CEPI

2023
Annual Progress Report

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Abbreviations

Africa CDC	Africa Centres for Disease Control and Prevention
ARC	Audit & Risk Committee (CEPI)
BARDA	Biomedical Advanced Research and Development Authority (US)
BPCV	Broadly Protective Coronavirus vaccine
CEPI	Coalition for Epidemic Preparedness Innovations
CfP	Call for Proposals
CHIM	Controlled Human Infection Model
CMC	Chemistry Manufacturing and Controls
COVAX	Vaccine pillar of Access to Covid-19 Tools Accelerator
COVID-19	Coronavirus disease 2019 (due to SARS-CoV-2 virus)
EA	Equitable Access
ECOWAS	Economic Community of West African Studies
EID	Emerging Infectious Diseases
FDA	Food and Drug Administration (US)
GISAID	Global Initiative on Sharing All Influenza Data
GMP	Good Manufacturing Practice
GPC	Glycoprotein Complex (Lassa)
HERA	Health Emergency Preparedness & Response Authority (European Commission)
IMS	Investment Management System
INB	Intergovernmental Negotiating Body
IPPS	International Pandemic Preparedness Secretariat
IAVI	International AIDS Vaccine Initiative
IVI	International Vaccine Institute
KPI	Key Performance Indicator
JCG	Joint Coordination Group (CEPI)
LMIC	Low- and Middle-Income Countries
mAb	Monoclonal Antibody
MCM	Medical Countermeasures
iMCM Net	Medical Countermeasures Network
MERS	Middle East Respiratory Syndrome
MSC	Manufacturing and Supply Chain (CEPI)
NEIDL	National Emerging Infectious Disease Laboratory (US)
NIAID	The National Institute of Allergy and Infectious Diseases (US)
OPEX	Operating Expenses
PMN	Preclinical Models Network (CEPI)
PPR	Pandemic Preparedness & Response
PPPR	Pandemic Prevention Preparedness & Response
RPPWA	Research Preparedness Programme West Africa
RVF	Rift Valley Fever
RVMC	Regionalised Vaccine Manufacturing Collaborative (hosted by CEPI)
SAC	Scientific Advisory Committee (CEPI)
SCARDA	Strategic Centre for Biomedical Advanced Research and Development (Japan)
SARS COV-2	Severe acute respiratory syndrome coronavirus 2 (coronavirus strain that causes COVID-19)
VMFN	Vaccine Manufacturing Facility Network (CEPI)
WHO	World Health Organization
XVAX	Network of wider ecosystem organisations involved in preparedness for public health emergencies building on COVAX partners

Introduction from Dr. Richard Hatchett, CEO

In 2023 the lives of hundreds of millions, if not billions, of people were impacted by climate change, conflict, food insecurity, and displacement. Each of these factors increases the risk of infectious disease outbreaks. Collectively, they create conditions that create grave risks for epidemics and pandemics.

While the world's perception of COVID-19 as a threat subsided in 2023, significant outbreaks of epidemic disease continued to occur globally. The incidence of mosquito-borne diseases such as Dengue and Chikungunya increased markedly over the year. India and Bangladesh saw outbreaks of Nipah, and the Democratic Republic of Congo experienced an intensifying and increasingly widespread outbreak of the most virulent form of mpox. Unusually high case numbers of Crimean-Congo Haemorrhagic Fever were recorded in Iraq, Afghanistan, and Iran. Large outbreaks of H5N1 influenza clade 2.3.4.4 in U.S. wild aquatic birds, commercial poultry, and backyard flocks that began in January 2022 accelerated alarmingly throughout the year, affecting almost 100 million birds and heralding the ongoing 2024 outbreaks in U.S. dairy herds and livestock.

In May, the World Health Organization (WHO) declared the end of the COVID-19 Public Health Emergency of International Concern, ending the acute phase of the pandemic. In October, vaccine technology pioneers Katalin Karikó and Drew Weissman received the Nobel Peace Prize for Medicine for work that enabled the development of effective mRNA vaccines against COVID-19. At the end of 2023, COVAX closed its doors after delivering just shy of 2 billion doses of COVID-19 vaccine to populations in need. In its successes and failures, COVAX simultaneously demonstrated what can be achieved through international collaboration while underscoring the need for greater effort and attention to ensure equitable access.

Support for the 100 Days Mission continued to grow. We were pleased to support work led by the Government of Japan under its 2023 G7 Presidency on what it called the "100 Days Mission PLUS". As highlighted in the International Pandemic Preparedness Secretariat's (IPPS's) Third Implementation Report, multiple actors contributed to advancing the thinking and innovation required to meet the 100 days target. CEPI established four new strategic partnerships with vaccine development leaders—the University of Oxford, Moderna, BioNTech and IQVIA—to jumpstart progress on the 100 Days Mission, while adding Bio Farma in Indonesia to its Global South manufacturing network alongside existing partners Institut Pasteur de Dakar in Senegal and Aspen in South Africa.

As the year ended, CEPI representatives attended the historic inauguration of BioNTech's new commercial-scale mRNA vaccine facility in Kigali, Rwanda and prepared to host the Secretariat of the Regionalized Vaccine Manufacturing Collaborative (RVMC) in the next phase of its work.

In other work to support the 100 Days Mission, CEPI:

- Signed collaborations to support mRNA thermostability and delivery innovations
- Invested in the use of artificial intelligence to design vaccines and predict future outbreaks
- Expanded its preclinical and Centralised Laboratory networks for the assessment of epidemic and pandemic vaccines
- Launched work to identify correlates of protection that can reduce the cost and time required to develop vaccines by serving as alternatives to clinical endpoints
- Issued an all-in-one call for innovations to simplify and accelerate the formation of new partnerships
- Introduced a new biosecurity function, in recognition of the crucial intersection between pandemic preparedness and biosecurity risks.

CEPI's efforts reflected its commitment, in alignment with the WHO and US National Institutes of Health (NIH), to get a head start against the viral families most likely to produces future pandemic threats. In 2023, CEPI initially prioritised four viral families, including coronaviruses, paramyxoviruses, arenaviruses, and filoviruses, and collaborated with the European Commission's Health Emergency Preparedness & Response Authority (HERA) to assemble a meeting in Brussels in October of global Medical Countermeasures R&D Funders to foster coordinated effort on the viral families approach.

CEPI's priority pathogen portfolio made important progress as well. In November, the United States licensed the first-ever Chikungunya vaccine, IXCHIQ, developed by Valneva with support from CEPI. This announcement marked a huge leap forward in the fight against this deadly disease. CEPI's investment, supported by the European Commission, aimed to accelerate access to the vaccine in areas where the disease is endemic and for younger age groups. CEPI announced new clinical trials in endemic countries to assess vaccines against Rift Valley Fever (RVF) and Middle East Respiratory Syndrome (MERS), while CEPI's partner International AIDS Vaccine Alliance (IAVI) geared up to begin Phase IIa trials of its Lassa vaccine in West Africa.

Global efforts to strengthen the pandemic preparedness and response architecture achieved important milestones. In September 2023, Member States approved a declaration calling for concerted action on pandemic preparedness at the UN General Assembly. At COP28, more than 140 countries backed a Declaration on Climate and Health that linked human, animal, environment and climate health and called for intensification of efforts to detect zoonotic spillovers. Negotiations continued on the Pandemic Agreement with CEPI focusing its advocacy on concrete proposals to advance the cause of vaccine equity. We also continued to work with national and regional health bodies, including HERA, Africa Centres for Disease Control and Prevention (Africa CDC), Biomedical Advanced Research and Development Authority (BARDA), Strategic Centre for Biomedical Advanced Research and Development (SCARDA), national ministries, research funders and others to promote cooperation and, where possible, coordinated funding.

My executive leadership team and I would be the first to admit that CEPI also faced abundant challenges in 2023. Some of these derived from CEPI's growth and bureaucratisation, some from the need to lay the foundations of new programmes (which always takes longer than one would want), some from the limited absorptive capacity of the research ecosystem in areas critical to CEPI's work, and some from the cumulative impact of years of remote working on CEPI's culture. CEPI 2.0 lays out an ambitious strategic framework and demands that CEPI be a forward-leaning, adaptive and resilient organisation. We took this challenge to heart and worked hard, particularly over the last quarter, to implement and deliver programmes, eliminate excess bureaucracy, simplify processes and improve our financial forecasting.

These efforts had begun to bear fruit by the end of the year and I am pleased to say that we have largely regained our momentum. The work undertaken in 2023 to improve investment management and realise organisational efficiencies has left CEPI better positioned to deliver on CEPI 2.0 moving forward. We now better understand the factors driving our performance and have streamlined our internal processes to ensure we proceed at pace. And science is dynamic, with every day bringing new opportunities. The Mid-Term Review process taking place in 2024 will undoubtedly identify key learnings and recommendations in areas where refinements to our strategy and key performance indicators may be needed and will guide us as we plan for CEPI 2.0's homestretch.

Despite today's many global challenges, I see reason for hope and optimism. We have a once-in-a-generation opportunity to change the way the world prepares for and responds to pandemics. Through the research and manufacturing efforts we support, our unwavering commitment to equity and international cooperation, we are making steady progress toward our goals.

I extend my warmest thanks to our Board, Investors and all partners who, inspired by the 100 Days Mission, continue to support CEPI in our efforts. We look forward to continuing our joint endeavour to create a world free from the threat of pandemics.

Dr. Richard Hatchett,
CEO of CEPI

2023: CEPI's achievements in numbers

12
Active CEPI-funded vaccine candidates advanced for priority pathogens

12
Technology platform projects aiming to validate rapid response capabilities

6
Manufacturing innovations to support thermostability, speed and scalability of platforms

1
World-first vaccine against Chikungunya virus licensed

3
Partners in the Vaccine Manufacturing Facility Network to expand the global footprint of vaccine production and outbreak response capacity

60
Established or planned clinical study sites across all continents of the globe

7
Vaccines licensed against COVID-19

4
Viral families prioritised for investment

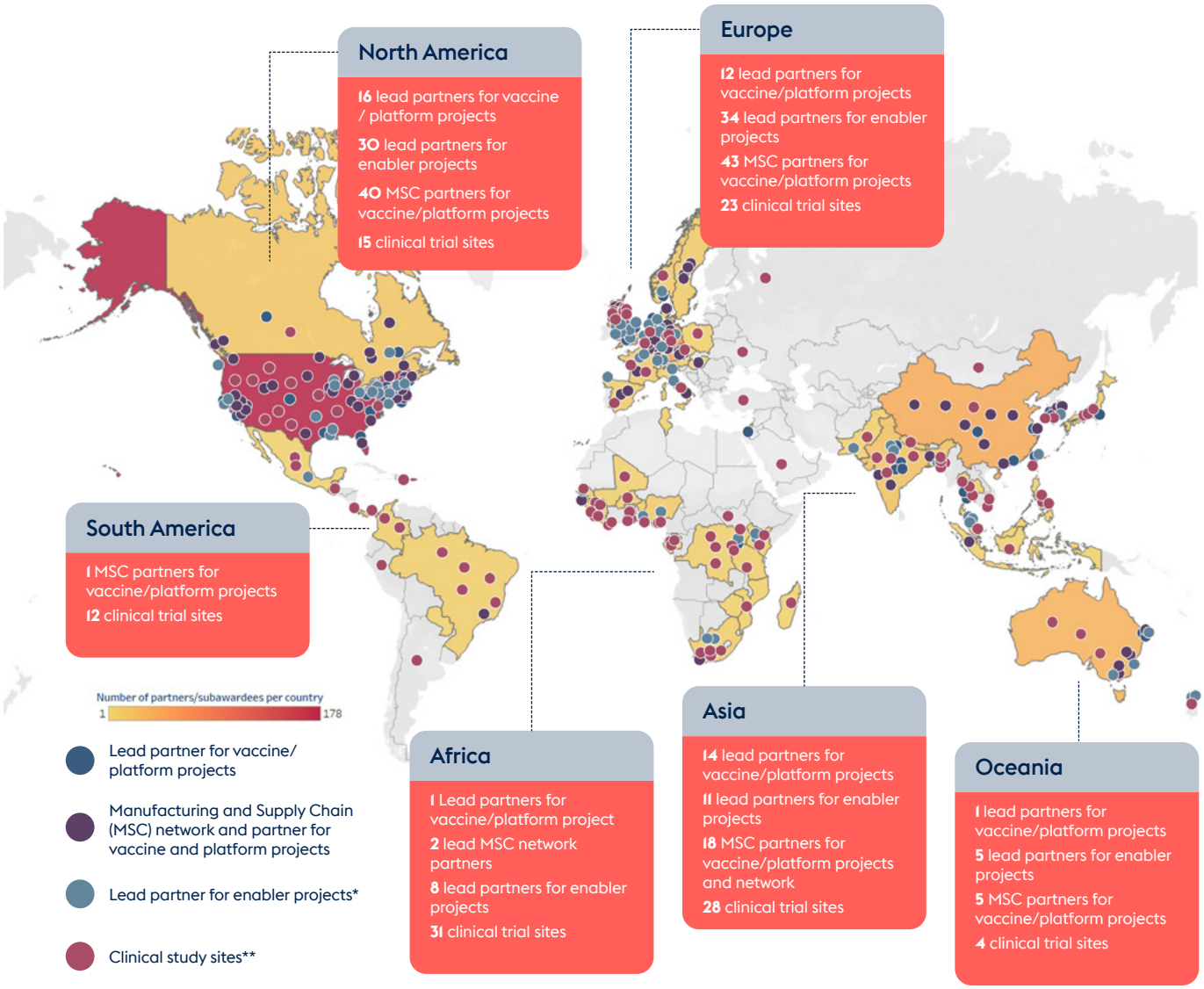
7
New laboratories in the Centralised Laboratory Network bringing the total to 17

70k
Clinical samples tested through the Centralised Lab Network using standardised SARS-CoV-2 assays

1
Biosecurity function established in recognition of the crucial intersection between pandemic preparedness and biosecurity risks in the 21st century

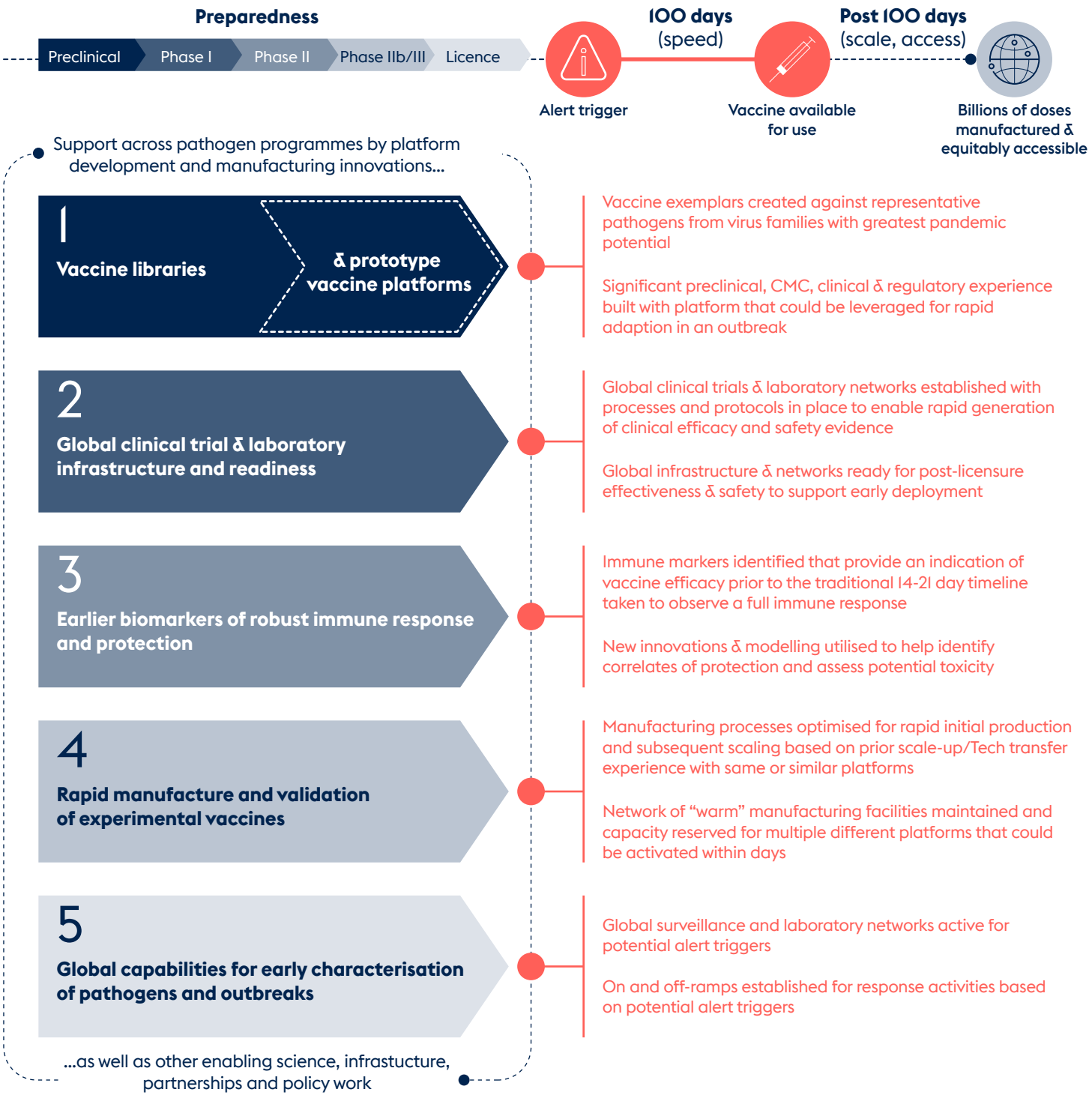
96
Pathogen-specific and cross cutting enabling science projects to support vaccine development for 100 Days Mission readiness

Figure I: Investments that support CEPI's mission as of December 2023



*Includes clinical research, standard & assay; animal model, epi, central lab, diagnostic, predictive modeling, system immunology and manufacturing innovation
**Planned and confirmed based on available information

