CEPI

2022 Annual Progress Report

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Abbreviations

ACT-A	Access to COVID-19 Tools – Accelerator
AMC	Advance Market Commitment (COVAX/ GAVI)
ARC	Audit and Risk Committee
BMGF	Bill and Melinda Gates Foundation
BPBC	Broadly protective betacoronavirus (part of the BPCV portfolio)
BPCV	Broadly protective coronavirus
BP-SARS-CoV-2	Broadly protective SARS COV-2 (part of the BPCV portfolio)
CfP	Call for Proposals (CEPI funding opportunity)
CEPI	Coalition for Epidemic Preparedness Innovations
CMC	Chemistry, Manufacturing and Controls
COVAX	Vaccine pillar of ACT-A (CEPI, GAVI, WHO & UNICEF)
COVID-19	Coronavirus disease 2019 (due to SARS-CoV-2 virus)
CCT	Complementary Clinical Trials
EC	European Commission
EDCTP	European Development Countries Clinical Trials Partnership
EMA	European Medicines Association
EUL	Emergency Use Licensure (WHO)
EIDs	Emerging infectious diseases
FDA	Federal Drug Administration (US)
HRIA	Human Rights Impact Assessment
IAVI	International AlDS Vaccine Alliance
IA/PA	Internal Audit/Partner Assurance
JCG	Joint Coordination Group (CEPI)
KPI	Key Performance Indicator
LMICs	Low- and middle-income countries
LPAP	Legal Preparedness Action Package
MERS	Middle East Respiratory Syndrome-CoV
MPox	Monkeypox
NIBSC	National Institute for Biological Standards and Control (UK)
OPEX	Operating Expenses
OEP	Outbreak/Epidemic/Pandemic
PPR	Pandemic Preparedness and Response
RfP	Request for Proposals
RVF	Rift Valley Fever
SAC	Scientific Advisory Committee
SARS COV-2	Severe acute respiratory syndrome coronavirus 2 (coronavirus strain that causes COVID-19)
TPP	Target Product Profile (WHO)
TRG	Technical Review Group (CEPI/COVAX)

Introduction from Richard Hatchett, CEO: 2022 a seminal moment for CEPI and the 100 days mission

2022, the first year in CEPI's second strategic period, was another difficult year for the world. The economies of many nations wobbled, the war in Ukraine erupted and food insecurity spread. We witnessed the resurgence of polio in rich countries, the outbreak of a rare strain of Ebola in Uganda, and multiple outbreaks of monkeypox (Mpox). Climate change is increasing the number of animal-to-human spill-over opportunities, heightening the risk of a new human virus or Disease X emerging, while the number of observed outbreaks is increasing.

All of which serve as a stark reminder of the fact that viral threats are everywhere and will continue to exploit every available chink in our collective armour.

Against the backdrop of these challenges, global focus on COVID-19 and pandemic preparedness was diminished. But the progress the world made against COVID-19 and the commitment to pandemic preparedness and the 100 Days Mission, has given me cause for hope.

The 100 Days Mission, initially endorsed under the UK G7 Presidency in June 2021, continued to gain traction in multiple policy fora in 2022, including under the German G7 and Indonesian G20 Presidencies. To further strengthen global collaboration and support international partners in their efforts to advance the 100 Days Mission, CEPI also published the "What Will It Take?" report, building on lessons learned from the COVID-19 pandemic. The report highlights how the world could deliver future pandemic-beating vaccines in 100 Days and outlines five key areas of innovation that are needed to contribute to accelerated development of vaccines: 1. pre-existing prototype vaccines for representative pathogens across multiple virus families; 2. global clinical trial infrastructure and readiness; 3. earlier biomarkers of robust immune response and protection; 4. global capacity for rapid manufacture and validation of experimental vaccines; and 5. global capacities for early characterization of pathogens and outbreaks.

As ever, equitable access remains at the heart of CEPI's mission. Building on the existing policy and efforts to date, we developed an Equitable Access Framework in 2022 to better articulate our overall approach to realizing the complex challenge of equitable access. The Framework acknowledges the important role that other stakeholders play in achieving systems equity and re-enforces CEPI's primary responsibility to accelerate the development of vaccines against emerging infectious diseases and enable access to these products by populations that need them. CEPI will continue to work with other stakeholders to strengthen the global health architecture. Our success ultimately depends on the structure of that architecture and on the partnerships which can deliver and enable equitable access.

COVAX stands as a beacon of progress toward equitable access. While the record of COVAX – which is co-led by CEPI, Gavi, WHO, and UNICEF - has been mixed, its accomplishments must be acknowledged. By the end of 2022, COVAX had raised almost USD 14 billion, supported the development of 14 vaccine candidates to 11 authorized products and delivered more than 1.85 billion doses to 146 countries. Importantly 1.66 billion of these doses were delivered to the 92 low- and middle-income countries. Building on the close collaboration of COVAX, and successes and challenges, the COVAX agencies are continuing to discuss how to build on the lessons from COVAX to support better coordination next time.

CEPI brought key stakeholders together at an inaugural Global Pandemic Preparedness Summit in 2022. The summit served as a platform to both reflect on lessons learned from COVID-19 as well as to secure funding pledges toward the USD 3.5billion target for CEPI 2.0. In light of the USD 1.6Bn raised at the time of the summit, we engaged in a re-prioritization of our CEPI 2.0 programme starting with our priority pathogens that primarily affect the global south, and on preparedness for the next Disease X, including shifting to a "viral family approach". Our initial focus is on two viral families: Paramyxoviridae and Arenaviridae (rather than four), as well as accelerating strategic roadmaps and key partnerships to help us deliver on our ambitions. CEPI 2.0 also signals a shift in our investment strategy to address changes in the COVID-19 virus and anticipate future needs in terms of second-generation vaccines focusing on optimized characteristics, alongside investments with existing partners for development of variant-adapted vaccines. In addition, as the pandemic evolved, CEPI has adjusted its investments to also pursue the goal of developing a broadly protective Betacoronavirus vaccine.

2022 was also a year for CEPI to take stock of our internal systems and processes to make them effective in a post-pandemic context, maintain our culture of innovation and partnerships and preserve our agility. We strengthened our resources in areas critical for CEPI 2.0 including by establishing a Manufacturing and Supply Chain division, strengthened our operations footprint to manage a 200 person organization and increased our capacity in key areas of Research and Development.

At the close of the first year of our second strategic period, this report outlines our progress to date in a complex world. We have adjusted to the challenges and taken steps to deliver on our ambitions over the next five years. There is no doubt that the journey ahead will be challenging—many scientific, regulatory, and political hurdles will need to be overcome. But there is reason for optimism. A number of COVID-19 vaccines have reached licensure. We are beginning to take priority pathogen vaccine candidates into clinical and late-stage development and have established global networks to enable R&D. G7 and G20 leaders have gotten behind the 100 Days Mission, as have the CEOs of many pharmaceutical companies. I am hopeful that if we are bold and make the right investments—today— the 100 Days Mission can be accomplished and a future free of epidemics and pandemics can be achieved in our lifetimes.

In closing, I would like to express my heartfelt gratitude to our many investors – new and long standing – for continuing to support our joint ambition to take the threat of pandemics off the table.

Richard Hatchett
CEO CEPI

Selected highlights 2022

Evolving global pandemic preparedness architecture

New international mechanisms were established in 2022 to strengthen global pandemic preparedness capacity. One key example is the Pandemic Fund, championed by Indonesia during its G20 presidency. Importantly, CEPI has been accredited as an implementing entity to help the Fund carry out its work, along with Gavi, the Global Fund, and others. Though undercapitalized, the Fund established, for the first time, a joint financing mechanism to support pandemic preparedness and response. 2022 also saw a growing number of health security agencies established to develop and produce medical countermeasures such as SCARDA (Strategic Center for Biomedical Advanced Research and Development) in Japan and HERA (Health Emergency Preparedness and Response Authority) under the European Commission with whom CEPI signed a Letter of Intent for joint cooperation. Supported by the Wellcome Trust an independent International Secretariat was established to help the G7 to track progress against the 100 Days Mission. In late 2022, Japan highlighted the 100 Days Mission as a key priority for its 2023 G7 Presidency which has been expanded to include manufacturing and delivery, including in the global south.

100 Days Mission Case study: Sudan ebolavirus in Uganda

When the Sudan ebolavirus broke out in Uganda in September 2022, the world didn't have countermeasures ready or stockpiled. But they were in advanced stages of development. CEPI and a consortium of other funders joined WHO in supporting Uganda's Ministry of Health and local investigators to accelerate the formulation of clinical trial material and adapt existing clinical trial protocols so that these products could be tested during the outbreak.

Thankfully, the outbreak was brought under control using traditional measures (isolation, contact tracing, and quarantine) and this trial did not need to be initiated. But we learnt a great deal from this experience. The fact that investigational products were delivered and ready to be deployed in early December, within about 70 days of the declaration of an outbreak, represents a new record for global response and a significant step towards achieving the 100 Days Mission. The response also reflected a new high-water mark for international cooperation and unity of purpose, with BARDA, CEPI, and the European Commission's HERA working well together in support of WHO and the Ugandan authorities.

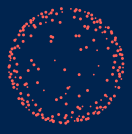
CEPI continues to work with the Uganda Virus Research Institute and the UK Medicines and Healthcare products Regulatory Agency to support the development of a reference antibody standard which will contribute to the eventual licensure of a vaccine.

The Global Pandemic Preparedness Summit

In March 2022, CEPI and the UK government cohosted the Global Pandemic Preparedness Summit in London, UK. More than 300 participants from governments, academia, industry, philanthropy, and civil society gathered to explore a proposed response to the next "Disease X" by making safe, effective vaccines, and other biologics within 100 days of identification—known as the 100 Days Mission. The 100 Days goal originally articulated by CEPI, forms a core part of CEPI's 2022–2026 pandemic plan, and has been embraced by the G7, G20, and other governments around the world. The summit concluded with representatives from industry, philanthropy, and governments pledging political and financial support of USD 1.6 billion against a target of USD 3.5 billion. In doing so, supporters emphasized the need to maintain momentum and break the cycle of panic and neglect by supporting rapid response technologies to build confidence in accelerated R&D responses to outbreaks.

By the end of 2022, approximately USD 2 billion had been secured in funding pledges.

Priority pathogen spotlight: Lassa Fever



- CEPI is the leading funder of research for Lassa vaccines and has candidate vaccines in development with four partners across the world.
- In 2022, the vaccine candidates being developed by Emergent Biosolutions and by IAVI began Phase I clinical trials in Ghana and Liberia, respectively, to assess safety and immunogenicity.
- To support the development of these vaccines, CEPI has also created and funded the largest ever Lassa fever study (the 'Enable' study) to provide a more accurate assessment of the incidence of Lassa fever infections in West Africa, and inform the design of late-stage Lassa vaccine trials. More than 20,000 participants are being recruited to take part in the study in Benin, Ghana, Guinea, Liberia, Mali, Nigeria, Sierra Leone, and Togo.
- In October, 2022, CEPI, WHO, and the Nigeria Centre for Disease Control and Prevention teamed up to host a workshop in Abuja, Nigeria, for scientists from across the West Africa sub-region to discuss and review progress of their ongoing Lassa fever research.

Priority Pathogen and Disease X Progress

Alongside its work on Disease X, CEPI is working to develop vaccines against 'priority pathogens' that have epidemic or pandemic potential. Despite the ongoing challenges of COVID-19, CEPI has been able to continue to advance its portfolio of vaccines against its priority pathogens – including Chikungunya, Lassa Fever, MERS, Nipah Virus, and Rift Valley Fever – in addition to platform technologies for use against Disease X.

As COVID- 19 demonstrated, the next Disease X is an ever-present threat. One critical tool, which will enable a rapid response to the next existential viral threat, is swiftly adapting technologies to speed up vaccine development. This concept has been adopted for annual influenza but CEPI is looking to build an armoury of these adaptive 'plug and play' technologies to help with future responses.

Crucially, CEPI's work to develop platform technologies against Disease X and priority-pathogen vaccines will also yield critical data and insights that will help the world accomplish the 100 Days Mission.

Strengthening collaborations in the Global South

CEPI's work on priority pathogens focuses on diseases that mainly affect lower- and lower-middle income countries. How and where such products are manufactured and stored, the costs of production and stockpiling, whether they are easy to deliver, their method of administration, their thermostability and any associated cold chain requirements, and of course their price, will heavily influence whether and to what extent equitable access is achieved.

To advance our goals, CEPI seeks to work with industry partners with a demonstrated commitment to equity. In October 2022, CEPI expanded its investment in the Korean vaccine developer and manufacturer SK Bioscience for a new rapid response platform technology. This partnership enhances equity by giving CEPI access to an mRNA platform that could be deployed against multiple potential threats, and to an industry partner that has committed to fair access by prioritizing supply for low- and middle-income countries at affordable prices.

To overcome some of the structural barriers to equity that we observed during the COVID-19 pandemic, CEPI supports the geographical diversification of vaccine manufacturing to promote regional vaccine self-sufficiency. We do this through our policy and technical contributions to global and regional initiatives – for example, as an active participant in Africa CDC's Partnerships for African Vaccine Manufacturing (PAVM). We also do this through targeted investments in a network of vaccine manufacturers in the Global South which will expand sustainable routine and outbreak vaccine manufacturing capacity in those regions.

A key example is CEPI's partnership with Aspen and the Bill & Melinda Gates Foundation, announced in December 2022, to improve access to vaccines in Africa and support sustainable manufacturing capacity for African-produced vaccines for future epidemics and pandemics. The new funding from CEPI and the Gates Foundation -each contributing USD 15 million- supports a 10-year agreement between Aspen and Serum Institute of India Pvt Ltd. that aims to expand the supply and sourcing of affordable vaccines manufactured in Africa.

Case study: CEPI Senegal, and the African Union

In December 2022, Senegal became the 35th country to join CEPI, pledging USD 1 million to support the organization's mission to prevent future epidemics and pandemics. The announcement built on CEPI's existing partnership with the Institut Pasteur de Dakar and its work to enhance vaccine R&D and manufacturing in Africa. In Senegal, CEPI is providing strategic and technical support to the Institut Pasteur de Dakar's MADIBA (Manufacturing in Africa for Disease Immunization and Building Autonomy) project, which will bolster health security in the region by developing a regional vaccine manufacturing hub making vaccines in Africa, for Africa. CEPI is funding vaccine R&D programmes in countries across the continent, as well as implementing a Memorandum of Understanding with the African Union/ Africa CDC to enhance vaccine R&D and manufacturing in Africa, and actively participating in the Partnerships for African Vaccine Manufacturing (PAVM).

Snapshot of other highlights in 2022

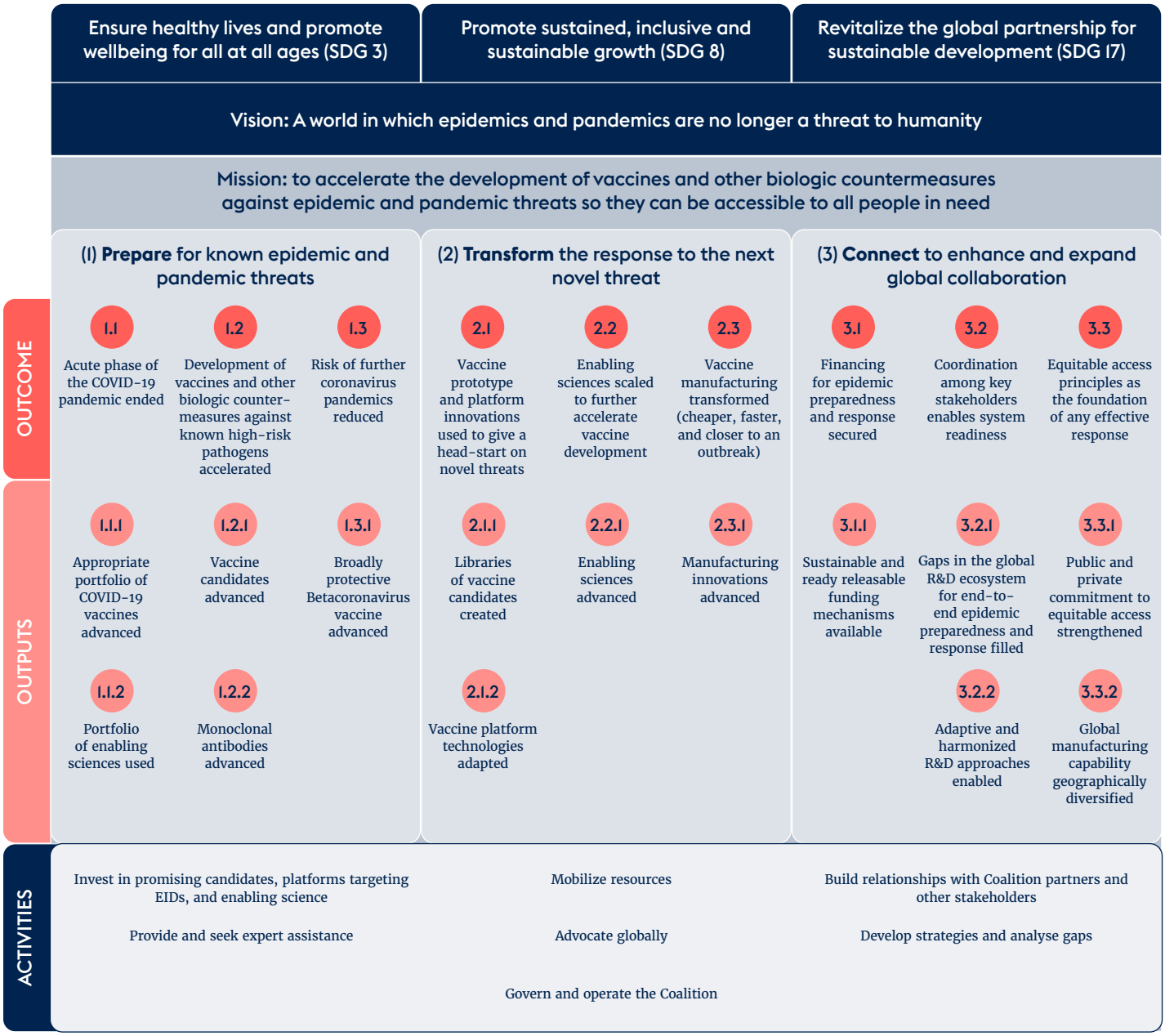
- COVID-19 status as a Public Health Emergency of International Concern (PHEIC) persists, new variants continue to emerge
- CEPI is the leading funder of SARS-CoV-2 vaccine candidates, with a portfolio of 7 candidates, by the end of 2022, with four vaccines receiving EUL
- CEPI is the leading funder of Broadly Protective Coronavirus vaccine candidates with 13 in the portfolio
- CEPI funds 14 complementary clinical trials to generate real world evidence for COVAX vaccines in Africa, Asia, Europe, South America and Oceania, aimed at supporting policy makers by advancing the understanding of the vaccines and immunization regimens
- Active portfolio of 12 vaccine candidates against CEPI priority pathogens
- The first partner was secured (Aspen Pharmaceuticals, Republic of South Africa) toward building CEPI's preferred Global Vaccine Manufacturing Network to support regional resilience
- Expansion of Central laboratory network for COVID-19 vaccines to 10 laboratories worldwide and increasing the number of immunology assays to six in order to cover gaps
- Successful compilation of interim Lassa epidemiology data that was made available to developers and key local stakeholders during a workshop held in Abuja, Nigeria
- First partnership signed for mRNA platform and virus family library prototypic approach (SK Bio in Republic of Korea)
- First in-human studies for Nipah vaccine

CEPI 2.0 Theory of Change

In 2022, CEPI began to implement the first year of CEPI 2.0 – its strategy for the second five-year business cycle (2022 to 2026). The objectives of the CEPI 2.0 strategy are threefold: to PREPARE for known epidemic and pandemic threats, to TRANSFORM the response to the next novel threat and to CONNECT to enhance and expand global collaboration. More information about CEPI's vision and approach for the current strategic period can be found in the CEPI 2.0 programme document.

The Theory of Change (Figure 1) visualises the CEPI 2.0 Strategy, highlighting the intended outputs and outcomes within each of the three strategic objectives and connects these with the mission and vision, linking to the Sustainable Development Goals on the impact level.

Figure 1: CEPI 2.0 Theory of Change



The 2022 Annual Progress Report provides an update on progress against the Key Performance Indicators (KPIs) described in the CEPI 2.0 Results Framework[1]. A snapshot of progress for the achievements against KPIs during 2022 can be seen in Figure 2 below.

Generally, KPIs for CEPI 2.0 have an expected end date of 2026, with the exception of COVID-19 indicators (Outcome 1.1, Output 1.1.1, Output 1.1.2) which have a target completion date of 2023. KPIs at output and outcome level measure progress towards the target in 2026. To track CEPI's progress more closely during the strategic period, year-on-year interim milestones have been set for KPIs (though some KPIs at outcome level do not have interim milestones).

Throughout the remainder of this report, a status box together with narrative commentary provides an assessment of progress for each indicator against the interim milestones for 2022, and the overarching target.

The 2022 Annual Progress report and other reporting are being used to assess measurability and relevance of the KPIs for CEPI 2.0. Potential adjustments to the KPIs will be considered at the mid-term review of CEPI 2.0 planned for 2024. Any adjustments to the KPIs will be made in consultation with the Board and Investors.

