, to ensure that products successfully developed with CEPI funding can be supplied to target populations, at affordable prices in ample supply, and with requirements around sharing data and transferring technology for manufacturing scale-up in low-resource settings. Specific conditions can include:

- Right of first refusal for LMIC procurement (e.g., COVAX) for CEPI-funded product
- Expectations around pricing, such as pricing limits in LMICs
- Data sharing requirements
- Manufacturing-related conditions such as technology transfer to manufacturing agents, manufacturing in new locations, or rights to reallocate unused CEPI-funded reserved manufacturing capacity
- Funding released conditional on reaching staged milestones



**Figure 4:**

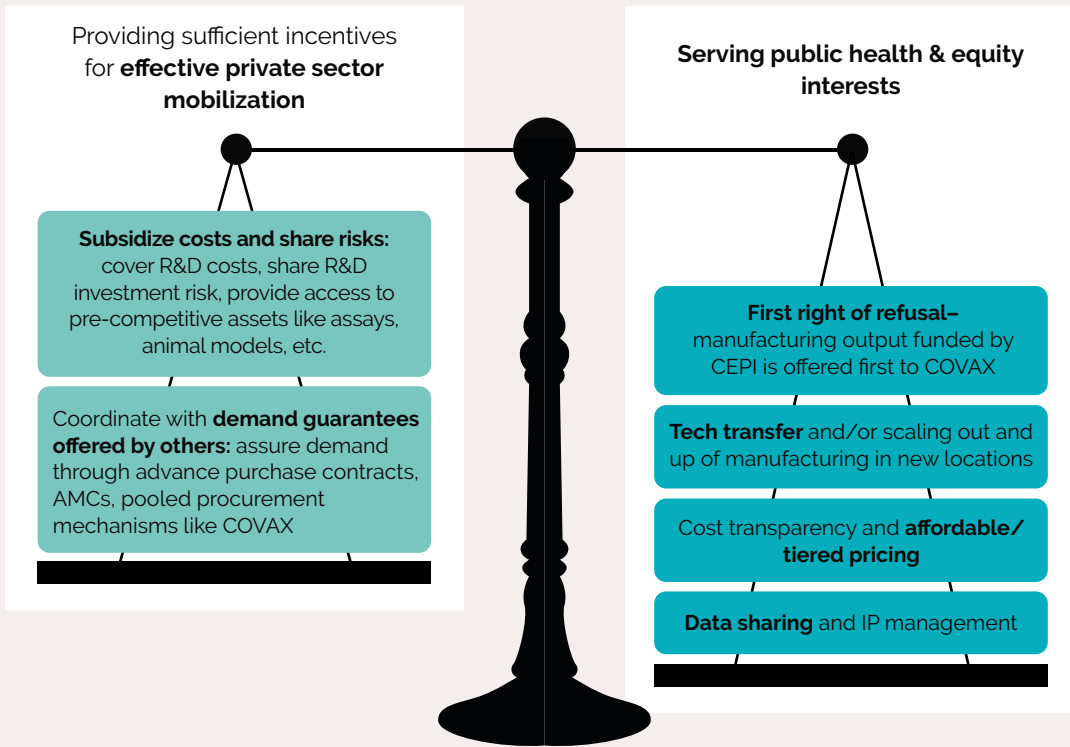
CEPI's instruments and terms

CEPI provides direct R&D “push” funding, coordinates with “pull” funding sources, and attaches conditions to its funding to help ensure its money is used to serve public health and equitable access

**CEPI's R&D funding instruments**

**Vaccine development agreements** generally include these activities: preclinical studies, clinical trials, regulatory planning and development of the manufacturing process at a small scale.

**Scale-up of manufacturing agreements** focus on developing manufacturing processes that can provide much larger amounts of vaccine than the more limited manufacturing processes needed for vaccine development.



**CEPI has the ability to deploy a range of incentive levers flexibly, based on the particular gaps of each disease market and in service of long-term global health security interests.** However, it still takes billions of dollars and many partners to get even one vaccine fully to market. The role of any single financing actor must be considered with this perspective, making it unrealistic to expect that one organization like CEPI (with relatively limited resources compared to other global actors) can fully address all market risk aversion. The COVID-19 experience shows that many, flexible, and dynamic incentives are important for quickly accelerating vaccine development during an emergency. Annex 4 details examples of how CEPI offers different incentives according to the different needs of each vaccine market.

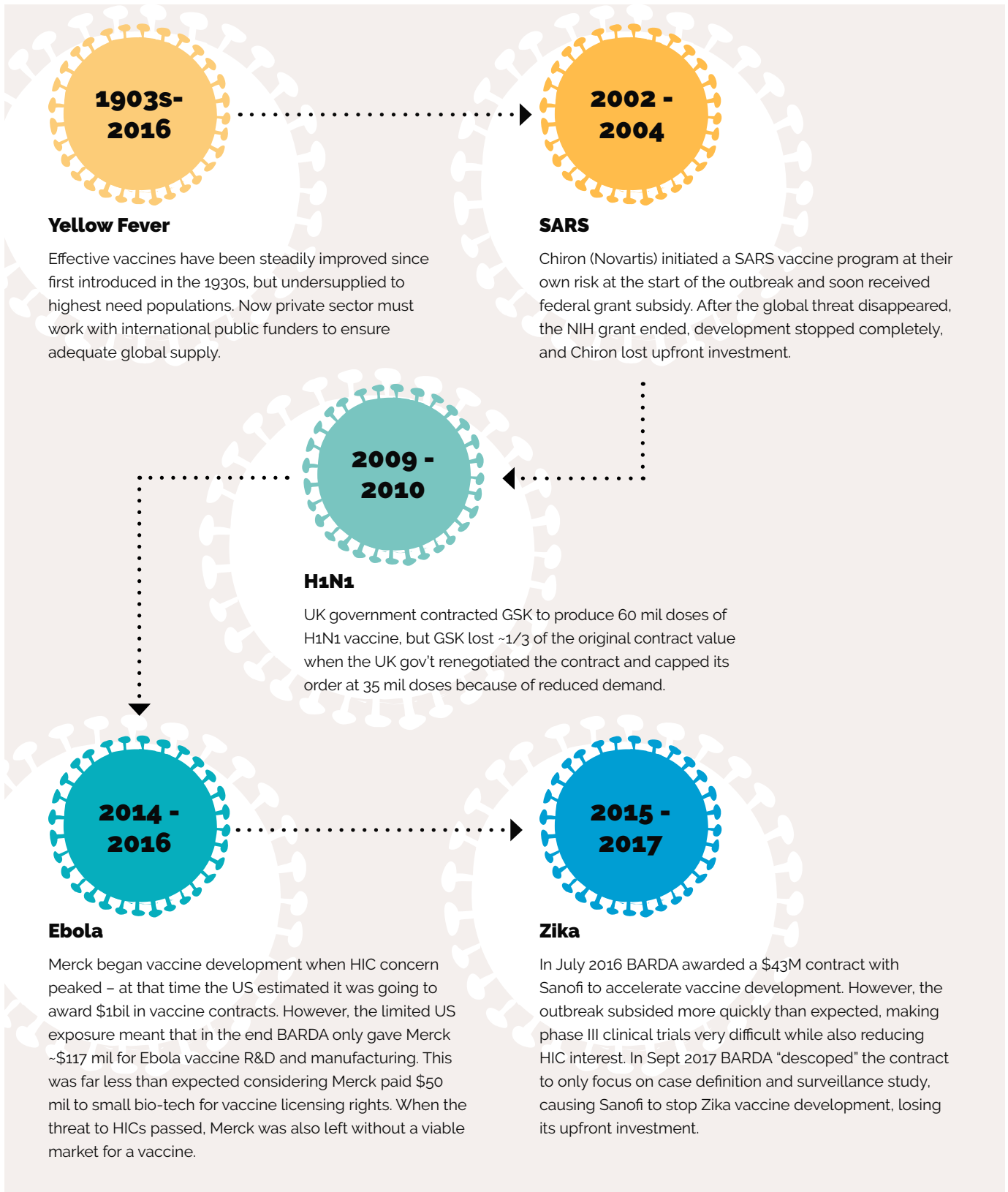
## 2B. Chronic underinvestment in vaccine R&D for preparedness

**Despite overwhelming epidemiological evidence and warnings of the threat of a novel respiratory virus growing into a global pandemic, the world has failed to sustainably prioritize and invest in pandemic preparedness.** R&D for vaccines and other medical countermeasures have been chronically underfunded aspects of preparedness that are required to ensure that the world has tools to contain and respond to a disease outbreak before it becomes a pandemic. From 2014-2018, only \$3.5 billion was invested in all stages of R&D for emerging infectious diseases, including for diseases prioritized by the WHO as those with epidemic and pandemic potential.<sup>17</sup> In comparison, the economic costs of the COVID-19 pandemic have been estimated at \$375 billion *per month*,<sup>18</sup> and the global economy is projected to lose a projected \$22 trillion from the pandemic over the next five years.<sup>19</sup>

Of the funding historically invested in EID R&D, 77% came from the public sector, 18% from the private sector, and the remaining 5% from philanthropy.<sup>20</sup> The market failures discussed in this paper point to the relatively small share of financing that comes from the private sector. Yet even public sector funding for EID R&D, while representing the majority of investments, is still extremely limited when compared to other public investments in medical and other R&D. This is in large part driven by a lack of prioritization, where EID vaccines are perceived as a nice to have, not need to have. Instead, public funding for pandemic R&D and pandemic preparedness overall is prone to boom-and-bust funding, with funding surging during an emergency, then quickly reverting to low levels once the perception of a threat has waned.