CEPI's contributions to the 100 Days Mission



Background to the 2023 Report

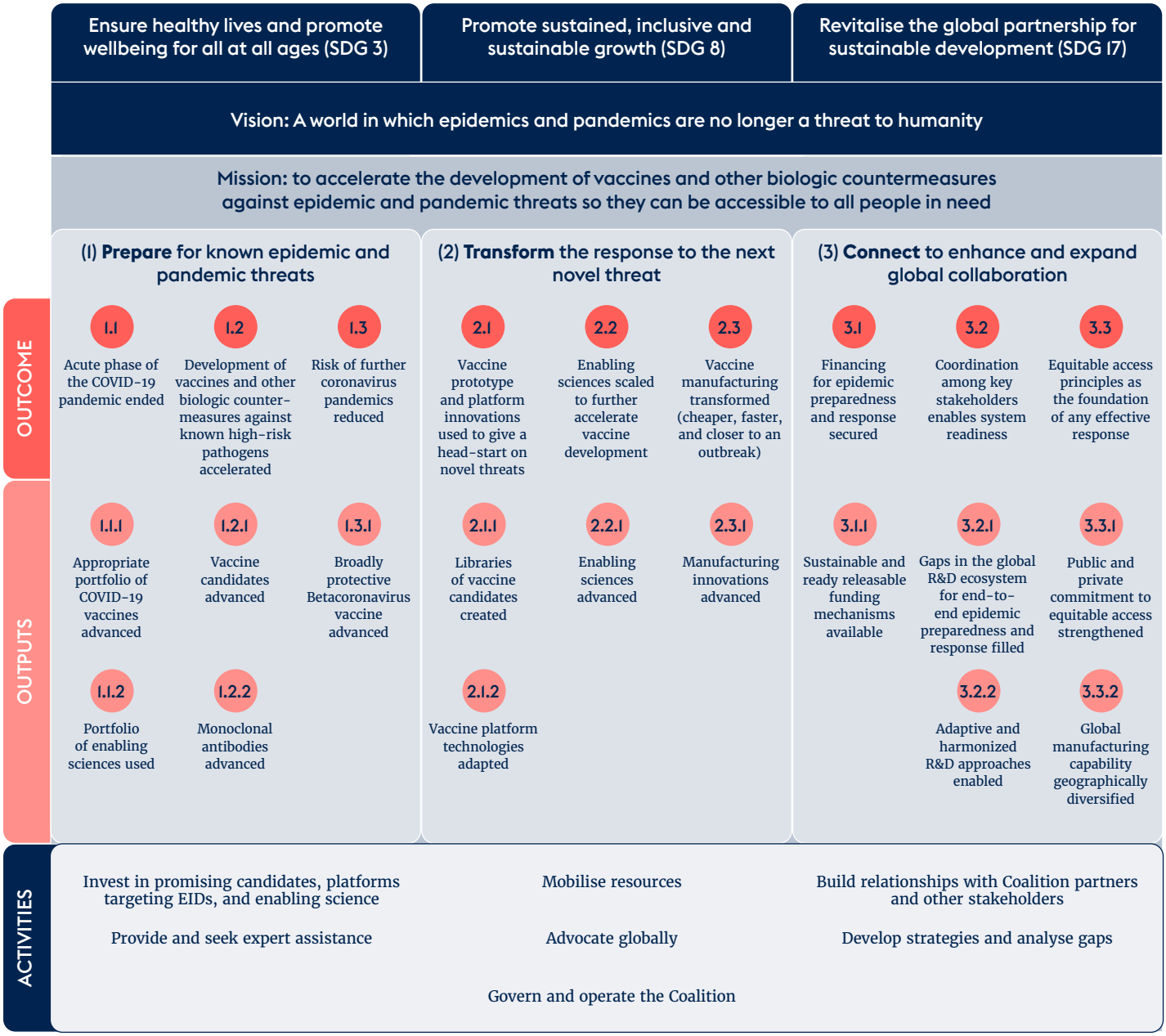
The 2023 Annual Progress Report provides an update on progress against the Key Performance Indicators (KPIs) under the three Strategic Objectives – PREPARE, TRANSFORM AND CONNECT – as described in the CEPI 2.0 Theory of Change and Results Framework. An overview of progress against KPIs is provided below and a detailed description is available on request.

As well as outlining CEPI's key successes, challenges and learnings in 2023 in relation to existing KPIs, this report outlines CEPI's achievements that fall outside of the 2.0 Results Framework but are necessary to support the delivery of CEPI's strategic objectives and mission. This reflects the fact that CEPI developed the initial strategy 2.0 while we were responding to the COVID-19 pandemic and we were building and leading COVAX with some significant successes. In taking forward CEPI 2.0, it has taken longer than anticipated to prioritise and translate high-level concepts into programmes. CEPI has worked intensively to address the factors within its control including building more robust financial management infrastructure and filling staffing gaps.

As a result of these efforts, CEPI has made significant strides in the latter half of 2023 towards bolstering its portfolio, entering new and strategically important partnerships and achieving more efficient investment management in a rapidly growing organisation. With agreement of our Board, CEPI has added or reframed some areas, such as reducing the level of activity on COVID-19 and adding mpox as a priority pathogen in late 2023, in recognition of its evolution and the critical needs. Other significant successes since publication of the 2022 Annual Progress Report include the U.S. Food and Drug Administration (FDA) Market Authorisation of the first ever Chikungunya vaccine Valneva's live-attenuated vaccine candidate (IXCHIQ), successful stage gate reviews of leading vaccine candidates now ready to enter Phase II against Lassa, Middle East Respiratory Syndrome (MERS) and Nipah, while the remainder of CEPI's active vaccine portfolio for these diseases and for Rift Valley Fever (RVF) moving into the clinic in 2024.

CEPI is approaching the midpoint of the CEPI 2.0 business cycle and an organisation-wide Mid Term Review will take place in 2024. This review will assess the strategic positioning of the portfolio in the context of CEPI's progress and the evolving global preparedness and response needs and will be reflected in the 2024 Annual Progress Report.

Figure 2: CEPI 2.0 Theory of Change



CEPI 2.0 Key Performance Indicators - Overview of progress in 2023

CEPI 2.0 Outcomes	KPI	2026 Targets	Progress update end of 2023	Status
1.1 Acute phase of the COVID-19 pandemic ended	1.1. Number of CEPI-funded SARSCoV-2 licensed vaccines that are favourable for LMICs and available for use	Two variant-proof broadly protective SARS-CoV-2 candidates demonstrate clinical proof of concept (by end 2023)	CEPI continued to support the remaining development and licensure activities of two SARS-CoV-2 vaccines favourable for the Global South (SK Bioscience and Clover). Seven preclinical models have been developed for the original prototype SARS-COV-2. CEPI's efforts have shifted to reducing the risk of future coronavirus pandemics. The variant-proof coronavirus targets and the Betacoronavirus targets have now been merged into pan-sarbecovirus. Progress is outlined under 1.3.	Completed
1.2. Development of vaccines and other biological countermeasures against high-risk pathogens accelerated	1.2. Number of CEPI-funded vaccine candidates and other biologic ountermeasures for priority pathogens ready for use	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 more priority pathogens to ready to use under outbreak conditions	Vaccine candidate portfolio: Preclinical: Three Phase I: Seven Phase II: One Phase III: Zero Licensure: One One candidate is currently in preclinical and ready to enter Phase I, and four candidates are currently in Phase I and ready to enter Phase II. There is a gap in the number of candidates in mid/late-stage development due to candidate down selection and delays due to COVID-19 which is being addressed through backfilling of additional candidates. Portfolio outperformed in terms of licensure target in 2023 (CHIK-Valneva) although a licensed vaccine for a second priority pathogen is unlikely before end of 2026.	In progress
1.3 Risk of other coronavirus pandemics reduced	1.3 Number of CEPI-funded broadly protective Betacoronavirus vaccines (BPCV), favourable for LMICs, assessed for clinical proof of concept	Two	The BPCV programme is focused on two approaches: (1) pan-sarbecovirus (+/- MERS-CoV) vaccine development, and (2) whole coronavirus family vaccine development. The portfolio is comprised of 11 candidates in preclinical phase, six of these which are fully funded and five are seed-funded projects. Of the 11 active projects, one has a precursor candidate in Phase I trial funded by Government of Canada. Three further projects have been terminated/are in process of being closed out.	In progress
2.1 Vaccine prototype and vaccine innovations used to give a head start on novel threat	2.1 Number of CEPI-funded innovations that can be rapidly adapted against unknown pathogens	Two licensed vaccines against viable targets for LMICs using prototype and/ or platform innovations. Clinical proof of concept for four virus family vaccine libraries	Four viral families (arenaviruses, paramyxoviruses, poxviruses, coronaviruses) have been prioritised. The planned workflow of antigen design and preclinical testing has started for two viral families – poxviruses and arenaviruses. A design has been selected by BioNTech for their mpox vaccine which initiated Phase I clinical trial. Production and testing of designs for Lassa and Junín viruses, members of the arenavirus family, was initiated. Seven new platform technology innovation projects onboarded in 2023, bringing the total to eight prototype vaccines against Japanese Encephalitis, SARS-CoV-2, Chikungunya, Rabies, Yellow Fever, and Influenza in development by end 2023.	In progress

CEPI 2.0 Outcomes	KPI	2026 Targets	Progress update end of 2023	Status
2.2 Enabling sciences scaled to further accelerate vaccine development	2.2 Enabling science programmes and innovative tools actively used by CEPI-funded developers 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	Ongoing work to develop preclinical models for BPCV via investments into MERS-CoV, SARS-CoV, and other pre-emergent coronavirus preclinical model discovery research. Seven original protype SARS-CoV-2 virus animal models and 17 SARS-CoV-2 variant-based models were made available as of end 2023. Additional preclinical model work in progress for MERS and pre-immune models based on approved on-market SARS-CoV-2 vaccines. Progress is on track and reflects the evolution of the SARS-CoV-2 variants and to the decision to redefine the focus of the BPCV portfolio in 2023. Active partnership with preclinical model network laboratories with capacity to contribute models for CEPI priority pathogens means that CEPI has in place resources for expedited preclinical testing. Development launched for Nipah natural history study models for vaccine and mAb preclinical testing in pivotal efficacy studies, planned for delivery in 2024. The Nipah antibody international standard was approved by WHO Expert Committee on Biological Standardization in October 2023.	 In progress
2.3 Vaccine manufacturing transformed	2.3 Number of new technologies demonstrating manufacturing cheaper, faster or closer to outbreak	At least three innovations which demonstrate manufacturing cheaper, faster or closer to an outbreak	Six manufacturing innovation projects were launched in 2023. CEPI-supported manufacturing innovations span seven countries covering the different aspects of thermostability, speed, scale and access as drivers of vaccine manufacturing transformation.	 In progress
3.1 Funding for epidemic preparedness and response secured	3.1 New financing mechanisms include funding for vaccines and other biologic ountermeasures preparedness and response R&D	Funding for vaccine and other biologic countermeasures preparedness and response R&D included (by end 2025)	CEPI played a catalytic role in shaping the PPR financial architecture including commissioning modelling efforts to inform PPR policymaking, engaging with G7 Development Finance Institutions and G20 Health and Finance efforts, and is actively coordinating with the newly established Pandemic Fund.	 In progress

CEPI 2.0 Outcomes	KPI	2026 Targets	Progress update end of 2023	Status
3.2 Coordination among key stakeholders enables system readiness	3.2 Alignment on key elements of a target ecosystem to accelerate development and promote equitable access of emerging infectious disease	RACI(s) - Responsible, Accountable, Consulted and Informed - for 80% of key elements in place	CEPI co-hosted the first Medical Counter Measures (MCM) R&D Funders Roundtable with the European Commission's Health Emergency Preparedness and Response (HERA) to increase visibility, coordination and opportunities for partnership. A second meeting is planned in 2024 to be co-hosted with South African Medical Research Council (SAMRC). CEPI provided thought leadership and staff support for the WHO-convened interim-Medical Countermeasures Network (iMCM Net), including R&D component of a report to be shared at 2024 World Health Assembly. CEPI's Joint Coordination Group (JCG) discussed stronger collaboration and identification of gaps for "hand-off" between organisations in the vaccine value chain. A tabletop exercise is planned for January 2024 alongside CEPI's Annual Portfolio Review. With Gavi, UNICEF, WHO, Africa CDC, PAHO, WHO SEARO, CEPI established the XVAX Network to support operational readiness to respond rapidly to emerging epidemic and pandemic threats. CEPI hosted session at World Health Summit on partnerships for a pandemic-free future with Africa CDC, EDCPT3, Fiocruz, GPMB and India Council for Medical Research. CEPI initiated development or revision of Memoranda of Understanding (MOU) with Africa CDC, Gavi, Korea DCA, and PAHO, to be signed in 2024. Agreement on collaboration priorities with UNICEF Supply Division.	 In progress
3.3 Equitable access principles as the foundation of any effective response	3.3 Removing at least one key systemic obstacle to access for LMICs	Guidance available to address potential injuries caused by vaccines/to establish a no-fault compensation-mechanism Three G20 countries making new funding and/or procurement commitment for vaccines development include reference to access provisions.	Ongoing advocacy to broaden the G20 Joint Finance and Health taskforce commitments, including with greater representation from the Global South, to establish and adequately fund surge financing mechanisms. One new partnership added to CEPI's network to support globally diversified manufacturing capability (Bio Farma, Indonesia) bringing the total number of partners in CEPI's Manufacturing network to three. Designed and secured support to launch the second phase of the Regionalised Vaccine Manufacturing Collaborative (RVMC). CEPI agreed to host the RVMC Secretariat from 2024. CEPI's equitable access positions were reflected in the interim draft of the Pandemic Agreement, and CEPI's role in the PPPR ecosystem was reflected in the G7 Leaders communique, the G20 Health Ministers meeting outcomes and in the work of the G20 Joint Finance and Health Task Force. Engaged with CEPI Investors Council members and their relevant agencies on need for equitable access terms in MCM R&D contracts. CEPI welcomed that the National Institutes of Health (NIH) proposed to develop and implement a new policy within its Intramural Research Program (IRP) to promote access to products stemming from taxpayer-funded inventions.	 In progress

Progress Against the Strategic Objectives

Strategic Objective 1: PREPARE for known epidemic and pandemic threats

A core part of CEPI's mission is to support the development of promising vaccine candidates against known priority diseases to rapidly activate R&D at the outset of an outbreak, with the ultimate goal of fast tracking the availability of vaccines that can be used to save lives and avert large scale epidemics or pandemics. CEPI's activities span the globe with 60 established or planned clinical study sites, spread across all continents. The portfolio incorporates a range of technology platforms, with investments split across viral vector, RNA and protein-based platforms as well as live attenuated/inactivated vaccines.

As of 31 December 2023, CEPI had an active Research and Development (R&D) portfolio of 12 vaccine candidates for its initial priority high risk pathogens: three vaccine candidates against Lassa virus, two vaccine candidates against Middle East Respiratory Syndrome-CoV (MERS), three candidates against Nipah virus, two candidates against Rift Valley Fever (RVF) and two candidates against Chikungunya, of which one candidate secured its first approval in 2023 and is technically not a candidate anymore but an approved vaccine. We continue to count this as a candidate as we fund studies to achieve approval in Brazil and other LMICs. Across the board, CEPI's portfolio has made robust progress. Highlights include:

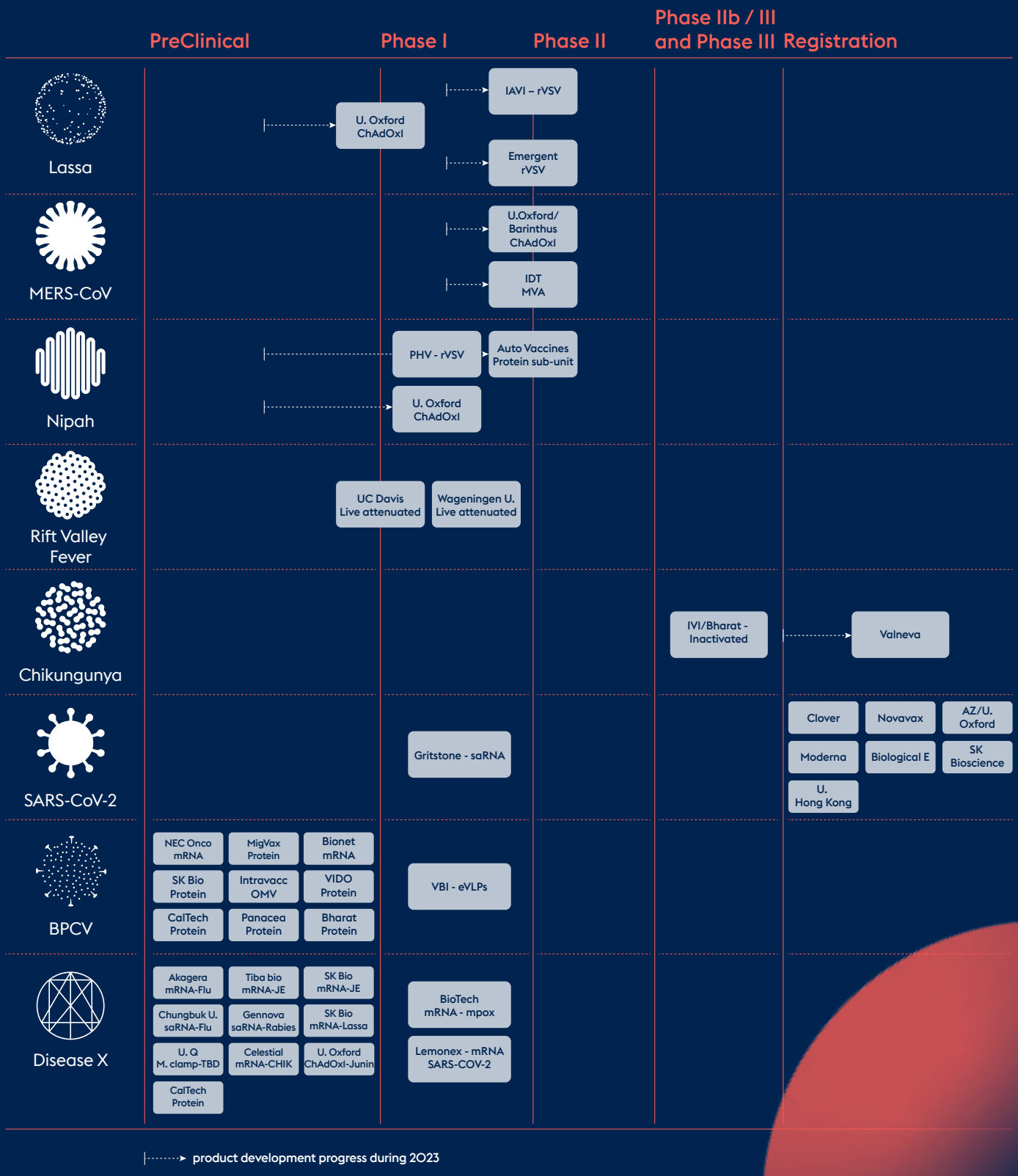
- Lassa: one partner prepared to begin a Phase II clinical trial, a global first.
- Nipah: commenced Phase I clinical trial (Oxford) and CEPI launched a Call for Proposals to develop monoclonal antibodies (mAbs) that could be used in an outbreak to provide immediate protection to recipients prior to vaccine-induced immunity.
- MERS: CEPI signed an agreement to advance two candidates into clinical trials.
- Chikungunya: with support from CEPI and the European Commission, Valneva's live-attenuated Chikungunya vaccine candidate was licensed by the US Food and Drug Administration (FDA), another global first, with ongoing work in Brazil to support licensure, especially in Low- and Middle-income countries (LMICs) in affected countries in the region.
- RVF: with support from CEPI and the European Commission, signed agreements to take two candidates into clinical trials in endemic countries for the first time.
- Covid-19: additionally, since 2020, CEPI has invested in 14 COVID-19 vaccine candidates, seven of which achieved either domestic or global licensure, including one that utilised a platform funded by CEPI in early-stage development. Three of these investments were procured by the COVAX Facility, thereby supporting the delivery of almost two billion doses of vaccine to 146 countries by the time COVAX closed at the end of 2023. With the acute phase of the pandemic declared over in May 2023, CEPI's investment strategy has transitioned to focus on developing Broadly Protective Coronavirus Vaccine (BPCV) candidates and associated efforts including new work on Controlled Human Infection Models (CHIM) to evaluate mucosal vaccine candidates with a view to preventing or reducing the risk of infection and/or transmission of SARS-CoV-2.