[1] See also CEPI's Monitoring and Evaluation Framework for CEPI 2.0 here

Figure 2: CEPI 2.0 KPI Targets - Overview of progress in 2022

PREPARE

1.1 Acute phase of the COVID-19 pandemic ended

- At least two SARS-CoV-2 vaccines favourable for LMICs available (by end 2022)
- Two variant-proof broadly protective SARS-CoV-2 candidates demonstrate clinical proof of concept (by end 2023)
- At least three enabling science programmes and innovative tools available for use in COVID-19 vaccine candidate development (by end 2023)

1.2 Development of vaccines and other biologic countermeasures against known high-risk pathogens accelerated

- At least two vaccines reaching licensure for two or more priority pathogens, including at least one WHO Prequalification
- At least two monoclonal antibodies for two priority pathogens ready to use under outbreak conditions

1.3 Risk of further coronavirus pandemics reduced

- Two broadly protective Betacoronavirus vaccines, favourable for LMICs, assessed for clinical proof of concept

Status Indicator

- On track
- Action may be required
- Action required

TRANSFORM

2.1 Vaccine prototype and platform innovations used to give a head-start on novel threats

- Clinical proof of concept for four virus family vaccine libraries and preclinical proof of concept for additional six virus family vaccine libraries
- Two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations

2.2 Enabling sciences scaled to further accelerate vaccine development

- Three or more of the enabling science tools developed through CEPI funding used by one or more of CEPI-funded vaccine developers
- Standards, preclinical models, assays, translational immunology, correlates of protection, Sentinel safety surveillance and epidemiological, mathematical models and studies advanced for all CEPI priority pathogens and the virus family approach

2.3 Vaccine manufacturing transformed

- At least three innovations which demonstrate manufacturing cheaper, faster or closer to an outbreak
- Five manufacturing innovation projects advanced

CONNECT

3.1 Financing for epidemic preparedness and response secured

- Funding for vaccine and other biologic countermeasures preparedness and response R&D included in new financing mechanisms
- USD 3.5 billion in commitments for CEPI 2.0

3.2 Coordination among key stakeholders enables system readiness

- RACI(s) for 80% of key elements of a target ecosystem in place
- At least three funded global networks expanded or established
- Regulatory database available as a pilot to CEPI-funded developers by 2023 with view to wider roll out towards 2026

3.3 Equitable access principles as the foundation of any effective global response

- At least one key systemic obstacle to access for LMICs removed
- 100% of CEPI-funded products/ platform with relevant access plans in place each year for each product passing a Stage Gate review
- At least five agreements in place over two regions that support manufacturing capacity strengthening in order to support LMICs

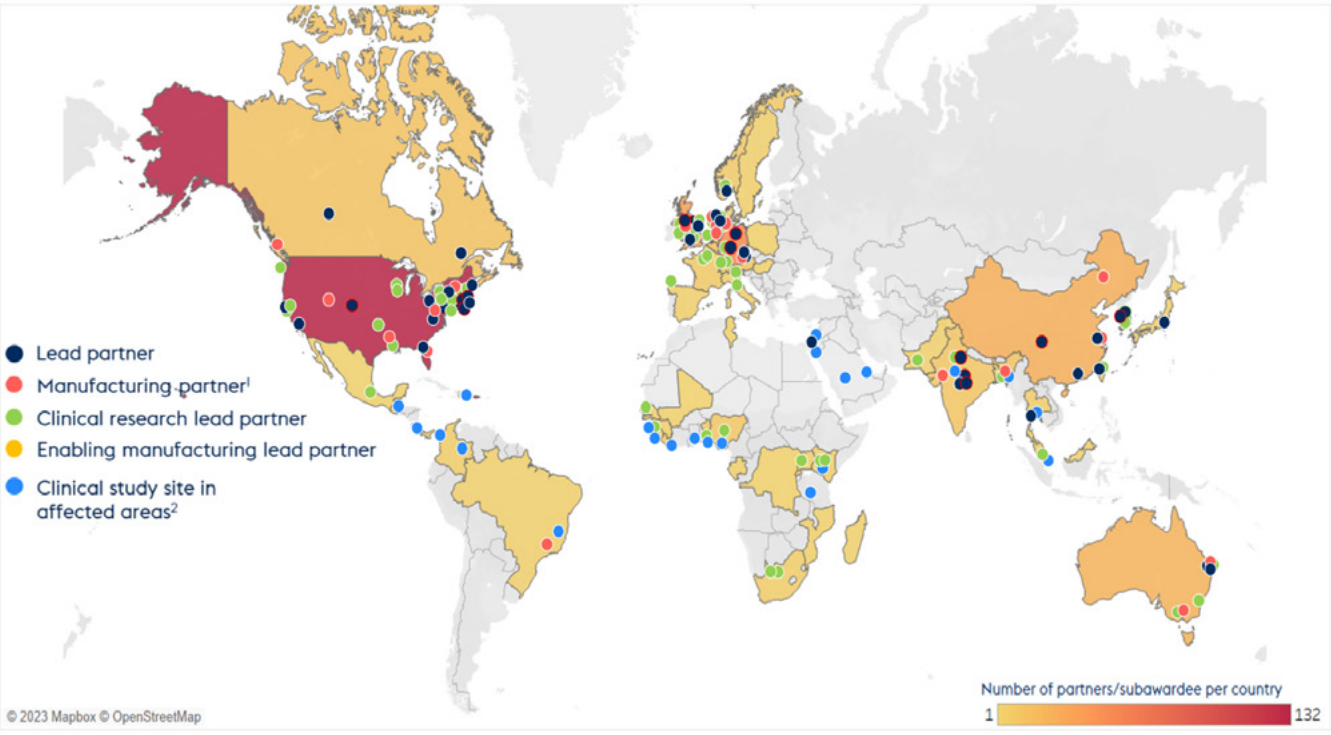
Progress Against the Strategic Objectives

1. Strategic Objective 1: Prepare for known epidemic and pandemic threats

To prepare for the next epidemic or pandemic, CEPI continues to invest in promising vaccine candidates against priority disease areas in order to rapidly activate R&D at the outset. The ultimate goal is to fast track the availability of vaccines that can be used to save lives and avert large scale crises.

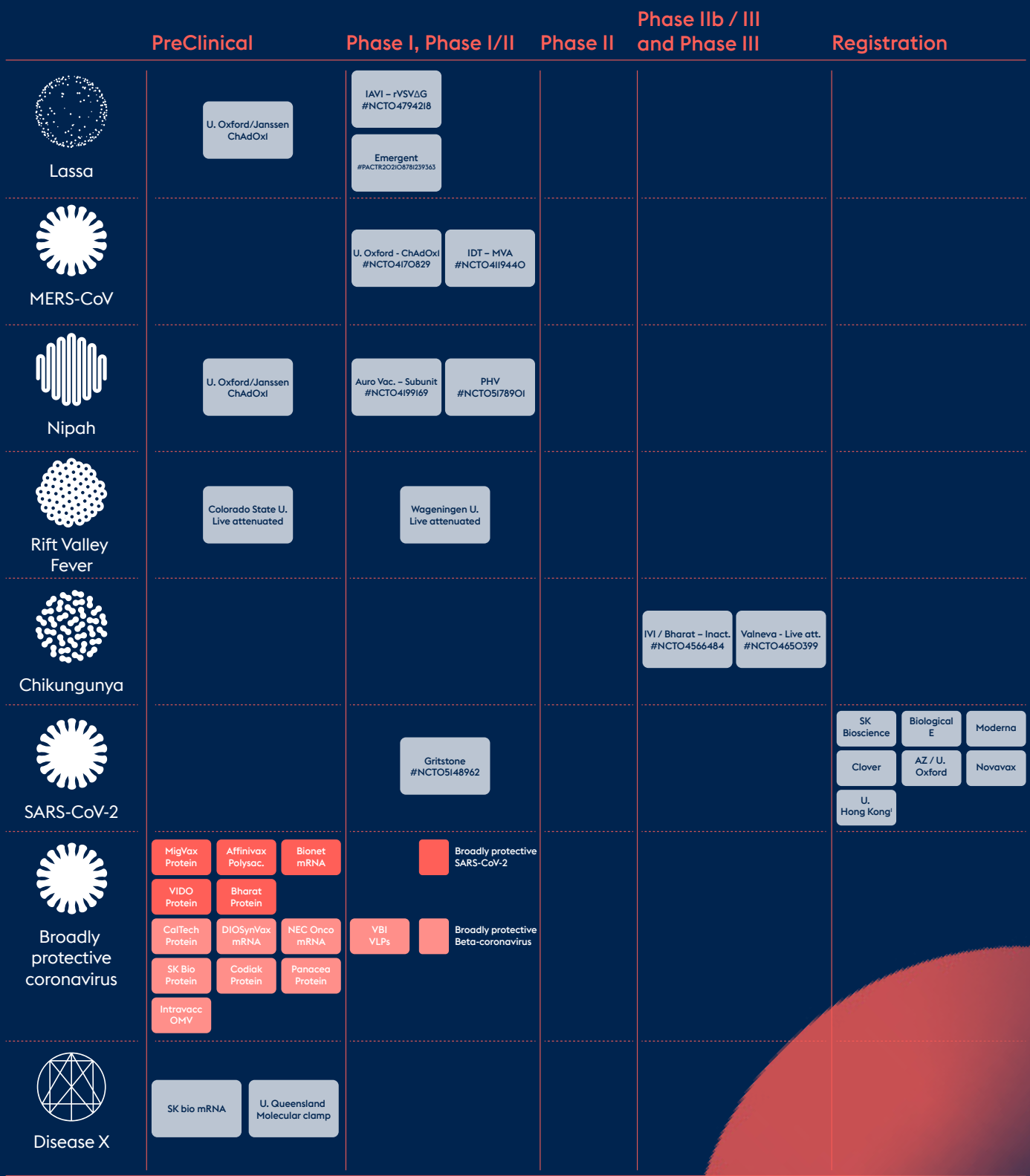
As of 31 December 2022, CEPI had an active research and development (R&D) portfolio of 12 vaccine candidates for its initial priority pathogens; three vaccine candidates against Lassa virus, two vaccine candidates against Middle Eastern Respiratory Syndrome-CoV (MERS), three candidates against Nipah virus, two candidates against Chikungunya, two candidates against Rift Valley Fever (RVF). CEPI also had eight candidates for COVID-19, and in our Broadly Protective Coronavirus (BPCV) portfolio five broadly protective SARS-CoV-2 candidates and eight broadly protective Betacoronavirus candidates (BPBC); and two rapid response platforms. CEPI has also invested in an array of enabling science programmes and established networked global laboratories to advance its vaccine development projects, and advance vaccine science, including standards and assays, animal models, diagnostics, epidemiological studies, clinical development, and regulatory initiatives.

Figure 3: CEPI's investments that support its mission as of December 2022



[2] Five of these, having received licensure are no longer actively managed

Figure 4: Portfolio overview – CEPI-funded vaccine candidate portfolio as of December 2022



[1] *Utilized a platform funded by CEPI during early stages of development*

Notable developments during 2022 to "Prepare for known epidemic and pandemic threats"

- Emergency-use authorization achieved for four SARS-CoV-2 vaccine candidates
- 10 new agreements signed for vaccine candidates / vaccine technology platforms[3]
- Termination of investment in nine vaccine candidates due to attrition and project reprioritization or rescoping
- Expansion of the centralized lab and animal model networks to support priority pathogen advanced development.
- Nine calls for proposals (CfPs) / expressions of interest (EoIs) launched across all strategic areas
- Progress in the clinical stage of development for three vaccine candidates for the priority pathogens Lassa, Nipah and RVF

To enhance the management of a larger, more complex portfolio of R&D, as well as the manufacturing investments anticipated during the CEPI 2.0 strategic period, CEPI adapted its portfolio management and governance framework in 2022. New external members were added to CEPI's portfolio management and governance bodies and new delegations of authority were established, enabling CEPI to bring a greater breadth of technical and low- and middle-income country (LMIC) perspectives, while also remaining agile and responsive to the evolving vaccine development landscape, which continues to be very dynamic. With that in mind, CEPI's investment strategy to end the acute phase of the pandemic has evolved to address changes in the virus and anticipated future needs. This includes investments in second generation vaccines (which focus on optimized characteristics), and investments with existing partners for development of variant-adapted vaccines. In parallel, CEPI has pursued near- and longer-term goals to tackle the challenge of achieving broader protection across the betacoronaviruses[4]. Investments in our broadly protective coronavirus (BPCV) candidate portfolio fall into two main categories:

1. Broadly protective SARS-CoV-2 variant targeted vaccine candidates (called BP-SARS-CoV-2 with a target by 2023. This work is captured in section 1.1),

2. Broadly protective Betacoronavirus vaccine candidates (called BPBC with a target by 2026. This work is captured in section 1.3).

Activities undertaken in 2022 to prepare for known epidemic and pandemic threats are described under following sections and subsections:

1.1 End the acute phase of the COVID-19 pandemic

1.1.1 Advance an appropriate portfolio of COVID-9 vaccine

1.1.2 Use portfolio of enabling science programmes

1.2 Accelerate the development of vaccines and other biologic countermeasures against known high-risk pathogens

1.2.1 Advance vaccine candidates

1.2.2 Advance monoclonal antibodies

1.3 Reduce the risk of further coronavirus pandemics

1.3.1 Advance broadly protective Betacoronavirus vaccine

[3] Technology platforms form part of CEPI's Transform Strategic Objective

[4] A snapshot of the BPCV portoflio can be found here

1.1. End the acute phase of the COVID-19 pandemic[5]

Building on work which commenced in at the outset of the pandemic in January 2020, CEPI continued to support the development of first-generation candidates that can offer vaccine doses through fair allocation mechanisms, such as the COVAX Facility.[6]

These investments included supporting evidence generation for policy decisions to optimize the use of available doses, and ensuring the availability of critical input supplies as well the possibility of manufacturing technology transfer. In addition, CEPI progressed on longer-term goals of funding next-generation approaches that address the specific needs of a diverse range of populations and settings, including vaccines against emerging variants of concern. CEPI also addressed critical R&D questions through investments in clinical research which could expand access to vaccines, such as how they might work in at-risk populations and whether some vaccines might be combined to boost efficacy or address supply disruptions.

Equitable access is central to CEPI's vision. To facilitate equitable access, CEPI actively seeks to fund the development of vaccines that are favourable for LMICs, defined in the context of CEPI's COVID-19 work as vaccines that meet at least three of the following criteria based on the relevant WHO Target Product Profile (TPP): one dose; long-acting; minimal cold chain requirements; heat-resistant / thermostable characteristics; affordable price; applicable for all segments of the population; ease of administration. CEPI is the only vaccine R&D funder globally that systematically includes equitable access terms in its partnership agreements.

Throughout the COVID-19 pandemic, CEPI made significant investments in R&D, and reserved raw materials and facilities for technology transfer for COVID-19 vaccines, with equitable access as a driving principle. As a key COVAX partner, CEPI will continue to support R&D and manufacturing into COVID-19 vaccine innovations, expanding and scaling technology transfer and supporting partners and regional bodies on manufacturing. CEPI has a portfolio of 13 BPCV candidates to take forward, and partnerships with LMIC manufacturers to establish a global vaccine manufacturing network designed to support agile and resilient manufacturing in, and for LMICs, thereby accelerating access to vaccines during future outbreaks and pandemics.

[5] Interim milestones have been set for 2022 for KPIs for outcome 1.1 and associated outputs. The target for these KPIs runs until 2023 when this piece of work is intended to finish.

[6] The global procurement mechanism of the COVAX vaccines pillar of the Access to COVID-19 Tools Accelerator (ACT-A)

KPI Outcome 1.1: Number of CEPI-funded SARS-CoV-2 licensed vaccines that are favourable[7] for LMICs and available for use

Baseline	Actual 2022	Target 2022 & 2023*	Status
Three licensed SARS-CoV-2 vaccines (one is favourable for LMICs) Three broadly protective SARS-CoV-2 vaccine candidates in preclinical phase Four variant proof SARS-CoV-2 vaccines	Seven (original COVID-19 strain based) licensed vaccines available. Six of which are favourable for LMICs Five broadly protective SARS-CoV-2 in preclinical phase and one variant-proof vaccine candidate in Phase I	At least two SARS-CoV-2 vaccines favourable for LMICs available (by end 2022) Two variant-proof broadly protective SARS-CoV-2 candidates demonstrate clinical proof of concept (by end 2023)	**ON TRACK**

Comment on progress in 2022 and status:

CEPI outperformed the target for 2022 in the number of licensed vaccines. Two broadly protective SARS-CoV-2 vaccine candidates were added to the portfolio in 2022. For more details, please refer to the narrative section and KPI Output 1.1.1.

**COVID-19 KPI targets under Outcome 1.1, Output 1.1.1, Output 1.1.2 are due in 2022 and 2023 when this piece of work is intended to finish.*

[7] Favourable for use in LMICs means vaccines should meet at least 3 of relevant WHO TPP criteria: one dose, long-acting, minimal cold chain requirements, heat-resistant/thermostable characteristics, affordable price, applicable for all segments of the population, and ease of administration.

1.1.1. Advance an appropriate portfolio of COVID-19 vaccines

CEPI's continued support for first generation vaccines against COVID-19 included five vaccines that achieved regulatory approval in 2022; Novavax[8] in multiple countries, SK bioscience in South Korea, Biological E in India, and Clover and University of Hong Kong in China. All of these vaccines meet the criteria for use in LMICs in addition to one other previously licensed vaccine funded by CEPI, thereby surpassing CEPI's 2022 interim milestone of achieving at least two SARS-CoV-2 vaccines favourable for LMICs available by end 2022. These exceptional results were the combination of multiple success factors, including strong political support, end-to-end rapid vaccine development based on pre-existing experience and global engagement, early investments by CEPI to scale up adjuvant and glass vial supplies, and centralized cross-agency coordination.

In the longer term, CEPI is investing in next-generation vaccine candidates that seek to provide broad protection against SARS-CoV-2 variants (BP-SARS-CoV-2). Initially focused on the wild type strain, additional investments were made to work on emerging variants which has evolved into a broadly protective portfolio. In 2022, CEPI signed agreements with two partners, BioNet-Asia and Bharat Biotech to develop their BP-SARS-CoV-2 vaccine candidates from the preclinical phase to clinical proof-of-concept. These two candidates add to the existing three projects in CEPI's BP-SARS-CoV-2 vaccine portfolio that CEPI has supported with seed funding (Affinivax, MigVax and VIDO) resulting in a total of five candidates, all of which are in preclinical phase. As with the first generation COVID-19 vaccines, equitable access and use in LMICs, remains at the heart of CEPI's mission. Overall, there is diminishing demand for COVID-19 vaccines and a clear preference for mRNA, while protein-based vaccines have not been taken up. Mindful of these factors, right-sizing the COVID-19 portfolio will be a priority for CEPI going forward.

[8] First licenced in 2021 in the UK, with additional EULs granted in other regions and countries in 2022

KPI Output I.I.I: Percent of interim milestones achieved for advancing CEPI-funded COVID-19 portfolio favourable for LMICs				
Baseline	**Interim milestone 2022**	**Actual 2022**	**Target 2023**	**Status**
N/A	100% of interim milestones achieved (Three for 2022)	Majority on track (see comment box below for more detail)	100% of interim milestones achieved (One for 2023): Two variant-proof broadly protective SARS-CoV-2 candidates demonstrate clinical proof of concept (by end 2023)	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:
CEPI outperformed the interim milestones for 2022, exceeding the number of licensed vaccines and interim data from clinical research. In terms of the SARS-CoV-2 broadly protective coronavirus portfolio, CEPI has down selected the large number of CfP applicants in 2022 and completed due diligence for most selected candidates. However, given the stage of development of all these candidates, the target of clinical proof of concept by 2023 is not feasible.

Interim milestone 2022 (1): Four licensed vaccines to maximize doses of existing vaccines to COVAX in 2022.
Actual 2022: Six (original COVID strain based) licensed vaccines to maximize doses of existing vaccines to COVAX in 2022; five of which are favourable for LMICs.

- Of seven licensed COVID-19 vaccines (Moderna, AstraZeneca/Oxford, Novavax, SK bioscience, Biological E, Clover, University of Hong Kong/Wantai), six are favourable for LMIC use.
- Three licensed vaccines (AstraZeneca/Oxford, Moderna, and Novavax) have been granted emergency use listing by the World Health Organization (WHO) and have been administered in countries around the world.
- One of the licensed vaccines (University of Hong Kong/Wantai), is one of the first intranasal vaccines, which utilized a platform funded by CEPI during the early stage of development.

Interim milestone 2022 (2): Two vaccines favorable for LMICs (including for new variants) clinical proof of concept by 2022 (and consider to licensure in 2023/24).
Actual 2022: Five broadly protective SARS-CoV-2 were in preclinical stage of development and one variant-specific vaccine candidate was in Phase I stage of development. No vaccines for variants achieved clinical proof of concept in 2022.

- Two broadly protective SARS-CoV-2 vaccine candidates were added to the portfolio in 2022 (Bharat Biotech and BioNet Asia).
- One variant-specific SARS-CoV-2 vaccine achieved partial clinical proof of concept in Phase I (Gritstone).
- CEPI phased out investment in variant-specific SARS-CoV-2 vaccines in 2022 and focused its effort on broadly protective SARS-CoV-2 and Betacoronaviruses, as next generation vaccine candidates offer advantages over so-called first-generation ones, to reduce the risk of further coronavirus pandemics. The three variant-specific vaccines were too early in development to play a role in the current global response and were discontinued or transitioned to the broadly protective coronavirus portfolio. Based on this trajectory CEPI will not reach the 2023 target.

Interim milestone 2022 (3): Interim data from eight clinical research studies to maximize access of existing vaccines.
Actual 2022: Out of 13 CEPI-funded clinical studies to address gaps in COVID-19 vaccine R&D, 12 have achieved interim data.

I.I.2. Use portfolio of enabling science programmes

Alongside vaccine development, CEPI invested in a portfolio of enabling science programmes to advance understanding of existing COVID-19 vaccines, support their manufacturing and maximize access.

CEPI developed and established a COVID-19 international antibody standards with partners (NIBSC and WHO). Assays and funding were also provided to support harmonized immunology assessments of over 70,000 serum samples from preclinical and clinical studies of COVID-19 vaccines from over 50 different developers through the CEPI established Centralized Laboratory Network. The ongoing Agility Programme is supporting global efforts to monitor the emergence, evolution, and spread of new SARS-CoV-2 mutations, and test whether antibody serum—known to neutralize the original virus—remains effective against emerging variants.

CEPI has expanded the number of Centralized Laboratory partners who can perform the core SARS-CoV-2 assays, and complemented this by using the updated international standard for SARS-CoV-2 which covers contemporary variants of concern. More assays will be added to the Centralized Laboratory as needed.

CEPI Agility and Predictive Modelling programmes are currently investing in clearly understanding the mechanisms of immune escape by SARS-CoV-2 variants, which will help CEPI offer better preclinical testing for the support of vaccine development projects. The Agility programme will expand in 2023 and work more closely with Predictive Modelling to synergize data analyses and strengthen the modelling tool in its prediction of important mutations in new variants.

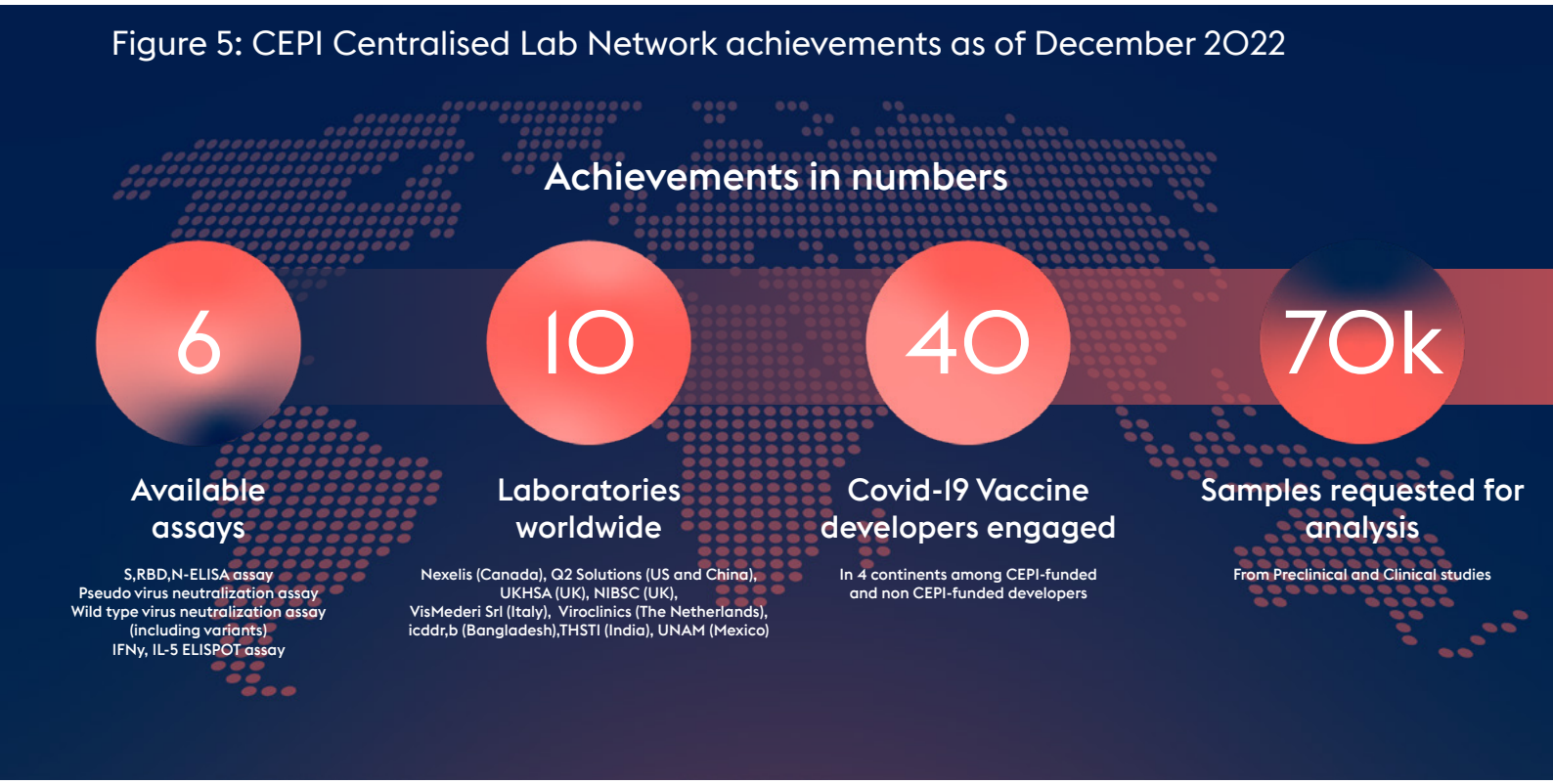
Additional enabling science programmes include:

- animal model development and preclinical testing of vaccine candidates;
- systems immunology studies to better understand factors contributing to successful immune responses (biomarkers) to COVID-19 vaccination;
- modelling to simulate vaccine supply chain networks.