**Figure 5:**

Historical Market Experience with Epidemic/ Pandemic Vaccine R&D

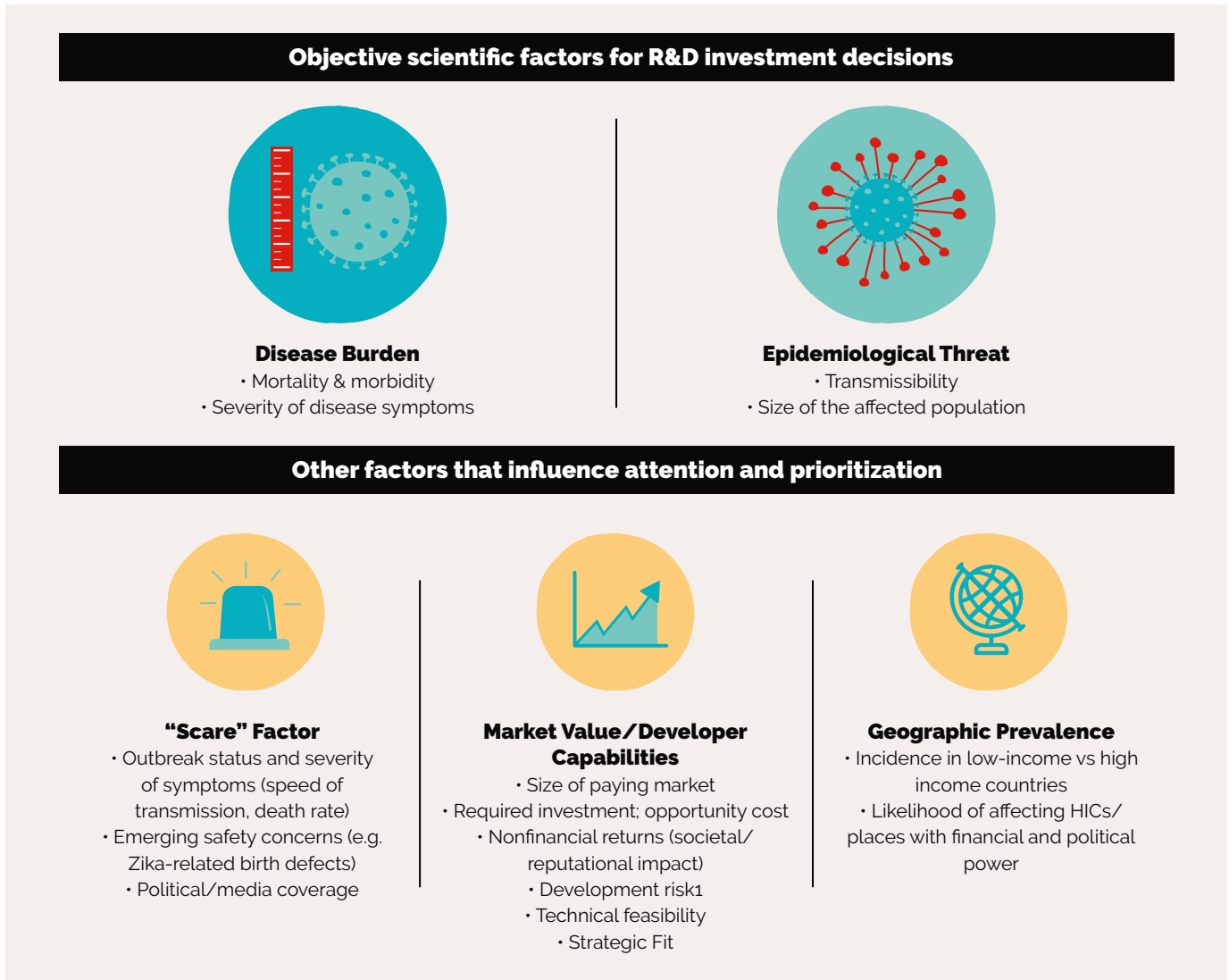


**This repeated cycle of panic and neglect dissuades proactive, forward-looking R&D efforts that could prevent a future infectious disease outbreak from spreading.** As an example, funding for Ebola & Marburg viruses more than tripled between 2014 and 2015 in response to the West African Ebola outbreak, peaking at almost \$600 million in 2015. As the virus waned in 2016—both reducing the immediate disease threat and challenging late-stage clinical trials that relied on disease in the population—Ebola funding dropped too, falling by around \$125 million in both 2016 and 2017.<sup>21</sup> This volatility in the market can “burn” industry partners who are in the middle of product development—leaving them without reliable resources to continue development of a risky product and effectively punishing them for diverting resources and time from other business opportunities. An industry partner who has been burned from an experience of developing a vaccine during an emergency may find engagement during the next health crisis too risky, effectively shrinking the pool of qualified partners; indeed, only a handful of the leading vaccine manufacturers decided to pursue a COVID-19 vaccine. In addition, if industry does not pick up the tab to continue the work, the decline in public funding can lead to premature stoppages of work, leaving the world without a finished tool when the same disease or virus emerges again despite large past investments. Because of funding fluctuations and shifting priorities, it was not until the 2018-2020 outbreak in the Democratic Republic of the Congo (DRC) that the development and regulatory approvals of Ebola vaccines were complete—a deadly delay.

**Underlying the critical failure of both the public and private sectors to invest in preparedness is the fact that political and/or commercial interests often trump science, epidemiological risk, and global needs.** Sometimes, when manifested by the private sector, this results in prioritization and funding of R&D with the greatest potential for long-term, sustainable profit—which usually benefits the endemic needs of high-income economies with the most resources (e.g., diabetes treatment R&D v. vaccine R&D). Other times, when manifested by the public sector, this is driven by political expediency, where headline-grabbing disease outbreaks generate a surge of attention and investment that may not necessarily be warranted by the actual transmission and mortality rates of the disease.

**Figure 6:**

Factors that Drive Actual R&D Funding Priorities<sup>22</sup>



**It is always easier to identify gaps and inefficiencies in pandemic preparedness, including gaps in R&D, with the benefit of hindsight.** When pandemic preparedness and response is viewed as a continuum—including other efforts needed to prevent epidemics/pandemics before they spread, rapidly suppress an outbreak with pandemic potential, and rapidly develop and deploy a vaccine and other health technologies when a novel pathogen emerges—the gaps in investment become more apparent in real time. “Preparedness” is not merely being ready to mobilize quickly during a pandemic, but rather all the steps and investments needed to prevent and/or curb a pandemic early, such as comprehensive investments in surveillance, pathogen research, vaccine, therapeutic, and diagnostic development and delivery, and creating functioning “peacetime” structures that can be stepped up in crisis response.

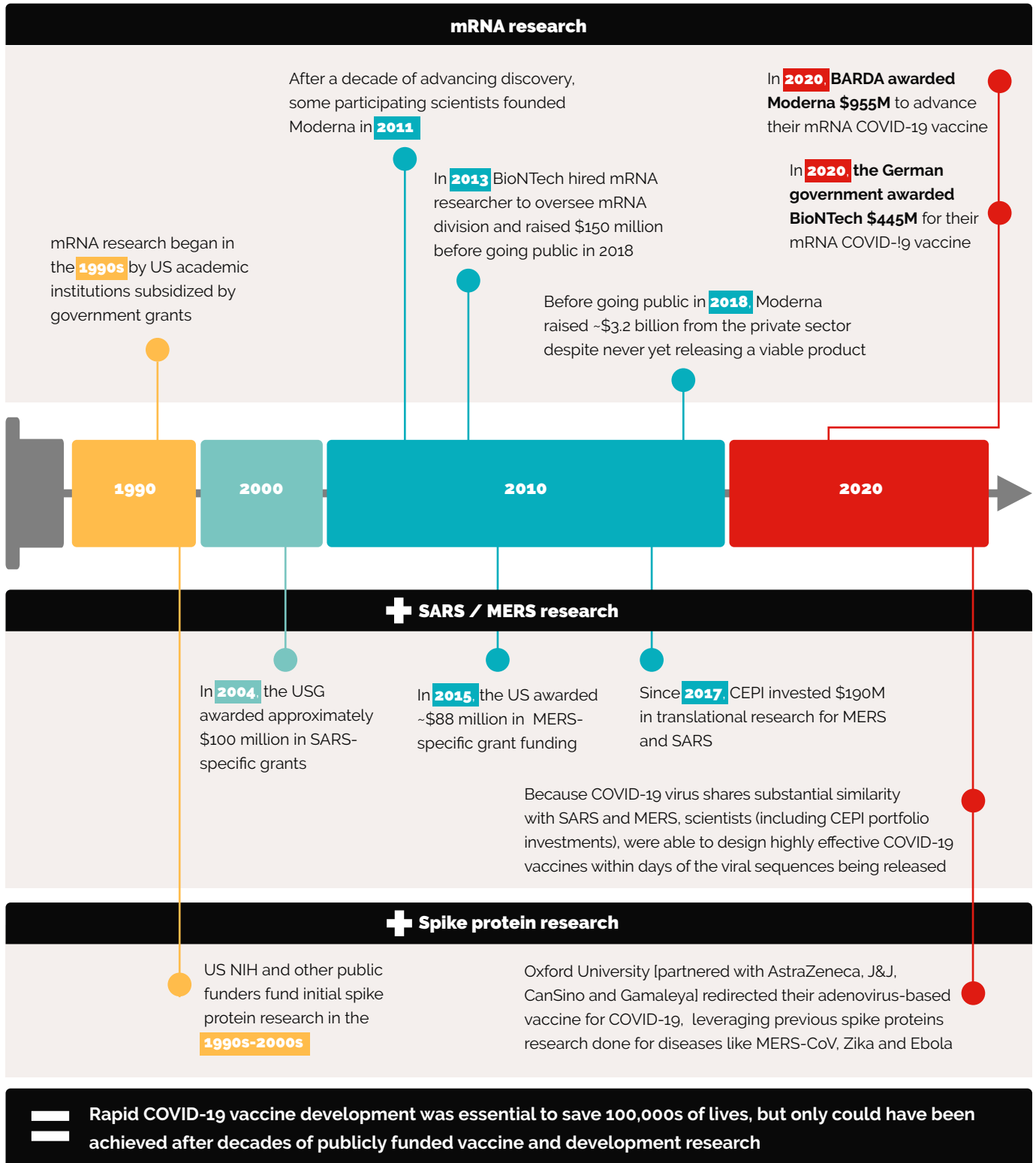
**Ultimately, preparedness means that outbreaks can be stopped in their tracks before they become devastating pandemics.** This requires substantial resources and capabilities from both the public and private sectors: the private sector brings unique know-how, capacity for innovation, and ability to scale, while the public sector can de-risk participation in uncertain markets and provide incentives to facilitate provision of public goods with high externalities,<sup>23</sup> thereby filling market gaps in foundational research, inter-organization collaboration and equitable access to lifesaving tools and supplies.