Monitoring of high-risk pathogens

In keeping with CEPI's mission prepare the world for emerging viral threats, CEPI continues to keep close track of emerging pathogens of interest, such as the Sudan strain of ebolavirus and mpox, and to use its resources and capabilities to support outbreak response. In 2023:

- Following prior investment in a vaccine against the Zaire strain, CEPI expanded its focus on the Sudan strain of ebolavirus and made a decision to support the development of broadly protective Filovirus vaccines. More information on this can be found in Outcome 2.1.
- The evolving epidemiology of mpox and the unmet medical need for effective vaccines in endemic countries, led CEPI to add mpox as a priority pathogen. With two mpox vaccines licensed in some countries, CEPI is focusing on filling evidence gaps to support access to the existing vaccines in low resource settings and developing immunological assays and standard reagents to support the global mpox outbreak response. CEPI also considered further investments in next-generation mpox vaccine candidates, given the potential limitations of current vaccines in terms of indications and effectiveness. The first such investment was made in 2023 under a broader strategic partnership with BioNTech, to initiate a Phase I/II clinical trial of the mRNA-based mpox vaccine programme, BNT166. This project constitutes an exemplar prototype vaccine for the mpox viral family that contributes to the PREPARE strategic objective.

Figure 3: Portfolio overview – CEPI-funded vaccine candidate portfolio as of December 2023



1.1. End the acute phase of the COVID-19 pandemic

Building on significant previous investments and taking into account the evolving nature of the pandemic, CEPI continued to progress a portfolio of first-generation COVID-19 vaccine candidates. In parallel, CEPI continued to progress 11 BPCV vaccine candidates, with most in preclinical development and one candidate in Phase I. Going forward, CEPI will continue support into clinical development including immunogenicity and clinical efficacy trials to support potential regulatory pathways.

In 2023, CEPI continued to support the remaining development and licensure activities for two additional SARS-CoV-2 vaccines (SK Bioscience and Clover Biopharmaceuticals) that had secured first licensures in 2022.

Following WHO's announcement in May 2023 that that COVID-19 no longer constituted a public health emergency of international concern, CEPI continued to co-lead COVAX until its closure in December and worked with COVAX partners on its replacement throughout the year. More information on this can be found in Outcome 3.2.

To enable researchers to compare results from different clinical trials of COVID-19 vaccines and to build on scientific advancements that were made during the COVID-19 pandemic, CEPI enables an ongoing supply of COVID-19 international antibody standards with partners, the National Institute for Biological Standards and Control (NIBSC) and WHO. Through CEPI's Centralised Laboratory Network, CEPI has supported harmonised immunology assessments of over 70,000 serum samples from preclinical and clinical studies of COVID-19 vaccines from over 70 different developers to date.

Progress on approaches that contribute to the 100 Days Mission

CEPI continues to seek increased understanding of new variants of SARS-CoV-2 as they emerge, and to provide the tools and knowledge for developers all over the world, including those in the Global South, to accelerate their programmes and enable smarter development decisions, including those that contribute to a BPCV.

Part of this work is implemented through CEPI's Agility programme. Established in 2020, Agility supports global efforts to monitor the emergence, evolution and spread of new SARS-CoV-2 strains on the effectiveness of COVID-19 vaccines using high quality, standardised assays and models and developing variant-specific antibody standard reagents and preclinical models. By the end of 2023, a CEPI supported-taskforce[1] had developed seven preclinical models for the original prototype SARS-CoV-2 and four variant models, and obtained and evaluated all newest SARS-CoV-2 variants for changes in virulence and immune escape. Informed by the Global Initiative on Sharing All Influenza Data (GISAID), the global database on variant importance and global prevalence, CEPI partners the UK Health Security Agency (UKHSA) and the NIBSC have obtained clinical swabs containing variant viruses to generate high quality master and working stocks and to assess the biological consequences of the rapid genetic changes using both in vitro and in vivo techniques.

[1] The taskforce was established in 2020 and comprises GISAID, UK Health Security Agency, and the National Institute for Biological Standards and Control.

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

Target 2023	Progress update
Two variant-proof broadly protective SARS-CoV-2 candidates demonstrate clinical proof of concept (by end 2023)	CEPI continued to support the remaining development and licensure activities of two SARS-CoV-2 vaccines favourable for the Global South (SK Bioscience and Clover). Seven preclinical models have been developed for the original prototype SARS-COV-2. CEPI's efforts have shifted to reducing the risk of future coronavirus pandemics. The variant-proof coronavirus targets and the Betacoronavirus targets have now been merged into pan-sarbecovirus. Progress is outlined under 1.3.

As part of this work, CEPI has been working closely with Harvard Medical School's Predictive Modelling programme to share data, samples and laboratory methods. Through these efforts, variants of 'high escape potential' have been identified (that is, the likelihood of a new variant evading vaccine- or infection-acquired immunity), underscoring the value of closer collaboration. CEPI's Agility and Predictive Modelling programmes are currently seeking to understand the mechanisms of immune escape by SARS-CoV-2 variants, which will help CEPI offer better preclinical testing for the support of BPCV development projects (see Outcome 1.3).

Identifying "correlates of protection" could significantly reduce the cost and time taken to develop vaccines by serving as alternatives to clinical endpoints, helping to inform earlier go/no-go decisions on which products are likely to meet efficacy endpoints, and guiding clinical trial designs where efficacy testing would otherwise be unfeasible. In 2023, and with the aim of identifying SARS-CoV-2 correlates of protection, CEPI funded two systems immunology studies to better understand the factors contributing to successful immune response biomarkers to COVID-19 vaccinations. The first study took place in the UK and Brazil during the emergence of the SARS-CoV-2 B.1.1.7 and P.1 variants, and the second took place in South Africa and the UK during the emergence of the Betacoronavirus variant in late 2023.

A significant gap in the current armoury of medical defences against viruses like SARS-CoV-2 is that none of the available COVID-19 vaccines can effectively prevent transmission of the virus from person to person. Since breaking the chains of viral transmission is critical to stopping outbreaks of epidemics before they expand into deadly pandemics, CEPI launched a new project with the support of the European Commission that will use so-called "human challenge" studies to discover how best to design effective vaccines that will provide a particular type of immunity — mucosal immunity — to stop viruses from infecting the body in the first place. This work is expected to gather pace in 2024.

CEPI's role in COVAX: Making Covid-19 vaccines available to the world

CEPI led COVAX's vaccine research and development work, investing in R&D and manufacturing across one of the world's largest portfolios of COVID-19 vaccines with the goal of developing safe and effective vaccines which could be made available to COVAX participating countries.

Seven CEPI-backed vaccines have been approved for use either globally or domestically: Biological E, Clover, Novovax, SK Bioscience, AZ/University of Oxford, University of Hong Kong and Moderna. Four of these have been granted Emergency Use Listing by WHO.

CEPI also made strategic investments in vaccine manufacturing to help scale-up supplies, supported enabling science and shared data that benefited the entire scientific field across the globe, and funded clinical trials designed to expand access to vaccines to additional populations.

CEPI is the only public sector funder of R&D that systematically leveraged its investments to enable equitable access to COVID-19 vaccines. Crucially, CEPI's investments secured first right of refusal for the COVAX facility to access hundreds of millions of doses of multiple vaccines at a time when global demand vastly outstripped supply.

COVAX shipped close to two billion doses of COVID-19 vaccine to 146 countries and territories, with the vast majority delivered to countries in the Global South. This represented the fastest and most complex deployment of vaccines ever seen, and modelling estimates that over 2.7 million deaths were averted by COVAX vaccines by the end of 2022.

While COVAX was unable to overcome the inequitable access to vaccines and other medical countermeasures which tarnished the global pandemic response, the global solidarity demonstrated during the pandemic was exemplary and must be harnessed ahead of the next pandemic. Through its investments in science, its commitments to access and its advocacy and policy engagements, CEPI is contributing to re-engineering the global health security system so the world can avoid a repeat of this tragic inequity and produce better, more equitable outcomes next time a pandemic threat strikes.

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[2], for which no licensed vaccines are currently available.

In 2023, CEPI progressed its portfolio of 12 active vaccine candidates against priority pathogens CEPI achieved a notable success with the US FDA approval secured for Valneva's Chikungunya vaccine. Significant efforts have been made to expand support to late-stage vaccine development. Where beneficial for rapid response, CEPI broadened its investment strategy beyond vaccines to consider use of prophylactic vaccine-like technologies, such as mAbs. CEPI is complementing this investment strategy through implementation of enabling science activities in epidemiology, standards and assays, and preclinical models, to inform demand and forecast need (see also Outcome 2.2).

The priority pathogen portfolio consists of candidates in the following stages of development:

- Three candidates in Preclinical
- Seven candidates in Phase I
- One candidate in Phase II
- One registered vaccine.

The 12 candidates are spread across different technology platforms as follows:

- Seven candidates using a viral vector platform
- One using a protein-based platform
- Four using a live attenuated/inactivated platform.

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

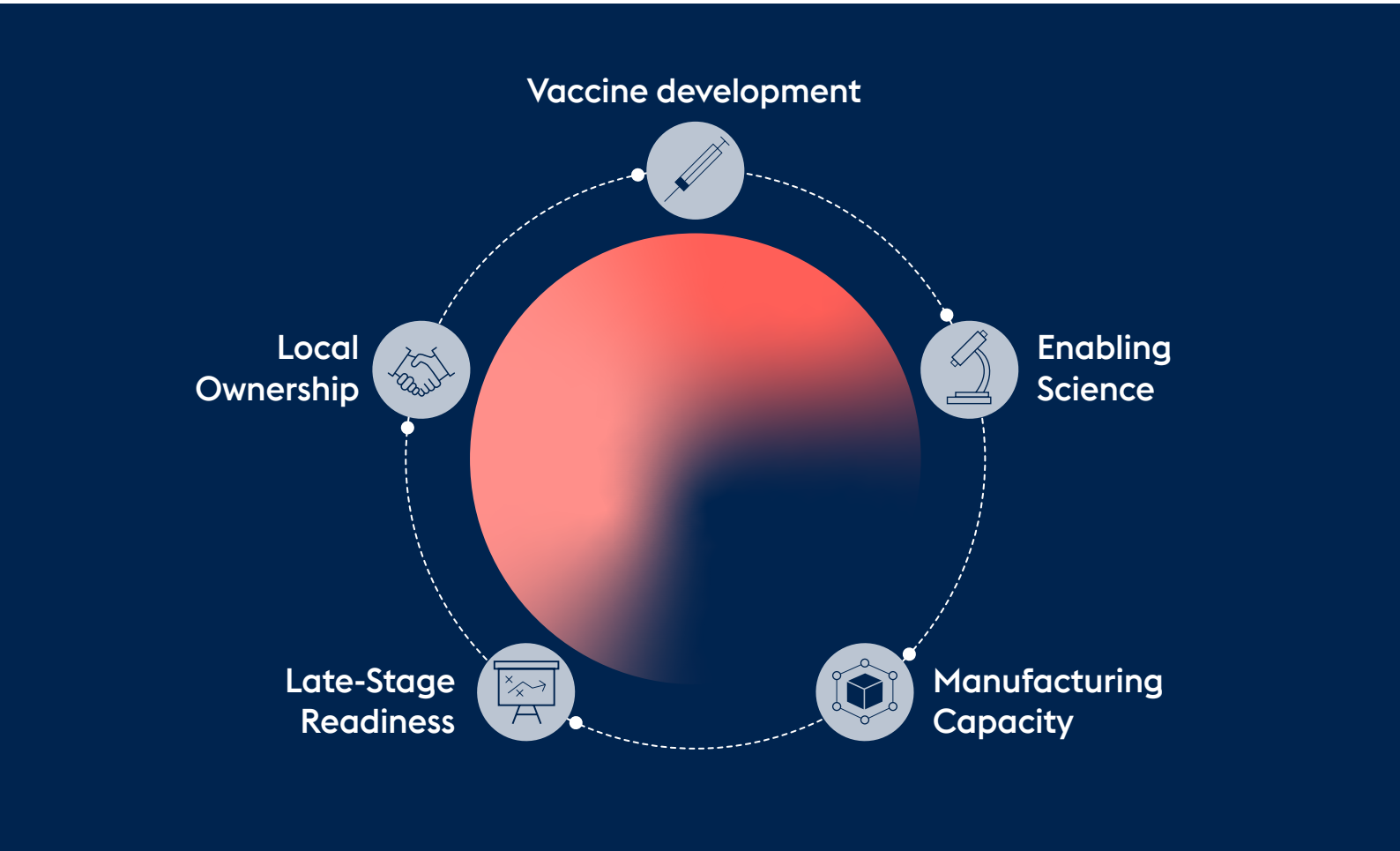
Lassa fever

CEPI aims to advance at least one Lassa vaccine candidate through to late-stage clinical development and towards licensure for both reactive and routine immunisation, while filling epidemiology gaps and strengthening clinical trial and regulatory capacity. The active Lassa portfolio consists of three vaccine candidates: University of Oxford (ready to enter Phase I), Emergent (Phase I) and IAVI (Phase I, planning to enter Phase II) with an additional mRNA lipid nanoparticle platform-based candidate in CEPI's Disease X portfolio targeting Lassa, developed by SK Bioscience (preclinical).

The portfolio is progressing well and the lead vaccine candidate, IAVI, achieved key milestones in 2023. These included the completion of studies to demonstrate vaccine efficacy in a well characterised preclinical model, as well as demonstrating that the vaccine is safe and well tolerated in healthy adult volunteers, with a durable, humoral immune response induced in preclinical models and humans. Using this data, CEPI worked with IAVI and local and regional partners to advance IAVI's Lassa vaccine into a Phase IIa clinical trial in West Africa which began April 2024 representing a critical step towards protecting those living in affected regions.

CEPI's enabling science programmes are critical in supporting vaccine development and biologic countermeasures projects. CEPI's Lassa Fever epidemiology study in West Africa, "Enable", is built on local partnerships and has been extended to further refine and inform clinical efficacy trial endpoints and disease definition. Further information on Enable can be found in Outcome 2.2. In addition, research preparedness efforts to build up good clinical practice is focusing on building capacity targeted to Lassa late-stage clinical trials.

Figure 4: CEPI efforts to facilitate end-to-end delivery of a Lassa vaccine



Middle East Respiratory Syndrome (MERS)

CEPI's active MERS portfolio consists of two viral vector vaccine candidates: with CEPI funding both IDT (Phase I) and University of Oxford/Barinthus Bio (Phase I). Both candidates are using viral vector platforms, with the University of Oxford/Barinthus Bio platform based on the same technology as the Oxford-AstraZeneca COVID-19 vaccine. In addition, four vaccine candidates in the BPCV programme are being developed to offer protection against MERS. These candidates include one or more MERS immunogens within the vaccine construct, in addition to SARS-CoV and SARS-CoV-2 immunogens.

CEPI is developing a new preclinical model for MERS that would best reflect the full spectrum of MERS infection and disease in humans, to provide immunogenicity data supporting vaccine development. As a coronavirus, MERS should be viewed together with CEPI's COVID-19 and the broadly protective work in Outcomes 1.1 and 1.3.

Nipah virus

CEPI's active Nipah portfolio consists of three vaccine candidates: University of Oxford (Phase I), Auro Vaccines (completed Phase I) and Public Health Vaccines (Phase Ib), with potential investment in an additional candidate being considered.

In addition, given the time required for immune responses to vaccines, the future inclusion of a Nipah mAb in the CEPI portfolio aims to provide immediate passive protection prior to the onset of vaccine-induced immunity, thereby potentially limiting the size and impact of a Nipah outbreak.