CEPI has also funded clinical research studies to assess the use of mixed COVID-19 vaccine regimens for several vaccines available through COVAX, evaluate fractional dosing, investigate vaccine effectiveness, and explore vaccine safety and efficacy in at-risk populations (e.g., HIV-positive, immunosuppressed, elderly and/or adolescent individuals). These studies are geographically varied, taking place in countries across Africa, Asia, Europe, Oceania, North America and South America. Evidence from these studies has, and will, contribute to the evidence base for policy decisions at both national and global level.

Together with BMGF and WHO, CEPI convened working groups of international experts in COVAX SWAT teams, to resolve product agnostic challenges and issues arising from the unprecedented speed and scale of vaccine development and manufacturing. COVAX SWAT teams provided expert guidance and solutions for manufacturing, clinical development and operations (with sub-working groups on vaccine safety and maternal immunization) and enabling sciences challenges. A Regulatory Advisory Group (RAG), co-chaired by CEPI and WHO, originally formed for COVAX, now consists of 13 global regulators representing all regions, and provides closed-door fora to discuss critical regulatory issues. The RAG was pivotal in driving discussions, and facilitating alignment of key regulatory challenges that enabled COVID-19 vaccine authorizations for emergency use and guidance for strain change.

Figure 5: CEPI Centralised Lab Network achievements as of December 2022



KPI Output 1.1.2: Number of CEPI-funded enabling science programmes and innovative tools available for use in COVID-19 vaccine candidate development

Baseline	Interim milestone 2022	Actual 2022	Target 2023	Status
One international antibody standard, three assays validated (Centralized Lab Network), 13 variants assessed (Agility project), two partners for systems immunology, eight complementary clinical trials projects and two fractional dosing trials ongoing	Seven interim milestones for 2022 across enabling science programmes and innovative tools	Six interim milestones achieved in 2022 and one achieved in March 2023 (see comment box below for more detail)	At least three	**ON TRACK**

Comment on progress in 2022 and status:

Interim milestone 2022 (1): Variant serum collection for SARS-CoV-2 and replacement of current SARS-CoV-2 WHO International Standard by Q4- 2022.

Actual 2022:

- Collaborated with partners to closely monitor and assess the impact of SARS-CoV-2 variants of concern and variants of interest.
- Worked with partners on updating the standard for SARS-CoV-2 to include contemporary variants of concern, and refining preclinical infection models for new SARS-CoV-2 variants in several laboratory animal species. The replacement of the current SARS-CoV-2 WHO International Standard has been approved by WHO as of March 2023.

Interim milestone 2022 (2): Preclinical models for COVID-19 and continuing refinement of models, as needed, as emerging variants arise; up to five variants per year would be examined for model refinement throughout 2022, and models will be made available for vaccine testing in the Preclinical Models Network.

Actual 2022:

- Five Preclinical models developed for SARS-CoV-2, with refinement of hamster models for four additional variants provided in 2022.
- Two developers were supported with refined variant models.

Interim milestone for 2022 (3): Developing assays for new emerging variants of concern for SARS-CoV-2 throughout 2022 and make them available in the Centralized Laboratory Network.

Actual 2022:

- Six assays across six variants are available and offered through CEPI's Centralized Laboratory Network.
- Sixty-seven of the most prevalent sub lineages of omicron are now being scored by Harvard Medical School and Massachusetts General Hospital in the predictive modeling programme.

Interim milestone 2022 (4 & 5): Assessments of new emerging SARS-CoV-2 variants through the Agility and Predictive Modelling programmes and results shared with vaccine developers.

Actual 2022:

- The Agility programme assessed 26 SARS-CoV-2 variants by end of 2022, investigating the variants of concern that showed the highest priority, as per WHO and other public health indicators.
- Ongoing assessments of new emerging variants through the Agility and Predictive Modelling programmes. Biweekly predictive modelling reports are being shared with the Agility project team.

Interim milestone 2022 (6): Systems immunology network functional and analyzing samples from COVID-19 clinical trials.

Actual 2022:

- Systems immunology partners Seromyx and Oxford have signed implementing partner agreements and are progressing on their respective projects.
- The Systems Immunology Team is collecting data from human clinical trial samples and preclinical laboratory animal samples to look for important signals and correlates of protection.

Interim milestone 2022 (7): Optimize manufacturing of COVID-19 vaccines by addressing manufacturing supply chain bottlenecks through the COVAX marketplace (Q1/2022).

Actual 2022: The COVAX marketplace was operationalized with 35 signed participants and a total of 13 matches between requester and suppliers of raw material.

1.2. Accelerate the development of vaccines and other biologic countermeasures against known high-risk pathogens

CEPI continues to invest in the development of vaccines and biologic countermeasures for its priority pathogens: Lassa, MERS, Nipah, Chikungunya and RVF. These are diseases with epidemic and pandemic potential, mostly identified in the WHO R&D Blueprint[9], for which no licensed vaccines are currently available.

In the CEPI 2.0 strategic cycle, CEPI will expand its support to late-stage vaccine development towards licensure, add new priority pathogen candidates as required to maintain a robust portfolio and increase probability of success, and, as part of CEPI's TRANSFORM strategic objective, invest in new rapid response vaccine platform candidates. Additionally, under PREPARE strategic objective CEPI will broaden its investments in countermeasures beyond vaccines to prophylactic vaccine-like technologies, such as monoclonal antibodies (mAbs), where this is beneficial for rapid response. As with the COVID-19 programme, CEPI will continue to support its vaccine development and biologic countermeasures projects with an array of enabling science programmes.

KPI Outcome 1.2: Number of CEPI-funded vaccine candidates and other biologic countermeasures for priority pathogens ready for use

Baseline	Actual 2022	Target 2026	Status
Zero	Vaccine candidates: Zero Monoclonal antibodies: Zero	• At least two vaccines reaching licensure for two or more priority pathogens, including at least one WHO Prequalification • At least two monoclonal antibodies for two priority pathogens ready to use under outbreak conditions	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:

Action may be required as progress on mid- and late-clinical development has not been achieved (see 2022 interim milestones for Output 1.2.1), and the funding opportunity for monoclonal antibodies was not launched in 2022 as planned.

[9] WHO R&D Blueprint can be found here

1.2.1. Advance vaccine candidates

At the end of December 2022, CEPI's active vaccine candidate portfolio against its five priority pathogens consisted of 12 candidates at the following stages of development:

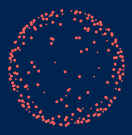
- Three candidates in Preclinical
- Seven candidates in Phase I
- Two candidates in Phase IIb/III

Lassa fever

CEPI's active Lassa portfolio consists of three vaccine candidates: University of Oxford (Preclinical), Emergent (Phase I) and IAVI (Phase I), with an additional mRNA lipid nanoparticle platform-based candidate in CEPI's Disease X portfolio targeting Lassa (Preclinical).

The Lassa portfolio progressed significantly in 2022, following delays due to the COVID-19 pandemic; one candidate progressed from Preclinical to Phase I; another candidate completed Preclinical and was approved to Phase I; the third candidate received conditional approval for CEPI investment in the next development phase. Two other candidates previously in the Lassa portfolio have been closed, one due to manufacturing technical issues and a second due to poor clinical data.

CEPI's Lassa epidemiology study in West Africa (ENABLE study) has started to deliver essential data to inform the design of a Phase III study. Importantly, the data indicates that a conventional licensure pathway for a Lassa vaccine is likely to be both feasible and appropriate. Continued analysis of epidemiological data, clinical trial protocol and site preparation and regional engagement are ongoing in anticipation of supporting late-stage development for the Lassa vaccine portfolio.



Lassa fever, a zoonotic disease associated with acute and potentially fatal haemorrhagic illness, is caused by Lassa virus and is one of the pathogens included in the WHO R&D Blueprint list of epidemic threats needing urgent action.

Transmitted to humans via contact with food or household items contaminated with rodent urine or faeces, both sporadic cases and prolonged outbreaks of the disease are observed in Benin, Ghana, Guinea, Liberia, Mali, Nigeria, and Sierra Leone, with between 100,000 to 300,000 cases reported each year. Nigeria has experienced a high incidence of Lassa fever in the past, with an overall case fatality rate among hospitalized patients of 20.6% in 2021.

CEPI, one of the largest funders of Lassa fever research, has been working with endemic countries to ensure that affected populations have access to a life-saving Lassa fever vaccine. This has involved gaining a better understanding of underlying epidemiology and disease burden, looking at ways to build clinical trial capacity in West Africa, as well as improving the regulatory environment to facilitate clinical research and vaccine licensure and finally, securing stakeholder support in endemic countries to enable equitable access. CEPI is the only institution funding the late-stage development of Lassa fever vaccines in endemic countries

The *Enable* Lassa Research Programme, launched in 2020, has captured the burden of disease information for Lassa virus across five West African countries. Interim data is now available and is being directly utilized by Lassa vaccine developers to inform clinical trial design. *Enable*, the largest-ever epidemiological study of Lassa fever, will publish the study results in 2024.

CEPI has invested in a portfolio of five Lassa vaccine candidates across affected countries in West Africa, resulting in the advancement of the first-ever vaccines into Phase 1 clinical trials. In addition, there are two Lassa vaccine candidate, which form part of the platform technologies portfolio (part of the TRANSFORM strategic objective). One of these completed preclinical development and an additional vaccine candidate was added to the vaccine library portfolio. Further information on this can be found in section 2.1.1.

CEPI is also focused on engaging key African and global partners and coordinating dialogue between various stakeholders (Africa CDC, NCDC, AVAREF, Gavi, UNICEF, WHO, National regulatory authorities, manufacturers, etc.) to help facilitate country decision-making on vaccine deployment strategy – whether prophylactic or outbreak response. In October 2022, CEPI held a regulatory workshop to discuss Lassa development plans, upcoming clinical trials, the data required for licensure and other collaborations.

Phase III efficacy trial protocol is under development for advanced stage clinical trials in West Africa. The final step will be to facilitate technology transfer of the lead candidates to an African-based vaccine manufacturer.

Middle East Respiratory Syndrome (MERS)

CEPI's active "standalone" MERS portfolio consists of two vaccine candidates: IDT (Phase I) and University of Oxford (Phase I). While some development activities were paused due to COVID-19, clinical trials resumed in 2022. As CEPI continues to support these two candidates, four vaccine candidates under the broadly protective Betacoronavirus (BPCV) programme are being developed to offer protection against MERS in addition to the two candidates in the standalone portfolio. These candidates include one or more MERS immunogens within the vaccine construct, in addition to SARS—CoV-1 and SARS-CoV-2 immunogens. Two candidates previously in CEPI's MERS standalone portfolio have been closed due to acquisition of a development partner or poor clinical data. Another candidate vaccine within the BPCV programme has also been closed due to poor clinical data.

Nipah virus

CEPI's active Nipah portfolio consists of three vaccine candidates: University of Oxford (Preclinical), Auro Vaccines (Phase I) and Public Health Vaccines (Phase I). Advances were made in 2022, with one candidate moving from Preclinical to Phase I, and another candidate receiving conditional approval to progress to the next development phase. A fourth candidate, previously in CEPI's Nipah portfolio, has been closed due to substantial project delays.

Recognizing the need for an alternative pathway to licensure for a Nipah vaccine, due to the nature of the disease, CEPI has funded a comprehensive set of enabling science projects in epidemiology, standards and assays, and animal models, to fill knowledge gaps. CEPI will bring together regulators in 2023 to discuss potential licensure pathways, and convene regional and global experts to discuss collaborative efforts to support studies advancing vaccine science and monitoring of epidemiology.

Chikungunya virus

CEPI's active Chikungunya portfolio consists of two vaccine candidates: IVI / Bharat (Phase IIb/III) and Valneva (Phase III). In a major milestone, Valneva completed rolling submission of the Biologics License Application to the United States Federal Drug Administration (FDA) for its vaccine candidate for adults in December 2022. Co-sponsors, Valneva and Butantan, completed enrolment and vaccination for a CEPI-funded technology transfer to Instituto Butantan, as well as Phase III clinical trials in Brazil for adolescents to support label extension to those aged 12-17 years, with first results expected mid-2023. These data will be used to achieve licensure in Brazil with material manufactured at Butantan. A third vaccine candidate is inactive due to acquisition of the development partner.

Working with Pan American Health Organization (PAHO) and the Brazilian Health Regulatory Agency ANVISA, CEPI brought together regulators in the region, as well as regulators from the FDA, Health Canada, European Medicines Association (EMA), Indonesia and South Africa, to learn the status of development for CEPI's Chikungunya vaccines and discuss the regulatory strategy.

To further advance one of CEPI's most mature disease portfolios, a CfP will be launched in 2023 (with support from the European Union) to fund Phase III and/or Phase IV studies to establish long-term safety and durability, and accelerate access and registration of Chikungunya vaccines in endemic countries.

Rift Valley Fever (RVF)

CEPI's active RVF portfolio consists of two vaccine candidates: Colorado State University (Preclinical) and Wageningen University (Phase I). In 2022, the Wageningen University candidate progressed from Preclinical to Phase I. To further develop the portfolio, a CfP, co-funded by the European Union, was launched to fund RVF vaccine candidates into Phase I/II in endemic countries; due diligence is currently ongoing for potential awardees.

KPI Output 1.2.1: Number of CEPI-funded vaccine candidates advanced for each priority pathogen				
Baseline	**Interim milestone 2022**	**Actual 2022**	**Target 2026**	**Status**
Preclinical: Seven Phase I: Seven Phase II: Three Phase III: One Registration: Zero Licensure: Zero	Preclinical: Two Phase I: Six Phase II: Four Phase III: Two Registration: Zero Licensure: Zero	Preclinical: Five (including two inactive[10]) Phase I: Nine (including two inactive) Phase II:Three (including two inactive) Phase III: One Registration: Zero Licensure: Zero	Two licensed vaccines, additional two vaccines in Phase III and four vaccines through Phase II with ready reserve of vaccine for use in an outbreak	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:
Across all priority pathogens (MERS, Lassa, Nipah, Chikungunya, RVF), CEPI is meeting the interim targets in Preclinical and Phase I, and progressing towards the interim targets in mid- and late-stage clinical development in 2022, with some delays mainly due to COVID-19 vaccine candidate developments having been prioritized during the pandemic.

The **Chikungunya vaccine portfolio** is the most advanced, with one candidate submitted for licensure to FDA through the accelerated regulatory pathway (i.e., not based on clinical efficacy) in 2022, another candidate having completed Phase II and seeking approval to move to Phase III in early 2023.

The **Lassa vaccine portfolio** is likely to be able to proceed through Phase III clinical efficacy trials, and contains one candidate in Phase I that has been approved to move to Phase II in 2022, and another candidate in Phase I. Preparatory activities are being conducted to move to Phase III efficacy trials in West Africa, with some of the ENABLE epidemiology sites potentially being able to take part in Phase III, and stakeholder and community engagement being conducted within endemic countries and among regional and global stakeholders. End-to-end vaccine development plans have been requested from developers, with iterative reviews to be conducted with CEPI and others.

The **Nipah vaccine portfolio** is likely to require an alternative regulatory pathway to licensure (i.e., not based on clinical efficacy). Potential pathways are being actively discussed with relevant regulatory authorities to support end-to-end development planning for Nipah vaccine developers (including the two currently in Phase I within CEPI's portfolio).

The **MERS vaccine portfolio**: Two MERS candidates are in Phase I, with a target to advance through Phase 2 clinical trials with ready reserve.

The **RVF vaccine portfolio**: One project progressed from Preclinical to Phase I, with the clinical trial ongoing in Europe. A CfP for vaccine candidate projects to enter Phase I/II clinical trials in endemic regions is currently being reviewed with the expectation to commence these projects in Q2 2023.

For all the priority pathogen vaccines in CEPI's portfolio, the specific requirements for late-stage development are being actively investigated on an ongoing basis in collaboration with key stakeholders, since development of these outbreak priority pathogen vaccines are unprecedented. As these requirements mature and plans become more defined, larger investments can be applied (as late-stage activities typically account for most development costs).

[10] Inactive means that the vaccine development project is currently being closed/under review for closure.

1.2.2. Advance monoclonal antibodies

As part of the current strategic cycle, CEPI will make some investments in biologic countermeasures beyond vaccines where they are beneficial for rapid response. Countermeasures like mAbs with rapid mechanisms of action can provide crucial pre- or post-exposure prophylactic protection, and possibly post-exposure treatment for diseases that cause short explosive outbreaks in which vaccines may not serve as the best initial course of action to bring the outbreak under control. To launch CEPI's investment in this area, a CfP for mAbs against Nipah is planned for Q2 2023, with accessibility as a core criterion.

KPI Output 1.2.2: Number of CEPI-funded monoclonal antibodies advanced for each priority pathogen

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
N/A	*Interim milestones and number of candidates will be added once the CfP is completed, and contracts are signed*	No candidates currently in the portfolio	At least two monoclonal antibodies ready for use in an outbreak situation	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:
Extensive landscaping was undertaken in 2022 to evaluate the current status of mAbs against outbreak pathogens across all phases of development – from discovery to clinical studies. Based on this assessment, it was concluded that CEPI's niche in the current mAb ecosystem should be in the later stages of development, building on the work of others by funding the clinical evaluation of promising mAb candidates and the stockpiling of investigational doses. Accordingly, a CfP for Nipah mAb candidates for outbreak use was generated, tailored to clinical-stage development and investigational ready reserve, and and has been published in 2023 (deferred from 2022).

Please note that the terminology for this area of work may move from "monoclonal antibodies" to "biologics" to be more inclusive of monoclonal-like technologies and innovations in biologics.

1.3. Reduce the risk of further coronavirus pandemics

Coronaviruses have caused three major epidemics or pandemics in the 21st century: Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and COVID-19. In order to reduce the risk of future coronavirus epidemics/pandemics, CEPI has initiated a broadly protective coronavirus (BPCV) programme to develop vaccines that will provide protection against multiple coronaviruses, including potentially against novel ones that have yet to emerge. To support the BPCV vaccine development programme, CEPI has also invested in a portfolio of enabling science activities to develop tools that will facilitate determining the breadth of protection and generate data required for regulatory approval.

The COVID-19 vaccine development landscape continues to be very dynamic. With that in mind, CEPI has structured its broadly protective coronavirus vaccine (BPCV) candidate portfolio into two main categories:

- Broadly protective SARS-CoV-2 variant targeted vaccine candidates (BP-SARS-CoV-2; target by 2023; captured in section 1.1),
- Broadly protective Betacoronavirus vaccine candidates (BPBC; target by 2026; captured in section 1.3).

There is ongoing discussion about developing broadly protective coronavirus vaccines based on a virus family approach similar to that being developed for Disease X. Conceptually, a series of off-the-shelf investigational BPCV vaccines, each targeting a range of pre-emergent viruses within one or more coronavirus subgenera, would be maintained in stockpiles as a ready reserve for a rapid response during an outbreak of a novel coronavirus. Candidates for such a repository would be selected based on their comparative breadth of protection potential, as determined by their capabilities to neutralize representative viruses in a standardized panel developed by CEPI and its partners, including the National Institute of Allergy and Infectious Diseases (NIAID).

KPI Outcome 1.3: Number of CEPI-funded broadly protective Betacoronavirus vaccines, favourable for LMICs, assessed for clinical proof of concept

Baseline	Actual 2022	Target 2026	Status
Zero	Zero	Two	ON TRACK

Comment on progress in 2022 and status:

In 2022, CEPI expanded its broadly protective Betacoronavirus vaccine candidates (BPBC) portfolio to include seven vaccine candidates in Preclinical and one vaccine candidate in Phase I (rescoped from COVID-19 to a broadly protective coronavirus vaccine candidate).

1.3.1. Advance broadly protective Betacoronavirus vaccine

In 2022, CEPI added six new BPBC vaccine candidates in the preclinical phase to its portfolio: Codiak, CPI / CalTech, DIOSynVax, Intravacc, NEC OncoImmunity and Panacea Biotec. Three of these candidates received seed funding to generate initial data, while the other three candidates are funded to demonstrate clinical proof of concept. An additional vaccine candidate in Phase I, VBI, originally in CEPI's COVID-19 portfolio, was re-scoped to become a BPBC candidate. These seven new candidates join an SK bioscience candidate in preclinical phase, signed in late 2021, resulting in a total of eight vaccine candidates in CEPI's BPCV portfolio.

KPI Output 1.3.1: Number of CEPI-funded broadly protective Betacoronavirus vaccine candidates, favourable for LMICs, advancing through preclinical and Phase I

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
One broadly protective Betacoronavirus vaccine candidate in Preclinical	*Interim milestones and number of candidates will be added once the CfP is completed, and contracts are signed*	Seven broadly protective Betacoronavirus vaccine candidates in Preclinical and one in Phase I	N/A	**ON TRACK**

Comment on progress in 2022 and status:
By end 2022, the BPBC vaccine candidate portfolio consisted of eight projects. In addition to the one project in the portfolio since end 2021, six projects were added to the portfolio throughout 2022 and one project was rescoped from a COVID-19 vaccine candidate to a broadly protective coronavirus vaccine candidate. Among the candidate vaccines in this portfolio, one candidate is currently in Phase I.

The interim milestones for the coming years have been defined (these projections do not account for portfolio attrition and/or down selection):

- For 2023, up to four candidates initiate Phase I studies; up to six, including seed funded and fully funded, demonstrate preclinical proof of concept (complete required preclinical work).
- For 2024, up to two more candidates demonstrate clinical proof of concept (complete Phase I); and one additional seed funded candidate demonstrates preclinical proof of concept (complete required preclinical work).
- For 2025, up to five candidates in Phase I and/or initiate Phase II studies, one additional candidate achieves clinical proof of concept.

2. Strategic Objective 2: Transform the response to the next novel threat

As the world becomes increasingly interconnected, a currently unknown pathogen with epidemic potential – a future Disease X – is inevitable, and is designated a priority under the 2018 WHO R&D Blueprint. CEPI has been preparing for the threat of an unknown pathogen, and will continue this trajectory by working to realize the 100 Days Mission and investing in innovations that will rapidly speed vaccine development and manufacturing.

To this end, CEPI is developing and characterizing rapid response vaccine platforms, and advancing the creation of vaccine libraries against virus families with high risk of causing outbreaks. In addition, CEPI is investing in enabling science programmes, such as real-time virus prioritization and computational immunogen design, as well as manufacturing initiatives such as the creation of a Manufacturing Network, and launching CfPs aimed at different areas of Chemistry Manufacturing, Control (CMC) innovation to improve speed, scale and access.

Activities to TRANSFORM the response to the next novel threat are described under the following sections and subsections:

2.1 Use vaccine prototypes and platform initiatives to give a head-start on novel threats

- 2.1.1 Create vaccine libraries
- 2.1.2 Adapt vaccine platform technologies

2.2 Scale enabling sciences to further accelerate vaccine development

- 2.2.1 Advance enabling science programmes

2.3 Transform vaccine manufacturing so it is cheaper, faster, and closer to an outbreak

- 2.3.1 Advance manufacturing innovations

2.1. Use vaccine prototypes and platform initiatives to give a head start on novel threats

In 2022, CEPI launched several CfPs, including for the development of advanced mRNA-based vaccine platform technologies, and generation of computational immunogen designs to support development of vaccine libraries against virus families with high epidemic/pandemic risk. The initial two virus families selected for vaccine library development were: 1. Paramyxoviridae (family of virus which includes Nipah and Hendra viruses) and 2. Arenaviridae (a family of viruses which includes Lassa virus and other deadly South American viruses like Junin and Machupo). These two families were selected as pilots since CEPI had already supported substantial vaccine development efforts against members of both two families and their outbreak potential in low- and middle-income settings.

At the end of December 2022, CEPI's Disease X platform portfolio consisted of two vaccine platforms in preclinical phase: SK bioscience's mRNA platform and University of Queensland's protein molecular clamp platform. In addition, vaccine platforms used for vaccine candidates in the priority pathogens portfolio can be leveraged for use as rapid response vaccine platforms for vaccine library development if appropriate (e.g., University of Oxford's adenoviral vector platform). Furthermore, a CfP for novel RNA technology innovations was published in 2022 and will remain open until 2023. This CfP is expected to support the advancement of next-generation mRNA vaccine platform technologies. Looking forward, a broader CfP for innovative platform technologies (both RNA and non-RNA) will be published in 2023 to support potential next-generation vaccine platforms.