**In examples where the public sector has made a serious investment to de-risk and promote health R&D over time, the results are notable.** Industry's ability to bring successful COVID-19 vaccines to market within a year was made possible by steady public investments in global health R&D, including R&D for coronaviruses and mRNA platform technologies that started decades before. Public sector funds basic science and research that builds a scientific base and platform enabling a sprint across the finish line during a crisis—a fact that is often overlooked as breathless headlines during an emergency celebrate the achievements of specific companies advancing successful technologies. Steady progress in the prioritization of global health and infectious disease R&D is evident in the speed of the COVID-19 response.

Ultimately, preparedness means that **outbreaks can be stopped in their tracks before they become devastating pandemics.**

**Figure 7:**

Recent COVID Vaccine Breakthroughs are Premised on Decades of Previous Public Investments<sup>24</sup>



## CEPI as a model for addressing lack of investment in preparedness

**CEPI was set up to overcome the chronic failures to invest in preparedness.** Its purpose is to forecast diseases with epidemic potential and invest in vaccine countermeasures to address them. In its current iteration, CEPI has jumpstarted needed research in EID vaccines, which has proved critical to accelerating pandemic R&D. Within three years of inception, CEPI built up a \$705 million portfolio of 20 vaccine candidates targeting 5 priority EIDs, along with three rapid response platforms to develop vaccines against Disease X and an array of enabling science projects.<sup>25</sup> As part of this portfolio, CEPI invested \$50 million to develop platform technologies that could enable development of rapid-response vaccines against newly emerging pathogens and over \$140 million to develop vaccines against MERS, a disease caused by a coronavirus related to the COVID-19 virus. CEPI's pre-existing partners working on these projects were able to quickly pivot to COVID-19 vaccine development when the pandemic struck. This enabled CEPI to make its first investments in potential COVID-19 vaccines just weeks after the genetic sequence for the virus was made public.<sup>26</sup> In the space of just 8 months, CEPI was able to build a portfolio of COVID-19 vaccine investments that, while not as large in dollar value as those of national HIC funders, represented a portfolio diversified by technology, product profile, geography and supplier.<sup>27</sup>

**Public sector and philanthropic funding are critical to lay the preparedness groundwork required for speed during a pandemic.** CEPI is one of several entities leveraging public funding for pandemic R&D, with other partners such as the U.S. National Institute of Health, BARDA, Wellcome Trust, Europe's Innovative Medicines Initiative, the Bill & Melinda Gates Foundation, and others. The extent to which these or other institutions may pivot to more actively prioritize "Disease X" research in the wake of COVID-19 remains to be seen. Meanwhile, CEPI has already built a program and foundation to accelerate this work including:

- Forecasting the top 10-15 virus families with Disease X potential;
- Leveraging mRNA and other vaccine platform technologies to develop multivalent vaccines for each virus family;
- Shepherding each family vaccine candidate through clinical trials and regulatory review processes to ensure they are safe and effective;
- Building clinical stockpiles of approved vaccines; and
- Developing monotypic vaccines for each new epidemic/pandemic threat virus and variant that emerges and gets genetically sequenced.<sup>28</sup>



This preparedness process is the foundation of CEPI's new five-year strategy to deliver safe, effective vaccines that are ready for use within 100 days of a novel disease outbreak. However, this dramatically accelerated R&D timeline will only be possible if investments are made proactively to develop, approve, license, and stockpile vaccines against a range of virus families well *before* an outbreak.

**Responding with countermeasures as quickly as possible is critical to stopping a pandemic and preventing tremendous loss of life.** With COVID-19, had vaccines become available within 100 days, countless lives could have been saved—not to mention the related social and economic devastation wrought by this pandemic. On May 8, 2020, fewer than 3.8 million cases of COVID-19 had been recorded and on December 8, 2020, when vaccines were first administered, more than 67 million cases had been confirmed.<sup>29</sup> But this type of system hinges on sustained, pre-allocated funding that is forward-looking, designed to anticipate need and disburse funding based on epidemiological data, rather than political or commercial attention which is too often reactive. When countries and companies scramble to provide surge funding and R&D capacity only after a health emergency has manifested, it is typically already too late to deliver effective tools fast enough to stem the crisis, resulting in greater loss of life and driving a system where vaccine developers “miss the market” as R&D can take longer than the natural cycle of disease. CEPI can help fill a critical gap by providing pre-positioned, anticipatory financing to drive a more comprehensive approach around the prevention-preparedness-response continuum.

## 2C. Equity and access failures

**The stark imbalance in the availability of COVID-19 vaccines between high- and low-income countries is the most egregious example of the failures of the global health R&D system to promote global access and equity.** Even if failures around risk and preparedness can be overcome, persistent failures in traditional R&D financing contribute to continued disparities between high- and low-income countries, with the most vulnerable nations and communities often shouldering disproportionate disease burden and risk. Just as different diseases generate different market dynamics, gaps, and risks, so too can they pose different types of failures when it comes to equitable access.

**Figure 8:**

Different Funding Gaps and Equity Failures for Regional EID Markets vs. Global Pandemic



On one end of the spectrum, there are neglected EIDs, such as Lassa fever, Nipah, and Rift valley fever, which are similar to poverty-related neglected diseases in that they traditionally receive little public/private investment based on a perception that they represent distant threats and primarily affect populations with low ability to pay. For these disease markets, there is generally underinvestment across all stages of the vaccine lifecycle, which means potentially life-saving vaccine do not get developed at all. While the U.S. government and other HICs do invest in research and development for such diseases, the majority of this funding is for basic research.<sup>30</sup> This leaves a particularly large gap in funding to bridge from early-stage R&D to commercialization, the “valley of death” of the R&D lifecycle where many promising new tools perish without sustained funding.

**When neglected EID vaccines manage to attract funding to escape the “valley of death”, they still face challenges further downstream in terms of access to finance for costly and limited manufacturing capacity.** Manufacturing capacity for vaccines is currently constrained and concentrated to a limited set of geographies. While some industry players have tried in the past to build greater distributed manufacturing capacity globally, including in LMICs where most of the global population resides, geographically diversified vaccine manufacturing remains a major gap, with most LMIC geographies lacking the infrastructure and human capital to establish reliable vaccine manufacturing capabilities at scale. Most manufacturers are hesitant to diversify geographically and few see a compelling business rationale to justify construction for multiple global hubs. Even if a sufficient supply of doses can be successfully manufactured, procurement and delivery to LMIC populations presents serious equity and access challenges. Successfully getting shots in arms requires a functioning and trained health workforce capable of reaching last-mile communities, as well as personal protective equipment (PPE) and often access to cold-chain infrastructure. Stories abound about finally getting vaccines delivered to rural clinics in low-resource settings, only to have them expire or be spoiled due to lack of healthcare personnel or infrastructure.<sup>31</sup>

On the other end of the spectrum are threats more widely seen as global pandemic threats, which receive more international and HIC attention—coronaviruses like COVID-19, MERS and SARS are recent examples. However, too often the funding and response to these threats serves primarily the interests of those nations with the most resources and the ability to control the market, to the detriment of the rest of the world. As has been extremely apparent during the COVID-19 pandemic, all countries necessarily prioritize their national interests in a global crisis, with political priorities and obligations to citizens taking precedence over epidemiological or equity considerations. Until vaccine production has scaled up to be widely available, the countries with higher purchasing power, production capacity, or access to inputs hold an advantage to monopolize scarce global supply, leaving the rest of the world waiting and vulnerable. Collective memory is short, and the distributed

networks for raw materials and inputs that have expanded in response to COVID-19 could prove to be a hard-won gain that is at risk of being reversed when the emergency subsides, as markets pivot back to form in search of the cheapest goods. For private industry, the more limited ability to pay and relative lack of purchasing power of LMIC buyers means that even though the global need and demand for vaccines in the context of a pandemic may be huge, they will favor working with the more “sure bets” from HICs with more accessible and reliable markets, higher risk financing capacity and greater ability to provide guaranteed demand incentives.