In 2023, CEPI launched a CfP to invest in the further clinical development of an existing Nipah mAb candidate and fund the storage, maintenance, and stability testing of a developer clinical trial inventory for five years in a Nipah-affected country. A Phase Ib/IIa safety trial of the mAb candidate is anticipated to be conducted in endemic countries starting in mid-2025, subject to regulatory approval. CEPI expects to fund additional preclinical studies to expand the indication of the Nipah mAb candidate to post-exposure prophylaxis, which will allow this mAb to become the first post-exposure option to prevent severe disease, hospitalisation, and mortality due to infection with Nipah virus.

To discuss potential licensure pathways for Nipah medical countermeasures, CEPI convened regulators in June 2023 bringing together regional and global experts to discuss collaborative support on studies advancing vaccine science and monitoring of epidemiology.

Information on how CEPI's enabling sciences programme is supporting the advancement of Nipah vaccines candidates can be found under Outcome 2.2.

Chikungunya

CEPI's active Chikungunya portfolio[3] consists of two vaccine candidates: International Vaccine Institute (IVI)/Bharat (Phase IIb/III) and Valneva/Instituto Butantan (Phase IV). Both vaccines differ in terms of geography and technology/antigen approaches.

A major milestone was achieved with the Valneva live-attenuated Chikungunya vaccine candidate, IXCHIQ, securing US FDA approval in 2023, making it the first Chikungunya vaccine licensed anywhere in the world. CEPI's funding for this vaccine – supported by the European Commission – is first and foremost intended to accelerate endemic country access. CEPI has facilitated technology transfer for filling and finishing the vaccine to Instituto Butantan in Brazil, a country that experienced a significant Chikungunya outbreak in 2023 and is funding late-stage studies to support regulatory approvals in the region. First results from Phase III clinical trials in Brazil to support label extension to those aged 12–17 years of age demonstrated safety and immunogenicity of the vaccine. These data can support potential licensure of a Chikungunya vaccine in Brazil, with material manufactured at Instituto Butantan.

CEPI is further advancing the Chikungunya portfolio to support Phase IV studies, with further co-funding from the European Commission. These studies are particularly important because US FDA licensure of IXCHIQ was based on immune biomarkers of protection with conditional requirements for post-authorisation effectiveness and safety studies. If alternative regulatory pathways are to be considered in the future, Phase IV study requirements and designs will be important. CEPI plans to fund clinical trials in vulnerable groups, including children, those who are immunosuppressed, as well as pregnant women with a view to expanding future use of the vaccine and accelerating access and registration of Chikungunya vaccines in endemic countries.

Engagement of regulators is key to identify and help overcome regulatory challenges and support efforts to align regulatory requirements (where appropriate). For the Chikungunya portfolio, CEPI works with Pan American Health Organization (PAHO) and the Brazilian Health Regulatory Agency (ANVISA). In 2023, CEPI brought together regulators in the Latin American region, as well as regulators from the FDA, Health Canada, European Medicines Association (EMA), Indonesia and South Africa to update on the status of development for CEPI's Chikungunya vaccines and to discuss and potentially harmonise the regulatory strategy.

Rift Valley Fever (RVF)

CEPI's active RVF portfolio[4] consists of two vaccine candidates: Colorado State University (Preclinical, entering Phase I) and Wageningen University (Phase I). In 2023, Wageningen University led a successful Phase I trial in Belgium with promising results in terms of vaccine safety and immunogenicity against RVF. Two candidates, University California Davis (which took over as lead awardee from Colorado State University for the same RVF vaccine) and Wageningen University, were subsequently funded to continue efforts and conduct Phase I/II clinical trials in Kenya, Uganda and Tanzania, marking important progress in ensuring vaccine development efforts benefit populations in endemic countries.

By the end of 2023, CEPI was exploring the inclusion of additional candidates to the portfolio in 2024 to enhance technological diversity and strengthen African RVF vaccine development. Furthermore, CEPI will host a workshop on epidemiology and modelling in Kenya to support a planned funding call for RVF epidemiology supporting vaccine development in late 2024.

[3] CEPI's work to accelerate the development of vaccines against Chikungunya virus and RVF has been co-funded with the European Commission (Horizon 2020 since 2019 and Horizon Europe since 2022).

[4] CEPI's work to accelerate the development of vaccines against Chikungunya virus and RVF has been co-funded with the European Commission (Horizon 2020 since 2019 and Horizon Europe since 2022).

Accelerating access in endemic countries to the world's first Chikungunya vaccine

2023 marked a historic milestone in terms of the fight against Chikungunya, a debilitating disease which is endemic in parts of the world home to over a billion people. In November 2023, Valneva's live-attenuated vaccine candidate (known as IXCHIQ) secured regulatory approval for the first time from the US Food and Drug Administration (FDA).

CEPI's funding for IXCHIQ, supported by the European Union's Horizon 2020 Programme, is first and foremost intended to accelerate endemic country access to a vaccine that, prior to CEPI's involvement, had been developed and funded by Valneva predominantly for travellers from high-income countries.

Following the US FDA approval of IXCHIQ, WHO added Chikungunya as a medium priority pathogen for pre-qualification (PQ) purposes. This will further enable equitable access to the vaccine as WHO PQ will accelerate the ability to supply to more countries.

To date, CEPI and the EU have committed up to USD 24.6 million to facilitate access to IXCHIQ, for those living in countries with the highest burden of disease. This funding primarily supports the following activities:

- Technology transfer of the drug product to Valneva's partner in Brazil, Instituto Butantan, who will manufacture and market the vaccine in the Global South enabling sustainable, reliable, and affordable access to the vaccine for endemic countries in the future.
- Late-stage studies designed to generate data that will contribute to future regulatory approval in Brazil, a country which experiences a high burden of Chikungunya disease.
- Access to an emergency stockpile of 200,000 vaccine doses which, at CEPI's direction, can be supplied to affected countries free of charge to help control disease outbreaks until the Instituto Butantan-produced vaccine becomes available.

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

Target by 2026	Progress update
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 more priority pathogens to ready to use under outbreak conditions**	Vaccine candidate portfolio: Preclinical: Three Phase I: Seven Phase II: One Phase III: Zero Licensure: One One candidate is currently in preclinical and ready to enter Phase I, and four candidates are currently in Phase I and ready to enter Phase II. There is a gap in the number of candidates in mid/late-stage development due to candidate down selection and delays due to COVID-19 which is being addressed through backfilling of additional candidates. Portfolio outperformed in terms of licensure target in 2023 (CHIK-Valneva) although a licensed vaccine for a second priority pathogen is unlikely before end of 2026.

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), MERS and COVID-19. The scientific progress made during the COVID-19 pandemic has indicated a realistic potential for broadly reactive immune responses against the sarbecovirus sub-genus i.e., SARS-CoV-like viruses (including those that have not emerged from animals) however, the potential for more broadly reactive immune responses across all coronavirus genera remains unclear. In order to reduce the risk of future coronavirus epidemics/pandemics, CEPI has initiated a BPCV programme to develop vaccines that will provide broad protection against multiple coronaviruses, including against novel viruses that have yet to emerge.

The BPCV programme has two major approaches:

- Pan-sarbecovirus vaccine candidate development (although some pan-sarbecovirus candidates also contain a MERS-CoV antigen to expand coverage) and;
- Coronavirus vaccine library development targeting non-sarbecoviruses (including MERS-CoV as a prototype pathogen) as part of wider vaccine library development.

Successful candidates in this programme would protect against SARS, MERS, COVID-19 and potential newly emerging threats from the broad animal reservoir of coronaviruses.

CEPI's pan-sarbecovirus vaccine candidate portfolio[5] expanded in 2023 and now consists of 11 candidates - six fully funded preclinical vaccine candidates: Bharat Biotech/University of Sydney/Excell Gene, VBI, CPI/CalTech/SpyBio, SK Bio/IPD, Panacea/THSTI and IVI, with a diverse geographic spread. The portfolio also consists of a five seed-funded projects: Intravacc (Preclinical), NEC OncoImmunity (Preclinical), VIDO (Preclinical), Gritstone bio (Preclinical/Phase I) and MigVax (Preclinical).

The ambition in CEPI 2.0 is to advance BPCV vaccine candidates favourable for the Global South through preclinical and Phase I. To support this, CEPI has also invested in a portfolio of enabling sciences activities to develop tools that will facilitate determining the breadth of protection and generate data required for regulatory approval. For example, the preclinical model work is gearing towards developing preclinical models for BPCV via investments into MERS-CoV, SARS-CoV, and other pre-emergent coronavirus preclinical model discovery. By the end of 2023, 17 original and variant SARS-CoV-2 models were developed and made available for ongoing development testing. There is steady progress in MERS, SARS-CoV and pre-immune models based on approved on-market vaccines. The progress on chosen models reflects the evolution of the SARS-CoV-2 variants as well as guidance from the discussions during 2023 to redefine the focus of the CEPI BPCV portfolio.

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

Target by 2026	Progress update
Two	The BPCV programme is focused on two approaches: (I) pan-sarbecovirus (+/- MERS-CoV) vaccine development, and (2) whole coronavirus family vaccine development. The portfolio is comprised of II candidates in preclinical phase, six of these which are fully funded and five are seed-funded projects. Of the II active projects, one has a precursor candidate in Phase I trial funded by Government of Canada. Three further projects have been terminated/are in process of being closed out.

[5] Excluding MERS-CoV which is covered in section 1.2 above

Partnerships to deliver the 100 Days Mission

The COVID-19 pandemic highlighted how important agile, resilient, end-to-end partnerships are in addressing the challenges posed by the volatility, uncertainty, and complexity of an outbreak.

To date, competitive Calls for Proposals (CfPs) have been the primary mechanism through which CEPI engages and contracts awardees. This typically results in a contractual agreement between CEPI and the selected partner to deliver a single project—such as the development of a vaccine candidate for an individual disease through to a pre-determined phase of clinical development—over a specified period, for a specified sum of funding. This model has delivered notable scientific successes, including four CEPI-backed COVID-19 vaccines receiving WHO Emergency Use Listing and CEPI-funded vaccine candidates leading the field in the race to develop vaccines against Chikungunya, Lassa fever and Nipah.

As CEPI continues to deliver CEPI 2.0, it will ramp up its ambition of developing pandemic-busting vaccines in just 100 days, by broadening the scope and scale of some key partnerships. By adding more strategic collaborations which move beyond funding individual projects, CEPI will enhance the way it works and partners with industry and academia whose unique capabilities or technologies are vital to the success of the 100 Days Mission.

For example, if positive trial data is emerging within a project, or it is desirable to incorporate additional scientific thinking or activities, having a new model of partnership already in place offers the flexibility and speed to better leverage research and broader pandemic preparedness opportunities. By grouping work into these strategic collaborations, when and where relevant, the need for additional grant applications to be written, processed and reviewed can be eliminated, allowing scientific innovation and evidence collection to move much more rapidly.

Strategic partnerships are assessed against four criteria:

- Technical impact: impact of the partner's technology and activities to enable the 100 Days Mission.
- Equitable access: commitment towards CEPI's Equitable Access Policy and Framework, and support for the health security of the Global South.
- Partner potential: the partner's demonstrated organisational capacity to successfully deliver products and services critical to the 100 Days Mission and enhance the global epidemic and pandemic response ecosystem.
- Public policy: influence with governments, policy makers, regulators, and other stakeholders across regions to advance the 100 Days Mission and system equity.

In 2023, CEPI signed four major strategic partnerships with the University of Oxford, Moderna, and BioNTech and IQVIA. The first three partnerships are intended to expand the use of partners' development and manufacturing platforms beyond the existing licensed COVID-19 vaccines to address viruses from other families deemed to present high epidemic or pandemic risk. The strategic partnership with IQVIA aims to help strengthen clinical research capability in the Global South and to develop a transferable toolkit to enable the 100 Days Mission.

In addition, CEPI continues to build and work with civil society, governments, the public and philanthropic sectors to support alignment on epidemic and pandemic preparedness and response. All this work is critical not only to CEPI achieving its goals but to the ultimate goal of ending pandemics in the future. Further highlights can be found in Outcome 3.

Strategic Objective 2: TRANSFORM the response to the next novel threat

Climate change, social disruption, population expansion and travel are some of the many reasons for increased global vulnerability to viral pandemics caused by the next unknown pathogen or Disease X. A key ambition of the TRANSFORM objective is a paradigm shift in the preparedness and response architecture for a safe and effective vaccine to be developed in 100 days from the next global outbreak which can subsequently be accessible to all people in need. CEPI has continued preparations for the threat of an unknown pathogen in 2023, making good progress on the 100 Days Mission – which is central to transforming response time – and investing in innovations that will rapidly speed vaccine development and manufacturing.

CEPI has introduced the concept of a vaccine library as a one element to achieving the 100 Days Mission. A vaccine library is envisaged as a repository of knowledge, seed materials and vaccine candidates based on smart antigen designs combined with rapid response vaccine platforms to be able to respond more quickly to Disease X. A key component of the vaccine library is the targeting of whole virus families with high risk of causing a Disease X outbreak and the development of "exemplar vaccines" against prototype pathogens representative of virus families through preclinical and clinical development.

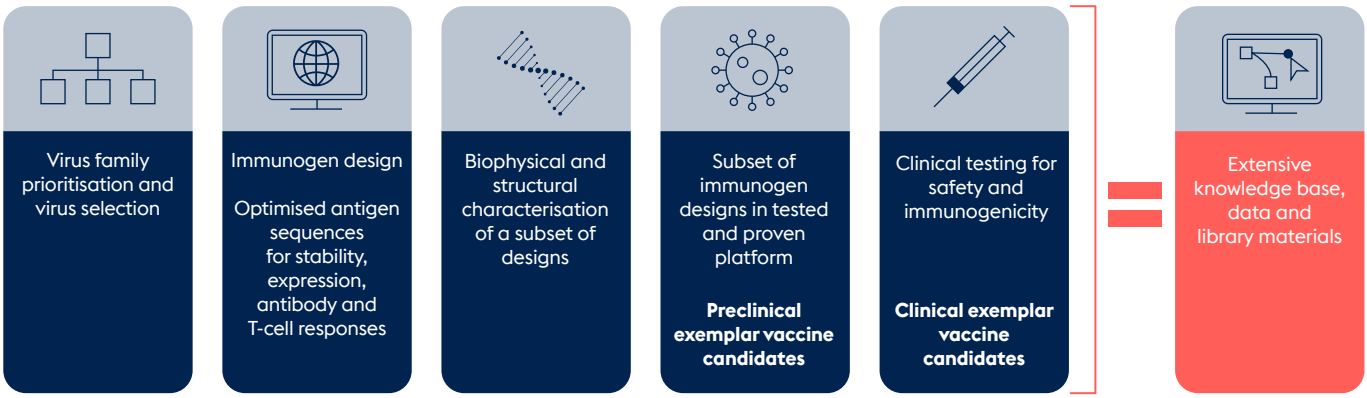
Other activities include the establishment of a virus ranking system for epidemic likelihood, and the development of protective immune responses in preclinical models and in humans for lesser-known viruses with high outbreak potential.

Additional transformative areas CEPI continued to progress in 2023 include: use of artificial intelligence to accelerate and improve vaccine design; regulatory system readiness in low resource settings; product development projects that aim to identify correlates of protection that could significantly reduce the cost and time taken to develop vaccines by serving as alternatives to clinical endpoints for regulatory approval; vaccine manufacturing innovations that aim to facilitate speed, scale and access, including more thermostable RNA vaccine platforms.

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

A key component of CEPI's 100 Days Mission is the development of a vaccine library targeting viral families with high risk of causing epidemics and pandemics. The vaccine library aims to generate optimised antigens against high-risk viruses within high-risk viral families and combine them with rapid response vaccine platforms e.g., mRNA, viral vector, others. These platforms would have common production characteristics to minimise the need to develop new processes for novel outbreak pathogens. The iterative technical, safety and efficacy data gathered from testing preclinical and clinical exemplar vaccines against prototype pathogens on rapid response platforms will add to the technical and regulatory experience with the relevant vaccine platforms. The body of knowledge, materials and capabilities developed during this exercise can then be used to generalise vaccine design, development and manufacturing for other viral species in the same families, giving the world a head start against newly emerging viral threats.

Figure 5: Components of a vaccine library



In 2023 CEPI targeted its efforts on four high-risk viral families:

- Paramyxovirus family which counts the highly contagious ancient diseases measles and mumps and the more recently identified and much more lethal Nipah and Hendra among its members (prototype pathogens include by Nipah and Hendra viruses).
- Arenavirus family, the first identified member of which was isolated in the 1930s, and which includes Old World and New World viral haemorrhagic fevers (prototype pathogens include Lassa and Junín viruses).
- Coronavirus family, which includes seven known coronaviruses with the ability to cause illness in people, such as MERS-CoV as well as SARS-CoV-2.
- Poxvirus family, a large family of more than 70 viruses, some of which are the largest and most complex in nature (prototype pathogen includes mpox). The family has been included as a priority pathogen.

CEPI will further expand viral family work to include the Filovirus family (with co-funding support from the European Commission) in 2024. Looking ahead, Phenuiviruses, Hantaviruses, Phenuiviruses and Nairoviruses are also under consideration.

In 2023 CEPI established a partnership with University of California at Davis (UC Davis) to build on their work to rank viruses based on their zoonotic risk. This work aims to expand their "SpillOver" database to identify virus families most likely to emerge as the next Disease X with pandemic potential by using cutting edge artificial intelligence. Through harnessing machine learning, the database has expanded to include viruses from domestic animals and vector-borne viruses, and viruses/sequences available in the International Committee on Taxonomy of Viruses and GenBank databases.

In parallel, CEPI is participating in discussions led by WHO, who is updating a list of risk factors for a Disease X emergence. An updated virus family prioritisation/ranking is expected in 2024.