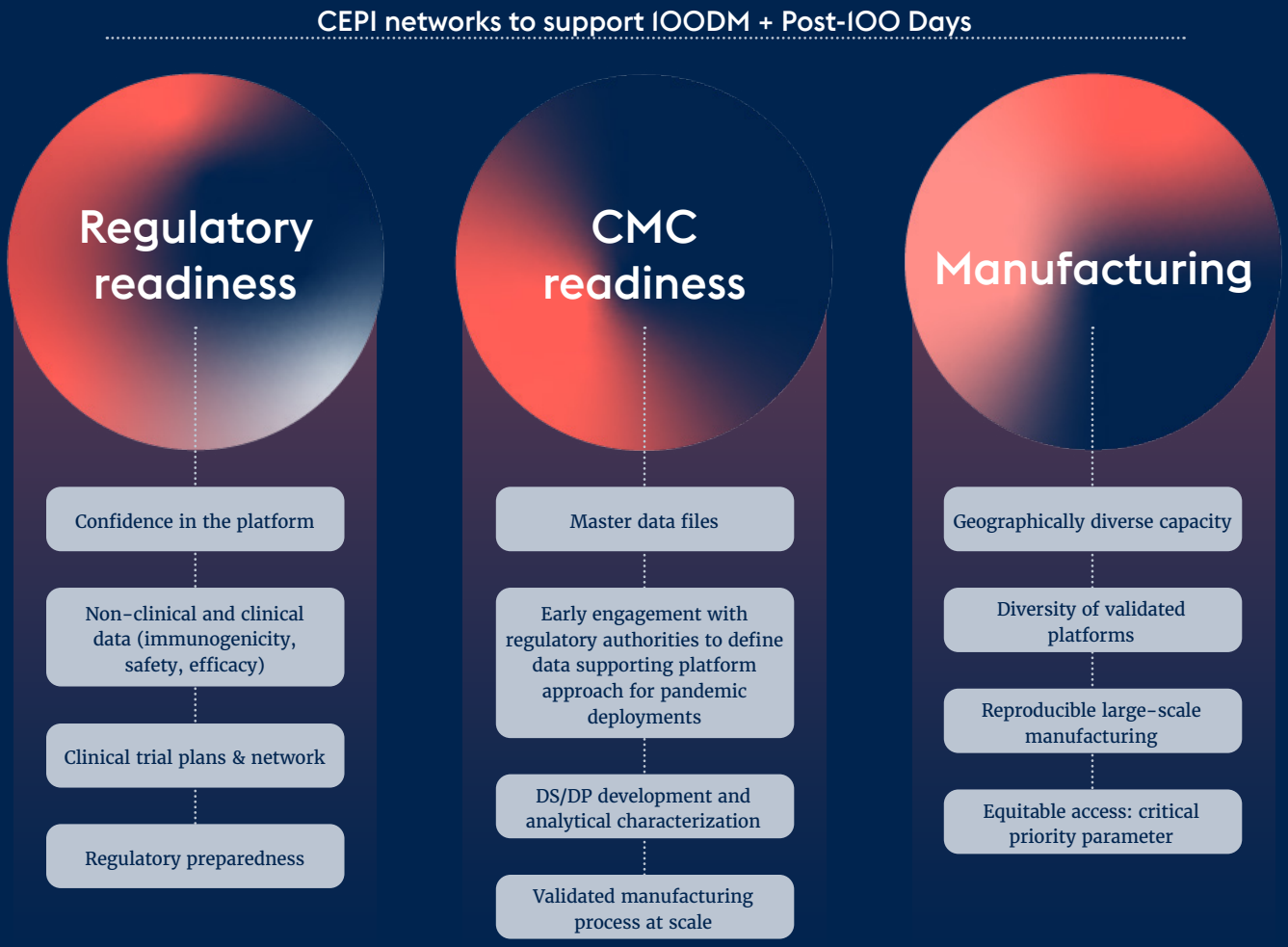
VACCINE LIBRARIES

The 100 Days Mission depends on the development of vaccine libraries targeting virus families with high risk of causing epidemics and pandemics. The concept of vaccine libraries is based on the creation of a range of library materials, including the knowledge base (e.g., antigen sequence, structure, assays, animal models, immune response, safety data, etc.) research-grade vaccine reagents and vaccine constructs, GMP-grade seed materials and vaccine formulations, and/or vaccine candidates taken through preclinical and clinical proof-of-concept.

The vaccine library concept relies on different antigens being applied to rapid response vaccine platforms (e.g., mRNA, viral vector, etc.) that have common research and manufacturing characteristics to minimize the need to develop new research and manufacturing processes in response to a novel pathogen. The vaccine library materials could then be leveraged to get a head start on developing safe and effective vaccines in response to the outbreak. The level of advancement of library materials, from just the knowledge base up to late-stage vaccine candidates against different target pathogens will vary. Therefore, the degree of the possible head start will also vary. However, as the vaccine libraries become more extensive and advanced over time, the likelihood of a substantial head start will progressively increase. In the first year of CEPI 2.0 strategic cycle, CEPI has prioritised two viral families for its vaccine library work: paramyxoviridae which includes Nipah and Hendra viruses and arenaviridae which includes Lassa virus and other deadly South American viruses like Junin and Machupo.

CEPI is also building regional networks of laboratories for animal model development and testing, human immunology labs and clinical trial networks that can support the vaccine development work of our partners.

Figure 6: Establishing rapid Response Vaccine Platforms: a critical element of CEPI's 2.0 strategy beyond R&D



KPI Outcome 2.1: Number of CEPI-funded innovations that can be rapidly adapted against unknown pathogens			
Baseline	**Actual 2022**	**Target 2026**	**Status**
Zero	Zero	• Clinical proof of concept for four virus family vaccine libraries • Two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:

Currently there is one project in the virus family vaccine library portfolio (SK Bioscience – exemplar for vaccine library Lassa, added in October 2022) and two projects in the prototypic / platform innovations portfolio (SK Bioscience – a prototypic vaccine against Japanese Encephalitis virus, added in October 2022. Tiba Biotech – a platform innovations project with a prototypic vaccine candidate against Japanese Encephalitis virus, added in January 2023).

In 2023, CEPI will release a new CfP to advance innovative vaccine platforms with the potential to transform Disease X outbreak response. This will include and expand beyond novel RNA technologies to include other platforms that can enable vaccine development within 100 days of an outbreak as well as innovations to deliver more safe, effective, and accessible vaccines. The CfP will also invite expressions of interest on novel vaccine candidates for Disease X, which will enable CEPI to expand the Disease X library to include additional developers and exemplar vaccine candidates.

2.1.1. Create vaccine libraries

The generation of Disease X vaccine libraries involves multiple components. First, virus families and viruses within each family will be prioritized for their risk of causing epidemics and pandemics. These viruses include those not yet documented in humans, but which are at risk of spilling over from zoonotic sources to people. Second, immunogens will be designed using computational methods, accounting for structure, receptor interactions and other characteristics. Third, these computational designs will be expressed as recombinant proteins in the laboratory and assessed using various laboratory analytical methods. Fourth, vaccine constructs will be created by combining promising immunogens with different rapid response vaccine platforms (e.g., mRNA, viral vector, etc.) and undergo laboratory and animal testing. Fifth, a subset of promising "preclinical exemplar vaccine" candidates may undergo further preclinical safety and efficacy testing. Sixth, a subset of promising "clinical exemplar vaccine" candidates following preclinical assessment may progress to Phase I/II clinical trials. Seventh, some clinical exemplar vaccine candidates may proceed to late-stage development as "prototype vaccine" candidates. The iterative technical, safety and efficacy data gathered from testing preclinical and clinical exemplar vaccines, and prototype vaccines on rapid response platforms will add to the "validation" of the corresponding rapid response platform on which the vaccine candidates are based.

In late 2022, WHO, CEPI, FIND, and other partners, convened the first meeting of Prioritization Advisory Committee to define priority pathogens of pandemic potential. In addition, CEPI began a partnership with University of California, Davis to develop a ranking system that assesses the likelihood of a Disease X emerging from a family of viruses. Work is ongoing to achieve a dynamic virus prioritization ranking list that is adopted globally, based on scientific evidence and modelling projections, with the collaboration of key stakeholders such as WHO and regional bodies.

In early 2022, a CfP on RNA vaccine platform technologies to support development of vaccine libraries against emerging and select endemic infectious diseases, and a CfP on State-of the-Art Immunogen Design using Computational Antigen Simulation Technologies for Vaccine Development Against Emerging Infectious Diseases, were launched.

Two applicant consortia were selected for the CfP on State-of the-Art Immunogen Design using Computational Antigen Simulation Technologies. Due diligence was undertaken in December 2022 with contract negotiations ongoing.

The RNA CfP sought vaccine developers with advanced mRNA vaccine platform technologies to develop a prototype vaccine candidate to go through full clinical development to licensure and support vaccine library development focused on high-risk virus families, with the initial target exemplar vaccine candidates being against Lassa virus and/or Nipah virus through clinical proof-of-concept.

The resulting development of RNA platforms will synergize with the outputs from the CfP for Immunogen Design to generate vaccine constructs and candidates for development of the vaccine libraries.

KPI Output 2.I.I: Number of virus family vaccine libraries which have demonstrated proof of concept for viruses with high probability of inducing outbreaks

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
Zero	Completion of vaccine libraries for two virus families (two pilot projects)	• Zero vaccine libraries completed • One virus family vaccine library onboarded (SK Bioscience - exemplar for vaccine library Lassa)	Clinical proof of concept for four virus family vaccine libraries and preclinical proof of concept for additional six virus family vaccine libraries	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:
Virus family and virus risk ranking was initiated in collaboration with the University of California, Davis, and is expected to deliver a preliminary risk ranking in 2023, with real-time ongoing updates thereafter. In 2022, vaccine library development was initiated on the first pilot virus family (Arenaviridae family with Lassa as the exemplar vaccine). Vaccine library development on the second pilot virus family (Paramyxoviridae family with Nipah as the exemplar vaccine) is expected to be initiated in 2023.
As soon as agreements with the two immunogen design consortia selected from the immunogen design CfP are executed (expected in 2023), computational immunogen design activities can progress on additional targets within other viral families. Generation, evaluation and development of vaccine constructs, including exemplar vaccines, will also be performed by additional strategic partners with advanced vaccine platforms (agreements expected in 2023).
Key milestones for the virus family vaccine libraries and exemplar vaccines in the coming years are:
- Immunogen designs for additional virus family libraries (libraries 3 and 4) are expected to be initiated in 2023.
- Additional strategic agreements with advanced vaccine platform developers are expected to be executed in 2023.
- Preclinical proof of concept for exemplar vaccines for Lassa and Nipah is expected by end of 2024.

To achieve the target in 2026, development of exemplar vaccine candidates for vaccine libraries 3 and 4 will be initiated by end 2024.

2.I.2. Adapt vaccine platform technologies

CEPI funds research to validate vaccine platforms which can be quickly pivoted towards Disease X, (including by applying them to known pathogen targets). Of the two RNA CfPs launched in 2022:

- The first RNA CfP yielded three applicants selected for due diligence. One awardee (SK bio) was signed in October 2022 to develop both a prototype vaccine against Japanese Encephalitis Virus to add to "validation" of their mRNA platform [Output 2.1.2], and an exemplar vaccine against Lassa to add to vaccine library development [Output 2.1.1]. Another awardee is anticipated to be signed in 2023.
- The second RNA CfP, seeking novel RNA technologies for next-generation vaccine platforms for the future – was launched in 2022 with due diligence ongoing to end of December 2022. One awardee, Tibia Biotech (a platform innovation project with a prototypic vaccine candidate against Japanese Encephalitis virus) added in January 2023.

CEPI also launched a CfP on improving vaccine thermostability, which will remain open until January 2023. In addition, CEPI and Wellcome Leap selected 17 organizations to co-fund seed awards. One area of focus is cost reduction and increased access to biologics through alternative delivery mechanisms (e.g., via needle-free delivery).

With a focus on innovative technologies to enable access for LMIC's, CEPI funded a new fill/finish, presentation, and multi-dose bag injection project (MedInstill); and through an expression of interest (EOI) matched the project with two vaccine developers one of which is Institut Pasteur Dakar.

KPI Output 2.I.2: Number of prototype vaccines for existing vaccine preventable diseases (with prevalence in LMICs) using rapid response vaccine platforms

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
Zero	Interim milestones and number of candidates and/or platforms will be added once the CfP is completed, and contracts are signed	One ongoing prototype vaccine candidate	Two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:

Three applicants for the CfP seeking advanced mRNA vaccine platform technologies entered due diligence. SK Bioscience was signed in October 2022 to develop both prototype vaccine against Japanese Encephalitis [Output 2.1.2], and exemplar vaccine against Lassa for vaccine library development [Output 2.1.1]. One other applicant is expected to sign in 2023 on a modified project to optimize the applicant's RNA vaccine platform. CEPI will continue to actively monitor the RNA vaccine technology landscape and may consider portfolio additions if opportunities arise. CEPI is also working towards strategic partnerships with some developers that may encompass several projects and /or vaccine libraries using a common RNA platform technology.

For the second RNA CfP (seeking novel innovations for next-generation RNA platform technologies), review and due diligence of applicants was ongoing by end of December 2022. Tiba Biotech – a platform innovations project with a prototypic vaccine candidate against Japanese Encephalitis virus – was added in January 2023.

CEPI and Wellcome Leap selected 17 organizations to co-fund seed awards, as part of Leap's USD 60 million RNA Readiness and Response (R3) programme on RNA-based biologic products (e.g., monoclonal antibodies, vaccines), including setting up manufacturing facilities.

The interim milestones for 2023 have been defined as:

- Demonstrate preclinical proof of concept for Japanese Encephalitis prototype vaccine by SK bioscience.
- Initiate development of exemplar vaccine based on non-mRNA vaccine platform.

CEPI will continue to actively monitor the RNA vaccine technology landscape and may consider portfolio additions if opportunities arise. CEPI is also working towards strategic partnerships with some developers that may encompass several projects and /or vaccine libraries using a common RNA platform technology.

2.2. Scale enabling sciences to further accelerate vaccine development

Complementing its portfolio of vaccine candidates and platforms, CEPI is also investing in enabling science programmes to accelerate vaccine development and deployment. These activities span standards and assays, animal models, epidemiology, predictive and mathematical modelling, clinical research, regulatory and diagnostics.

CEPI is developing concepts for clinical research preparedness and operational strategies, informed by epidemiology, for optimal design of evidence generation for the use of biological countermeasures. For priority pathogens and Disease X platforms, CEPI is facilitating the development of the regulatory framework, regulations, organizational structure as well as conducting a risk ranking of viruses with the highest risk of zoonotic spillover to prepare for the next pandemic.

In addition to filling gaps in knowledge and producing innovative tools, these enabling science programmes expand CEPI's network of collaborators across the globe. Two examples of networks include CEPI's Centralized Laboratory Network established in 2020, which provides sample testing services that both CEPI-funded and non-CEPI-funded developers can access, and CEPI's Animal Model Network established in late 2019, which CEPI-funded developers can utilize.

These networks have been essential for advancing CEPI supported COVID-19 vaccine development projects and CEPI's general BPCV programme. In particular, from its establishment in 2020 to the end of 2022, the Centralized Laboratory Network expanded its operations to include six assays and 10 laboratories worldwide, engaging over 50 COVID-19 vaccine developers across four continents and receiving more than 70,000 samples for analysis, from preclinical and clinical (Phases I-II-III) studies. Meanwhile, the Animal Model Network supported 17 vaccine developers with infection models, offering seven animal models for COVID-19 testing across its eight laboratories.

In 2023, the Central Laboratory Network will expand to include pathogens, other than the SARS-CoV-2, and will also assist the harmonization of immunological assessment. Similarly, the Animal Model Network is expanding to support CEPI's Disease X programme and build capabilities to conduct licensure-enabling studies, in line with CEPI 2.0 goals for priority pathogens.

The Lassa fever research programme, ENABLE, was extended to mid-2024 due to the COVID-19 pandemic. However, interim data was successfully compiled and made available to developers and key local stakeholders during a workshop held in Abuja, Nigeria in October 2022. Enable Programme study data and further site readiness activities will be completed in 2024.

In relation to COVID-19 CEPI supported 14 complementary clinical trials (CCT) taking place in countries across Africa, Asia, Europe, South America and Oceania, including fractional dosing (FraCT-CoV) aimed at supporting policy makers by advancing understanding of the vaccines, e.g., immunogenicity within at-risk populations, and maximizing access to them including through heterologous boosting and fractional dosing. As supply outstrips demand for COVID-19 vaccines, fractional studies are being deprioritized. In 2023, as bivalent omicron-specific vaccines become available, studies comparing monovalent and bivalent vaccines will be initiated.

Figure 7: CEPI Centralised Lab Network as of December 2022

KPI Outcome 2.2: Enabling science programmes and innovative tools actively used by CEPI-funded developers to further accelerate vaccine development			
Baseline	**Actual 2022**	**Target 2026**	**Status**
N/A	Six enabling science programmes and innovative tools are actively in use by CEPI-funded developers	Three or more of the enabling science tools developed through CEPI funding used by one or more of CEPI-funded vaccine developers	**ON TRACK**

Comment on progress in 2022 and status:

Enabling science programmes and innovative tools actively in use by CEPI-funded developers to further accelerate vaccine development, include:

- **Antibody standards and antigens** for Lassa, MERS and SARS-CoV-2- are used by all CEPI-funded developers.
- **Central laboratory network**: 20 CEPI developers are using the CEPI Central Laboratory Network for testing samples.
- **Animal Models network**: At least four developers used the Animal Model Network in 2022; and 17 developers have used the network since its inception.
- **Systems immunology**: One CEPI developer.
- **The ENABLE Lassa fever Research Programme**: Launched in 2020, this has captured burden of disease information for Lassa virus across five West African countries. Interim data is now available and is being directly utilized by Lassa vaccine developers to inform clinical trial design.

2.2.I. Advance enabling science programmes

To further advance the CEPI 2.0 strategy and 100 Days Mission, CEPI carries out enabling science activities such pathogen monitoring, prioritization and risk assessment, collection of real-world evidence (in respect of COVID-19), and mathematical modelling, with a view to identifying and addressing critical knowledge gaps and to provide innovative tools and critical data to internal and external stakeholders including vaccine developers and other CEPI partners to accelerate their work.

As part of the generation of real-world evidence, in 2022 CEPI launched a COVID-19 Vaccine Effectiveness CfPs. Among the 16 applications received, four applications were approved for funding and two one-year contracts were signed (with University of the Philippines and Mutala Trust in Zimbabwe). CEPI also launched an Impact Assessment project and commissioned Imperial College London and a consortium of Oxford University and Liverpool School of Tropical Medicine, to investigate the likely health and health-economic impacts of accelerated vaccine development. In addition, CEPI published a Systematic review on RFV in PLoS Neglected tropical Diseases (January 2022).

Other highlights from CEPI's enabling science programmes in 2022 include:

- The launch of the Predictive Modelling Programme;
- A strategy to advance mAb development;
- The establishment of vaccine platform technology regulatory master files;
- A second partnership established with the Brighton Collaboration on the Safety Platform for Emergency Vaccines (SPEAC) to provide cross-pathogen and cross-platform vaccine safety oversight.

Figure 8: CEPI Preclinical Animal Model Network as of December 2022

KPI Output 2.2.I: Number of enabling science programmes and innovative tools to accelerate vaccine development advanced				
Baseline	**Interim milestone 2022**	**Actual 2022**	**Target 2026**	**Status**
International standards developed for Lassa and MERS, initiated for Nipah, RVF. Serology assay completed for Lassa and MERS	Six interim milestones for 2022 across enabling science programmes and innovative tools	Three are on track with one completed in Q1 2023, three interim milestones are delayed (see comment section below)	Standards, preclinical models, assays, translational immunology, correlates of protection, sentinel safety surveillance and epidemiological, mathematical models and studies advanced for all CEPI priority pathogens and the virus family approach	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:
Interim milestone for 2022 (1): Develop RVF WHO international standard.
Actual 2022: The RVF working standard and panel is available, the WHO international standards have been developed and were approved by WHO (Q1 2023).

Interim milestone for 2022 (2): Target Product Profile for Disease X vaccine modelled and shared with stakeholders.
Actual 2022: Draft TPCs are available but need to be refined by modelling.

Interim milestone for 2022 (3): Nipah consortium to assess the epidemiological diversity of Nipah strains established and study activities launched.
Actual 2022: Study is ongoing with University of Malaya (Malaysia) since 2022 and has started in Bangladesh in Q1 2023 to assess the epidemiological diversity of Nipah strains.

Interim milestone for 2022 (4): Systematic review on RVF vaccine trial design published.
Actual 2022: Systematic literature review of RVF virus epidemiology was published in January 2022 here.

Interim milestone for 2022 (5): Develop translational immunology concepts supporting the establishment of 'correlate of protection' libraries supporting rapid vaccine development and authorization strategies.
Actual 2022: Work started on translational immunology concepts for correlates of protection in December 2022 and there is a plan to launch a CfP in July 2023 for crosscutting pathogens. Transmission blocking approaches started in 2022 for COVID vaccines.

Interim milestone for 2022 (6): Advance concepts around innovative trial designs to support rapid clinical development strategies based on pre-defined benefit-risk scenarios (contributing to CEPI's 100 Days Mission).
Actual 2022: Work on advancing concepts around innovative trial designs will start in 2023.

2.3. Transform vaccine manufacturing

Following the establishment of the Manufacturing and Supply Chain division with experienced staff expanding the team from the vaccine industry, a CMC framework and technical transfer guidance were developed to support CEPI's awardees through the respective development phases. The Supply Chain Services team managed COVAX Marketplace and supported CEPI's portfolio, partnering initiatives, supply chain modelling collaborations and outbreak response. During recent outbreaks CEPI's experienced manufacturing team supported the delivery of clinical trial doses using the mechanisms of matching partners.

CEPI's Manufacturing Innovation programme will focus on vaccine process platforms, thermostability, speed, cost and other characteristics that are particularly relevant for LMIC markets.

KPI Outcome 2.3: Number of new technologies demonstrating manufacturing cheaper, faster or closer to an outbreak

Baseline	Actual 2022	Target 2026	Status
N/A	0	At least three innovations which demonstrate manufacturing cheaper, faster or closer to an outbreak	**ON TRACK**

Comment on progress in 2022 and status:

A CfP to develop heat-stable vaccine technology for use against epidemic and pandemic threats (Thermostability CfP) was launched in 2022. One partnership agreement was signed in December 2022 (Vaxxas) and another one in January 2023 (20Med).

2.3.1. Advance manufacturing innovations

After the CEPI 1.0. investment in innovative fill, finish and presentation technology, thermostability was prioritized as the first CEPI 2.0 area in which to invest, as a key criterion to support equitable access, in particular for mRNA-based vaccines. A CfP resulted in 69 applications which were reviewed in 2022 and early 2023. The first project was signed in December 2022, for the development of microarray patches for mRNA-based vaccines, improving thermostability, distribution and delivery, and equitable access for this platform. Two additional projects moved into due diligence in 2022. In parallel, innovation prioritization was performed with internal and external stakeholders, to define the scope and criteria for the next CfPs.

CEPI has also identified key CMC innovations to accelerate vaccine development and manufacturing in response to an outbreak, thereby contributing directly to the 100 Days Mission. This work forms the basis of new CfPs, to be published in 2023, one focusing on speed-related manufacturing innovations to accelerate the response to a new outbreak, and the second focusing on scale- and access-related manufacturing innovations to make vaccines equitably accessible. Innovation prioritization has been performed for both calls with internal and external stakeholders, and the first CfP is scheduled to be open from May 2023. Projects are anticipated to start from the end of 2023 and throughout 2024.