**Even when new products can be developed with remarkable speed, other significant bottlenecks remain that prevent equitable access to vaccines.** Chief among these is manufacturing and supply chain bottlenecks which, if left unaddressed, will continue to affect equitable access during the next pandemic. As of April 2021, the 6 countries with the largest manufacturing capabilities (U.S., India, Japan, Canada, Mexico, South Korea) have 33% of the world's population but represent 63% of the world's COVID-19 vaccinated population.<sup>32,33</sup> This statistic demonstrates that countries with greater vaccine production capacity have greater access to vaccines produced. Yet expanding global manufacturing capacity requires sustained investment in both costly infrastructure and human capital—and ongoing use of this infrastructure keeping it “ever warm” is critical so that it does not fall stagnant or into disrepair. Intense debates about intellectual property (IP) and whether requiring developers to waive IP protection in the event of a global health crisis can facilitate faster technology transfer and diversified manufacturing/access to novel technologies continue to rage on. However, vaccine manufacturing is more complex than simply making IP available; in fact, Africa CDC's experience shows that IP has *not* been the primary hold up. The recent announcement by WHO, Africa CDC and industry partners to establish a South African mRNA technology transfer hub will allow for greater and more diversified vaccines manufacturing capability.<sup>34</sup>

**Many of the same equity challenges for regional EIDs are also equity challenges for global pandemic threats, so it is dangerous to treat them as disconnected markets.** While at a high level there are different market dynamics for neglected EIDs and global pandemic threats, it is important to appreciate that what makes a disease a pandemic threat is its epidemiology—its ability to spread and ease of transmission, along with its lethality—not its geography of origin. If HICs drive pandemic R&D and create tools that are not appropriate for or accessible to all global settings or available in a timely manner, disease threats may dissipate in some countries while lingering in others. Not only does this mean that the needs and lives of vulnerable populations are overlooked, but also that the pandemic threat never truly disappears. Without changes to priorities and incentive structures to prioritize global access and equity, this is likely to be true for the next “Disease X” that could be far worse than COVID-19.

**All told, equity failures have potentially far-reaching repercussions that threaten the health, security, and prosperity of LMICs and HICs alike.** The impact of COVID-19 continues unabated as the virus ravages countries without access to sufficient vaccines. As of July 15, 2021, only 4.2% of total population in Africa has received at least 1 dose of a COVID-19 vaccine, while that number was 63% in Israel, 70% in Canada, and 69% in the UK.<sup>35</sup> Death tolls are believed to be far higher than official numbers suggest, particularly in developing countries, with an estimated 7-13 million excess deaths worldwide since the start of the pandemic.<sup>36</sup> The deadly third wave of COVID-19 in Africa that started in late spring 2021 is directly related to widespread lack of access to vaccines. As long as the virus continues to spread (and mutate) in LMICs that have no or very little access to vaccines, not only does this threaten all countries with continued health and economic fallout, but it also threatens geopolitical stability. Fragile states can deteriorate to failed states under the health and economic burdens of new waves of infection. The longer these global vaccine inequities are allowed to continue, the greater the risk of new COVID-19 variants emerging that have greater potential to evade the current vaccines, as well as to foment unrest as populations in already resource-poor settings rightly demand to know why they have been left behind. Yet HICs overall have been slow to share COVID-19 vaccine doses to lower-income countries that do not have them: At their June 2021 summit, G7 leaders committed 870 million doses by the end of 2022, falling far short of global demand.<sup>37</sup>

**Structural inequities in the pandemic R&D ecosystem will continue to threaten global health security for all if they remain unaddressed.** These inequities perpetuate underinvestment in the highest epidemiological threats, purchasing power imbalances, development of products that are not appropriate for all settings, and exacerbating manufacturing and delivery challenges. As with many other global threats, it is easy for individual countries to mobilize large amounts of funding quickly to protect their citizens, and then move on to the next political priority. It is much harder to collectively address deeply-ingrained structural and systems inequities required for meaningful change and progress in global health security.

## Responses to equitable access challenges

**One of the most important and additive roles of public sector funding for epidemic- and pandemic-related R&D is to provide for the global good and ensure equitable access to lifesaving tools.** Along a spectrum of EIDs with epidemic or pandemic potential to realized pandemics, public sector funding can target the distinctive market failures in equitable access observed in each. For EIDs with epidemic or pandemic potential, public sector funding can fill gaps throughout the entire vaccine development lifecycle to ensure needed vaccines are developed and produced: from basic research and pre-competitive investments, to both early-stage and late-stage

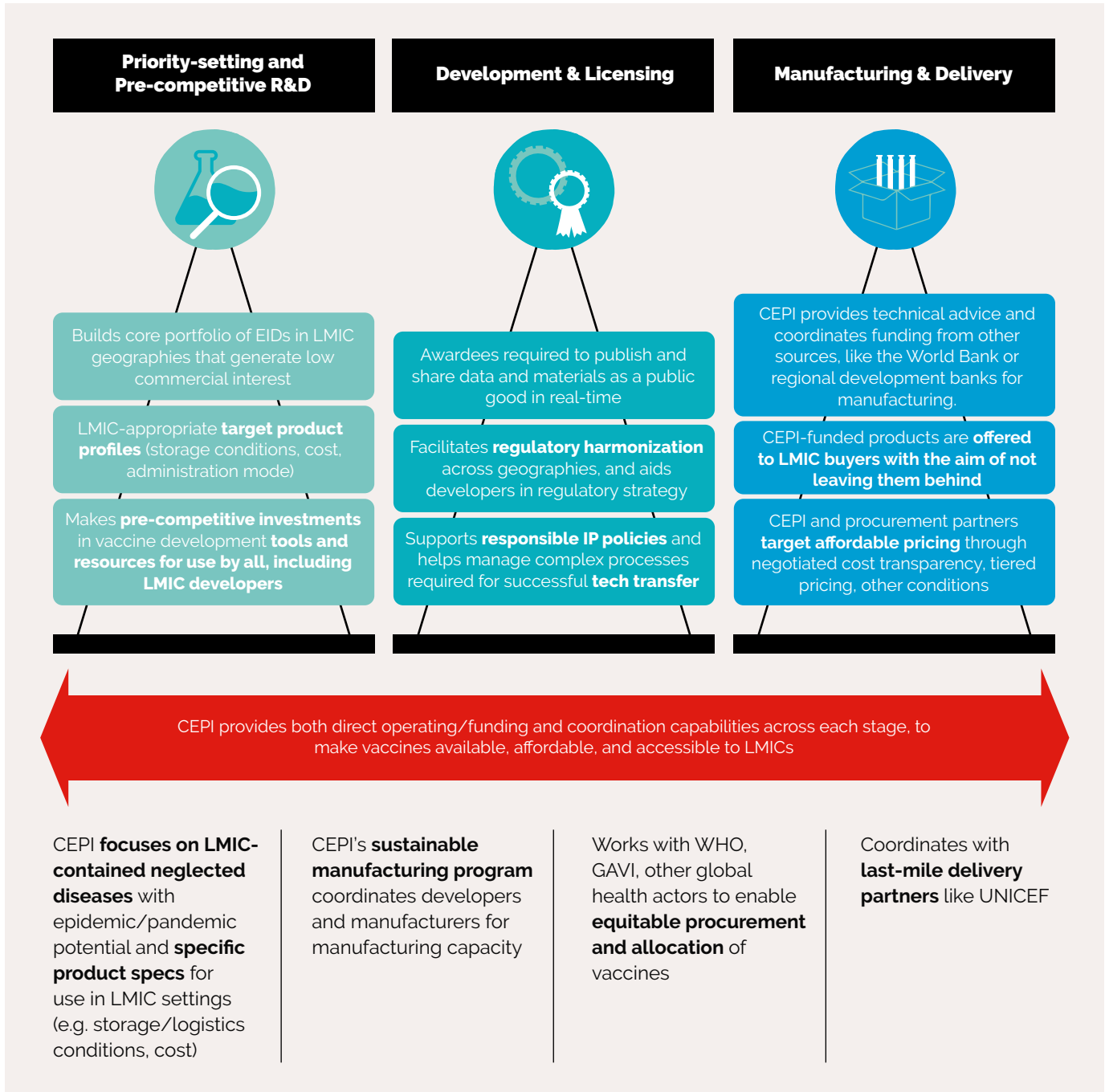
R&D, to explicit coordination with manufacturing and delivery actors. CEPI was created to help fill major gaps in this development cycle, with a focus on supporting translational research to convert basic science all the way to marketable vaccine products for neglected EIDs. For viruses like Lassa and Nipah, where there are no biomedical countermeasures currently available, CEPI has enabled some of the first-ever vaccines for those diseases to proceed into Phase 1 clinical trials. CEPI will never be at the scale to compete with entities like the U.S. National Institutes of Health for funding basic research for EIDs, but it can be additive in focusing on translational research for vaccines for diseases with epidemic or pandemic potential that otherwise might not get developed.