Progress on Arenaviruses in 2023

In 2023, CEPI signed partnerships with a consortium led by Houston Methodist Research Institute and the Institute for Drug Discovery at Leipzig University. These partners have started the work on Arenaviruses by designing antigens for Lassa and Junín viruses. At the end of 2023, thousands of Lassa Glycoprotein Complex (GPC) antigen designs had been generated in silico, and down selected for expression as cell surface proteins and screened with a panel of 24 Lassa virus neutralising antibodies. It is expected that the top five to 20 designs will be moved to the in vivo screening stage (either as mRNA and/or recombinant protein vaccines) in early 2024, by performing preclinical immunogenicity studies.

In silico and in vitro work on the Junín virus GPC, will be tested in preclinical experiments in the first half of 2024 and the conceptual in silico and structural work on Nipah G and F antigens has also started. The knowledge base for the Paramyxovirus and Arenavirus family will be complemented with additional immunogen designs, preclinical and/or clinical testing of other viruses within these two families.

An additional area of activity in relation to the vaccine library is to combine some of the antigens designed by CEPI's immunogen design partners with rapid response platforms to generate safety, immunogenicity, and efficacy data in preclinical and clinical studies. CEPI has identified three partners for this work:

- The Lassa exemplar vaccine will be tested on SK Bioscience mRNA platform.
- For the Junín exemplar vaccine, the partner is Oxford University using ChAdOx compared with a benchmarked mRNA platform, with preclinical work planned to start in 2024.
- The additional exemplar vaccine, currently in clinical testing, is an mpox vaccine developed by BioNTech using BioNTech's mRNA vaccine technology.

Other efforts to advance the 100 Days Mission

Besides the creation of a vaccine library, CEPI continues to fund research to gain increased experience with vaccine platforms which can be quickly pivoted towards Disease X. CEPI invests in both advanced RNA vaccine platform technology and emerging innovations in RNA vaccine technology. The main goal is to build significant preclinical chemistry, manufacturing and control (CMC) and clinical and regulatory experience with a platform that could be leveraged for rapid adaptation in an outbreak to improve the efficacy, speed and access to vaccines.

By the end of 2023, seven new platform technology innovation projects had been onboarded. Including one existing project, a total of eight prototype vaccines against Japanese Encephalitis, SARS-CoV-2, Chikungunya, Rabies, Yellow Fever, and Influenza are in development. A project with SK Bioscience uses a platform technology similar to those established during the COVID-19 pandemic. In 2023, the selection and preclinical immunological characterisation of a Japanese Encephalitis vaccine candidate was completed. All other projects test novel innovative technologies, one of which (Lemonex) has entered into Phase I.

In October 2023, CEPI launched a new CfP aimed at advancing cutting-edge vaccine development and manufacturing science and technologies that will contribute to speed, scale and equitable access during future outbreak response. Once partners are selected, this work will initially support transformative innovations in vaccine platforms, manufacturing technologies and vaccine candidates against high-risk viruses, which are critical to the success of the 100 Days Mission.

KPI-Outcome 2.1: Number of CEPI-funded innovations that can be rapidly adapted against unknown pathogens

Target 2026	Progress update
Two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations. **Clinical proof of concept for four virus family vaccine libraries.**	Four viral families (arenaviruses, paramyxoviruses, poxviruses, coronaviruses) have been prioritised. The planned workflow of antigen design and preclinical testing has started for two viral families – poxviruses and arenaviruses. A design has been selected by BioNTech for their mpox vaccine which initiated Phase I clinical trial. Production and testing of designs for Lassa and Junín viruses, members of the arenavirus family, was initiated. Seven new platform technology innovation projects onboarded in 2023, bringing the total to eight prototype vaccines against Japanese Encephalitis, SARS-CoV-2, Chikungunya, Rabies, Yellow Fever, and Influenza in development by end 2023.

2.2. Scale enabling sciences to further accelerate vaccine development

CEPI's enabling science programme spans the production of research tools such as standards and assays, preclinical models, epidemiology, predictive and mathematical modelling, as well as strengthening clinical research approaches, regulatory science, and diagnostics.

CEPI has advanced partnerships that have been globally networked to accomplish clinical research preparedness and operational strategies, informed by epidemiology, for evidence generation and the optimal development and use of biological countermeasures. These networks of partners aim to support standardisation of tools to assess and compare vaccine candidates, build capacities closer to where outbreaks might happen and are critical in supporting the 100 Days Mission goal.

To further advance the priority pathogen and viral family work toward the 100 Days Mission, CEPI is expanding its enabling sciences programmes on preclinical modelling and standard development and regulatory activities as outlined below.

Preclinical modelling and standard development work

Much of the preclinical modelling for CEPI priority pathogens is achieved through CEPI's Preclinical Model Network (PMN). The Network is growing with 11 PMN partners onboarded across six countries. Highlights in 2023 include:

- By the end of 2023, seven preclinical models were developed for original prototype SARs-CoV-2 in addition to 17 SARS-CoV-2 variant-based models. Nine vaccine development partners were supported with testing using those models.
- CEPI made specific investments in preclinical models for Chikungunya to improve performance of passive transfer studies, where vaccine-driven antibody protection is likely to be shown to be the correlate of protection.
- Partners in CEPI's PMN have developed models for Ebola, Marburg, RVF via non-CEPI funding, and CEPI can further invest to refine those models for use in ongoing development research.
- Preclinical modelling is underway for MERS as a target pathogen, and this CEPI investment supports MERS vaccine developers.
- Modelling work in relation to Lassa and Junín, as two important Arenaviruses, as well as Sudan Filovirus progressed through ongoing model establishment work in the network.
- Significant progress was made during 2023 to support Nipah preclinical model development at the National Emerging Infectious Diseases Laboratories (NEIDL) in Boston, with plans to deliver these models for use in 2024. These models will be essential for testing Nipah vaccines and mAb in pivot preclinical efficacy trials supporting regulatory decisions. Not only will CEPI-funded developers use these models, but we are actively publicising this work so that developers, such as those funded by US BARDA and NIAID, will also be encouraged to use these models.

In October 2023, the WHO Expert Committee on Biological Standardization approved the Nipah antibody preparation invested by CEPI through laboratory partners. This standard is essential for calibration and standardised performance of Nipah immunoassays in preclinical and clinical trials.

Regulatory and quality activities

CEPI continues to act as a pivotal connector between developers and regulators with the aim of developing disease-specific regulatory strategies and undertaking detailed regulatory engagement plans for each of CEPI's priority pathogens (see section 1.2 for specific examples). CEPI's approach is to engage regularly with regional regulatory authorities, strengthening their individual capability, building a knowledge base of diseases and vaccines in development, and critically establishing trust and collaboration.

Activities in 2023 continued to support CEPI's priority pathogen portfolio through building partnerships with Global South regulators and progressing regulatory initiatives to maximise use of platform data and pre-approved documentation. This includes the development of platform master files and pre-approved CMC and clinical documentation. CEPI also continued to evaluate product development pathways for any opportunities for acceleration and streamlining.

In addition, regulatory work continues to progress the identification of immune correlates of protection, based on anticipated benefit-risk. This includes establishing harmonised guidelines and templates for benefit-risk assessments and a risk-based framework for the use of immune correlates of protection.

CEPI also continued activities to gather real world effectiveness data, harmonise outbreak ready pathways and maximise speed of review and regulatory reliance. In 2023 this included:

- Establishing a global database of emergency regulatory licensing requirements
- Developing a cloud-based tool to enable real-time exchange of information for regulatory review
- Establishing study designs and data gathering tools appropriate to different outbreak scenarios to enable quality data capture.

Tracking incidence and prevalence of Lassa Fever in West Africa and informing late-stage clinical trials

In 2019 CEPI launched the largest Lassa fever epidemiology study "Enable" to give researchers a better picture of the true disease burden and the number of people who are at risk of Lassa virus infection who might benefit from Lassa fever vaccination. Findings from the study will also guide the design of future vaccine trials and could help define future vaccination strategies if and when a Lassa fever vaccine has been approved for use.

So far, the study has recruited and is monitoring more than 23,000 participants across West Africa to clinical trial compliance standards. Extensive data has been acquired and should provide a better understanding of the underlying epidemiology and disease burden, and in turn inform future Lassa virus burden of disease studies. Interim data is now available and is being directly utilised by Lassa vaccine developers to inform clinical trial design with final study results due in 2024. Further work under an expanded study is due to commence in 2024.

Regional and national leadership from Lassa-affected countries is critically important to advance the development of vaccines that protect against the disease. In 2023, CEPI established a new partnership with the Economic Community of West African States (ECOWAS) Regional Centre for Surveillance and Disease Control, a part of the West African Health Organisation. CEPI maintains close engagement with national public health agencies, such as the Nigeria Centre for Disease Control (NCDC), and Ministries of Health in the most affected countries.

CEPI also initiated coordination of a collaborative project, with support of the European Union between regulators, ethics committees, and the African Vaccine Regulatory Forum to enhance regulatory and ethics oversight of clinical trials in West Africa. With a focus on Lassa Fever vaccine development, the project aims to boost preparedness for possible future outbreaks of Lassa Fever in the region.

KPI-Outcome 2.2: Enabling science programmes and innovative tools actively used by CEPI-funded developers to further accelerate vaccine development

Target 2026	Progress update
Three or more of the enabling science tools developed through CEPI funding used by one or more of CEPI-funded vaccine developers	Ongoing work to develop preclinical models for BPCV via investments into MERS-CoV, SARS-CoV, and other pre-emergent coronavirus preclinical model discovery research. Seven original protype SARS-CoV-2 virus animal models and 17 SARS-CoV-2 variant-based models were made available as of end 2023. Additional preclinical model work in progress for MERS and pre-immune models based on approved on-market SARS-CoV-2 vaccines. Progress is on track and reflects the evolution of the SARS-CoV-2 variants and to the decision to redefine the focus of the BPCV portfolio in 2023. Active partnership with preclinical model network laboratories with capacity to contribute models for CEPI priority pathogens means that CEPI has in place resources for expedited preclinical testing. Development launched for Nipah natural history study models for vaccine and mAb preclinical testing in pivotal efficacy studies, planned for delivery in 2024. The Nipah antibody international standard was approved by WHO Expert Committee on Biological Standardization in October 2023.

Case Study: How Enabling Science supports Nipah Vaccine development

CEPI has three Nipah vaccine candidates (Auro, Oxford, and PHV) currently in clinical trials. In 2023 and CEPI commenced exploring investment in an additional Nipah mRNA vaccine and Nipah monoclonal antibody. As these programmes mature, they will need to generate efficacy data in appropriate preclinical models to complement human safety and immunogenicity data.

Preclinical studies are anticipated to form a core element of the licensure packages for Nipah vaccines and therefore must be conducted in a rigorous manner to stand up to regulatory scrutiny. CEPI has partnered with Boston University to make sure suitable preclinical models of Nipah infection are available to developers for testing the efficacy of their products. The National Emerging Infectious Disease Laboratory at Boston University has first conducted a series of dose-finding viral infection studies to be followed by a model-defining natural history of Nipah disease study. Input from the FDA will be sought prior to initiation of the natural history studies to ensure that the models provide a suitable testing system in which to collect data supportive indirect evidence for efficacy.

Key national health bodies including NIAID, BARDA and SCARDA are enthusiastic about using the preclinical models that CEPI has established to test their own products because efficiencies are created by reducing duplicative model development by multiple funders at multiple sites.

Additional laboratory tools under development for the Nipah programme are the International Antibody Standard, and binding assays available through CEPI's CLN. CEPI has also invested in retrospective and prospective sample and data analysis from Nipah cases, plus clinical research preparedness in South Asia.

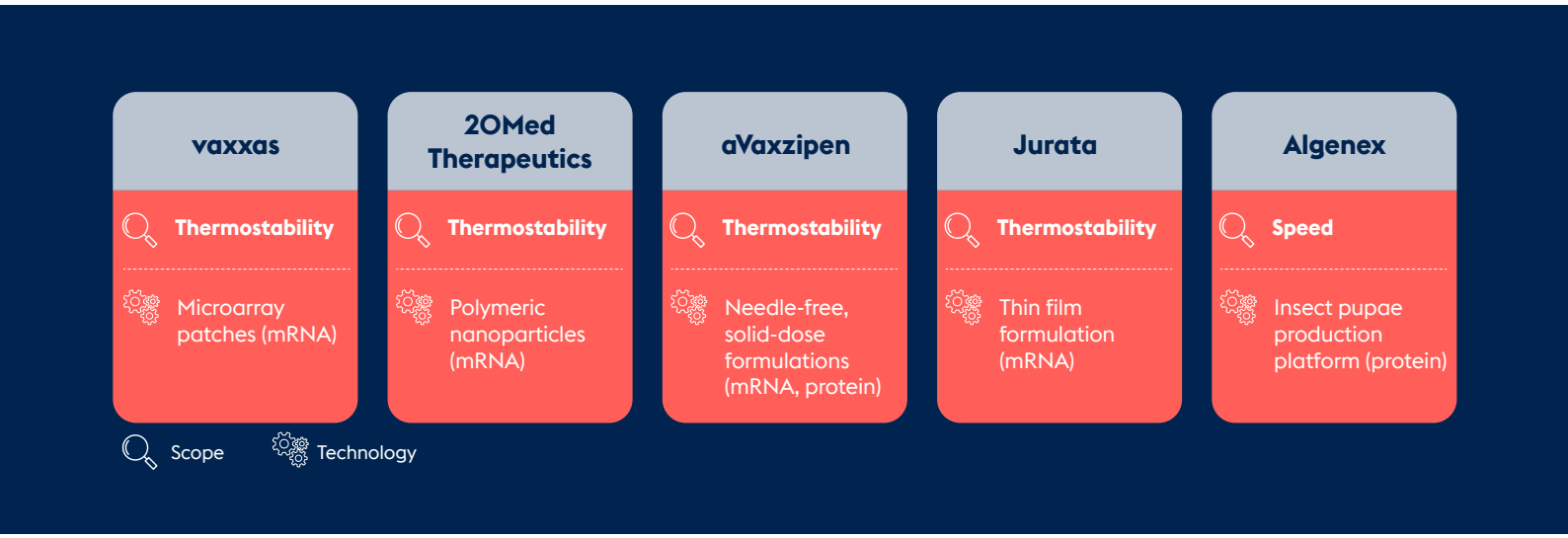
2.3. Transform vaccine manufacturing

Achieving the 100 Days Mission will require transformative innovations in vaccine platform and manufacturing technologies and CEPI's Manufacturing Innovation programme continued to focus on vaccine process platforms, thermostability, speed, costs that are particularly relevant for Global South markets and critical to supporting equitable access. In line with this commitment, investing in innovative fill, finish and presentation technology in addition to thermostability, have been prioritised, particularly for mRNA-based vaccines.

In 2023 four additional projects were selected bringing the portfolio to five innovative technologies. These projects focus on improving thermostability and enabling equitable access to RNA-based vaccines using different presentations including the microarray patch work, different RNA carriers, solid dosage forms, sublingual films and continuous spin-freeze-drying. Projects take technologies to proof of concept, after which they can be matched with vaccine and facility partners for implementation.

Through two additional CfPs published in 2023, CEPI aims to make investments in speed-related manufacturing innovations to accelerate the response to a new outbreak, and scale-and access-related innovations to make vaccines equitably accessible. One "speed" project to develop novel protein expression systems aimed at turning protein-based vaccines into a rapid response platform was signed in 2023, while additional projects related to speed, scale and access are under review and due diligence.

Figure 6: CEPI MSC innovations portfolio snapshot



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

Target 2026	Progress update
At least three innovations which demonstrate manufacturing cheaper, faster or closer to an outbreak	Six manufacturing innovation projects were launched in 2023. CEPI-supported manufacturing innovations span seven countries covering the different aspects of thermostability, speed, scale and access as drivers of vaccine manufacturing transformation.

Improving access to vaccines by removing the need for frozen storage

Advances in vaccine technology have been critical to the global response to COVID-19. One of the challenges the world faced in getting these lifesaving vaccines to vulnerable populations—particularly those people in poorer countries—was the need to store them at low, or very low temperatures.

The current generation of mRNA vaccines require frozen storage due to the fragility of mRNA molecules. Once removed from the freezer, these vaccines must be used within a short timeframe.

As part of a wider goal of harnessing innovative technologies to improve the speed, scale and access of vaccine development and manufacturing in response to epidemic and pandemic threats, CEPI is continuing to invest in solutions that improve the thermostability of—and thereby improving equitable access to—a variety of new vaccine platforms.

One example of this investment is CEPI's support, since 2022, for preclinical testing of Vaxxas' platform—a needle-free, high-density microarray patch (HD-MAP) to assess its stability, safety and immunogenicity and to evaluate its potential as a rapid-response technology for heat-stable, dried-formulation mRNA vaccines. HD-MAPs are made up of thousands of microscopic points attached to a small patch. Each of these micro-projections contains a tiny dose of vaccine in a dried formulation. When applied to the skin, the patch delivers vaccine to the abundant immune cells immediately below the skin surface.

HD-MAP vaccine delivery offers many potential advantages over more traditional ways of administering vaccines and could enable a future in which vaccine patches could be mailed directly to peoples' homes, workplaces, and schools, in turn avoiding the delay and inconvenience of traditional needle-and-syringe vaccine scheduling and administration.

Strategic Objective 3: CONNECT to enhance and expand global collaboration

CEPI's 100 Days Mission and its Equitable Access Framework highlight the need for a robust ecosystem and strong partnerships to achieve speed, scale, and equitable access to vaccines and countermeasures.

CEPI is a part of this wider ecosystem of epidemic and Pandemic Preparedness and response (PPR) actors and organisations who are responsible for financing, purchasing, stockpiling, and delivering vaccines to communities that need them. The CONNECT strategic objective builds relationships to align CEPI's R&D and manufacturing partners with institutions and partners that shape the enabling environment for innovation and vaccine production including public R&D funding organisations. CEPI's activities supports vaccine procurement, allocation, and delivery through partnerships with organisations such as WHO, Gavi, UNICEF, regional organisations, and sovereign Ministries of Health.

In an increasingly dynamic external environment, CEPI continued to build effective working partnerships internationally and regionally that can adapt to changing priorities and geographic shifts in PPR leadership and capacity, evolving international and regional policy developments and organisational responsibilities (e.g. the Pandemic Agreement) or new regional strategies.