KPI Output 2.3.1: Number of manufacturing innovations advanced

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
N/A	Centralized process for manufacturing innovations selection and funding implemented Support two projects on manufacturing innovations that can accelerate epidemic and pandemic responses or enable the scaling of production of vaccines, particularly in LMIC settings	Process for Chemistry, Manufacturing and Control (CMC) innovations selection and funding implemented for the Thermostability CfPs and the prioritization for the Speed CfP One manufacturing innovation project was signed by the end of 2022, and the second one in early January 2023	~5 manufacturing innovation projects advanced	**ON TRACK**

Comment on progress in 2022 and status:

- A CfP to develop heat-stable vaccine technology for use against epidemic and pandemic threats (Thermostability CfP) was launched in 2022.
- The call received 69 applications with three entering due diligence. Several still undergoing review in early 2023.
- One manufacturing innovation project was signed by end of 2022 – with Vaxxas to advance development of its high-density microarray patch for mRNA vaccines.
- In parallel, an innovation prioritization exercise was performed with internal and external stakeholders, to define the scope and criteria for the next CfPs to be announced in 2023.
- A second manufacturing innovation project was signed in January 2023 with 20Med to advance development of their polymeric nanoparticle platform technology for mRNA stablilization and delivery.

3. Strategic Objective 3: Connect to enhance and expand global collaboration

CEPI's Connect strategy emphasizes connections beyond those needed for Prepare and Transform (the vaccine development partners, laboratories, clinical trial partners, and manufacturers) to engage with global, regional, and national institutions to reinforce the overall global health security and pandemic preparedness and response (PPR) systems, to help ensure that developed products reach where they need to go. Given no single organisation can accelerate the research, development and manufacturing of vaccines (R&D&M) against EIDs alone – and support system equity - CEPI connects and collaborates closely with organizations responsible for financing, manufacturing, purchasing, stockpiling, and distributing these products to streamline access to all people in need.

This strategic objective focuses on activities that support the establishment of needed financing for epidemic and pandemic preparedness, including fully funding CEPI 2.0, establishing networks to fill gaps in the present ecosystem, promoting adaptive and harmonized ways to accelerate R&D and strengthen systems equity, including through the establishment of more geographically diverse manufacturing capacities.

3.1. Secure financing for epidemic preparedness and response

CEPI helps to ensure that critical resources are available to support vaccine R&D and other initiatives essential for addressing the continued evolution of COVID-19 and future global health threats. This will require both long term sustainable funding for the preparedness ecosystem at large, including fully funding of CEPI 2.0, and ready-releasable surge funding when faced by a new threat.

CEPI is working to ensure that R&D&M funding remains a key focus in global fora. In addition to advocating for the new Pandemic Fund mechanism to also fund vaccine R&D (see KPI Outcome 3.1), CEPI participated in various financing initiatives and high-level fora including:

- Submission of proposals to the Organization for Economic Cooperation and Development (OECD) to assess the eligibility of CEPI 2.0 programmes for official development assistance (ODA), presented to the OCED's DAC Working Party on Development Finance Statistics (WP-STAT) in December 2022[11].
- Active engagement in shaping understanding of development of health technologies that disproportionately benefit LMICs. This has included engagement with the OECD Health Team as part of its flagship project to promote investment in strengthening health system resilience.
- Engagement with G20 Joint Finance-Health Task Force, under the co-leadership of Italy and Indonesia, where CEPI has helped place surge financing for international pandemic response on the official agenda for discussion during the 2023 India G20 Presidency, including in the establishment of the Pandemic Fund.
- Advocacy and engagement with the early investors to the Pandemic Fund to enable accreditation as an implementing agency.
- Working closely with the G7 Presidencies (held by Germany in 2022 and transitioning to Japan in 2023) to explore innovative approaches to surge financing and to reform the finance component of the Health Pandemic Preparedness and Response ecosystem.

[11] The revised OECD assessment of 88% ODA eligibility, for the core contributions to CEPI 2.0, was approved by the WP-STAT at their meeting from 21-23 March 2023.

KPI Outcome 3.1: New financing mechanisms include funding for vaccines and other biologic countermeasures preparedness and response R&D				
Baseline	**Interim milestone 2022**	**Actual 2022**	**Target 2026**	**Status**
N/A	Mechanism(s) proposed for consideration	The Pandemic Fund has been established as a new financing mechanism for Pandemic Preparedness and Response CEPI has been accredited as an Implementing Entity	Funding for vaccine and other biologic countermeasures preparedness and response R&D	**ON TRACK**

Comment on progress in 2022 and status:

- Throughout the lead-up to the establishment of the Pandemic Fund[12], CEPI successfully advocated for designation as an Implementing Entity.
- As a result, CEPI is now able to apply for funding to support vaccine R&D and other critical initiatives.
- Being an Implementing Entity means that CEPI is also an Observer on the Pandemic Fund's Governing Board. This recognition highlights CEPI's proven track record in the field and its commitment to support essential initiatives to address the ongoing COVID-19 pandemic and future global health threats.

[12] The Pandemic Fund, approved by World Bank's Board of Directors, June 2022, established September, 2022 (link)

3.1.1. Advocate for availability of sustainable and ready releasable funding mechanisms

To achieve its mission CEPI needs diversified funding sources that are robust enough to mobilize the USD 3.5 billion programme budget, including from departments of health, health security, defense, research, science, technology, and development budgets, as well as from a diversity of non-governmental sources (sovereigns, philanthropies, private sector, high-net-worth individuals). Important attributes for financing are that funds are available when needed, for both preparedness (just-in-case) and response (just-in-time/surge); sustainable – in order to facilitate long-term, non-earmarked financing that is easy to renew – as well as being investable at-risk; where needed, to accelerate product development and availability at-scale.

Mindful of these criteria, CEPI's resource mobilization strategy is to use a multi-year replenishment mechanism and ongoing donor engagement to increase predictability of resource flows. High-level political support for a replenishment pledging event was a central success factor in 2022, the first year of CEPI's second five-year strategy. After a 12-month long advocacy campaign, CEPI held its first replenishment conference, the Global Pandemic Preparedness Summit, in March 2022 in London, United Kingdom. International policymakers, scientists, and representatives of industry, philanthropy and civil society were united at the Summit—co-hosted by the UK Government—in endorsing the ambition to have safe, effective, and globally accessible vaccines against the next pandemic threat ready in just 100 days.

KPI Output 3.1.1: CEPI fully funded for 2.0

Baseline	Actual 2022	Target 2026	Status
Investor commitments of USD 310 million in 2021 for CEPI 2.0	USD 1.98 billion* in 2022 for CEPI 2.0	USD 3.5 billion in commitments	**ACTION REQUIRED**

Comment on progress in 2022 and status:

- In March 2022, the first CEPI replenishment event raised USD 1.667 billion towards its USD 3.5 billion target from existing and new investors[13].
- By the end of 2022 an additional USD 315 million had been raised from Ethiopia, European Commission, Germany, Lithuania, and Luxembourg.
- CEPI anticipates securing a further USD 0.6 billion in pledges in 2023.
- By December 2022, 14 out of 18 pledges were converted into commitments to pay, amounting to USD 875.61 million (Bill & Melinda Gates Foundation, Austria, Finland, Germany, Indonesia, Italy, Japan, Luxembourg, Mexico, New Zealand, Norway, Singapore, Switzerland, United States).

Challenges:

- Heavy competition with multiple other fundraising events / global health organization replenishments.
- Changes in government and/or donor policy caused some countries to reduce or postpone their pledges.
- Fiscally constrained environment due to costs of the pandemic, eruption and ongoing war in the Ukraine and rising energy and cost of living forced other governments to shift priorities or delay funding decisions.

**Non-USD figures calculated at pledge date exchange rates.*

[13] Includes downpayment contributions received in 2021 amounting to USD 267.81 million.

Global Pandemic Preparedness Summit, on 8 March 2022

March 2022 saw the first ever public-facing replenishment event for the Coalition for Epidemic Preparedness Innovations, the Global Pandemic Preparedness Summit, co-hosted in London by the Government of the United Kingdom.

CEPI sought commitments from the global community to fund a 5-year plan to reduce the risk posed by epidemics and pandemics by developing vaccines for known disease threats (such as Lassa fever, MERS and Nipah virus), and by building on the scientific advances made during COVID-19 to prepare in advance for Disease X – the threat of an unknown pathogen with pandemic potential.

Central to the plan is CEPI's ambition – endorsed by G7 members and the G20 – to compress the time taken to develop safe, effective, globally accessible vaccines against emerging diseases to as little as 100 days. Achieving the 100 Days Mission would give the world a fighting chance of tackling and containing outbreaks close to the source in future, before they spread around the world and become pandemics.

The Covid-19 pandemic has dramatically highlighted the need for better pandemic preparedness and an even more rapid response to the demand for effective vaccines. Leading figures highlighted the importance of access-focused R&D as a cornerstone of global health security, and explored how to boost and sustain vaccine manufacturing across the world.

Dr Tedros Adhanom Ghebreyesus, Director General, World Health Organization, welcomed the Summit, "COVID-19 will not be the last Disease X. Epidemics and pandemics are a fact of nature, exacerbated in our time by urbanization, encroachment on habitats, the climate crisis, and insecurity. We need to strengthen efforts to develop, evaluate and distribute vaccines, tests and treatments as rapidly and equitably as possible when a new pathogen emerges."

As a result of the Summit, a total of USD1.6 billion was raised to kick start CEPIs plan to tackle epidemics and pandemics, potentially saving millions of lives and trillions of dollars in lost economic output. More information on the governments and philanthropies that pledged their support for CEPI can be found section 4.1. in the Investors Overview here. The Global Pandemic Preparedness Summit marked a moment in the global community's collective efforts to build a world that is better prepared to respond to epidemic and pandemic threats. This funds put CEPI on the path to raising the USD 3.5 billion it needs over the next five years.

3.2. Coordinate among key stakeholders to enable system readiness

In 2022, CEPI engaged with several processes related to policy, financing and influencing the evolving architecture for global pandemic preparedness and response, including negotiating for an International Pandemic Accord[14] CEPI:

- Collaborated with partners to align and leverage a unified voice for a more responsive health ecosystem, shaping focus of the Pandemic Fund and ensuring R&D investments are within scope. CEPI was appointed as an Implementing Entity with an observer seat on the Board.

- Supported the African Union's Partnerships for African Vaccine Manufacturing (PAVM), providing consultancy support to the secretariat and participating in technical working groups. CEPI supported the establishment of and is the co-chair of the Regional Vaccines Manufacturing Collaboration, hosted by the World Economic Forum, to promote regional sustainable vaccine manufacturing eco-systems.

- Engaged with successive G20 presidencies (Italy, Indonesia), participated in the G20 Joint Finance-Health Task Force and, in late 2022, engaged the G7 Japan Health Working Group, to contribute to the development of end-to-end thinking on equitable access and acceleration of R&D of vaccines in shaping the Pandemic Preparedness and Response ecosystem. This resulted in the recognition of CEPI and the 100 Days Mission in the 2022 G20 Health Ministers' and joint Finance and Health policy outcome documents.

- Worked with WHO, and other international and regional organizations towards preparedness and collaboration for future outbreaks and pandemics. CEPI was invited to participate in a WHO convened working group to develop proposals for a Medical Countermeasures platform (MCM) that could support a rapid collaborative response to an emerging pandemic threat. The MCM platform will be a 'minimum viable product' to be updated following the conclusion of the Pandemic Accord negotiations in 2024.

- Worked with Gavi, Unicef and WHO, consulting with regional and other international organizations, to agree how partners focused on vaccines will work together operationally (triggers, roles and responsibilities, risk-sharing, hand-offs etc.) to respond to different types of outbreak and pandemic threats. This work is complementary to the MCM Platform (which focuses on coordination across vaccines, therapeutics, and diagnostics).

[14] International Pandemic Accord: WHO Member States legally binding instrument designed to protect the world from future pandemics. Zero draft in development, anticipated for approval by the WHA in 2024.

Negotiations started in 2022 on a Pandemic Accord, with agreement expected at the World Health Assembly in May 2024. CEPI has engaged actively with the INB (Intergovernmental Negotiating Body) and at every opportunity to help shape the Accord. Through consultations, in-depth discussions, and sharing of CEPI's experiences and perspectives, the Zero Draft Pandemic Accord now contains commitments to increase R&D capacities, link public R&D funding to equitable access measures, as well as rapid sharing of pathogens of pandemic potential.

In 2022, CEPI played an active role in a range of global events, summits, and conventions that significantly influenced the pandemic preparedness and response ecosystem, including the World Health Assembly, World Health Summit, United Nations General Assembly, Munich Security Conference, and G20 Summit.

CEPI utilized existing platforms while also creating new opportunities to drive ecosystem reform. One of CEPI's primary focuses was addressing the gaps in the Health Emergency Preparedness and Response (HERA) architecture. Additionally, CEPI worked towards strengthening the International Health Regulations (IHR) and advancing its policy objectives. Some of these goals involved maintaining the 100 Days Mission as a central component of a responsive PPR architecture, promoting equitable access to Medical Countermeasures (MCMs) with distributed manufacturing, and addressing sustainability and surge financing gaps.

CEPI's active participation in these global fora continues to contribute to establishing the organization as a leading global influencer in PPR, and CEPI plays a prominent role in shaping the global platform for MCM, establishing regional vaccine manufacturing capacity, and advocating for additional funding of vaccine R&D&M, among others.

In addition to pursuing the R&D&M agenda, CEPI's increasing participation and contribution at these global events has established CEPI as a global thought leader in PPR. Consequently, CEPI now has "a seat at the table" in the ongoing processes toward shaping a global MCM platform that will continue into 2023 – and beyond.

KPI Outcome 3.2: Alignment on key elements of a target ecosystem to accelerate development and promote equitable access of emerging infectious disease countermeasures

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
N/A	Landscaping, gap exercises and discussions with key partners, countries and regions	• Landscaping was carried out • CEPI actively engaged with key multilateral –and regional partners	RACI(s)[15] for 80% of key elements in place	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:

Landscaping was carried out and a draft internal document outlining the role of various ecosystem partners, CEPI's engagement with them and potential areas of collaboration.

CEPI actively engaged with key partners (WHO, UNICEF and GAVI) and regional partners to discuss operational coordination (roles, hand-offs, risk sharing, etc.) for rapid, at-scale and equitable responses to different outbreak and pandemic scenarios.

CEPI also engaged parliamentarians, CSOs, patient and health organizations, particularly from the Global South, on the 100 Days Mission and Equitable Access through various platforms. These engagements facilitated an improved understanding of the varied challenges in health systems strengthening and the associated policy reforms and fiscal commitments required before countries can connect with the 100 Days Mission.

CEPI participated in a WHO convened working group to develop proposals for a Medical Counter Measures Platform.

[15] RACI referring to a responsibility assignment matrix.

3.2.1. Fill gaps in the global R&D ecosystem for end-to-end epidemic preparedness and response

Throughout 2022 CEPI enhanced regional capacity and partnerships by expanding existing networks and launching new ones. These networks serve as prepositioned, ready to act entities for epidemic preparedness activities spanning countermeasure development, enabling science and vaccine manufacturing. Highlights include:

- With a special focus on Global South, expansion of CEPI's Centralized Laboratory Network; contract negotiations underway with additional partners to add to the 10 partners in the global network already. An additional five partners were signed in 2022, with a further four ongoing, and expected for signature in 2023.
- Launch of a CfP in December 2022, to work with laboratory partners to facilitate networking on clinical and pre-clinical functions, including model discovery/development research and proof of concept studies; and/or advanced product testing/ IND-enabling preclinical studies; and/or toxicology and biodistribution studies; and/or in vitro or ex vivo tissue modelling studies.
- Initiation of work towards developing a Clinical Research Network / Sentinel Partner Sites with landscape and gap analyses, and a Lassa workshop in Abuja to engage clinical trial stakeholders in West Africa. A CfP for clinical trial site and research readiness in West Africa is planned to launch Q2 2023. Initiation of discussions with WHO Global Hub for Pandemic and Epidemic Intelligence to align on pathogen monitoring / early risk assessment to save valuable time in a pandemic situation for timely decision-making / investment in a 100 Day Mission.

KPI Output 3.2.1: Number of identified areas with funded global networks established (or expanded)				
Baseline	**Interim milestone 2022**	**Actual 2022**	**Target 2026**	**Status**
Three networks (Preclinical Model Network, Centralized Lab Network for COVID-19, systems immunology network and epidemiology networks)	Four interim milestones: (1) Clinical Research Network concept, (2) Launch first version of Clinical Research Network, (3) Launch CEPINET, (4) COVID-19 VIEW-hub	Two interim milestones completed; the approach for two interim milestones has changed and these will not to be taken forward (see comment box below)	At least three networks expanded or established	**ON TRACK**

Comment on progress in 2022 and status:

Interim milestone: (1) Develop a concept for Clinical Research Network/Sentinel Partner Sites*, explore landscape of existing trial site networks (suitable for both, preventive and reactive interventions) and (2) launch a first version of the Network/Sentinel Partner Sites.
Actual 2022:

- Clinical site readiness in West Africa work started in Q1 2022; landscape and gap analysis conducted at workshop in Abuja.
- A 'Research preparedness and emergency evidence generation readiness' RfP was published in May 2023 which will lead to the launch of a first version of the CEPI Clinical Research Network / Sentinel Partner Sites.

Interim milestone 2022 (3): Launch CEPINET stakeholder management online platform and establish CEPINET Community Advisory Boards (CABs) in Sub-Saharan Africa.
Actual 2022:

- The CEPINET stakeholder management online platform and CEPINET Community Advisory Boards in sub-Saharan Africa have not been established as the purpose of these platforms is already being addressed by initiatives led by other stakeholders.

Interim milestone 2022 (4): COVID-19 vaccine efficacy, effectiveness, impact, neutralization and safety VIEW-hub modules available for public consumption.
Actual 2022:

- Three publicly accessible modules on VIEW-Hub delivered: Vaccine effectiveness, Vaccine efficacy, and Neutralization studies.

In addition, the following progress was also achieved in 2022:

- The Vaccine Manufacturing Network was launched; one framework agreement was signed in December 2022 with Aspen; and one framework agreement was negotiated in 2022 through to signature in January 2023 with Institut Pasteur de Dakar.
- CfPs were launched for expansions of the Preclinical and Centralized Laboratory Networks. The Centralized Laboratory Network selection process has concluded in late 2022 and 9 additional laboratory partners were selected, rounding out participation from Africa and Asia in the newly expanded network.
- The CfP for model development and testing innovations to identify and select potential partners to expand the Preclinical Laboratory Network was released in December 2022.

** Please note that the terminology for the "Clinical Research Network / Sentinel Partner Sites" has changed to "Research preparedness and emergency evidence generation readiness hubs" as this better reflects what this area of work aims to address, and it will not necessarily be set up as a network but for example hubs of partner sites.*

3.2.2. Enable adaptive and harmonized R&D approaches

All regulatory activities within CEPI, and the cross-functional enabling science activities that support them, are to promote adaptive and harmonized R&D approaches across Disease and Vaccine Development Programmes of CEPI. To this end, the CEPI works to enable maximal use of platform data and pre-approved documentation, accelerate or streamline product development pathways, harmonize legal frameworks that exist for emergency public health use to increase the speed of regulatory review for rapid regional and global roll-out, and finally, identify circumstances to accelerate development and deployment based on anticipated benefit risk.

Considering these activities aimed at enabling adaptive and harmonized R&D approaches, CEPI made progress in following areas in 2022:

- Set up working groups to move ahead with initiatives of enabling maximal use of platform data and pre-approved documentation;
- Identified regulatory challenges from lessons learned to inform engagements with stakeholders to optimize epidemic response tools, guidelines, ways-of-working and to drive global alignment (see the KPI table below);
- Reviewed outbreak/epidemic/pandemic (OEP) emergency legislation and reliance, and initiated engagement with various stakeholders to ensure that appropriate legislation in place for the timely access to MCMs for future OEPs (see KPI table below); and
- Established a harmonized benefit-risk tool which can be applied to the CEPI core portfolio together with the Brighton Collaboration.

KPI Output 3.2.2: Regulatory database available and accessed by developers

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
N/A	• Review lessons learned • Work with coalition partners to align pathways	• Both interim milestones have been achieved in time • Cortellis Regulatory Intelligence tool was established in January 2022 • Identified potential partner to house database	Database available as a pilot to CEPI-funded developers by 2023 with view to wider roll out towards 2026	**ON TRACK**

Comment on progress in 2022 and status:

KPI is on track to be achieved by 2026; upcoming activities for 2023 include establishing the database (based on defined parameters) and launching it to CEPI-funded developers towards 2024.

- CEPI was invited to be a member of the Legal Preparedness Action Package (LPAP) of the Global Health Security Agenda (GHSA). Participation and collaboration in the GHSA Legal Preparedness Action Package broadens CEPI's outreach to the GHSA countries and other key stakeholders. CEPI is also working on setting up a Regulatory Sub-Working Group under the LPAP.
- Reviewed Cortellis Regulatory Intelligence tool for legal emergency frameworks and conducted a survey of legal emergency frameworks from a small number of regulatory authorities.
- The Cortellis Regulatory Intelligence tool research and regulator survey will supply information for the database.

3.3. Equitable access principles as the foundation of any effective global response

In 2022 CEPI developed its Equitable Access (EA) Framework, as a means of articulating it's overall approach to realizing this complex challenge. Approved by CEPI's Board in December 2022, the framework builds on existing policy and activities and acknowledges the important role to be played by other stakeholders in achieving systems equity, and re-enforces CEPI's primary responsibility which remains to accelerate the development of vaccines against emerging infectious diseases and enable access to these products by populations that need them. To enable equitable access CEPI will continue to work with other stakeholders to strengthen the global health architecture. CEPI's success ultimately depends on the structure of that architecture and on partnerships which can deliver and enable equitable access. This framework will underpin the work aimed at removing obstacles for access in LMICs, and it will guide CEPI's strategic engagements and interventions, including advocacy activities.

CEPI enables equitable access directly through its financial investments and partnerships, and indirectly through advocacy and its analytical and policy contributions to the evolving ecosystem.

The CEPI 2.0 Equitable Access Framework describes work in four main areas:

1. Rapidly advancing product development,

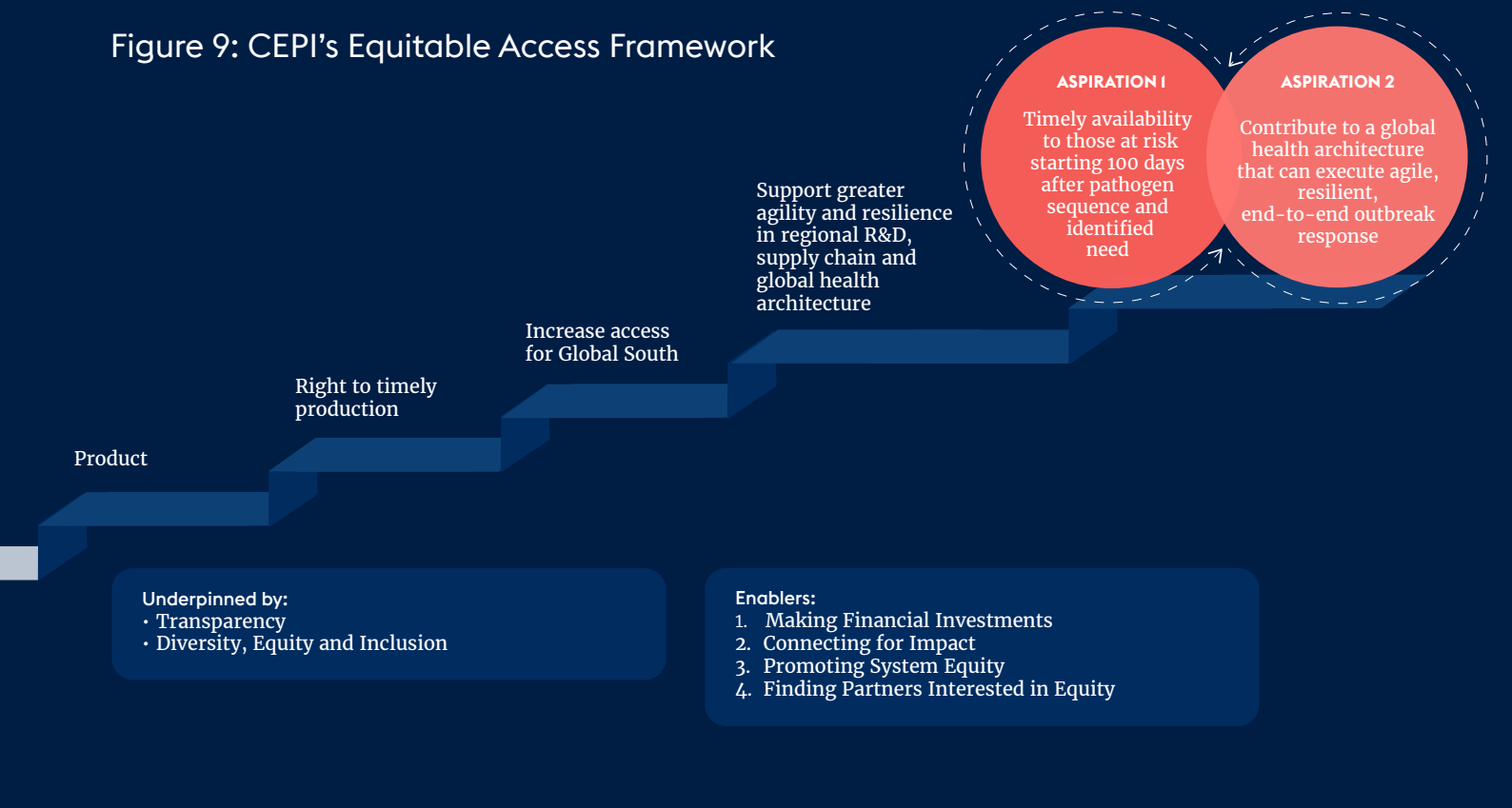
2. Securing rights for the timely production of that product for at-risk populations,

3. Increasing access to vaccines and other medical counter measures for LMICs, and

4. Supporting greater agility and resilience in regional supply chains and the global health architecture to achieve the 100 Days Mission.