COVID-19 has shown that when a pandemic is occurring, this translational support may not be as necessary if industry can run quickly and is incentivized to move from research to product. Yet access and equity challenges remain in areas such product design, procurement, delivery and pricing. For example, due to provisions on how government funding could be used, the first-wave COVID-19 vaccine developers who secured large amounts of funding from HIC governments were obligated to supply products first and foremost to the donor markets, creating significant delays to vaccine access in LMICs. Global COVID-19 vaccine access and supply constraints are projected to continue well into 2023—meaning there could be *a gap of more than two years* between most HICs and LMICs in their ability to protect the majority of their populations and contain the pandemic.

**The experience with COVAX points to how access and equity in R&D must be pursued strategically and proactively.** CEPI was a driving force with Gavi in creating COVAX, the pooled procurement mechanism designed to ensure global equitable access to vaccines as soon as possible. Although it got off to a promising start, due to massive funding, supply, and downstream delivery constraints, of the 2.1 billion COVID-19 vaccine doses that had been administered worldwide as of mid-June 2021, COVAX had been responsible for less than 4%.<sup>38</sup> Although in early 2020 CEPI had modeled an investment case for COVAX to deliver a forecasted 2 billion COVID-19 vaccine doses in 2021, it was not until much later that governments stepped up to close the financing gap so that Gavi and COVAX could deliver on this plan and legally cut advance purchase agreements. Indeed, the funding made available to CEPI and COVAX (and speed at which it was made available) to help drive COVID-19 vaccine R&D and procurement for global needs has paled in comparison to the funding supplied by HIC governments, such as through OWS, whose efforts were focused on securing vaccine access for their national populations first and foremost. This disparity in funding and speed of action for the global good vs. national interests provides important lessons for future R&D and delivery planning and coordination during a global health emergency.<sup>39</sup>

**Figure 9:**

CEPI's End-to-End Approach to Ensuring Equitable Access



## 2D. Collective action failures

**Effectively addressing the market and system failures requires numerous actors in the pandemic preparedness R&D ecosystem to come together, collaborate, and leverage their respective skills and resources.** Yet the persistent challenges that prevent governments, institutions, and other stakeholders from aligning and working together for the global public good of health security and pandemic preparedness represent another system failure. Instead of global partnership, national approaches tend to dominate, and the limitations of multilateral structures built to specifically tackle pandemic preparedness and response R&D further inhibits multilateral coordination.

### National and bilateral approaches

**While governments will inevitably look out for their own populations first, there are inherent flaws in relying on strictly national and bilateral approaches to vaccine development for pandemic response and preparedness.** Not all nations have the capacity—both human and financial—to translate basic research into safe and effective vaccines within their own borders. The list of countries with near “end-to-end” capacity for vaccine R&D gets even smaller when considering capacities and funding for the upstream and downstream aspects of vaccine development from basic research through to manufacturing. This limited capacity, paired with global need and demand, make clear the need to collaborate, share, and coordinate across borders to leverage resources and skills to develop and supply vaccines to fuel global pandemic response and preparedness. If vaccine development is concentrated in high-income settings, the resulting products may be unsuitable for use in all global settings. There are also logistical risks: as manufacturing capacity remains concentrated in HICs, if there are production or supply chain bottlenecks in a vaccine producing country, global supply could be significantly threatened.

**A well-prepared, inclusive global R&D infrastructure will be based on a foundation of global coordination and cooperation to produce and deliver products that are appropriate and acceptable for universal use around the globe.** Effective global pandemic preparedness and response is put in jeopardy when national vaccine R&D translates to bilateral vaccine sharing and distribution. Bilateral vaccine sharing leads to “vaccine diplomacy” risks—where national agendas and strategic foreign policy dictate where vaccine supplies go, not needs or risk assessments. Without a strong, well-financed and efficient global alternative to channel investments, nationalism and vaccine diplomacy may leave entire countries and populations behind, exacerbating existing power imbalances between vaccine producing countries and those that may not have end-to-end capacities.



## Multilateral approaches

**ACT-A was formed to serve as a multilateral platform to accelerate R&D and delivery of innovations for COVID-19, and its record has been decidedly mixed to date.** As COVID-19 was spreading rapidly in its first wave in spring 2020, no global entity (or set of actors) was charged with the mission to develop, produce and deliver the medical countermeasures and tools the world needed to end the pandemic. ACT-A emerged as an important expression of global solidarity in the fight against COVID-19, and it forced a breaking down of siloes among international organizations and has driven new models of collaboration that are welcome and necessary for greater impact. However, as noted by the Independent Panel for Pandemic Preparedness and Response, “the fact that [ACT-A] did not exist before the COVID-19 pandemic and had to be created for that purpose is reflected in its shortcomings. A coherent, strategic, inclusive, and fully funded framework has not been achieved, to this day . . . and there is a lack of shared vision among all stakeholders, that the therapeutics, vaccines and diagnostics needed to counter pandemics are global health commons.” “Without that shared vision,” the Panel concluded, “the ‘business-as-usual’ approach dominated by the development and sale by global corporations of proprietary products designed for wealthy countries prevails, leaving the rest of the world dependent on the goodwill of donors, development assistance and charity to gain access—eventually—to life-saving health technologies.”<sup>40</sup>

**ACT-A’s shortcomings underscore the larger failures in the multilateral space for pandemic R&D.** These include: *limited and reactive funding; challenges in strategic engagement with the private sector; lack of systemic global coordination to mitigate risks, gaps, and bottlenecks; and lack of country ownership, among others.* As with other components of pandemic preparedness, multilateral funding for R&D is often too little, too late, coming after a crisis hits. As of June 2021, more than a year after its creation, ACT-A still had not secured full funding for its investment case for 2021, let alone to reach the much higher target of 60-70% of vaccine coverage in each country that is necessary to control and bring an end to the acute phase of the pandemic. In addition, there is no structure to coordinate and leverage resources to prevent gaps and address bottlenecks in real-time, such as at-risk vaccine manufacturing. ACT-A’s vertical structure means that in practice, different COVID-19 technologies compete for limited funding. Vaccines have attracted by far the bulk of attention and financing, while support for other technologies like diagnostics, therapeutics, oxygen and PPE fall behind. And even with this multilateral coordination structure in place, there remains a lack of clear and muscular global leadership, ownership, and oversight for the entire global COVID-19 response to ensure that research is translated into accessible products that can be manufactured, delivered and deployed.

In response to the failure of the world to share and deliver COVID-19 vaccines quickly and equitably, the **African Union** launched two initiatives of its own to drive access across the continent: a pooled procurement and financing mechanism for COVID-19; a new regional manufacturing initiative to build manufacturing capacity for the future. These are important emerging models of regional leadership, coordination, and cooperation that can inspire new thinking and structures to bolster local and regional capacity for pandemic preparedness and response.

## CEPI's role in the collective response

**The insufficiency of national and bilateral approaches coupled with the failures of the current multilateral system, calls for a variety of measures to better mobilize and facilitate collective action for pandemic preparedness R&D in the future.** CEPI's COVID-19 experience points to lessons for how some collective action measures can be operationalized and strengthened, including:

**A neutral broker function can help address the R&D bottlenecks that stall vaccine development.** CEPI is designed to bring partners together and match pieces of the vaccine development puzzle to drive research, production, and coordinate with further downstream actors. It has the mission and network to coordinate skills and resources and prevent vaccine technologies from languishing in one stage of development for want of a leader for the next phase. As co-leaders in COVAX, CEPI is working with Gavi and WHO to help shepherd end-to-end development and delivery of COVID-19 vaccines, regardless if they are vaccine technologies financially supported by CEPI.

**An inherent partnership mentality can help build a better multilateral structure to fill gaps and address coordination and alignment failures across countries.** For example, when a clear gap emerged in global manufacturing capacity for COVID-19 vaccines, CEPI stepped in to finance at-risk manufacturing to provide a distributed geographic footprint to bolster global capacity and mitigate against vaccine nationalism. In its new strategy, CEPI seeks to build partnerships to bolster manufacturing capacity in under-served regions like sub-Saharan Africa. In addition, because CEPI is generally seen as “politically neutral” it can be effective at balancing diverse stakeholder interests to tackle sensitive coordination and priority-setting challenges. This is also evident in COVAX's operating principles to distribute vaccines on a needs and at-cost basis, rather than following diplomatic or profit interests.

**Diversification is beneficial when it comes to building/managing a global vaccine portfolio optimized to deliver the best results.** Experts emphasize that public funders like CEPI and BARDA should ideally build a portfolio of projects that balances speed to market, vaccine platform risk, vaccine-specific risk, clinical trial capacity, regulatory capacity, and manufacturing

capacity.<sup>41</sup> This can be effectively and efficiently done through a central actor with expertise and access to the best technologies globally, rather than individual governments trying to make bets to construct their own portfolios. CEPI's diversification strategy has helped shepherd first-ever vaccines candidates for Lassa and Nipah, two of the first generation COVID-19 vaccines to receive emergency license and deployment, and holds promise to deliver wave 2 COVID-19 vaccines with more diverse, globally appropriate product profiles.

**Global funding and global coordination yields global benefits:** Not only do HICs contribute to CEPI, but so do LMICs like Ethiopia and Indonesia. This distributed funding structure, combined with CEPI's mission and mandate to enable equitable access, promotes country ownership helps ensure that vaccines developed benefit a global population, rather than a model where those that invest the most benefit the most—as is often the case with national programs.