In 2023 CEPI bolstered its engagement and activities to support:

- Alignment of key stakeholders around shared goals for the PPR ecosystem – including strengthened regional leadership.
- Improved strategic engagement and coordination with ecosystem processes at the global and regional levels, and highly targeted engagement at national levels (where CEPI has significant R&D or manufacturing partnerships) to support the goal of rapid and equitable access to vaccines against emerging infectious diseases.
- Policy analysis, development and engagement to support improved ecosystem effectiveness and equitable access – including with international processes, such as the Pandemic Agreement negotiations.
- An improved ability to stay abreast of, inform and adapt to ecosystem changes, to strategically pursue opportunities and collaborations – such as an improved Ecosystems Insights Model.
- Strengthened collaboration and respectful partnerships in regions and with key regional institutions, especially recognising the PPR leadership in Africa, Latin America and Asia.
- Establishment of necessary financing for the epidemic and pandemic preparedness ecosystem.
- Building networks to fill gaps in the present ecosystem, including through the establishment of more geographically diverse manufacturing capacities.
- Promoting adaptive and harmonised ways to accelerate R&D and strengthen system equity.

3.1 Secure financing for epidemic preparedness and response

CEPI continued to engage with partners and policymakers to ensure that critical resources are available to support vaccine R&D and other initiatives essential for addressing existing and future global health threats. This requires both long term sustainable funding for the preparedness ecosystem at large, including fully funding of CEPI 2.0 needs, and ready-releasable surge funding when faced by a new threat. Additional pledges to CEPI secured in 2023 include CAD 80 million from the government of Canada, USD 100 million from the USA and CHF 10 million from Switzerland. In addition, several pledges were converted into contribution agreements. These include the government of Spain's EUR 75 million (via the International Finance Facility for Immunisation) as well as EUR 35 million from the European Commission. Furthermore, a philanthropic resource mobilisation strategy was developed and engagement initiated, with the aim of bringing in additional philanthropic funders including from the Global South.

CEPI is working to ensure that R&D&M funding remains a key focus in global fora participating in various financing initiatives and high-level fora including advocating for the new Pandemic Fund mechanism to also fund vaccine R&D. CEPI also continues to work with international and regional health partners to define pandemic financing response needs. These include day zero and high-risk funding for accelerated R&D and manufacturing scale-up, and aggregated financing for advanced procurement agreements and timely funding to prepare for and support immunisation roll-out. CEPI commissioned the University of Chicago, Dartmouth College, Imperial College and Linksbridge to develop integrated health and macro-economic impact models for different investment combinations in preparedness and response interventions to accelerate the development and at-scale introduction of vaccines. The project is guided by a Policy Advisory Group that includes the WHO, the World Bank, Africa CDC, PAHO, US Treasury, the Italian Ministry of Finance and the G20 Joint Health and Finance Taskforce Secretariat. The project will report in the second quarter of 2024.

To ensure that R&D&M funding remains a key focus in global fora CEPI worked alongside Gavi, the Global Fund and other partners to coordinate advocacy positions ahead of G20 Joint Finance-Health Task Force meetings in March and June 2023, emphasising the role that each organisation played in the COVID-19 pandemic response and continues to play in R&D preparedness and future response financing. The 100 Days Mission and the need for at-risk R&D and manufacturing financing was emphasised in the G20 Report on Mapping Pandemic Response Financing Options and Gaps and was welcomed in the 2023 G20 Leaders Declaration. Both CEPI and the 100 Days Mission were also mentioned in the 2023 G20 Health Ministers Outcome Document.

CEPI continues to advocate for sustainable, long-term, non-earmarked financing for CEPI's activities that is easy to renew in the context of a challenging funding environment. In March 2023, CEPI's Official Development Assistance (ODA) coefficient with the Organisation for Economic Co-operation and Development Assistance Committee Working Party on Development Finance Statistics was raised from 66% to 88%. This means that a greater proportion of CEPI's operational and administrative costs are able to be reported as ODA eligible, signalling acknowledgement that all categories of CEPI's work either uniquely or primarily benefit countries in the Global South.

KPI-Outcome 3.1: New financing mechanisms include funding for vaccines and other biologic countermeasures preparedness and response R&D

Target 2023 (no 2026 target)	Progress update
New funding mechanism(s) in place	CEPI played a catalytic role in shaping the PPR financial architecture including commissioning modelling efforts to inform PPR policymaking, engaging with G7 Development Finance Institutions and G20 Health and Finance efforts, and is actively coordinating with the newly established Pandemic Fund.

3.2 Coordinate among key stakeholders to enable system readiness

A key determinant of the evolutionary path of the PPR architecture is the negotiations on the Pandemic Agreement. CEPI engaged actively with the Intergovernmental Negotiating Body (INB) to shape the final agreement which is expected to be presented at the World Health Assembly in May 2024. Building on the advocacy successes in 2022, in 2023 CEPI has made the case for sustained investments in R&D preparedness that support equitable access, for the establishment of a network of partnerships for end-to-end collaboration on medical countermeasures development and response, and for technology transfer that supports expedited R&D and that has equitable access at its core. CEPI's continued advocacy for system equity at the INB contributed to the inclusion of equitable access measures in the draft Pandemic Agreement text. This included provisions for Governments to develop national policies to include equitable access provisions in government-funded R&D, publication of access terms in government-funded R&D agreements, and commitment to achieving a more equitable geographical distribution of global production of pandemic MCMs.

In addition to advocating for a more robust and equitable PPR framework in multilateral fora, CEPI collaborates with leading organisations that will shape epidemic and pandemic responses, including WHO, Gavi, UNICEF, the European Commission (with HERA as the primary contact), SCARDA, BARDA, Africa CDC, PAHO, the Global Fund, the World Bank, and with civil society organisations (CSOs) more broadly.

CEPI's many engagements in strategic and high-profile events in the ecosystem marks its expanded role as a global influencer in PPR. Highlights in 2023 include:

- Under the 2023 G7 Presidency held by Japan, CEPI participated in G7 health working group meetings, bilateral engagement with the Government of Japan, and the Hiroshima Multi-stakeholder Dialogue, organised by the Japan Centre for International Exchange and supported by CEPI, Wellcome, and the Gates Foundation. CEPI's critical role in supporting PPR, the 100 Days Mission and equitable access remained central themes in G7 discussions, ultimately with both CEPI and the 100 Days Mission mentioned in the 2023 G7 Ministers of Health and the Leaders' Communiques. In addition, engagement with the Government of Italy and the Italian think-tank, Istituto Affari Internazionali, helped ensure the 100 Days Mission and equitable access, particularly African vaccine manufacturing, remain key priorities in the handover of G7 Presidency from Japan to Italy for 2024.
- CEPI strengthened coordination with interlocutors at the European Commission, including HERA, RTD, INTPA and SANTE to progress discussion on R&D funders collaboration, specific EU initiatives such as its pharmaceutical strategy, its pandemic preparedness partnership, and the shared global PPR agenda such as the pandemic treaty and MCM platform. CEPI co-hosted the first MCM R&D Funders Roundtable with HERA in October 2023 bringing together 20 organisations and government agencies funding medical countermeasures R&D. A follow-on event was agreed with the South African MRC to be held in May 2024.
- CEPI participated in the World Health Summit and hosted side and panel sessions bringing together delegates from the across the globe, including the Global South.

To galvanise relationships with key ecosystem partners, CEPI hosts the Joint Coordination Group (JCG). CEPI succeeded in getting partner buy-in to the concept of the 100 Days Mission and discussed operationalisation of the Equitable Access Framework throughout the value chain in 2023. A significant focus for 2024 will be exploring and solidifying the roles and responsibilities of partners in implementing the 100 Days Mission.

Other key JCG activities include:

- The first version of the Core Outbreak Response Plan (a living document) was completed and shared with JCG and other partners to increase awareness of CEPI capabilities and plans, identify opportunities for synergies, and model preparedness practice.
- A lessons-learned exercise was conducted based on the 2022 Sudan virus outbreak in Uganda. CEPI worked with Gavi and WHO to advance discussions about needs, roles, and responsibilities in prepositioning outbreak response elements for investigational products. These discussions have influenced Gavi's thinking on its expanded role in pandemic preparedness and response and its approach in Gavi's 6.0 strategic cycle.

CEPI recognises the civil society community as integral to a strong PPR ecosystem. Through 2023, CEPI deepened its collaboration with CSOs through engaging in bilateral dialogues with international and national CSOs, particularly to discuss PPR policy developments and country-specific progress. CEPI continued to co-organise COVAX-CSO dialogues and exchange updates with the CSO community. Highlights include:

- In June 2023, a virtual "CEPI-CSO dialogue" with nearly 100 attendees. The focus was the 100 Days Mission, CEPI's investments, and equitable access.
- In September 2023, a CSO roundtable in Kigali, Rwanda, in partnership with the Pandemic Action Network, Rwanda Biomedical Centre, Rinda Ubuzima and the Centre for Family Health Research. The group discussed local community engagement in clinical trials and shared best practices, while also discussing the importance of CSO engagement for the 100 Days Mission.
- CEPI facilitated relationships between CSOs and CEPI-funded clinical trial sites.
- A quarterly CSO newsletter was launched in December 2023, creating a platform to regularly communicate CEPI's updates and latest partnerships with civil society and continue to build relationships with CSOs.

In 2023, CEPI continued to enhance regional capacity and partnerships by expanding existing networks and adding new partnerships across the world. These networks support expedited vaccine development and a paradigm shift towards preparedness for the 100 Days Mission, acting as prepositioned entities for preparedness activities. Synergies across networks aim at enabling regional support for preclinical testing and support to CEPI's Global South focus. Highlights include:

- Centralised Laboratory Network (CLN): seven new projects were signed in 2023 bringing the total to 17. The projects span across 14 countries including five in the Global South (Bangladesh, India, Kenya, Senegal, and Uganda).
- Preclinical Model network: three new partners signed in 2023, bringing the total to 11 partners available in the network from six countries (Australia, Canada, Germany, UK, Netherlands, and USA), with negotiations ongoing with laboratories in Global South locations.
- Standards and assays: a global network for collection of specimens and assay development has been established, aiming to connect existing networks with four partner organisations also part of the CLN and PMNs. In 2023:
  - Seven international antibody standards have been developed (RVF, Nipah, SARS-CoV-2, SARS-CoV-2 VOC, Lassa, mpox and MERS) through CEPI's partnership with NIBSC
  - Four of these standards were made available in 2023 (Nipah, Marburg, RVF, SARS-CoV-2 VOC).
  - The serum collection process was conducted in partnership with CEPI partners in Bangladesh, Uganda, Korea, Malaysia, Kenya, UK, Nigeria, Sierra Leone.
  - In addition, several immunological assays have been initiated in 2023 including for mpox and Nipah.

Figure 7: CEPI Centralised Lab Network as of December 2023

Bringing protection against Lassa one step closer

In November 2023, CEPI along with partners IVI and Gambia's Medical Research Council Unit launched the Research Preparedness Programme West Africa (RPPWA) which aims to bolster regional clinical trial capacity and disease outbreak readiness.

Supported by USD 3.9 million of CEPI funding, the RPPWA will lay the groundwork for the first-ever high-quality, multi-country Phase IIb and Phase III trials to evaluate the efficacy of Lassa vaccines. Such trials are a prerequisite to a Lassa vaccine being approved by regulatory authorities and can only take place in countries in West Africa where the potentially deadly virus is circulating. The RPPWA will work with partners across the region to strengthen existing clinical trial infrastructure in West Africa, while also establishing additional good clinical practice-compliant Phase IIb /III trial facilities capable of conducting the crucial research that will advance a Lassa vaccine on its path to licensure.

The CEPI-backed programme will support regional stakeholders to strengthen clinical research capacity to conduct Phase IIb/III clinical trials of Lassa fever vaccines for the region to be better equipped to tackle both known and future viral threats. The strengthened research capacity and capability will heighten outbreak preparedness in the region with the aim of generating high-quality clinical trial data during regional disease outbreaks in as little as 100 days.

Having high-quality clinical trial capacity at the ready in outbreak-prone areas so that vaccine trials can begin within weeks of a new outbreak is a crucial enabler of the 100 Days Mission.

Regulatory efforts in 2023

All regulatory activities, and the cross-functional enabling science activities that support them, are to promote adaptive and harmonised R&D approaches across CEPI's programmes. To this end, CEPI works to enable maximal use of platform data and pre-approved documentation, accelerate, or streamline product development pathways, harmonise 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.

Other highlights include:

- Continued efforts to enable maximal use of platform data and pre-approved documentation by authoring a contribution to European Federation of Pharmaceutical Industries and Association's White Paper on the use of Master Files in the EU/EEA. CEPI also assessed the updated EU Draft Pharmaceutical Legislation in the areas of Master Files and Platform Technologies and provided feedback to the EU Commission and the European Medicine Agency.
- Drafted a COVID-19 lessons learned paper in collaboration with International Federation of

Pharmaceutical Manufacturers and Associations and industry representatives with key messages to be disseminated in 2024.

- Carried out a review of outbreak/epidemic/pandemic 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 outbreaks. This included collecting information on emergency regulations from multiple countries using a regulatory intelligence tool and partnering with the FRPath Project[6] that will take collected data to populate their existing database of regulated pathways for all countries in 2024 with a view to rolling out to regulators and developers.
- Establishing a harmonised benefit-risk tool which can be applied to the CEPI core portfolio together with the Brighton Collaboration. The Brighton collaboration standardised module for vaccine benefit-risk assessment – ScienceDirect was developed and published in the journal Vaccine in early 2024. Use testing of the module and associated digital tool is ongoing with the Ghana FDA Pharmacovigilance team with other regional socialisation engagements and uptake by CEPI awardees being planned.

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

Target by 2026	Progress update
RACI(s) - Responsible, Accountable, Consulted and Informed - for 80% of key elements in place	CEPI co-hosted the first Medical Counter Measures (MCM) R&D Funders Roundtable with the European Commission's Health Emergency Preparedness and Response (HERA) to increase visibility, coordination and opportunities for partnership. A second meeting is planned in 2024 to be co-hosted with South African Medical Research Council (SAMRC). CEPI provided thought leadership and staff support for the WHO-convened interim-Medical Countermeasures Network (iMCM Net), including R&D component of a report to be shared at 2024 World Health Assembly. CEPI's Joint Coordination Group (JCG) discussed stronger collaboration and identification of gaps for "hand-off" between organisations in the vaccine value chain. A tabletop exercise is planned for January 2024 alongside CEPI's Annual Portfolio Review. With Gavi, UNICEF, WHO, Africa CDC, PAHO, WHO SEARO, CEPI established the XVAX Network to support operational readiness to respond rapidly to emerging epidemic and pandemic threats. CEPI hosted session at World Health Summit on partnerships for a pandemic-free future with Africa CDC, EDCPT3, Fiocruz, GPMB and India Council for Medical Research. CEPI initiated development or revision of Memoranda of Understanding (MOU) with Africa CDC, Gavi, Korea DCA, and PAHO, to be signed in 2024. Agreement on collaboration priorities with UNICEF Supply Division.

[6] FRPath Project is an educational research project designed to serve as the repository of expertly evaluated and organized information about Facilitated Regulatory Pathways (FRPs) – regulatory approaches used by ministries of health to reduce the burden of duplicative regulatory activities, thereby promoting efficient access to important medicines worldwide. https://frpath.org/about-frpath

Enhancing Global Biosecurity Capabilities in Support of the 100 Days Mission

Enabled by generous support from Global Affairs Canada, CEPI announced establishment of a new Biosecurity function in August 2023.

CEPI has a critical responsibility to ensure its investments in vaccine and biologic research, development, and manufacturing do not inadvertently cause the next epidemic or pandemic due to an accident or deliberate misuse by malevolent actors. This is particularly salient given an ongoing reassessment by many policymakers in the wake of the COVID-19 pandemic of social tolerance for biosafety and biosecurity risks associated with research on high consequence pathogens, as well as rapid advances in biotechnology and other converging technology areas which are creating extraordinary new opportunities to accelerate global progress towards the 100 Days Mission, but also quickly evolving biosafety and biosecurity risks.

CEPI is uniquely positioned to elevate and prioritise the important role of biosecurity in vaccine development and across the end-to-end preparedness ecosystem while accelerating responsible global progress toward achieving the 100 Days Mission safely and securely.

In 2023, the new Biosecurity function began a series of internal and external consultations to identify areas of relevance to inform the priority areas of focus of CEPI's biosecurity work and proposed mission to "protect society from epidemic and pandemic threats, with an emphasis on preventing accidental and deliberate misuse of pathogens". To inform and support biosecurity strategy development, a Biosecurity Strategy Group of external advisors was established.

In parallel, CEPI is already advancing key biosecurity goals in support of the 100 Days Mission, for example by demonstrating CEPI as a thought leader on harnessing the benefits and mitigating the risks of artificial intelligence for vaccine development and adding biosecurity as a key pillar of CEPI's renewed Joint Action Plan with Africa CDC to advance African biosecurity and drive biosecurity for equity.

A biosecurity strategy is anticipated to be developed and approved in 2024.