The current innovation ecosystem does not routinely or reliably result in equitable access to innovative new products. The causes of inequity relate to the concentration of scientific and productive resources in certain regions, the fragility of healthcare delivery in others, the complexities and inertia of regulatory systems, the positive and negative incentives provided by current intellectual property regimes, differential access to capital, shifting political priorities, and other factors.

Figure 9: CEPI's Equitable Access Framework



While CEPI develops vaccines for specified outbreak prone diseases, it also seeks to remedy these structural causes of inequity by investing in platforms and prototype vaccines for virus families as a means of improving global R&D robustness to support outbreak/pandemic response, in line with the 100 Day Mission. CEPI will contribute to an overall preparedness and response ecosystem that increasingly addresses system inequities and puts equitable access at the heart of future outbreak response. While CEPI's primary focus remains the "product", which could be data, a vaccine, a platform, or an enabling innovation, CEPI will also work to strengthen the architecture and ecosystem in ways that will help CEPI accomplish its mission with respect to equitable access. During the ongoing negotiations for a pandemic treaty, there is a growing recognition that the current PPR ecosystem has suffered from a lack of equity, which has contributed to its breakdown. This acknowledges that the issue of ensuring universal and equitable access and distribution of medical countermeasures could be effectively addressed within the framework of a potential new instrument or treaty, and CEPI continues to engage with this.

CEPI can most effectively contribute to strengthening "system equity" by concentrating its efforts on:

- Geographical diversification;
- Policy engagement and advocacy;
- Co-amplification of resources and efforts of key stakeholders;
- Regulatory readiness;
- Networked, collaborative approaches.

KPI Outcome 3.3: Removing at least one key systemic obstacle to access for LMICs

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
N/A	Guidance available to address potential injuries caused by vaccines/to establish a no-fault compensation-mechanism: review of system set up by COVAX	Review of system set up by COVAX is ongoing	At least one (key systemic obstacle to access for LMICs removed)	**ACTION REQUIRED**

Comment on progress in 2022 and status:

- Plans have been made, in consultation with WHO, for the development of a no-fault compensation beyond the mechanism used by COVAX, in order to cover other vaccines/diseases. In 2023, more time and resources will be committed to developing the liability risk management framework.
- Initial stakeholder discussions held with WHO on the COVAX No-Fault Compensation to identify lessons learned and areas of opportunity.
- Concept note and proposed budget developed to support countries in developing liability risk management frameworks for pandemic preparedness.

3.3.1. Strengthen public and private commitment to equitable access

Mapping a path to access for each of CEPI's priority pathogens has continued, with the greatest focus being on Chikungunya as the pathogen with the most advanced candidates. Together with GAVI and UNICEF, the challenges and opportunities facing a possible Chikungunya vaccine have also been considered. For example, for GAVI to assess Chikungunya for funding in its next five-year cycle, either under VIS or the Living Assessment, key data will be needed. CEPI and GAVI are working together to fund the generation of that data and inform those decisions.

For each priority pathogen, CEPI has two or more private partners that it funds to develop appropriate vaccine candidates. Each of these funding arrangements contains a project access plan, partner commitments to rapidly advance product development of a vaccine candidate suitable for use by all affected populations including LMICs, and to secure rights for the timely production of that product for at-risk populations. It is this right to secure the timely production of product that will need a hand-off to another public partner such as GAVI/UNICEF or PAHO. These arrangements also include provisions for an outbreak response. Early in the life cycle of a vaccine candidate, the commitments may be at a high level, increasing in specificity as the vaccine candidate moves towards late-stage development and more is known about both the candidate and the relevant pathogen access plan. These equitable access plans are reviewed and updated as the project progresses through CEPI's internal governance processes.

When CEPI funds the development or validation of a platform technology that could potentially be used across relevant vaccines or other technologies, the focus is on access to the resulting project vaccines and across multiple vaccines that are relevant to CEPI's portfolio. In all cases CEPI is mindful of the developer's need to have a financially sustainable business model, to ensure that the partnership is in place in the event that an outbreak occurs.

The CEPI 2.0 objectives include new types of outcomes supportive of equitable access. These include:

(i) technologies that enable other work often as a component needed for CEPI's Disease X focus;

(ii) stronger and/or more agile preferred partner capabilities and;

(iii) manufacturing capacity and commitments for outbreak response. Examples of enabling technology include a partnership agreement signed with Vaxxas, and an Australian biotech advancing microarray patch technology (MAPs) for development of mRNA based vaccines under the Thermostability Call for Proposals (see output 2.3). This innovative technology has potential to combine the rapid response capabilities of the mRNA platform with equitable access advantages for MAPs which enable ease of administration, storage and distribution.

The improved preferred partner capabilities and manufacturing capacity are addressed in the next section.

KPI Output 3.3.1: Percent of CEPI-funded products / platforms with relevant access plans in place

Baseline	Interim milestone 2022	Actual 2022	Target 2026	Status
100%	100% each year for each product passing a stage-gate review	80%	100%	**ACTION MAY BE REQUIRED**

Comment on progress in 2022 and status:

Funding agreements have secured terms for equitable access consistent with the project objectives, and access plans are being developed as appropriate to the stage of development and in accordance with the project's short-term or longer-term timelines.

One project was permitted to pass a stage-gate review without completing all the partner's access milestones for that stage-gate in order to maintain R&D momentum at a critical point in the lifecycle. CEPI is in active discussions with that partner to address the resulting delay in access milestones.

3.3.2. Diversify global manufacturing capability geographically

To meet the objective of geo-diversifying vaccine manufacturing, CEPI launched an expression of interest in 2022 to identify vaccine development and manufacturing facilities with whom to partner and promote disease outbreak response preparedness, particularly in underserved LMICs. From the resulting respondents, CEPI initiated a Vaccine Manufacturing Preferred Partner Facility Network focused on improving capacity and capability of the selected facilities. The aim being to improve global public health security by supporting the establishment of agile, contemporary, geographically diverse vaccine manufacturing, closer to where vaccines will be used – thus facilitating their equitable access. CEPI has begun funding capacity-capability improvements at the onboarded facilities to make them attractive to vaccine developers. The CEPI preferred partner Vaccine Manufacturing Network may, in due course, also support the CEPI vaccine candidate portfolio.

To date, facility partnership funding agreements have been signed with Aspen (RSA – December 2022) and IPD (Senegal – January 2023). Opportunities to onboard a further six facilities to the CEPI Vaccine Manufacturing Network from LMICs are in-progress through 2023, with plans to further expand the network in 2024.

Thus far, required facility improvements include establishing suspension vaccine fill/finish capability, quality management systems, supporting transfer of novel technology capacity, improving workforce capability, implementing bioprocess development/ Good Manufacturing Practice clinical trial material laboratories, maturing the regulatory landscape, and scoping strategies to sustain vaccine manufacturing in the interpandemic period. Additional challenges being addressed include securing stable and reliable supply chains of single use consumables/raw materials for vaccine manufacturing (including relevant import/export permits and free flow of goods), overcoming trade barriers, maintaining government/political/ financial support, managing intellectual property, and ensuring freedom to operate. Whilst many of these are outside CEPI's role, MSC makes these and other issues visible so that they can be raised in the appropriate forums.

Leveraging the success of the COVAX Marketplace which supported the global COVID-19 response, CEPI Supply Chain Services (SCS) will support manufacture of vaccines by the preferred partner network facilities. Thereby building equitable, reliable systems to support consumable/raw material production, procurement, quality, storage, and distribution. To help overcome the inherent disadvantages of vaccine manufacture (low volumes, non-steady demand), there is an opportunity for CEPI to help partners secure more favorable terms for the supply of consumables. Standardization of consumables/ raw material supply across development partners and manufacturers is a key enabler for the 100 days challenge; it could also drive down costs and increase assurance of supply.

KPI Output 3.3.2: Number of agreements in place that support manufacturing capacity strengthening in order to support LMICs

Baseline	Actual 2022	Target 2026	Status
N/A	One agreement signed in 2022 – with Aspen (South Africa) covering the African region	At least five over two regions	**ON TRACK**

Comment on progress in 2022 and status:

- Aspen (South Africa) was the first facility to join CEPI's Vaccine Manufacturing Network, signing a funding agreement in December 2022. Activities instigated in 2022 have similarly concluded with Institut Pasteur de Dakar (Senegal) joining the network signing a funding agreement with CEPI in January 2023.
- The Expression of Interest launched in 2022 resulted in a further six facilities (of ≈100 respondents) being on track to join the CEPI Vaccine Manufacturing Network in 2023, expanding its reach beyond Africa and Southeast Asia, to include facilities in Latin America and Western Pacific regions.
- Given the large number of Expression of Interest respondents and vaccine manufacturing funding opportunities emerging in LMICs since April 2022, the CEPI Vaccine Manufacturing Network looks likely to expand further between 2024–2026, and support manufacturing capacity strengthening in more LMICs, including the Middle East Region.

4.Funding and finance

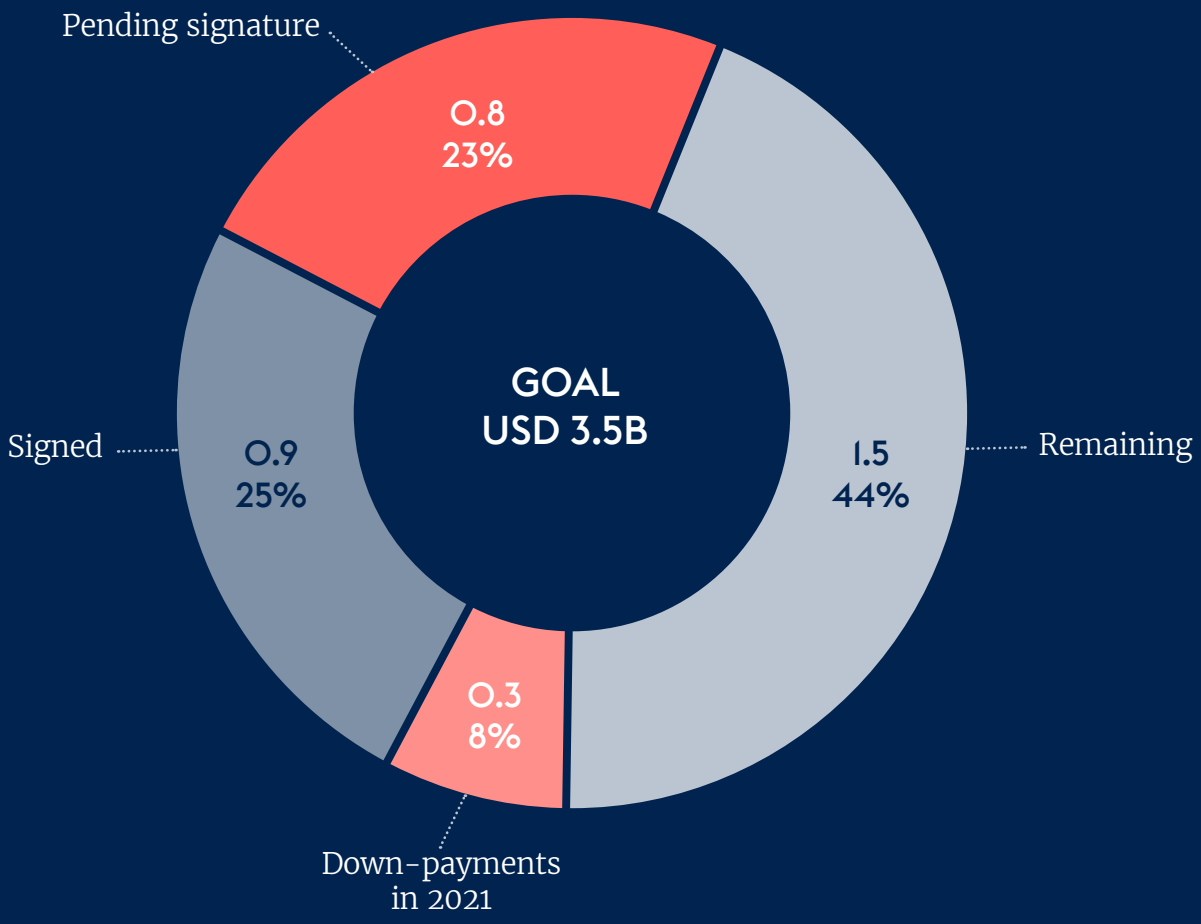
4. Funding and finance

Figures presented in the finance section represent cash flows (except for operating expenses) and are expressed in USD equivalents using actual exchange rates for the years 2017–2022 and 2023 budget rates for years beyond 2022. Further details on CEPI finances can be found in Appendix 2: Finance. Reference is also made to CEPI's Annual Audited Accounts and Board of Directors Report 2022.

4.1. Contributions from investors

In March 2021 CEPI launched its USD 3.5 billion plan for its second funding period (2022–2026) and by year-end 2022, USD 1.95 billion had been raised toward this goal (CEPI 2.0). Out of the USD 1.95 billion, close to USD 0.3 billion was already received in 2021 as a down-payment for continued COVID-19 investments under CEPI 2.0, USD 0.9 billion was secured through contribution contracts in 2022 and USD 0.8 billion had been pledged but is still pending contract signature.

Figure 10: Funds raised towards CEPI 2.0 in 2022[16]



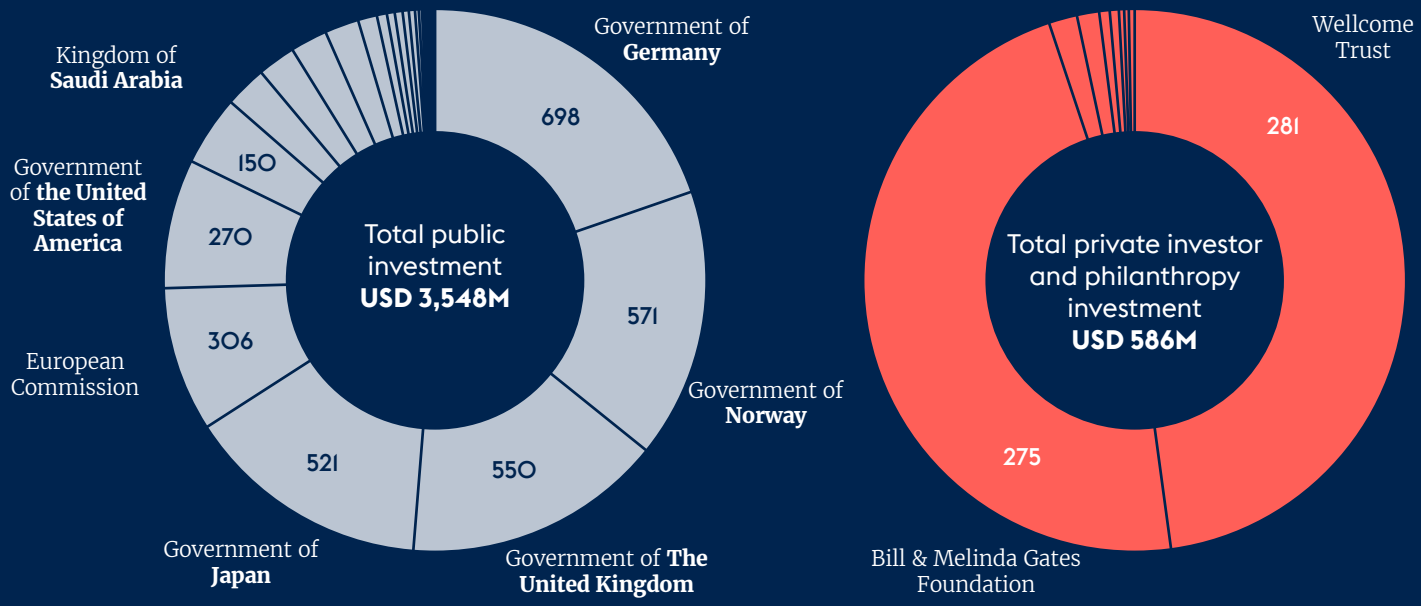
[16] Figures shown using actual exchange rates for contributions received and budget 2023 exchange rates for pledges not yet received.

Overall, more than USD 4.1 billion has been pledged to CEPI since its launch in 2017, whereof USD 2.6 billion had been received at the close of 2022. The remaining funds pledged are expected to be received in years 2023–2026.

CEPI receives funding from sovereign investors, the European Commission, philanthropies, and private organizations. Sovereign public investors represent the largest investor group with 86% of the USD 4.1 billion pledged to date (see Appendix 2: Finance).

The overall number of individual contributors has grown from 14 at the end of 2019, to 80 by the end of 2022[17]. Traditionally, most donations are pledged to CEPI's common/core pool of funds, while in the last couple of years, CEPI has also received earmarked donations directed to the COVID-19 pandemic. Earmarked funds, including funds softly earmarked toward activities that are considered ODA eligible, are pooled and spent on eligible groups of projects[18].

Figure 11: Total contributions and pledges to CEPI in 2022



[17] Including sovereign, philanthropic, and private sector contributions.

[18] COVID-19 funds are either earmarked through contract, or funds intended for COVID-19 investments. The overall OECD ODA co-efficient for CEPI 2.0 portfolio is 88% (see Appendix 2).

4.2. R&D&M Project disbursements

CEPI's investments in 2022

CEPI came to the end of its first strategic cycle at the end of 2021. The formal starting year of CEPI 2.0, 2022, was a transitional year in which new investment programmes were started and many new programmes were prepared.

Overall, spend in 2022 was lower than expected as a number of programmes were initiated, but contracting volume and disbursements across all strategic areas were lower than initially anticipated and will be skewed towards 2023 and beyond.

The evolving COVID-19 pandemic and steep decline in the need for COVID-19 funding, alongside slower progression of some projects in the portfolio contributed to a lower spend than expected. CEPI has launched an Operational Agility initiative aiming to streamline various processes and improve efficiency.

In total, CEPI disbursed USD 327 million to its awardees in 2022, compared to a budgeted amount of USD 613 million. See Appendix 2, Tables 2 and 3 for further details.

A large part of the spend in 2022 related to projects started before 2022, overlapping into CEPI 2.0. The spend included tail-end development funding for COVID-19 vaccine development projects and clinical trials (USD 200 million), progressing CEPI's broadly protective coronavirus candidates (USD 27 million), as well as funding for Enabling Science and vaccine development projects for CEPI's priority pathogens (USD 56 million).[19]

During 2022, CEPI launched large-scale multi-year and multi-phase investment programmes for mRNA platform-based prototypic vaccine development and vaccine library development, preparing for the next Disease X. CEPI also launched the establishment of a global vaccine manufacturing network focused on increasing access to doses in low- and middle-income countries. Spend was modest in 2022, with first contracts signed at the end of the year, in part due to the need to pause and reprioritise the CEPI 2.0 programme related to funds raised at the summit and projected to come in. Investments will increase significantly from 2023 as existing projects advance and new projects are added to the portfolio.

[19] Specifically late stage development of RVF in a co-funding arrangement between CEPI and the European Commission's Horizon Europe programme

CEPI portfolio at the end of 2022

As of the end of 2022, CEPI had entered into partnership agreements with total portfolio value of up to USD 2.5 billion[20], with more than USD 1.7 billion disbursed to date. Disbursements are made in tranches, dependent on the completion of pre-specified project milestones. The largest portion of the USD 1.5 billion pertains to COVID-19 investments (excluding Broadly Protective SARS-CoV2 projects), of which USD 1.3 billion have been disbursed to date. USD 343 million of these disbursements were made in the form of forgivable loans, financing at-risk manufacturing and capacity reservations, and USD 81 million have been repaid to CEPI at the end of 2022[21]. Investments into vaccine development and Enabling Science[22] projects supporting for CEPI's priority pathogens constitutes USD 0.5 billion of CEPI's portfolio, while over USD 0.3 billion remain for Broadly Protective Coronavirus (including Broadly Protective SARS-CoV2) and MERS vaccine development projects. USD 265 million and USD 95 million, respectively, have been disbursed to partners for these parts of the portfolio at the end of 2022. CEPI's portfolio of platform and Disease X projects amounted to USD 0.1 billion at the end of 2022, with USD 44 million disbursed to date. Apart from that, CEPI has also invested in a number of cross-cutting (not pathogen specific) enabling science activities and partnerships, and most recently started the establishment of a global manufacturing network focused on low- and middle-income countries. In total, these agreements have a value of USD 31 million so far, with USD 21 million paid out to date.

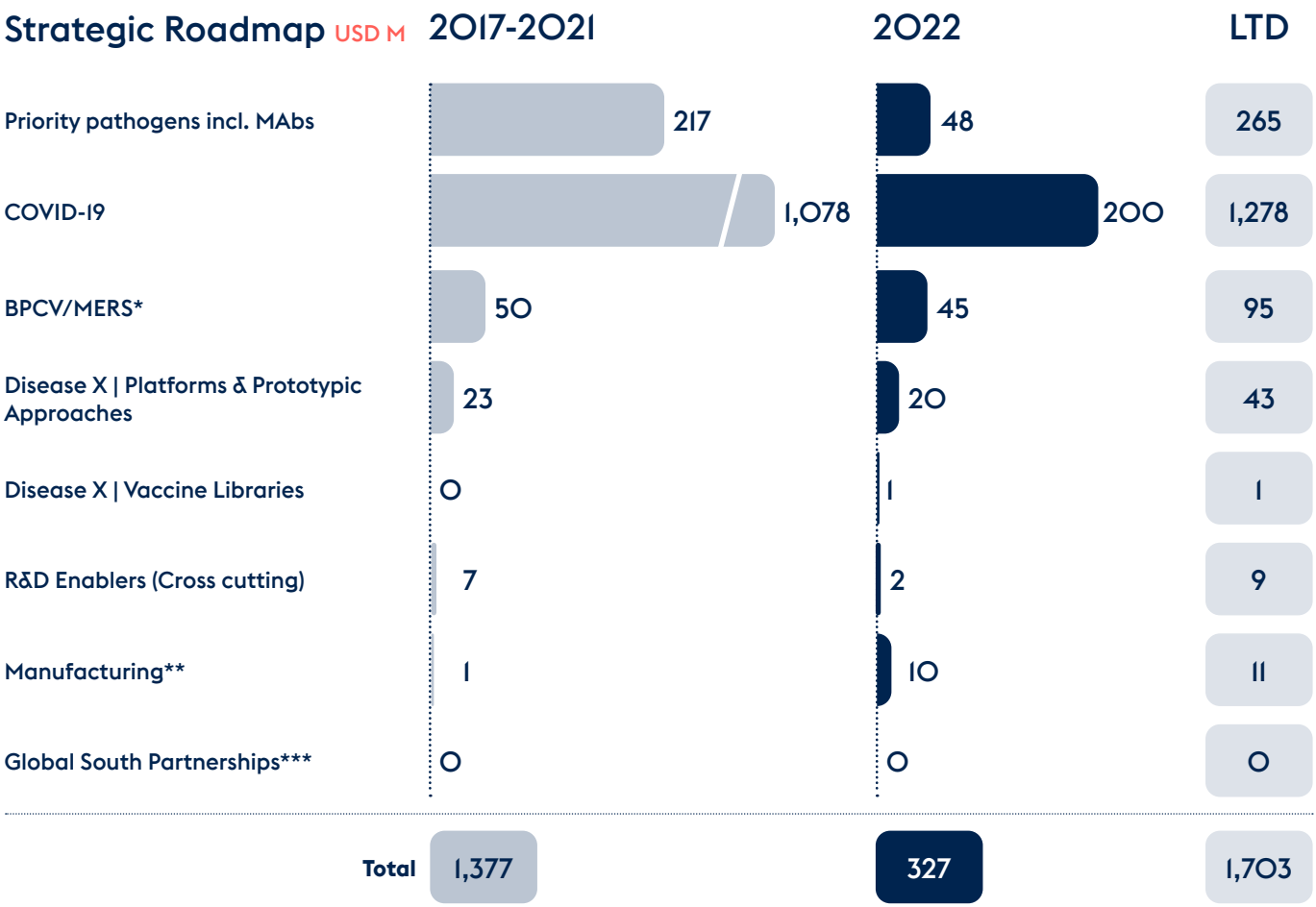
Many of CEPI's vaccine development investments are long-term, multi-phase investments, and therefore release of funding tranches is contingent on key milestones that candidates will have to meet as they transition between phases of development ('stage gates'). Therefore, not all contracted funding is expected to be committed and disbursed, as CEPI's portfolio management approach takes into account expected phase-to-phase attrition.