**3**

**Towards a Better  
Ecosystem  
for Pandemic  
Preparedness R&D**

**As health security experts and world leaders assess the global response to the COVID-19 pandemic, many are rightly calling for a new, coordinated, and permanent system or structure to accelerate end-to-end R&D for emerging pandemic threats.** CEPI has an important role to play in this evolving future ecosystem, with a structure and mission that address both system and market failures for vaccines as a global public good. It can also bring to the table its experience in R&D for neglected EIDs, as well as filling gaps for COVID-19 vaccine development and manufacturing, to inform and advise on what's needed for an effective and equitable system.

### What is needed to strengthen the ecosystem for the pandemic vaccine R&D ecosystem?

**The end-to-end ecosystem for vaccine development—from basic research to regulatory review, manufacturing, and delivery—is complex, and alignment and coordination among many actors are needed.** The Sabin-Aspen Vaccine Science & Policy Group recently released an analysis of the sector entitled *Powering Vaccine R&D: Opportunities for Transformation*<sup>42</sup> which discusses the successes and challenges of vaccine R&D for COVID-19. The report called for the following reforms:

- **DEFINE** leadership roles, responsibilities, and mechanisms of accountability to prepare for the R&D demands that surface in a pandemic;
- **PROPEL** a transdisciplinary research effort built around partnerships to expand and advance vaccine science;
- **REIMAGINE** clinical trials;
- **RESTRUCTURE** regulatory science to reflect advances in vaccine R&D;
- **POSITION** vaccines as a public good and align incentives so that benefits accrue to all sectors of society.

Coordination among all public sector R&D funders is another reform that could promote alignment and a divide-and-conquer strategy for prioritization of resources, human capital and expertise.

**While CEPI cannot fill all of these gaps, it is well positioned to address some of the market and systems failures that have been identified in this paper.** CEPI's new strategy<sup>43</sup> outlines a Prepare, Transform, and Connect agenda to: 1) advance vaccines and stockpiles for known threats like COVID-19, Ebola, and Lassa Fever; 2) create a "library of vaccines" targeting different virus families likely to trigger epidemics or pandemics to pave the way for product development during an emergency; 3) develop manufacturing innovations that enable quick production and scaling of vaccines, especially in low-resource settings; 4) form alliances with key manufacturers and invest in manufacturing capacity; 5) establish global lab networks to advance collaboration in vaccine research; 6) connect actors in the global vaccine R&D ecosystem to drive preparedness and equitable access.

**CEPI's new strategy aims to address the emerging lessons learned from COVID-19, including its own successes and failures.**

When the COVID-19 pandemic struck, CEPI quickly pivoted to fill market gaps with the modest resources it had on hand because there were no other actors with a global mandate to full this role. However, CEPI's limited funding power at the onset of COVID-19 contrasts with the much greater resources deployed by OWS and similar HIC efforts in the global race for vaccine supply. With the limited resources it did have, CEPI proved to be fairly nimble and adaptive in targeting what market failures that it could usefully address and pursuing strategic partnerships that could extend its impact. With its new 2.0 strategy, CEPI is further defining its role and responsibilities in the pandemic vaccine R&D space, propelling partnerships for research and manufacturing, and working with other actors to connect-the-dots and bridge gaps to promote end-to-end development and delivery of vaccines. For both COVID-19 and for future pathogens with pandemic potential, CEPI has a vital role in the global health security architecture to ensure that lower-income countries are not left behind.

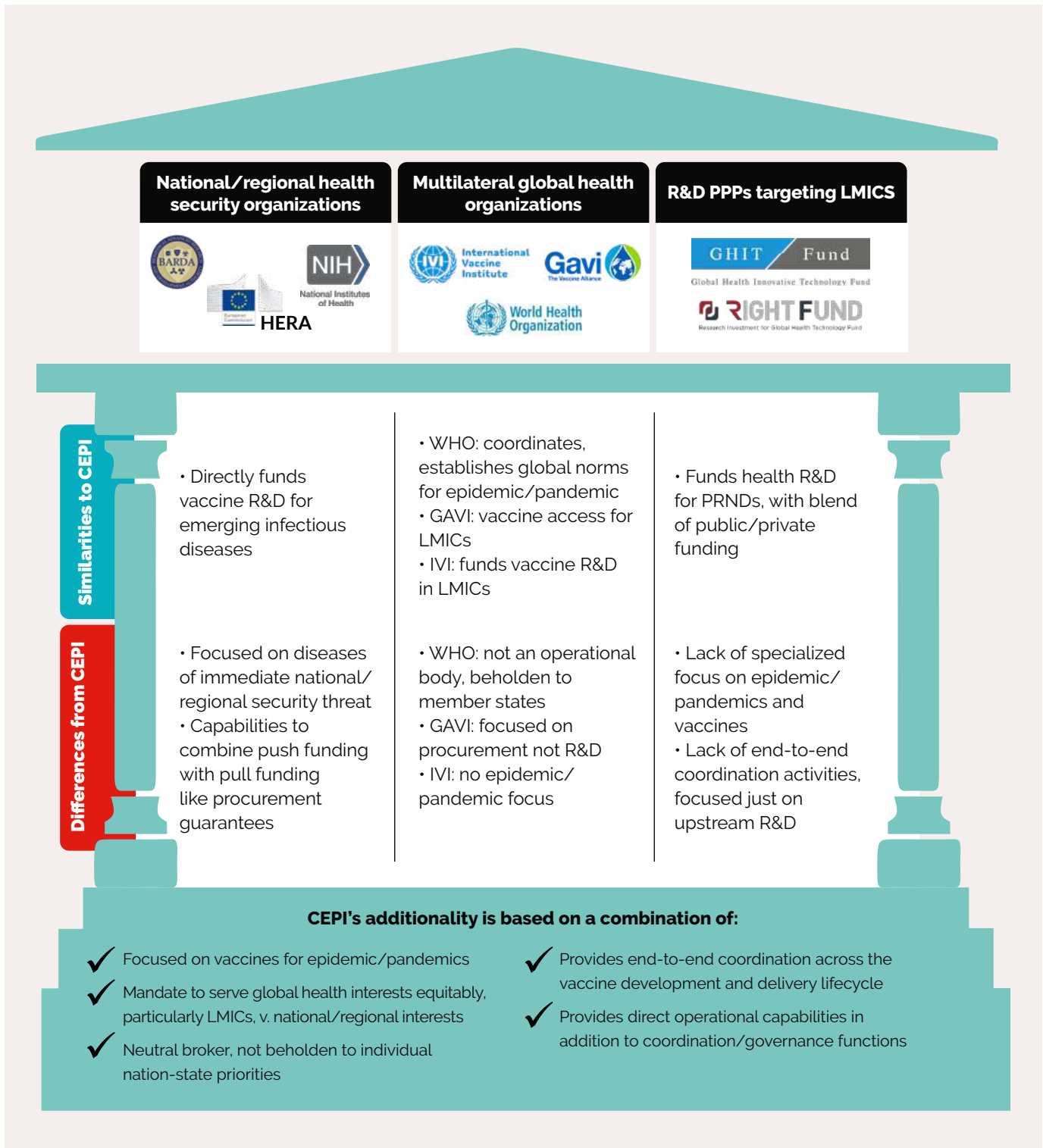
**But CEPI is just one element of a pandemic vaccine R&D ecosystem that is better prepared to prevent, detect, and response to emerging pandemic threats.**

The world needs a forward-looking, preparedness mindset to vaccine R&D that is supported by a well-funded set of actors who coordinate to provide vaccines against emerging infectious disease threats as close to "ready-to-go" when we need them as possible. As policymakers look to the future of the pandemic vaccine R&D field, they will need to consider these and many other important questions:

- What level and composition of funding is required to trigger sustainable, forward-looking investment and work in vaccine R&D for emerging infectious diseases?
- How can/should countries and regions with strong vaccine R&D programs balance investments in and prioritization of vaccine R&D for national versus global interests? How can/should global interests compete with well-financed national interests?
- What is the ideal and/or appropriate role of the private sector in vaccine R&D for emerging infectious disease threats? How do you balance profit with public sector push or pull funding?
- What does a better end-to-end system for vaccine development and delivery look like, and how does it function? How do you build and sustain manufacturing capabilities to produce and deliver vaccines at scale during a pandemic?
- How does the global system organize and coordinate for pandemic vaccine R&D? Is a new system or governing body needed? What is the future/evolution of ACT-A and COVAX?

**Figure 10:**

CEPI's Role in the Global Architecture<sup>44</sup>



**While vaccines are a critical component of pandemic preparedness and response, they are not a silver bullet—the world must also ensure more resilient systems and adequate funding for R&D and equitable delivery of drugs, diagnostics, PPE and other lifesaving tools.** Market and systems failures that plague vaccine R&D challenge the broader pandemic R&D space as well. And many of the questions raised about the future of the pandemic vaccine R&D field could be posed about the broader pandemic R&D space. However, each product area is also distinct, with unique challenges and bottlenecks. A strong future ecosystem needs to balance the realities and nuances of each of these critical product areas.