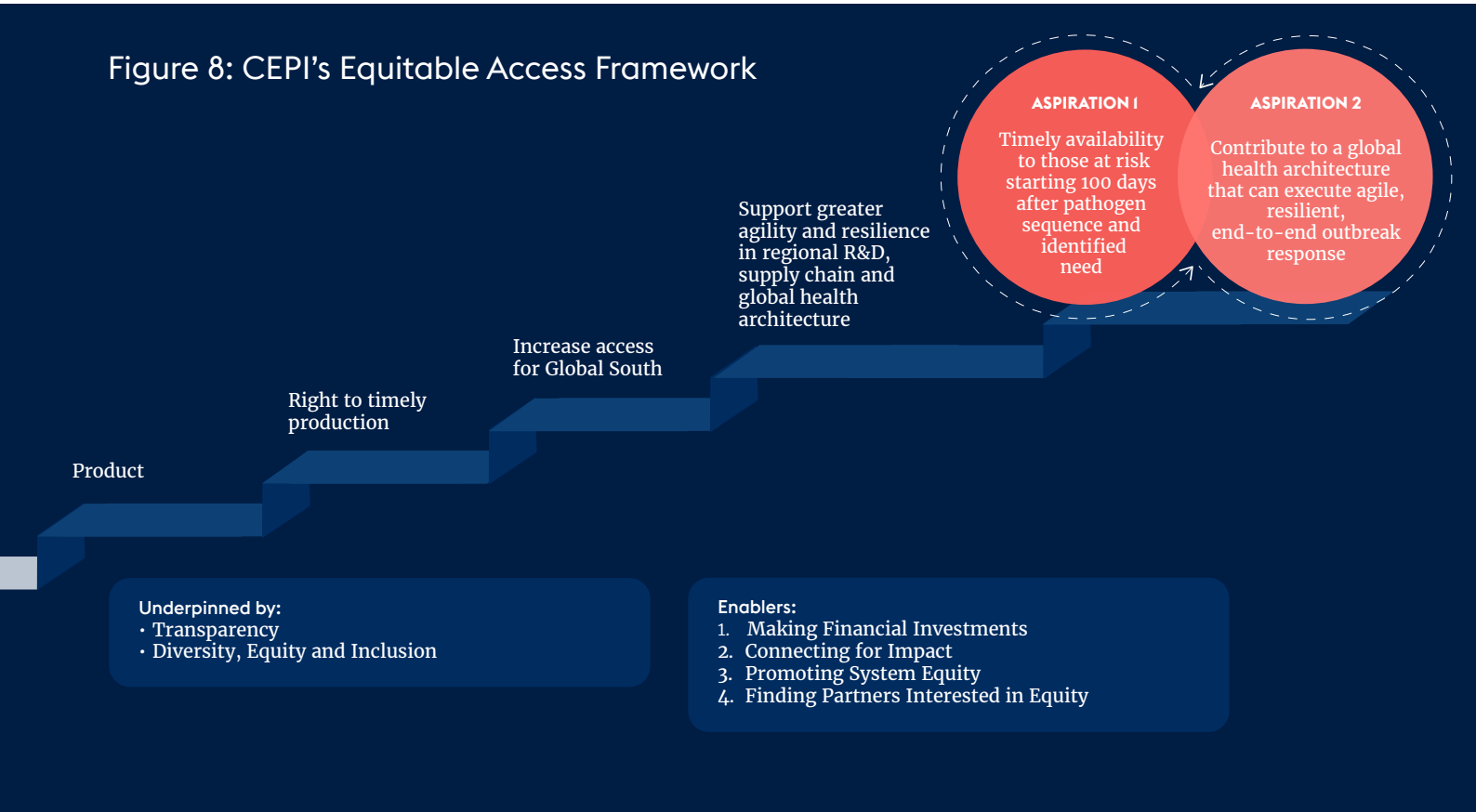
3.3 Equitable access principles as the foundation of any effective global response

An overriding commitment to equitable access informs every aspect of CEPI's work and has done so since the very beginning. In the context of an outbreak, equitable access to vaccines means that appropriate vaccines are first available to populations when and where they are needed to end an outbreak or curtail an epidemic or pandemic, regardless of ability to pay.

The COVID-19 pandemic has arguably done more than any other health crisis in history to expose the tragedy of unequal access to life-saving medicines. 'Vaccine nationalism' — first manifesting as a phenomenon during the 2009 H1N1 swine flu pandemic, which then dominated the COVID-19 response— is a term now widely understood. With a view to producing better outcomes in the future, CEPI's approach is to understand the systemic and structural roots of the inequity that hobbled the response to the COVID-19 pandemic and attempt to re-engineer the system so that future responses are characterised by the swift and equitable attainment of protection and health security for everyone.

In 2023, CEPI published its Equitable Access (EA) Framework which sets out how CEPI operates within an imperfect global health ecosystem, accelerating R&D&M to prepare for and respond to emerging infectious disease threats with EA as a core mandate. Approved by the Board in 2022, the framework articulates CEPI's aspirations concerning equitable access, why they are important and how they will be met. It also outlines the end-to-end life cycle process from creation to deployment of product with particular focus on how investments are made with both public and private strategic partnerships, engaging other stakeholders, to strengthen the global health architecture to ensure clear and efficient hand-offs to public partners. Finally, it emphasises the importance of promoting diversity, equity and inclusion to achieve equitable access as well as transparency with respect to the commitments obtained and the resulting impact.

Figure 8: CEPI's Equitable Access Framework



CEPI's investments and activities are focused on four enablers where CEPI can have the greatest impact – either directly or indirectly – on equitable access:

- Supporting system equity in the PPR ecosystem.
- Connecting with other stakeholders for impact and system equity.
- Making financial investments to drive equitable access by including equitable access obligations in all its investment agreements, based on the principles laid out in CEPI's equitable access policy.
- Investing in partners with an interest in equity.

Two aspirations will provide direction for CEPI's efforts:

- Directly – CEPI aspires to enable timely availability of CEPI-supported products to those at risk, starting just 100 days from pathogen sequence and identified need.
- Indirectly – CEPI aspires to support and contribute to a global health architecture that can execute agile, resilient, end-to-end outbreak response.

In 2023, in pursuit of a systems equity approach, CEPI participated in multilateral fora including the G7, G20 and provided inputs into the Pandemic Accord negotiation at the UN High-Level Meeting on Pandemic Prevention, Preparedness, and Response (PPPR) held on the sidelines of the UN General Assembly. As a result of these advocacy efforts, CEPI's equitable access positions were reflected in the interim draft of the Pandemic Agreement, and CEPI's role in the PPPR ecosystem was reflected in the G7 Leaders communique, the G20 Health Ministers meeting outcomes and in the work of the G20 Joint Finance and Health Task Force.

Diversify global manufacturing capability geographically

CEPI recognises that both bolstering global capacity to make new vaccines and establishing a global network of vaccine manufacturers are crucial innovations needed to make the 100 Days Mission a reality. In 2023, CEPI developed a Manufacturing and Supply Chain (MSC) strategy to strengthen efforts to manufacture and supply vaccines cheaper, faster, and closer to outbreaks.

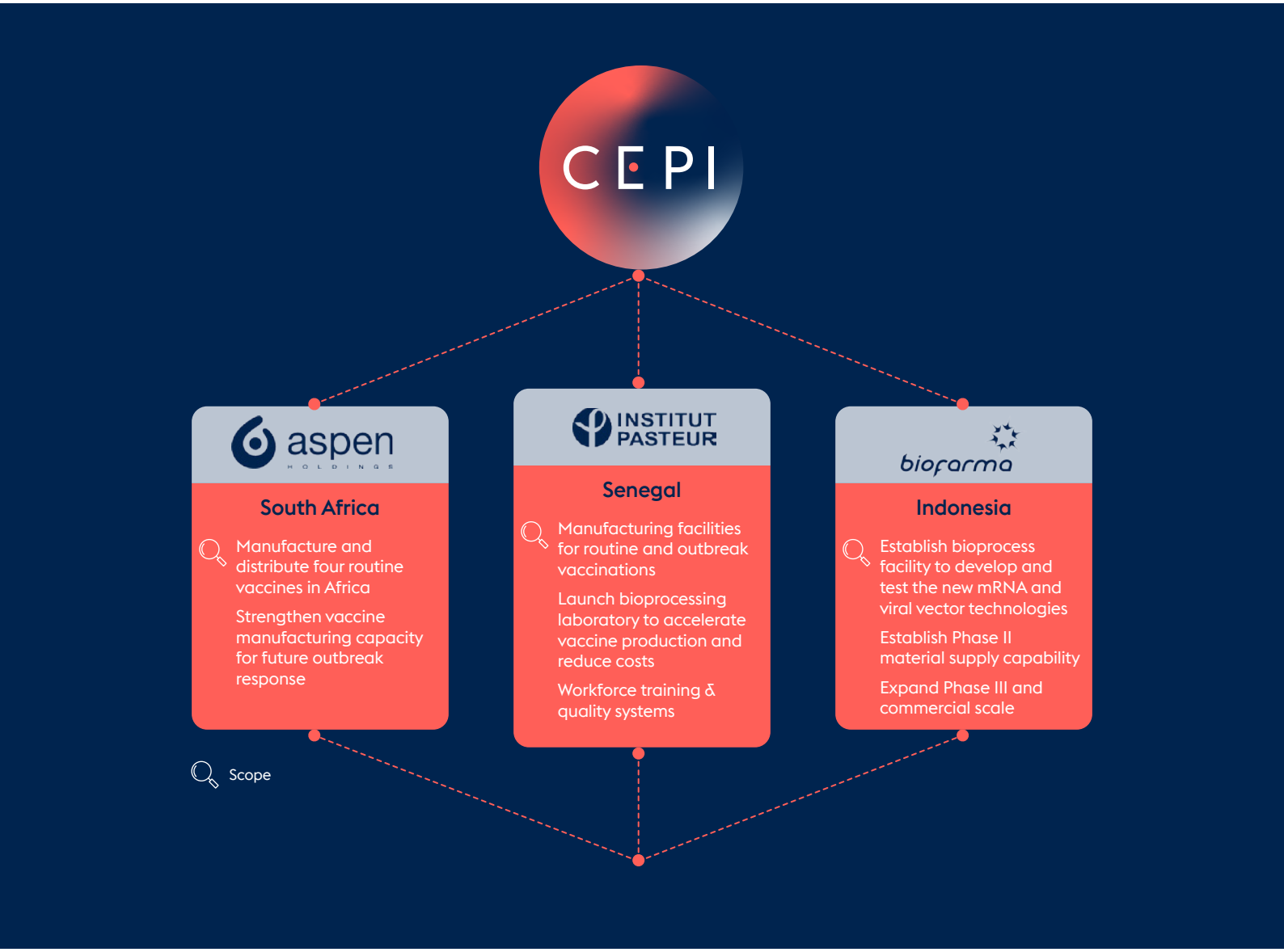
Central to this strategy is the establishment of the Vaccine Manufacturing Facility Network (VMFN).

The network aims to expand the global footprint of vaccine production and therefore heighten outbreak response capacity while supporting network members to remain sustainable during inter-epidemic periods. The VMFN focuses on established vaccine makers in the Global South, that are located near areas at high risk of outbreaks caused by viral threats like Lassa Fever, Nipah, and other pathogens with epidemic or pandemic potential. Shortening the time taken to manufacture and qualify the first batches of experimental vaccines will be key to enabling a response to an escalating outbreak within just 100 days.

The evolving VMFN delivers the MSC key performance indicator to have at least five signed funding agreements that support Global South vaccine manufacturing capacity and capability strengthening in at least two LMIC regions by 2026. One new partnership agreement was signed in 2023 with Bio Farma in Indonesia, complementing existing agreements with Aspen in South Africa and Institut de Dakar, Senegal bringing the total number of partners to three at the end of 2023. These collaborations will strengthen manufacturing capacity to supply Global South countries during future outbreaks and pandemics. The agreement with Bio Farma is expected to bring cutting-edge mRNA and viral vector rapid response vaccine manufacturing technologies to Indonesia and the ASEAN region.

CEPI expects that further VMFN partnership agreements will be signed in 2024, including with organisations based in Latin America, Asia and Africa. VMFN investments and partnerships are being coordinated with the RVMC and global agencies working on similar initiatives to ensure complementarity and synchronisation.

Figure 9: CEPI agreements with three VMFN organisations as of end December 2023



Building equitable, robust supply chains of critical input materials for vaccine manufacturing is critical to address the inherent challenges of low volumes, non-steady demand and location as vaccine manufacturing geo-diversifies in the Global South. CEPI is working with VMFN organisations to secure stable, reliable single-use raw material and consumable supply chains. This work aligns with activities undertaken to mitigate input material supply chain challenges during the COVID-19 pandemic and thus builds on the successes and lesson of the COVAX Marketplace. In addition, CEPI undertook preparatory work for an Africa Supply Chain Forum to address regional supply chain challenges similarly experienced by VMFN partner organisations, held in Kenya in early 2024. Building equitable, robust supply chains of critical input materials for vaccine manufacturing is critical to address the inherent challenges of low volumes, non-steady demand and location as vaccine manufacturing geo-diversifies in the Global South.

Supporting the 100 Days Mission: A Spotlight on the Regionalised Vaccine Manufacturing Collaborative

In recognition of RVMC's potential to help solve the challenges the world faced with vaccine manufacturing during the pandemic, CEPI continued to dedicate resources to the Secretariat throughout 2023 by providing consultancy support and co-chairing the RVMC Steering Committee alongside the US National Academy of Medicine.

The RVMC Secretariat convened several meetings throughout 2023, including on the sidelines of the World Health Assembly and the UN General Assembly, which focused on championing regional initiatives and promoting inter-regional learnings regarding diversifying vaccine manufacturing. To conclude the RVMC's first phase, a technical framework was produced outlining eight pillars on which efforts to expand regional-scale vaccine manufacturing should be based.

CEPI played a leading role in designing the second phase of RVMC, following broad support from partners for the continuation of RVMC as a unique, regionally led initiative focused solely on sustainable regionalised vaccine manufacturing. In consultation with partners, it was agreed that CEPI would host the Secretariat from 2024 to 2026 and provide USD 15 million in funding with Dr Frederik Kristensen, former Deputy CEO of CEPI, becoming the inaugural Managing Director of the RVMC Secretariat.

In its next phase, RVMC will focus on enabling regionally-led efforts including facilitating exchanges between lead countries, lead manufacturers and supply chain actors. The RVMC will seek to align partners and their support under the auspices of regional political bodies in regions such as Africa, Latin America and the Caribbean, and ASEAN.

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

Target by 2026	Progress update
Guidance available to address potential injuries caused by vaccines/ to establish a no-fault compensation-mechanism **Three G20 countries making new funding and/or procurement commitment for vaccines development include reference to access provisions.**	Ongoing advocacy to broaden the G20 Joint Finance and Health taskforce commitments, including with greater representation from the Global South, to establish and adequately fund surge financing mechanisms. One new partnership added to CEPI's network to support globally diversified manufacturing capability (Bio Farma, Indonesia) bringing the total number of partners in CEPI's Manufacturing network to three. Designed and secured support to launch the second phase of the Regionalised Vaccine Manufacturing Collaborative (RVMC). CEPI agreed to host the RVMC Secretariat from 2024. CEPI's equitable access positions were reflected in the interim draft of the Pandemic Agreement, and CEPI's role in the PPPR ecosystem was reflected in the G7 Leaders communique, the G20 Health Ministers meeting outcomes and in the work of the G20 Joint Finance and Health Task Force. Engaged with CEPI Investors Council members and their relevant agencies on need for equitable access terms in MCM R&D contracts. CEPI welcomed that the National Institutes of Health (NIH) proposed to develop and implement a new policy within its Intramural Research Program (IRP) to promote access to products stemming from taxpayer-funded inventions.

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 2017–2023 and 2024 budget rates for years beyond 2023. Further details on CEPI finances can be found in Appendix 2: Finance which includes reference to CEPI's Annual Audited Accounts and Board of Directors Report 2023.

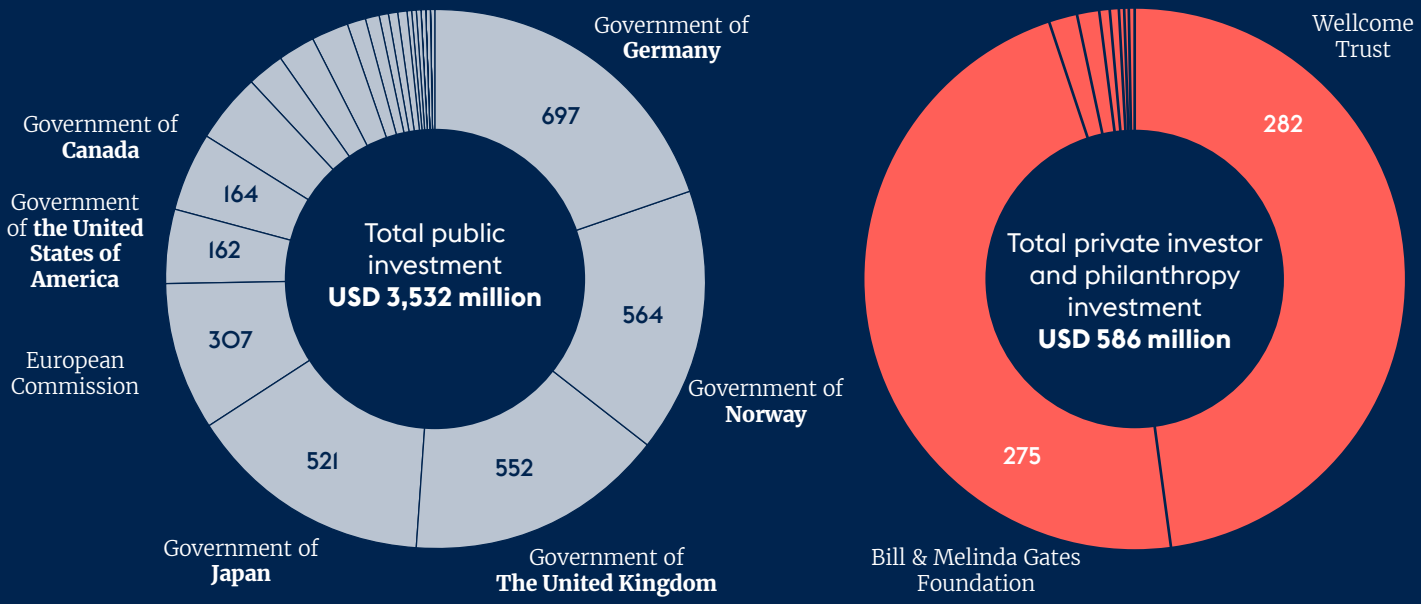
4.1 Contributions from investors

In March 2021, CEPI launched its USD 3.5 billion plan for its second strategic cycle, CEPI 2.0 (2022–2026). By December 2023, close to USD 2 billion has been pledged. O this figure, USD 1.8 billion has been secured through financial contribution agreements with USD 0.2 billion pending contract signature.