[20] This figure includes only current contract value of signed contracts (signed as of 31.12.2022).

[21] A total of USD 380 million of COVID-19 investments was provided in the form of forgivable loans, out of which USD 343 million have been paid out as of 31.12.2022. The remaining USD 37 million may not need to be paid out to the awardees. USD 81 million have been repaid to CEPI as of 31.12.2022, and USD 6 million will not be recovered. CEPI does not consider it likely that the outstanding amount of USD 255 million will be recovered.

[22] Enabling Science activities include e.g., standards & assay development, diagnostics, preclinical studies, epidemiology studies and clinical development work.

Figure 12: R&D&M Project disbursements 2022 – by Strategic Roadmap

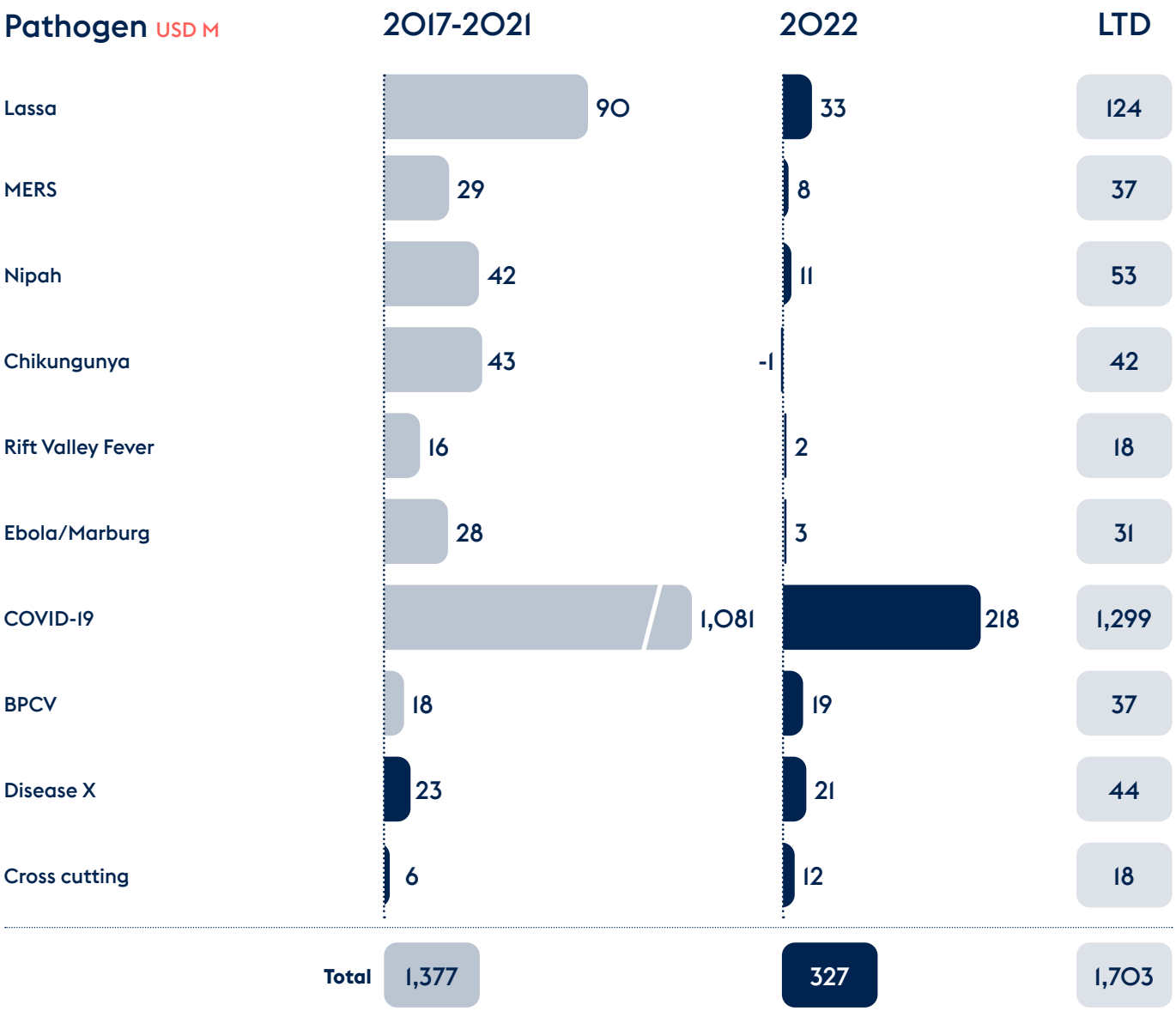


*includes Broadly Protective SARS-CoV2

**includes funding contributed from the original Global South Partnerships budget for the establishment of a Global Manufacturing Network focused on low- and middle-income countries.

***includes only Global South investments that are cross cutting in nature and not pertaining to a specific pathogen or Strategic Roadmap. Beyond that, CEPI has made significant investments in or directly benefiting the Global South through its funding of e.g. the ENABLE study (Lassa) in West Africa, Centralized Lab and Animal Model Network partnerships, or manufacturing partners for its Global Manufacturing Network.

Figure 13: R&D&M Project disbursements 2022 – by pathogen



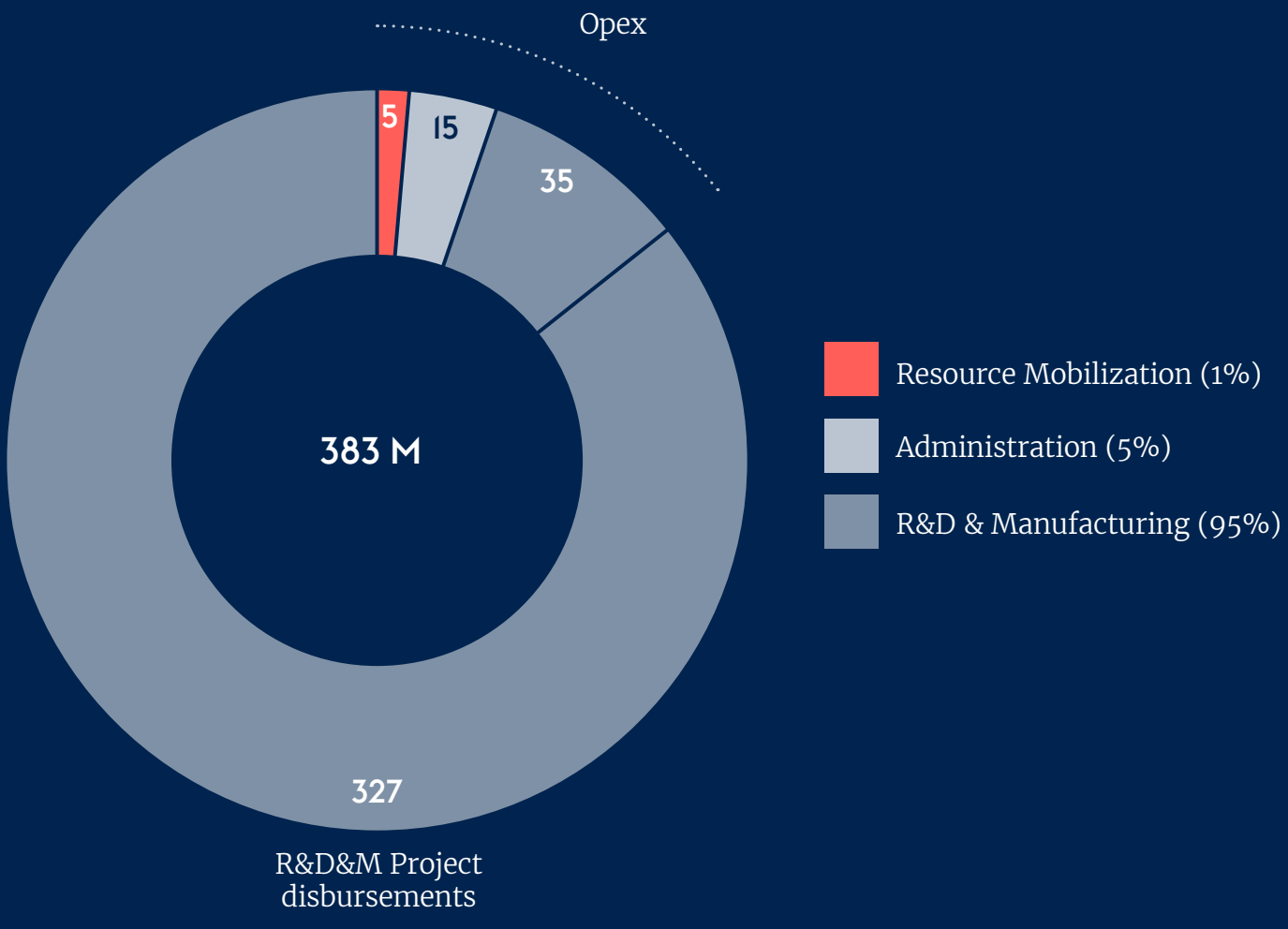
4.3. Operating expenses (Opex) and total expenditure

Out of the overall expenditure for 2022 (Appendix 2: Finance), CEPI spent 95% on its main activity, vaccine R&D and manufacturing, leaving a spend of 5% on overheads (resource mobilization and administration).

CEPI has had a significant year-on-year increase in staff since inception. This was also the case in 2022 as CEPI continued to prepare for the expanded scope under CEPI 2.0. Opex amounted to USD 55 million in 2022, an increase of 21% over 2021, but well within the approved 2022 budget (see Appendix 2 for details). The increase in Opex for 2022 was a result of continued hiring, full-year effect of increased headcount in 2021, resumed travel activities, and operational expenses for investments in IT infrastructure, development of business support processes, and the CEPI 2.0 replenishment event.

The overall expenditure is depicted below by activity and refers to whether an expense is channeled towards R&D and Manufacturing, project disbursements and project support, resource mobilization[23] or administration[24]. This provides insight into whether Opex are directed towards adding value to the portfolio of investments through project support, or to raising funds or organization management and administration. The last two are typically labelled overhead costs. Of CEPI's Opex, 64% relates to R&D project support which is largely driven by CEPI's R&D and Manufacturing department, staffed with technical experts responsible for launching CfPs and conducting technical follow-up of CEPI's portfolio of projects.

Figure 14: 2022 Total expenditure by activity



[23] Refers to CEPI's efforts to increase ongoing, and secure new funding commitments.

[24] From 2022, shared costs like IT, Office facilities, Finance & Operations and HR are distributed to the different activities. Total shared costs for 2021 was USD 12.3 million.

4.4. Procurement

The CEPI procurement policy and procedure includes general rules and principles, eligibility criteria for tenderers, specification of tender procedure types and duration of contracts. It also defines a set of thresholds that trigger different procurement processes (Direct purchase / Direct procurement / Request for quotation (RfQ) / Request for proposal (RfP)), whereby the number of steps and scrutiny undergone reflect the value and type of procurement.

Together, the policy and the procedure reflect international best standards and EU directives. They were also drafted in close consultation with CEPI's investors, ensuring the approach was in line with legal requirements. The procurement policy and procedure were reviewed in 2022, which included simplification and adjustment of the procurement thresholds. The new versions were approved by the board and implemented in September 2022.

In 2022, CEPI further strengthened its procurement capability through specific developments in the areas of people and skills, processes, and system support. The procurement team maintains a strong focus on cross-functional collaboration and knowledge sharing with, in particular, the legal team.

Furthermore, CEPI has mapped its procurement processes and developed corresponding checklists which were implemented alongside the updated policy and procedure mentioned above. CEPI is also working on improving the controls within procurement throughout the full life cycle of a contract. The current and planned contract life-cycle management software enables the procurement managers to store and track signed contracts and ensure that CEPI always has valid contracts for all procurements. Additionally, CEPI is working on developing a set of Key Performance Indicators (KPIs) in procurement with the aim to better measure controls and effectiveness in the end-to-end procure-to-pay process.

Under the procurement policy during 2022, a total of 25 RfPs were published (for consultants, travel, IT, infrastructure etc). Around 10 direct procurements were performed after the new procurement rules were implemented and a significant number of procurements below the RfP threshold were undertaken and completed in accordance with CEPI's previous procurement procedure. Additionally, six exceptions from the current procurement procedure were approved by CEPI management.

Table 1 below gives an overview of CEPI's procurement thresholds across the different procurement processes.

Table 1: Overview of procurement thresholds in USD

Type of procurement processes and corresponding thresholds
Direct purchase (up to USD 5,000)
Direct procurement (value USD 5,000-50,000)
Request for Quotation (value USD 50,000-210,000)
Request for Proposal (value above USD 210,000)

5. Risk management, Resilience and Assurance

5. Risk management, Resilience and Assurance

Risk management, compliance and internal audit processes are key components in assuring that proper governance and monitoring are in place and continuously improved in CEPI. Monitoring of risk in CEPI is carried out by the CEPI Board, the Board Audit and Risk Committee and the CEPI Leadership Team, with the support of the Governance, Risk and Compliance function (GRC).

As a second- and third-line function, the GRC function has a dual responsibility. It supports the work to ensure CEPI's internal governance, systems and process are robust, that it reliably achieves its objectives, addresses uncertainty and acts with integrity in the delivery of the strategic objectives. It also provides assurance to the Board and to CEPI's investors of the same.

Over the past twelve months, the GRC team underwent a reorganization and strategic prioritization of its objectives and resourcing, so it is better positioned to deliver on CEPI 2.0.

5.1. Risk Management

The continued growth of CEPI and the considerable scale-up required in response to the COVID-19 outbreak has resulted in significant change in the risk landscape for CEPI. As CEPI grows and becomes a more complex operation, the approach to managing risks has evolved. CEPI has improved and established new processes to stay abreast of changes. The organization's risk management framework, developed in 2018, needed to evolve and mature to align with the strategic shift to CEPI 2.0.

In December 2021, the CEPI Board endorsed the need to revise CEPI's risk management framework. An independent and comprehensive assessment of the organization's approach to risk management followed in 2022, prioritizing:

1. Risk governance and controls;
2. Ensuring an enterprise-view on risk management;
3. Developing a risk appetite framework, and;
4. Ways of working, decision-making and risk reporting.

The report, shared with the Board and the Audit and Risk Committee (ARC), highlighted many positives around the current governance structure, including the strong tone from the top- and high-level acknowledgement across the organization of the importance of risk management.

Several improvements to strengthen the current framework are already underway. In particular:

- **Developing the Risk Appetite Framework**: Risk Appetite is the amount of risk, at the strategic level, that CEPI is willing to accept in pursuit of its strategic objectives. The framework helps ensure that decisions are taken in the context of CEPI's strategy and objectives. It adds clarity over the risks that the organization (and the Board) wants to assume and assists management to take informed trade-off decisions in this respect, improving transparency across all internal and external stakeholders. Significant strides have been made on this since the last annual progress report starting with a comprehensive and thorough review of the organization-level risks which constituted a cross-departmental exercise involving CEPI's senior leadership. For CEPI, Risk Appetite will be set for each top organizational risk[25]. An approach to the risk appetite framework, including some examples, were discussed at the March 23 ARC and Board meeting. With the approach approved by the Board, CEPI will be defining the risk appetite for the other organizational key risks and present the full framework to the Board during 2023.

[25] Risks with a high residual risk level, which, if they materialize, will have a profoundly negative impact on CEPI.

- **Improvements to the Risk Management Framework**: Linked to developing the Risk Appetite Framework, several improvements have been made to the Risk Management Framework:
  - Revisions made to the rating methodology (more objective with better defined metrics) to minimize subjectivity and allow better comparison across categories and in prioritization of risks that would drive better oversight.
  - A targeted workshop with Senior Management team in Q3 2022, focused on critically reviewing and agreeing the key risks. This informed the roster of key organizational risks for 2023, also embedded in the annual planning for each division.
  - Risk monitoring and reporting is being strengthened by defining and agreeing on key risk metrics (KRIs) for the key risks. This is a cross-divisional task aimed at strengthening CEPI's oversight of the key organizational risks. Similar initiatives are also being rolled out for the individual projects and the overall investment portfolio.
- **Strengthening and embedding risk assessment in Governance and ways of working**: With a revised operating model and a larger organization, the importance of an effective risk review increases and is a strategic, as well as an organizational, exercise. Risk reviews are being embedded in organizational planning and discussed consistently at the Governance meetings for investment decisions, for projects and portfolios. With more multiple lines of activity and investment, the importance of managing the portfolio holistically, judging how all the parts contribute to the overall objective, how funds are allocated, and how risks integrate and support this thinking, is critical.

5.2. Compliance

In 2022, CEPI continued to evolve its Compliance Programme, strengthening its capacity through strategic recruitment in compliance and data privacy. This section addresses activities undertaken and developments throughout the year:

- **Third party due diligence**: Building on the establishment of an enhanced Integrity Due Diligence (IDD) process in 2021, Compliance continued to conduct robust and risk-based reviews of awardees. This included leveraging an in-house operated tool for screening and monitoring of all relevant entities, key individuals, ownership structures and ultimate beneficial owners, and sent automated alerts if there are any relevant changes related to ownership, directors, adverse media, and sanctions. The process also assessed awardees' capabilities relating to compliance with CEPI's Third Party Code, which is a requirement in all funding agreements. In line with the requirements of the new Norwegian Transparency Act, in 2022 CEPI also formalized the IDD process for suppliers, and operated a risk-based approach to assessing integrity and human rights risk in these supplier relationships.

- **Sanction compliance programme**: To ensure compliance with sanction regimes, in particular the US, EU, UK, and the UN, as well as complying with requirements of CEPI's funders, CEPI continued strengthening its sanctions compliance programme in 2022. Key activities included conducting risk-based screening of entities, beneficial owners, and key individuals to identify potential sanctions risks and to ensure that CEPI does not engage with sanctioned entities or individuals; board approval of a revised sanctions policy; providing risk-based sanction training; and an assessment of financial internal controls environment to adequately address sanctions risks.

Business integrity training: In 2022, all employees and long-term consultants (engaged more than three months), received business integrity training. The training addressed topics such as code of conduct, modern slavery, corruption and bribery, gifts and hospitality, confidential information, whistleblowing, and sanction requirements. Compliance also launched a mandatory e-learning on anti-bribery and mandatory Code of Conduct sign-off for all employees, and an online compliance programme for all new employees via CEPI's digital learning platform. Further, deep-dive gifts and hospitality trainings have been provided across the organization.

- **Human rights programme**: CEPI's human rights programme was further improved in 2022. A human rights impact assessment (HRIA) was completed in 2022 with support from BSR, a non-profit advisory organization. The assessment identified ten risks and opportunities where CEPI may have an impact on human rights.
  The assessment entails a set of recommendations, and implementation of those recommendations have been initiated and will continue to be implemented in 2023. The HRIA supports CEPI's compliance with the Norwegian Transparency Act and the UK Modern Slavery Act.

- **Policy management**: CEPI's current policy framework is comprehensive and covers a broad range of organizational subjects. To further strengthen the policy framework, as well as ensuring that changes in both CEPI's external and internal environment are addressed, a policy review was conducted in 2022 which identified several new policy requirements, as well as updates to existing policies, which were approved by the EIC in early 2023. Compliance will support an annual policy review process which will ensure regular policy reviews as well as strengthen CEPI's ability to ensure it complies with all investor requirements.

5.3. Internal Audit / Partner Assurance

The Internal Audit/ Partner Assurance (IA/PA) function has increased. In alignment with the review of CEPI's risk management framework, the priorities and strategic focus of the team have been reviewed. While the function has had a specific focus on auditing CEPI's partners and projects, a priority is to enhance the internally focused audit and assurance activities.

The IP/PA Function reports to Director of Governance, Risk and Compliance for administrative purposes and to the Board ARC for its functional role.

In 2022, IA/PA activities continued their assessments of CEPI awardee activities by carrying out four awardee audits in total. CEPI's PA activities are currently focused on finance management and related risks for projects selected in collaboration with the Finance Department. The awardee audit activities identified relevant findings and areas of improvement to be resolved and implemented by awardee management. The recommended improvements are outlined in the form of an action plan and agreed with the awardee to facilitate continuous improvement of the awardee's management of granted funds. CEPI monitors the status of the awardee's progress on the agreed-upon action plan until the action items are considered effectively implemented or resolved.

IP/PA conducted assessment of CEPI's Business Process Support Programme (BPS). This was the first internal audit conducted for this area and the scope of work included testing controls around how data is being managed, as well as how CEPI is managing this process to ensure it is being delivered to plan.

IP/PA function also commenced work to revise and further develop the scope of work. This will facilitate future development and maturity of the assurance function. To date IA/PA has developed new Vision/ Mission statement and a new Internal Audit Charter.

5.4. Security and organizational resilience

In 2022, CEPI continued to mature its security function and formally integrate security with resilience. CEPI hired its first in house Senior Security and Resilience Manager. The security function supports CEPI's commitment to establishing a safe and secure working environment for employees, associates and partners. It does this by putting in place measures which mitigate security risks for CEPI while at work, during events, and during travel. The function also leads CEPI's approach to resilience, including emergency response, incident management, and business continuity, which are essential parts of CEPI's ability to minimize disruptions when facing extraordinary events, and to respond to severe incidents and crisis situations.

Appendices

Appendix 1: Organizational update

CEPI's Growth and the need for a review of processes and systems

CEPI has grown from 150 to 194 employees in the last year alone. This 40% organic staff growth, and the evolution from CEPI 1.0 to CEPI 2.0 has introduced new challenges for the organization. Therefore, it is important for CEPI to take stock of the current processes, systems, and procedures, and to examine how to make them more effective for a larger and more complex organization.

In 2022 CEPI undertook an internal review of systems and processes and carried out a "voice of customer" exercise to understand from external partners what is currently not as agile or operationally effective as it could be. This initiative aimed to ensure that CEPI preserves its agility and remains an attractive partner to work with, continues to build on its existing strong culture of innovation and partnership, with the objective of future-proofing its already solid position in the ecosystem.

The project was carried out with the support of all CEPI divisions and the participation of an independent consultancy firm to provide the necessary confidentiality for the awardees and partners. The awardees were selected to represent a diverse sample of geographies, types of institutions, types of relationships, and sizes of projects.

CEPI gained valuable information on the agility and effectiveness of its operations and has helped identify key operational improvement areas from the exercise. The final report has provided a frank assessment of both strengths and challenges in CEPI's current customer experience, both across the end-to-end journey from CfP application, to project closure and for cross-cutting journey stages, such as ad-hoc partnership activities. In 2023 CEPI will further improve processes and systems by closing the gaps identified and measure and capture the value of more a gile and enduring relationships with key awardees and partners.