**A transformed pandemic R&D ecosystem depends on the following core priorities:**

- sustainable predictable, sufficient, nimble funding for forward-looking, proactive research and product development, not reactive funding during crisis time only;
- balanced investments in vaccines, diagnostics, therapeutics, and other tools to tackle all components of prevention and response;
- active collaboration between the public and private sectors to take advantage of complementary skills and resources;
- fixing bottle necks in global supply chains and manufacturing capacities, particularly during emergencies;
- oversight and coordination of actors and investments in pandemic R&D; and
- system architecture to incentivize product design, development and deployment for access and equity.

These priorities are at the same time straightforward and existential—requiring both tweaks and fundamental reshaping of the R&D and globalized landscape that's become status quo.

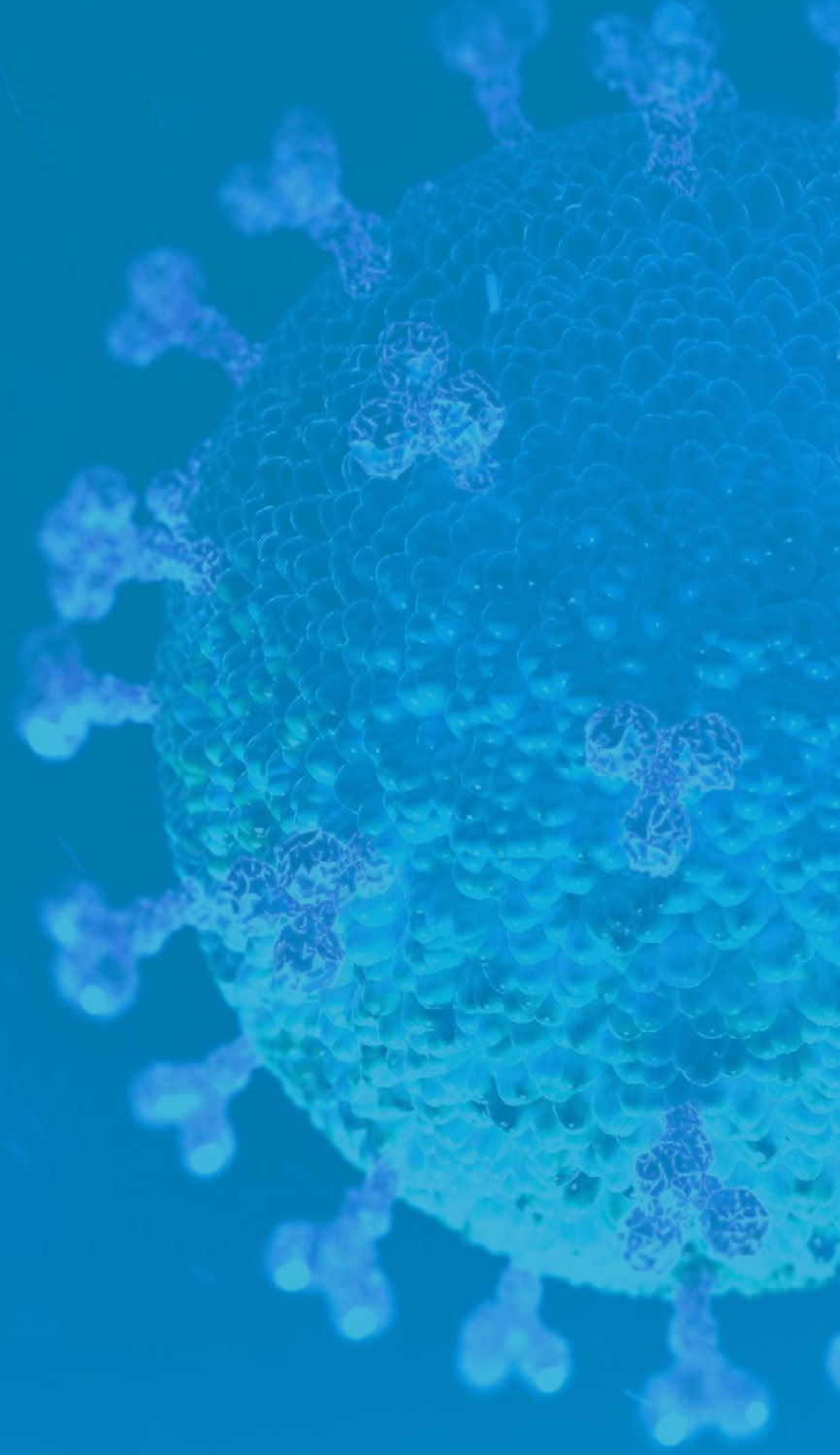
While many of these areas needing change may not be new to actors entrenched in the global health R&D space, the COVID-19 pandemic has elevated these issues to the global spotlight and could force a long overdue reckoning on challenges that have previously been too complex and not “urgent enough” to tackle. But this effort is vital and valuable, and indeed a key area where the world must “build back better” after COVID-19. Not only would transformative system change help prevent another devastating pandemic of this scale, but it can also lay the foundation for more efficient, equitable R&D for other longstanding health threats such as HIV, malaria and tuberculosis.





**4**

# Conclusion



**COVID-19 has exposed once again that there are persistent market and system failures in global health and pandemic preparedness R&D.** These failures have left the world at grave risk of deadly and costly pandemics and have resulted in the glaring inequities we see today in global access to COVID-19 vaccines. Addressing these failures requires strong public-private partnerships and financing solutions that incentivize preparedness and collective action.

**No single organization can fill all the gaps in a complex and evolving pandemic R&D landscape. However, CEPI has an important role to play to address some of the critical failures in global vaccine access and help ensure that lower-income countries are not at the back of the line.** If fully resourced, CEPI's new five-year strategy would enable it to:

- **Accelerate pandemic preparedness and counter chronic underinvestment** by investing in technologies and processes to advance a 100-day goal for pandemic vaccine development and build a library of novel vaccine technologies against emerging threats.
- **Deploy a flexible set of incentives to de-risk pandemic vaccine R&D**, attracting private industry R&D actors into the space, and coordinating closely with national governments, philanthropy and other actors who can bring additional and needed resources for risk-sharing in product development.
- **Ensure access and equity are front and center in pandemic vaccine R&D efforts** by continuing to prioritize vaccine product profiles that are appropriate for diverse and low-resource settings, linking CEPI funding to access provisions, and partnering with downstream actors to facilitate the affordable, efficient manufacture and delivery of vaccines once they are developed.
- **Partner with other global R&D actors to build a more robust global preparedness ecosystem** and facilitate end-to-end vaccine development to ensure timely, affordable vaccine access for all in the face of the next deadly epidemic or pandemic.

**As the world continues to fight COVID-19, it is also time to get ready for the next pandemic.** In addition to fully resourcing CEPI's new strategy to accelerate pandemic vaccine R&D, world leaders should commit now to increased and sustained investments in the requisite regional and national core capacities, resilient supply chains, and distributed manufacturing to quickly develop and deploy an array of medical countermeasures and tools. The sprint to develop COVID-19 vaccines in record time has shown that science can deliver amazing innovations. But breaking the past cycles of panic and neglect to ensure those innovations are advanced and delivered in time to save lives will require strong and sustained political will, collective alignment and action, and integrated end-to-end approaches with a steadfast commitment to keep all of humanity safer from pandemics.

# **Annex**

## 1. Private sector R&D industry market structure

The pharmaceutical industry is not monolithic, but rather composed of firms ranging from large multi-national companies (MNCs), to small- and medium-sized biotechnology companies to low- and middle-income country-based firms. Each of these players has different access to capital, different risk tolerance, and responds to different incentives. An increasingly common pattern is for academia and specialized biotechs to take earlier-stage scientific risk, shouldering the burden of the discovery of vaccines and underlying technology. These firms rely on venture capital for financing that can be volatile and short-lived. Larger firms, armed with capital from a wider range of sources and large in-house balance sheets, often step in to acquire intellectual property from biotechs once proof of concept has been established, to continue investing in costlier later-stage R&D phases and take on commercialization risks. R&D players in low- and middle-income countries have domestic and peer target markets that are high-volume and lower-price than those most often targeted by large MNCs. While their R&D activities are generally less intensive and novel when compared to their HIC peers, this segment is wide and diverse, supplying at least half the vaccine doses procured by Gavi and UNICEF for longstanding health challenges.<sup>45</sup> LMIC R&D actors are more reliant on blended public/private funding sources because of their target market dynamics, and some of their institutional funding sources may be less flexible and adaptable during periods of crisis, which can prevent surge capacity.

Each of these actor groups plays a particular role in the current vaccine R&D market structure, each balancing different parts of vaccine development risk and reward. If one piece is not able to perform, due to lack of capital or other reasons, then there will be a failure and gaps in end-to-end vaccine development and equitable access to all populations.