Appendix 2: Finance

Table 2: Total Contributions and pledges by 31.12.2022 with expected received year (in USD M)

Investors USD M	2017 - 2021	2022	2023 - 2026	Total contributions & pledges[1]	% of Total contributions & pledges
European Commission	124.40	29.94	152.13	306.47	7.41%
Government of Australia	8.77	1.31	68.28	78.36	1.90%
Government of Austria	2.36	1.68	3.45	7.49	0.18%
Government of Belgium	6.04	-	-	6.04	0.15%
Government of Canada	86.85	1.94	-	88.79	2.15%
Government of Denmark	1.45	-	-	1.45	0.04%
Government of Ethiopia	0.17	0.13	-	0.30	0.01%
Government of Finland	5.50	2.08	5.39	12.97	0.31%
Government of Germany	507.73	146.94	43.11	697.79	16.88%
Government of Greece	1.78	-	-	1.78	0.04%
Government of Hungary	0.84	-	-	0.84	0.02%
Government of Iceland	1.92	-	-	1.92	0.05%
Government of Indonesia	1.00	1.00	4.00	6.00	0.15%
Government of Italy[2]	17.67	4.21	17.24	39.12	0.95%
Government of Japan	221.27	10.00	290.00	521.27	12.61%
Government of Kuwait	10.00	-	-	10.00	0.24%
Government of Lithuania	0.11	-	-	0.11	0.00%
Government of Luxembourg	0.94	0.21	0.86	2.02	0.05%
Government of Malaysia[3]	1.00	1.00	1.00	3.00	0.07%
Government of Mexico	0.90	-	1.00	1.90	0.05%
Government of the Netherlands	58.64	-	12.93	71.57	1.73%
Government of New Zealand	10.82	1.16	5.06	17.05	0.41%
Government of Norway	469.37	-	101.97	571.34	13.82%
Government of Philippines	0.01	-	-	0.01	0.00%
Government of Portugal	0.34	-	-	0.34	0.01%
Government of Romania	0.24	-	-	0.24	0.01%
Government of Senegal	-	-	1.00	1.00	0.02%
Government of Serbia	1.23	-	-	1.23	0.03%
Government of Singapore	1.41	0.60	15.00	17.01	0.41%
Government of Spain	-	-	80.83	80.83	1.96%
Government of Switzerland	10.28	10.82	-	21.10	0.51%
Government of the Republic of Korea	3.00	6.00	-	9.00	0.22%
Government of the United Kingdom	355.81	12.11	181.71	549.63	13.30%
Government of the United States of America	8.00	54.00	208.00	270.00	6.53%
Kingdom of Saudi Arabia	150.00	-	-	150.00	3.63%
Total Public Investors	**2,069.87**	**285.15**	**1,192.96**	**3,547.98**	**85.82%**

Investors USD M	2017 - 2021	2022	2023 - 2026	Total contributions & pledges[1]	% of Total contributions & pledges
Avast	8.00	-	-	8.00	0.19%
Bill and Melinda Gates Foundation	121.40	33.88	120.00	275.28	6.66%
Fidelity Charitable gift funds	1.49	-	-	1.49	0.04%
Goldman Sachs Gives	1.63	-	-	1.63	0.04%
Néstle	1.04	-	-	1.04	0.03%
Paul G. Allen Familiy foundation	3.50	-	-	3.50	0.08%
Sumitomo Mitsui Banking Cooperation	1.14	-	-	1.14	0.03%
UN Foundation C19 Solidarity Fund	10.00	-	-	10.00	0.24%
Wellcome Trust	88.41	-	192.35	280.76	6.79%
Other Private Investors and Philanthropies[4]	3.23	0.05	-	3.28	0.08%
Total Private Investors & Philanthropies	**239.85**	**33.92**	**312.35**	**586.12**	**14.18%**
Total Contributions & Pledges	**2,309.72**	**319.07**	**1,505.31**	**4,134.10**	**100.00%**

1. Includes pledges made through 31.12.2022. Contributions received are expressed in USD equivalents using the exchange rates on the dates funds are received. Contributions Funds pledged but not yet received are expressed in USD equivalents using CEPI Budget 2023 exchange rates.

2. Includes EUR 5M contribution in 2021 received via the International Finance Facility for Immunizations (IFFIm).

3. Includes contributions of NOK 600M frontloaded in 2019 through IFFIm, and NOK 2B frontloaded through IFFIm for COVID-19 in 2020

4. Private Investors with contributions of less than USD 1M are grouped under "Other Private Investors and Philanthropies".

Table 3: R&D&M Project disbursements 2022

Strategic Roadmap USD M	2022 Actual	2022 Budget	2022 Variance
Priority pathogens incl. mAbs	48.0	87.2	-39.2
COVID-19	200.0	372.8	-172.7
BPCV/MERS	45.0	68.4	-23.4
Disease X | Platforms & Prototypic Approaches	19.6	45.3	-25.7
Disease X | Vaccine Libraries	1.1	26.2	-25.1
R&D Enablers (Cross cutting)	2.4	9.7	-7.3
Manufacturing*	10.1	2.5	7.7
Global South Engagement**	0.4	0.8	-0.4
Total R&D&M projects/investments	**326.6**	**612.9**	**-286.2**

** includes funding contributed from the original Global South Engagement budget for the establishment of a global manufacturing network focused on low and middle-income countries.*

*** includes only Global South investments that are cross cutting in nature and not pertaining to a specific pathogen or Strategic Roadmap.*

Strategic Roadmaps include pathogen specific Enabling Science activities. Cross cutting (not pathogen specific) Enabling Science activities included under "R&D Enablers (Cross cutting).

Table 4: R&D&M Project disbursements 2017-2022

Strategic Roadmap USD M	2017-2022 Actual
Priority pathogens incl. mAbs	265.2
COVID-19	1278.5
BPCV/MERS	94.7
Disease X | Platforms & Prototypic Approaches	42.6
Disease X | Vaccine Libraries	1.1
R&D Enablers (Cross cutting)	9.7
Manufacturing*	10.7
Global South Engagement	0.6
Total R&D&M projects/investments	**1,703.1**

** includes funding contributed from the original Global South Engagement budget for the establishment of a global manufacturing network focused on low and middle-income countries.*

Strategic Roadmaps include pathogen specific Enabling Science activities. Cross cutting (not pathogen specific) Enabling Science activities included under "R&D Enablers (Cross cutting).

Table 5: CEPI 2.0 ODA eligible project disbursements as of December 2022

ODA Category USD M	ODA %	Project disbursements USD M
1. Priority pathogens	100%	1.8
2. BPCV	55%	20.5
3. Disease X – viral families	68%	0.7
4. Rapid response platforms for LMICs	100%	19.6
5. Monoclonal antibodies	100%	0.3
6. Manufacturing networks	100%	10.0
7. Manufacturing Innovations	68%	0.1
8. LMICs capabilities and engagement	100%	0.4
9. Benefits both PP and Disease X	90%	0.5
Total ODA eligible investments	**88%**	**53.9**

The OECD has assigned an ODA eligibility co-efficient of 88% to 2022 reporting and the overall CEPI 2.0 investment portfolio and has further split the portfolio into groups with an individual eligibility co-efficient.

CEPI's Opex in 2022 were USD 8.7 million lower than the budget for the year. Part of it is explained by currency effects due to the strengthening of the USD against CEPI's operating currencies. The remaining variance is primarily due to a delay in hiring, slower than expected pick up in travel as well as lower spend on consultancy as some planned initiatives were postponed.

Table 6: Operating Expenses (Opex) 2022

Opex USD million	2022 Actual	2022 Budget	2022 Variance
Employment	28.4	31.4	-3.0
Consultancy	12.8	17.2	-4.4
Travel	2.7	4.0	-1.2
Infrastructure	6.6	7.0	-0.4
Other	4.1	3.8	0.3
Total Opex	**54.7**	**63.4**	**-8.7**

Management of Financial Risk

CEPI currently receives its donations predominately in USD, NOK, GBP, and EUR, and makes grants to awardees in USD. CEPI has a Trustee agreement with the World Bank through which most of the committed funds to CEPI are channelled. Available funds are invested in the World Bank or with selected commercial banks, with the main investment goal being capital protection.

To cover operational costs and to minimize the currency risk, CEPI is keeping cash in the donated currency for natural hedging purposes. CEPI has also established a hedging facility with its current commercial bank, as means to minimise currency risk caused by a mismatch between funding received and grant currencies.

Annual Accounts and Board of Directors Report

CEPI's Annual Accounts and Board of Directors Report can be found on CEPI's website. In the Annual Accounts, revenue and costs are recognised in accordance with the Norwegian Accounting Act and Generally Accepted Accounting Principles for Non-profit Organisations. As CEPI usually prepares its internal and external reporting based on a cash flow principle for revenue and investments, the Annual Accounts profit and loss deviate from CEPI's other financial reports, including the Annual Progress Report.

Appendix 3: Human resources

The CEPI organization has grown rapidly since the onset of the pandemic and the workforce has continued to increase and develop to meet the expanded scope and new expectations from its partners. Skills and capacity have been built in all CEPI's three locations (Oslo, London and Washington D.C.). CEPI has also established a partnership with a company offering Employer of Record (EoR) services that enables engaging with workers across the globe and to attract scarce resources. Deliberate and continuous efforts have been made and have contributed to developing CEPI's staff into a diverse and international group of employees.

On January 1, 2022, there were 150 permanent and temporary employees on board while at the end December, the number had increased to 194. In addition, the number of workers engaged through an Employer of Record service, grew from 5 to 18. There were 88 starters (includes 7 internal transfers, i.e. move from one CEPI legal entity to another) and 33 leavers (includes 10 internal transfers) over the year. CEPI´s activities were otherwise supported by consultants on direct consultancy contracts. Finally, CEPI is also supported by a strong cadre of international expert consultants that serve to broaden CEPI's global reach and operational flexibility.

In 2022, CEPI made a number of key leadership hires such as in Operations, Manufacturing and Supply Chain, Legal and Policy. A few managerial roles were also established and filled, mainly as a result of internal growth and the establishment of a new leadership level.

The most important staff increase in 2022, has come as a consequence of CEPI's role in the COVID-19 response and the demands on the COVID-19 portfolio, the build-up of a Project Management Office to help ensure excellent project management and administrative partnership with CEPI partners, CEPI's decision to expand its support into later phase development for select pathogens, a stronger emphasis on manufacturing and quality, and preparation of other activities and responsibilities laid out in the CEPI 2.0 strategy. With this growth also comes the need for enhancing internal organizational management, improving risk management practices, and implementing digital technology and information security arrangements commensurate with the organization's size.

The CEPI workforce is global, and the organization's employees originate from 51 different countries. About 28% of the employees originate from an LMIC. This number has steadily increased since CEPI started: 13% in 2018; 17% in 2019; 22% in 2020, and 25% in 2021.

Appendix 4: CEPI Board Summary

CEPI's Board met four times in 2022, and there were over 20 CEPI Board Committee meetings.

Administrative items

In the first half of 2022 there were the following changes to membership:

- Peter Piot and John Nkengasong resigned from the Board, following appointments to new positions
- Nadine Gbossa's term as a Board member ended
- A number of new appointments were made:
    - Emmanuel Hanon was appointed as Chair of the Scientific Advisory Committee (SAC) for 3 years. Laura Palomares was appointed as a second vice chair of the SAC, for 3 years
    - The Board reappointed Richard Hatchett as CEO for another 5-year term
    - Before the June 2022 meeting, Dr L. Rizka Andalucia, Director-General for Pharmaceutical and Medical Devices at the Ministry of Health of the Republic of Indonesia, as Board voting member (investor)
    - Mr. Cyrus Ardalan, Chairman of OakNorth Bank, Trustee of the Charities Aid Foundation (CAF), and a senior adviser at Alvarez and Marsal, as Board voting member (independent)
    - Dr Githinji Gitahi, Group Chief Executive Officer, Amref Health Africa, as Board voting member (independent)
    - Professor Samba Sow, Director General of the Center for Vaccine Development – Mali (CVD-Mali) and former Minister of Health for Mali, as Board voting member (independent).

Table 7: CEPI Board Members as of December 2022

CEPI Board Members as of December 2022 Organisation/Affiliation Independent Members	Name	Position
	Jane Halton	(Board Chair)
Oak North Bank	Cyrus Ardalan	Chairman
The Wellcome Trust Research Laboratory	Cherry Kang	(Board Vice-Chair) Professor
Oswaldo Cruz Foundation (Fiocruz)	Peter Piot	Director
Medicines for Malaria Venture	David Reddy	Chief Executive Officer
Center for Vaccine Development – Mali (CVD-Mali)	Professor Samba Sow	Director-General
Aerium Therapeutics	Rajeev Venkayya	CEO
Investor Representatives		
Gender Equality and Director, Vaccine Development and Surveillance and Director, Enteric and Diarrheal Diseases programmes, Gates Foundation	Anita Zaidi	President/Director
Pharmaceutical and Medical Devices at the Ministry of Health of the Republic of Indonesia	Dr L. Rizka Andalucia	Director-General
German Federal Ministry of Education and Research	Veronika von Messling	Director-General
National Institute of Infectious Diseases, Japan	Ichiro Kurane	Former Director-General
Non-voting Members		
Coalition for Epidemic Preparedness Innovations	Richard Hatchett	Chief Executive Officer
Viome	Emmanuel Hanon	(Chair SAC) Head of R&D
American Association for the Advancement of Science	Peggy Hamburg	(Chair JCG) Chair of the Board
World Health Organization	Soumya Swaminathan	(WHO representative) Chief Scientist
World Bank (Health, Nutrition and Population)	Juan Pablo Uribe	(World Bank representative) Global Director

Appendix 5: Summary of the Scientific Advisory Committee (SAC)

In 2022, the SAC appointed a new Chair, Emmanuel Hanon, and then continued to meet on a roughly quarterly basis, with the first meeting taking place on 19 July. Throughout 2022, the SAC focused on the following topics:

1. SARS-CoV2 and broadly protective coronaviruses and portfolio balance

2. Mucosal delivered vaccines and controlled human infection models

3. Optimizing rapid response platforms

4. CEPI's role in R&D&M for mPox during the Public Health Emergency of International Concern (PHEIC).

In addition, in November 2022, the SAC led a comprehensive portfolio review focusing on the performance and composition of the BPCV, Disease X, Lassa and Nipah portfolios.

Table 8: Members of CEPI Scientific Advisory Committee (SAC) as of December 2022

Members of CEPI Scientific Advisory Committee (December 2022)	
Organisation/Affiliation	Name
International Research Center of Excellence, Institute of Human Virology, Nigeria/ University of Maryland School of Medicine Institute of Human Virology, US	Alash'le Abimiku
Cambridge University Hospitals Foundation Trust, UK	Sani Aliyu
Indian Institute of Science Education and Research, Pune, India	Vineeta Bal
University of Texas Medical Branch, US	Alan D. Barrett
Arch Venture Partners, US	Luciana Borio
National Institute of Allergy and Infectious Diseases, National Institutes of Health, US	Paula Bryant
Centers for Disease Control and Prevention, US/ Emory University, US	Inger Damon
MDW Consultant, LLC, US	Michel De Wilde
Charité – Universitätsmedizin Berlin, Germany	Christian Drosten
Bill & Melinda Gates Foundation, US	Peter Dull
Chinese Center for Disease Control and Prevention/ Institute of Microbiology, China	George Gao
Imperial College London, UK	Azra Ghani
Wellcome Trust, UK	Josie Golding
Pasteur Network, France	Rebecca Grais
Vicebio, Belgium	Emmanuel Hanon
International Vaccine Design Center, The Institute of Medical Science, The University of Tokyo, Japan	Ken J. Ishii
IAVI, US	Kent Kester
University of Virginia, US	Michael King
WHO, US	Phil Krause
Harvard T.H. Chan School of Public Health, US	Marc Lipsitch
RH Solutions, FR	Dominique Maugeais
Bharat Biotech International, India	Krishna Mohan Vadrevu
ModeX Therapeutics, US	Gary Nabel
Instituto de Biotecnología, Universidad Nacional Autónoma de México (UNAM)	Laura Palomares Aguilera
Paradiso Biologics Consulting, LLC, US	Peter Paradiso
University of Pennsylvania, US	Stanley Plotkin
GHD|EMPHNET, Bangladesh	Mahmudur Rahman
Fondazione Biotecnopolo di Siena, Italy	Rino Rappuoli
Santa Casa de Sao Paulo School of Medical Sciences, Brazil	Marco Safadi
WHO, UK	Vaseeharan Sathiyamoorthy
London School of Hygiene & Tropical Medicine, UK	Peter Smith
SUNY Upstate Medical University, US	Stephen Thomas
Duke-NUS Medical School, Singapore	Linfa Wang

Appendix 6: Summary of the Joint Coordination Group

Table 9: Members of CEPI Joint Coordination Group (JCG) as of December 2022

Members of CEPI Joint Coordination Group (December 2022)	
Organization / Affiliation	Name
American Association for the Advancement of Science	Peggy Hamburg (JCG Chair)
AVAREF	Diadié Maiga
DCVMN	Rajinder Suri
European Medicines Agency	Marco Cavaleri
US Food and Drug Administration	David Kaslow
FIND	Bill Rodriguez
GAVI the Vaccine Alliance	Derrick Sim
International AIDS Vaccine Initiative (IAVI)	Mark Feinberg (Advisor)
International Federation of Red Cross and Red Crescent Societies	Petra Khoury (joined October 2021)
Médecins Sans Frontières	Sidney Wong
UNICEF	Andrew Owain Jones
Wellcome Trust	Charlie Weller
World Health Organization	Ana Maria Restrepo
World Bank	Mukesh Chawla
Working Group (Regulatory)	Rogerio Gaspar
Working Group (Regulatory)	Daniel Brasseur
Working Group (Regulatory)	Murray Lumpkin

Appendix 7: 2022 update on actions independent outcome evaluation of CEPI 1.0

In 2022, an independent outcome evaluation of CEPI 1.0 was conducted to assess:

1. The impact of CEPI – through its activities and investments;
2. The sustainability of the results achieved; and
3. Main lessons learned from CEPI's first five-years to contribute to the implementation of CEPI's new strategy (CEPI 2.0 2022-2026).

The independent evaluator report and a response from CEPI management can be found on CEPI's website here. Following this evaluation, CEPI management has committed to actions responding to the findings. An update on these actions can be found in the table below.

Table 10: Update on actions responding to findings of the independent outcome evaluation of CEPI 1.0

Follow up actions	Status update end of 2022
CEPI scope of work	
Based on CEPI's objectives, ensure partnerships are in place to ensure the ultimate success and utility of CEPI's projects.	Ongoing
CEPI has established a Manufacturing and Supply Chain division to support the organization's revised objectives to include supporting diversification of manufacturing and contribute to the global preparedness for rapid manufacturing response.	Completed. The division has been established and will be expanded with recruitments and capacity as needs evolve
A consultation on the role of the JCG is being conducted and revised terms of reference will be discussed with the Board and published. This will strengthen CEPI's role as a facilitator.	Completed. The Board approved the updated Terms of Reference for the Joint Coordination Group at the December 2022 Board meeting; published on CEPI's website here.
The annual budget exercise will review priority activities according to funds CEPI has received and anticipates receiving.	Completed. The budget for 2023 was developed as part of an annual strategic and operational planning exercise. The exercise took into account prioritization for CEPI's R&D&M activities to initiate at this point based on the funds CEPI has raised and hopes to raise, the financial runway CEPI has, and towards achieving CEPI's strategic objectives. The Board approved the 2023 budget at the December 2022 Board meeting.

Equitable access	
Increase transparency and measurement of implementation of CEPI's Equitable Access Policy, including: • Publishing an Equitable Access Framework • Conducting independent reviews of CEPI's access agreements for portfolios other than COVID-19	Ongoing
All investment proposals and pathogen portfolios will have a clear articulation of Equitable Access objectives and approach	Ongoing
Host roundtables with relevant stakeholders including CSOs on further strengthening access and transparency	Ongoing
Engaging industry	
Develop a strategic partnerships framework in discussion with CEPI Board	Ongoing. Management is developing a strategic partnerships framework, considering if there are circumstances where CEPI would look to directly partner with an organisation, and the rationale and rubric for doing that. Management presented an evolved framework, selection process and high-level view of how strategic partners may fit into the wider context of CEPI's objectives at the March 2023 Board meeting.
Seek to broker partnerships for academics and biotechs with successful technology as they progress	CEPI is actively linking developers to the growing networks CEPI is developing, including enabling sciences networks as well as the manufacturing network. For more details, please refer to section 3.2.1 – Fill gaps in the global R&D ecosystem for end-to-end epidemic preparedness and response.
CEPI has set up SWAT teams and the Manufacturing Taskforce to address broad R&D and Manufacturing issues with vaccine developers and manufacturers for COVID-19 vaccines and other CEPI priorities	Ongoing

LMIC engagement	
Proactively encourage applications to Calls for Proposals and strategic partnerships with partners from LMICs	Ongoing Careful landscaping and outreach to encourage applications occurs with each Calls for Proposals.
Continue to engage proactively with national and regional manufacturing preparedness and response initiatives, acting as a technical adviser where appropriate. CEPI's manufacturing network activity will work with partners from all Global South regions.	Ongoing In December 2022, CEPI signed a funding agreements with South Africa's Aspen (announcement here) to support its capabilities to manufacture lifesaving routine and outbreak vaccines for Africa. In January 2023, CEPI signed a funding agreement with Institut Pasteur de Dakar (announcement here) to boost manufacturing of affordable vaccines for the Global South. CEPI is in active discussions with additional vaccine manufacturers in the Global South about joining the manufacturing network and expects to make additional announcements. For more details, please refer to section 3.3.2 -Diversify global manufacturing capability geographic.
As CEPI's portfolio progresses, proactively engage affected countries/regions to prepare for availability of new vaccines (including discussing ideal profiles/characteristics of vaccines as they are developed)	Ongoing
Hold one of CEPI's two in-person Board meetings a year in an LMIC	Ongoing In 2023, the in-person meetings of CEPI's Board will take place in Washington DC, US and in Senegal.
Work with clinical trial networks to support work on products CEPI supports, clinical trial capacity, and readiness to respond to epidemics and pandemics and pandemic preparedness more generally	Ongoing This topic, among others, were discussed at the SAC meeting in April 2023.

Effectiveness	
Review the CEPI 2.0 Results Framework and identify opportunities to increase measurability and relevance of KPIs for CEPI's second business cycle.	Ongoing The work leading up to the 2022 progress and status update on the Key Performance Indicators in this Report and other reporting initiatives are being used to assess measurability and relevance of the KPIs. Potential adjustments to the KPIs will be considered at next year's CEPI 2.0 mid-term.
Use mid-term review as an opportunity to adjust KPIs and/or strategic targets if no longer fit for purpose and propose/agree any adjustments in consultation with the Board and Investors	Ongoing Preparations for the independent mid-term review of CEPI 2.0 will kicked off in 2023. The mid-term review will be conducted in 2024.

LMIC engagement	
Actively seeking to reach CEPI's fundraising target in full	Ongoing
Conduct a project to review how CEPI works with partners it provides funding to.	Ongoing Management conducted a "Voice of customer project" in 2022 to understand views of partners. The outcomes of the voice of customer exercise were reported to the Board in March 2023. Implementation of specific recommendations is ongoing. For more details, please refer to section Appendix I – Organizational update.
Revise Investor Council Terms of Reference for Board approval	Completed. The Board approved the updated Terms of Reference for the Investors Council at the December 2022 Board meeting; published on CEPI's website here.
Revise JCG Terms of Reference for Board approval	Completed. Management conducted a consultation on the role of the Joint Coordination Group and revised the Terms of Reference. The Board approved the updated Terms of Reference for the Joint Coordination Group at the December 2022 Board meeting; published on CEPI's website here.
CEPI's Audit and Risk Committee will oversee an external risk framework review and implementation process	Underway, through 2023 Management is working on revising CEPI's risk management framework. The target in 18 months is for a comprehensive approach, covering all areas, which will have a dashboard that can help the Board by indicating risk tolerance, appetite limits, and be actionable. The Board will receive timely, and frequent updates. For more details, please refer to section 5.1 – Risk Management.
Conduct Board effectiveness review	Ongoing

Reporting Period and Contact Information

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