	Large multi-national firms	Small/mid- size pharma and biotech firms	Developing country vaccine firms
Firms	"Big 4": GSK, Pfizer, Sanofi, Merck with vaccine franchises/platforms <sup>46</sup>	Thousands of private and publicly-listed firms globally <sup>47</sup>	DCVMN <sup>48</sup> : 40+ vaccine manufacturers across 14 countries, predominantly based in India and SE Asia, with some manufacturers in Brazil and Africa.
Avg product portfolio size	~10+ vaccines at any given time	~2 vaccines and or multiple candidates in development	~3-4 vaccines
R&D strategy	<ul style="list-style-type: none"> <li>• Blockbuster vaccine (high revenue, first to market)</li> <li>• Larger diversified portfolio including vaccines and other products</li> <li>• Often partner or acquire IP from small/mid-sized firms</li> </ul>	<ul style="list-style-type: none"> <li>• Specialized focus on one or more "big bets" in precommercial phases</li> <li>• Main drivers of novel innovation in vaccine R&amp;D</li> <li>• Market IP to larger companies</li> </ul>	<ul style="list-style-type: none"> <li>• Ensure a consistent supply of traditional, lower-cost vaccines to LMICs</li> <li>• Less intensive R&amp;D activities and weaker R&amp;D capabilities compared to HIC peers</li> </ul>

	Large multi-national firms	Small/mid- size pharma and biotech firms	Developing country vaccine firms
Access to capital	<ul style="list-style-type: none"> <li>• Use of retained earnings</li> <li>• Can leverage their expertise/ capacity to drive large/ dependable sources of government (including tax credits) and/or investor capital on their terms</li> </ul>	Initially funded by venture capital firms or other private investors, subsequent sustained access to capital is more variable.	<ul style="list-style-type: none"> <li>• Limited self-funding due to lower vaccine prices in LMICs + less product diversity and sales networks than MNCs.</li> <li>• LMIC govt. capital availability is limited, especially for R&amp;D and pre-pandemic planning.</li> <li>• More reliant on public funding sources like CEPI, BMGF, WHO, UNICEF, impact investors</li> </ul>
Typical performance	Revenues: \$30 billion Profits: \$7 billion R&D spending: \$5 billion	Revenues (typical earlier stage startups): \$0 Profits (typical earlier stage startups): \$0 R&D spending: \$25 million Often lack the revenues or margins to generate scale or gain market share, lack true end-to-end capabilities, but drive innovation: small biotechs and startups represented 64% of new molecular entities registered with FDA in 2018. <sup>49</sup>	Revenues: \$10-\$100 million Profits: \$0.3-\$3 million R&D spending: \$1.2-\$12 million Rely more heavily on volume to generate revenue rather than high margins (as with MNCs). Achieve high volume through domestic procurement or international programs like WHO and UNICEF.
Utility of public sector funding incentives	MNCs find vaccine R&D a low productivity, high risk area. More interested in: <ul style="list-style-type: none"> <li>• High-cost product development sectors (PII, PIII, and post launch clinical studies and surveillance)</li> <li>• Facility, Manufacturing capacity and cold chain distribution scale up funding</li> <li>• Demand guarantees</li> </ul> Public funding can help incentivize/de-risk development of vaccines that serve public health/LMIC interests	Funds key innovation in R&D space for companies unable to self-finance or get VC money/not already partnered with a large firm. Public funding can also catalyze further private investment as startups develop viable technology.	DCVMN vaccines are a key supply source for LMIC market – DCVMN comprised approximately half of UNICEF's 2017 procurement supply by volume. <sup>50</sup> 55 percent of Gavi's procurement supply by volume between 2012 and 2018, <sup>51</sup> and are likely to comprise more than 55% of total COVID vaccine volume in 2021 and beyond. <sup>52</sup> Public funding to DCVMs can also help build capacity and distributed manufacturing network for better preparedness + response, and more LMIC-appropriate TPP.
Challenges of applying public sector funding incentives	<ul style="list-style-type: none"> <li>• Pharma can and often prefers to fund most of the basic science and early development on their own or acquire smaller companies' IP as a source of R&amp;D, although this may leave gaps in equitable access.</li> <li>• Much prefer to manufacturer product end-to-end and reserve X% of production and final product for LMICs (deliver in parallel to DCs) rather than take gov funding with conditions.</li> </ul>	Small/mid-size firms may lack internal end-to-end capabilities, requiring a more matrixed and complex set of partnerships to manage rather than working with a single firm	Funding from international donors, and conditions associated with that funding, can conflict with those of developing country governments where vaccines are produced. For example, India was intended to be a major supplier of COVID-19 vaccines to Africa and elsewhere via ACT-A, but when COVID cases surged there the Indian government restricted export of any domestically produced vaccines in spite of equitable distribution clauses in agreements. <sup>53</sup>

## 2. Public sector funders in the preparedness and response ecosystem<sup>54</sup>

Just as with the private sector, **the public sector is diverse**, made up of HIC governments, LMIC governments, multilateral institutions, development banks/international financial institutions, philanthropic organizations, and others. In an ideal world, these various actors would work together in a coordinated way and pool money to efficiently solve market failures at each stage of the vaccine development life cycle. Yet political and coordination challenges, coupled with the overarching failure to prioritize preparedness investments, often prevent this type of proactive planning.

	HIC ODA	HIC non-ODA	MDBs/IFIs	DFIs	LMIC governments	Philanthropy
Size of funding available						
Upstream R&D funding track record						
Downstream delivery/health systems funding track record (LMICs)						
Ability to finance pre-licensed products						
Ability to finance licensed products						
Flexible, rapid funding deployment						
Low conditionality on funding						
Coordinating power/ systems influence						
Not beholden to national agendas						

### 3. Benefits and drawbacks of push v. pull funding incentives

	Benefits	Drawbacks	
Push	<ul style="list-style-type: none"> <li>• Speed to market</li> <li>• Needed when technical R&amp;D risk is too high for developer to engage, even with viable market demand if successful</li> <li>• Relatively lower amounts of \$ required compared to pull</li> <li>• Can come with pre-emptive rights to priority access</li> </ul>	<ul style="list-style-type: none"> <li>• No differential reward for better products, may be biased to speed/ease of production rather than quality/efficacy</li> <li>• Money needs to come up front, by design funding is spent regardless of outcome with funders absorbing development risks</li> <li>• Outside of pre-competitive investments, involves funders picking winners that may not have the optimal product profile and may not be actually demanded by market once produced</li> </ul>	
	<ul style="list-style-type: none"> <li>• Better stimulates ongoing R&amp;D risk-taking by private sector</li> <li>• Results-based whereby funding can be drawn over time based on demand and only once product specs are met</li> <li>• Depending on instrument design, may be able to offer differential incentives to attract better quality products or differential pricing for LMICs</li> </ul>	<ul style="list-style-type: none"> <li>• Requires bigger up-front \$ commitment and complex cross-organization coordination</li> <li>• Funders take on demand risk that disease threat wanes and vaccines are not needed</li> <li>• Potentially insufficient to attract developer engagement given high upfront technical risks</li> <li>• If advance purchase contracts with specific firms, buyers may be locked into purchasing low-efficacy vaccines even if better ones become available</li> </ul>	Pull

## 4. Examples of CEPI Transactions<sup>55</sup>

Transaction	Bottleneck/ market failure	CEPI instruments/ terms (USD)	CEPI additionality
Ebola Janssen Vaccines	<b>Late-stage trials/ regulatory approval (2019)</b>	<b>\$25.7M</b> to Janssen Vaccines to trial an Ebola vaccine in DRC in 2019 and get approval for its compassionate use; Janssen agreed to deliver up to 500k doses	Lack of attention and investment from other sources due to outbreak location and lack of paying market.
MERS portfolio	<b>Sustained R&amp;D funding</b> – once it became clear that MERS' transmission rate was relatively low, most public funding dried up	<b>\$140M</b> of R&D funding for four vaccine candidates	Laid groundwork for COVID-19 vaccine (mRNA tech) and quickly pivoted 4 projects to COVID-19 vaccine development when pandemic hit.
Moderna [COVID-19]	<b>Early-stage R&amp;D funding</b>	<b>\$0.9M</b> in gap funding to for the manufacture of an mRNA vaccine against COVID-19 for Phase 1 trials; Moderna agreed to publish project results and to CEPI's equitable access principles and an advance purchase agreement (APA) was entered into by Gavi for COVAX for up to 500 million doses of the Moderna COVID-19 vaccine	Lack of other funding sources available as of January 2020
AstraZeneca [COVID-19]	<b>At-risk manufacturing</b>	<b>\$383M</b> CEPI investment, \$338m of which is a bridge loan recoverable upon product sales, to reserve at-risk manufacturing capacity and enable tech transfer to additional manufacturing sites; AZ will supply up to 300 million doses to COVAX on a non-profit basis	At-risk manufacturing financing
/CureVac [COVID]	<b>At-risk development and manufacturing</b>	<b>\$15.3M</b> for accelerated vaccine development, manufacturing and Phase 1 clinical trial; CureVac agreed to provide 10-15% of total doses to COVAX, with pricing tiered based on country income level	CEPI supported development of more heat-stable mRNA technology better suited to LMIC delivery
Novavax [COVID]	<b>At-risk development and manufacturing</b>	<b>\$388M</b> for preclinical studies, P1/2 clinical trials, and manufacturing, \$142.5M of which is forgivable loan recoverable upon products sales; Novavax would transfer tech at no cost to a developing country manufacturer, and supply up to 1.1 billion doses to COVAX	Developing country technology transfer and large-scale supply to COVAX
Disease X	<b>Early-stage R&amp;D Funding</b>  <b>Other bottlenecks unknown</b>	<b>\$120M</b> long-term budget allocation, pre-COVID portfolio comprised of three rapid response platforms supported through phase 1 testing (based on pre-COVID budgets, which is dynamically evolving since COVID onset).	Specific, uniform approach to Disease X preparedness by funding development, approval/licensure, stockpiling of prototype vaccines for top virus family threats such that vaccines can be deployed within 100 days of outbreak onset



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