CEPI receives funding from sovereign investors, the European Commission, philanthropies and private organisations. Sovereign public investors represent the largest investor group with 86% of the USD 4.1 billion pledged to CEPI since its launch in 2017 (see Appendix 2: Finance).

The overall number of individual contributors has grown from 14 at the end of 2019, to 80 at the end of 2023[7]. The majority of donations are pledged to CEPI's common pool of funds. Earmarked funds, including funds softly earmarked toward activities that are considered ODA eligible, are pooled and spent on eligible groups of projects[8].

Figure 10: Total contributions and pledges to CEPI as of 31.12.2023



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

[8] The overall OECD ODA co-efficient for CEPI 2.0 portfolio is 88% (see Appendix 3).

4.2 R&D&M Project disbursements

CEPI portfolio at the end of 2023

At the end of 2023, CEPI had entered partnership agreements with total investment commitments of up to USD 2.583 million and has disbursed USD 1.928 million in funding across its portfolio. Approximately 37% of the funds remaining to be disbursed are gated (USD 245 million of USD 655 million), the release of which is conditional on key milestones that awardees will have to meet.

COVID-19, MERS and BPCV represent the largest signed budget in the portfolio accounting for ~67% (USD 1.7 billion). Priority pathogens account for ~18% (USD 474 million), with the largest proportion of the priority pathogen budget assigned to Lassa projects (USD 234 million). CEPI's Disease X portfolio investments have been increasing rapidly and represent ~8% (USD 222 million).

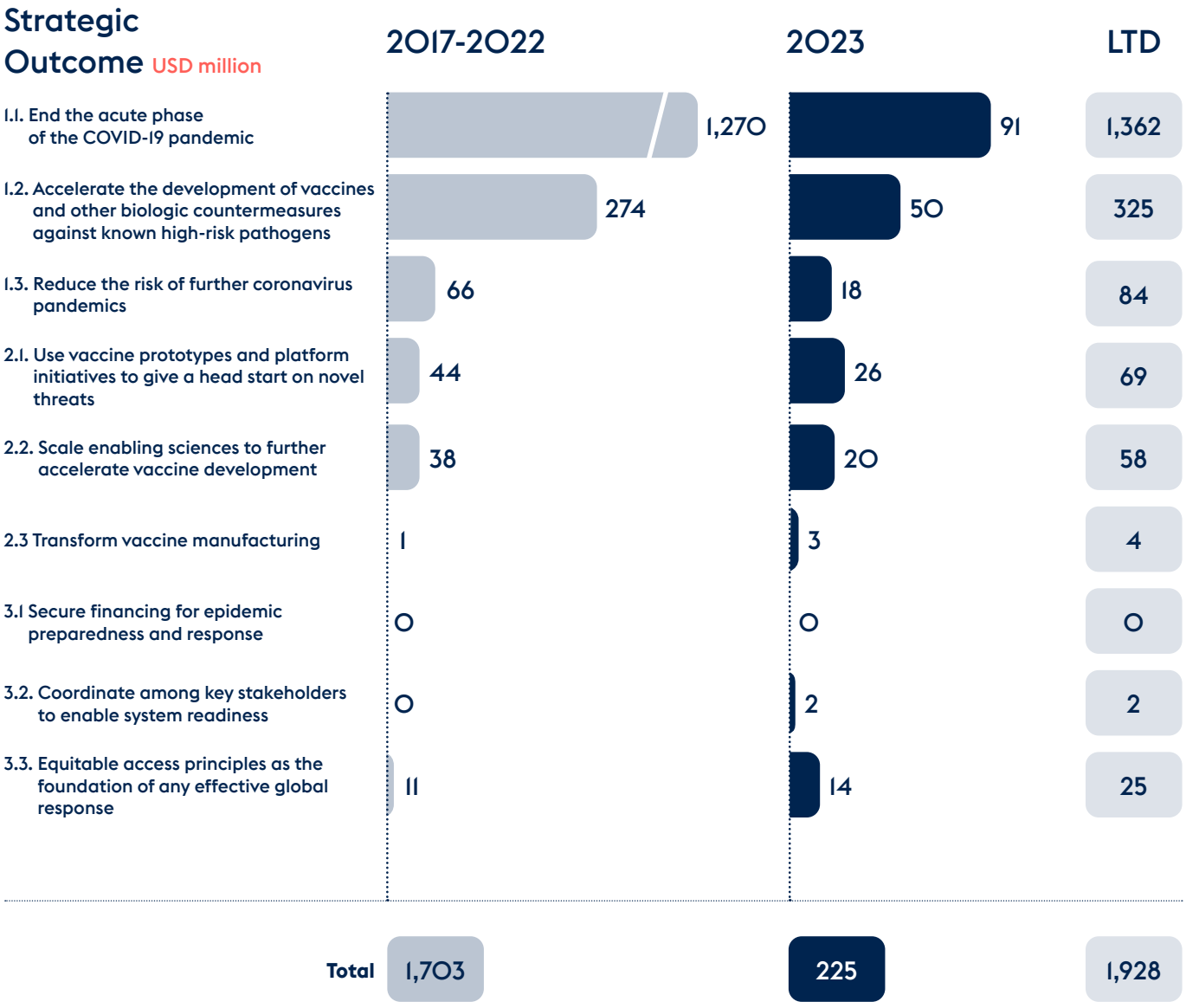
In terms of its financial allocations, ~85% (USD 2.2 billion) of the signed portfolio supports priority pathogen vaccine development, while ~8% (USD 222 million) has been allocated to Disease X, and ~6% (USD 154 million) to manufacturing and cross-cutting non-pathogen specific enabler projects (clinical research, preclinical models, standards and assays, CLN, epidemiology and regulatory). Signed vaccine projects (by value) represent 62% (USD 1.2 billion) and utilise protein-based platforms; and the share of mRNA investments has increased significantly in 2023, approaching ~9% (USD 181 million).

Many of CEPI's vaccine development investments are long-term, multi-phase investments and therefore the release of funding tranches is contingent on key milestones that awardees 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 considers expected phase-to-phase attrition.

CEPI's investments in 2023

In total, CEPI disbursed USD 225 million to its awardees in 2023. Most funding went towards the target of ending the acute phase of the COVID-19 pandemic (Outcome 1.1), specifically the remaining ongoing vaccine development programmes and clinical trials (USD 91 million). USD 50 million in funding was disbursed towards development of vaccines against known high-risk pathogens (Outcome 1.2), primarily for bridging the transition of Lassa candidates into late-stage development, as well as advancing CEPI- funded Chikungunya programmes, contributing to Valneva achieving the world's first licensed Chikungunya vaccine in November 2023. Further disbursements went to the advancement of mRNA and platform technologies to prepare against 'Disease X' (Outcome 2.1, USD 26 million) and preclinical proof of concept development of BPCV (Outcome 1.3) to reduce the risk of future coronavirus pandemics (USD 18 million). Lastly, CEPI has funded numerous enabling sciences initiatives to accelerate vaccine development as well as activities to improve equitable access and global manufacturing and response capabilities totalling around USD 40 million.

Figure 11: R&D&M Project disbursements 2023 – by Strategic Outcome



The 2023 disbursements of USD 225 million represent a shortfall compared to the planned budget (see Appendix 3, Table 3 for further details) due to a range of internal and external factors, including:

- A reduced need in the ecosystem for continued funding of COVID-19 R&D. In May 2023, WHO determined that COVID-19 no longer constitutes a public health emergency of international concern.

Evolutions to the COVID-19 vaccine landscape and overall reduced demand for COVID-19 vaccines resulted in changes to the scope of some large CEPI-supported vaccine development programmes which came with significantly lower funding needs. It also reduced the need for additional clinical evidence generation studies beyond the ones already ongoing and funded by CEPI.

- Slower than anticipated contracting for certain strategic areas. CEPI has established more agile funding mechanisms, including a broad rolling CfP, to help address this challenge.
- Delays in existing portfolio projects, in part due to the impact of COVID-19 on other vaccine R&D programmes. While delays are natural in vaccine R&D, better anticipation and resolution of the issues within CEPI's control e.g. project operations, as well as improved management and mitigation of issues not directly within CEPI's control e.g. R&D landscape evolution, supported by the IMS, will improve CEPI's programmatic execution and delivery on its investment plan going forward.

While CEPI fell short of its investment expectations for 2023, significant strides were made towards bolstering its portfolio, entering new and strategically important partnerships, and achieving more efficient investment management in a rapidly growing organisation. These have already resulted in tangible progress in the latter half of 2023, including:

- Entering into four major strategic partnerships anticipated to generate projects with the University of Oxford, BioNTech, IQVIA and Moderna, for accelerating pandemic preparedness and response capabilities in support of CEPI's 100 Days Mission.
- Signing new funding agreements to access BioNTech's mpox vaccine programme and development of an exemplar vaccine against Junín virus with the University of Oxford, as well as adding one new vaccine manufacturing network partners and funding to several partners to advance mRNA vaccine delivery technologies.
- Establishing an Investment Management System (IMS) to rapidly identify and resolve execution challenges. The IMS is an organisational, data-driven approach to recognise programmatic and operational challenges in CEPI's portfolio and investment plans early, manage them efficiently, and resolve them. The ultimate goal is to accelerate programmatic execution and thereby enable delivery of CEPI's strategic objectives and mission.
- Publication of a new Broad Call for Innovations to Prepare for Future Epidemics and Pandemics as a new mechanism to attract innovative partners and through more agile and fit-for-purpose processes.

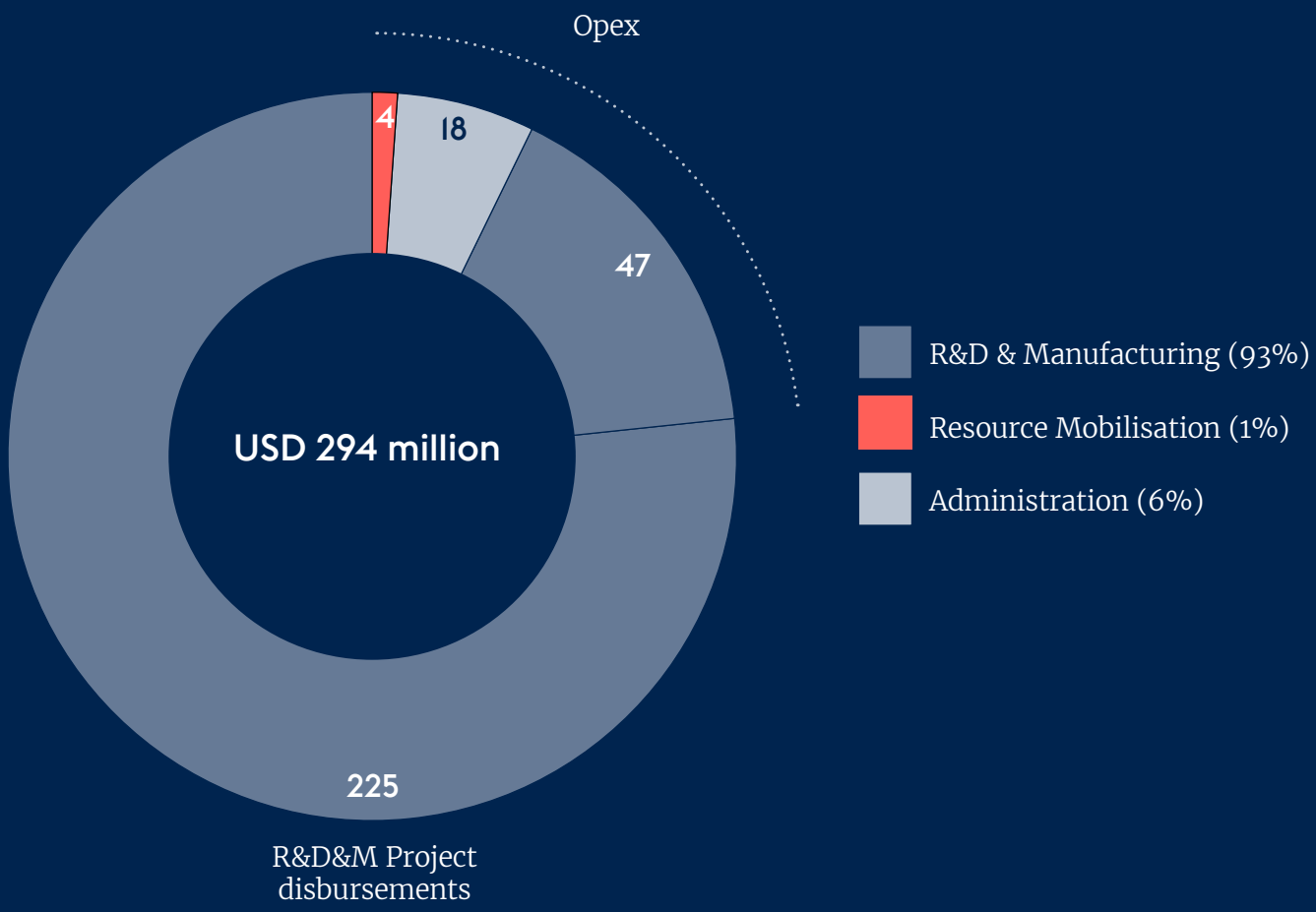
4.3 Operating expenses (Opex) and total expenditure

Out of the overall expenditure for 2023 (Appendix 3: Finance), CEPI spent 93% on its main activities in relation to vaccine R&D and manufacturing, leaving a spend of 7% on overhead (resource mobilisation and administration). With this, CEPI has demonstrated the ability to keep administrative costs low, while continuing to increase its portfolio and build the organisation accordingly.

The significant year-on-year increase in staff since inception continued in 2023, reflecting CEPI's ambition to build a fit-for-purpose organisation to implement the CEPI 2.0 strategic cycle. Opex amounted to USD 69 million in 2023, an increase of 26% over 2022, but well within the approved 2023 budget (see Appendix 3). The increase in Opex for 2023 was a result of continued hiring, full-year effect of increased headcount in 2022, increased travel activities and consultancy support related to investment management improvements.

The overall expenditure is depicted below by activity and refers to whether an expense is channelled towards R&D and Manufacturing, project disbursements and project support, resource mobilisation[9] or administration[10]. This provides insight into whether Opex are directed towards adding value to the portfolio of investments through project support, or to raising funds or organisation management and administration. The last two are typically labelled overhead costs. Of CEPI's Opex, 68% relates to R&D project support which is largely driven by CEPI's Vaccine R&D and Manufacturing and Supply Chain departments, staffed with technical experts responsible for launching CfPs and conducting technical follow-up of CEPI's portfolio of projects.

Figure 12: 2023 Total expenditure by activity



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

[10] Shared costs like IT, Office facilities, Finance & Operations and HR are distributed to the different activities. Total shared costs for 2023 was USD 13.9 million.

4.4 Procurement

CEPI has a robust procurement policy and procedure in place reflecting international best standards to include general rules and principles, description of risk management and eligibility criteria for tenders. They also define a set of thresholds that trigger discrete procurement processes whereby the number of steps and scrutiny undergone reflect the value and type of procurement. Rules related to exceptions from the threshold requirements are also outlined.

In 2023, CEPI strengthened its procurement capability related to internal capacity and skills, processes and system support. The Procurement team maintains a strong focus on cross-functional collaboration and knowledge sharing, particularly with the Legal, Governance and Risk & Compliance teams.

Furthermore, improving the controls within procurement throughout the full life cycle of a contract is an ongoing focus. The current contract management software enables the procurement managers to store and track signed contracts and ensure that CEPI always has valid contracts for all procurements. In 2023, CEPI developed a set of KPIs in procurement with the aim to better measure controls and effectiveness in the end-to-end procure-to-pay process.

In 2023, a total of 14 Requests for Proposals were published including for consultants, travel, IT and infrastructure under the current procurement policy. Additionally, 24 Requests for Quotation and almost 30 direct procurements were performed during the year with 12 exceptions from the current procurement procedure approved by CEPI management.

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)

Risk Management

5. Risk Management

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 risks in CEPI is carried out by the Board, the Audit and Risk Committee and the CEPI Leadership Team, with the support of the Governance, Risk and Compliance Department. Ensuring robust risk management, ethical conduct and compliance with laws and regulations is critical to CEPI's operations and central to CEPI's Risk Management Strategy.

The Governance Risk and Compliance Department has four functions: risk management, compliance, audit and partner assurance, and security and resilience. Section 5.1 below provides an update on how the individual functions contribute to CEPI's overall risk and assurance framework.

5.1 Risk Management

The evolving ecosystem, CEPI 2.0 and the growth of the organisation necessitated a review of CEPI's overall Risk Management Strategy, to ensure that it remains fit-for-purpose. Following an independent review of the risk management framework in 2022, several improvements were rolled out in 2023:

- **Approval of the Risk Appetite Framework:** The Risk Appetite Framework, was approved by the Board and the Audit and Risk Committee of CEPI in September 2023. Every organisation needs to factor risk into strategic planning and operation to achieve its strategic objectives. Clarity on CEPI's risk appetite is needed both to limit excessive and unrewarded risk taking as well as prevent undue risk aversion, both of which can impede progress. CEPI's business mandate, investing in vaccine development and manufacturing programmes, working to enable equitable access, and working alongside other stakeholders in an increasingly complex ecosystem, is inherently high risk. While CEPI needs to take risks to deliver on its mandate, it must also ensure operational and financial efficiency, stability and controls are able to safeguard CEPI's resources and investments. In agreement with the Board and the Audit and Risk Committee, CEPI's risk appetite is set for each of the four risk areas related to Strategic Goals, Programmes, Finance and Funding and Operations which forms the guiding principles on assessing, monitoring and reporting on risks and explicit risk-reward trade-off decisions.
- **Strengthening Organisational Level Risk Management:** In line with CEPI's strategy and priorities, the organisation-level risks were agreed in tandem with the Risk Appetite Framework. Risks critical to CEPI are detailed and monitored in CEPI's Risk Register that is maintained by the Risk Team (categorised into Strategy, Finance, Programmes and Operational risks). Detailed progress on the most important risks that impacts the organisation's ability to achieve its objectives is tracked quarterly. This is a cross-functional initiative led by the Risk Team, with individual risks owned by the respective Executive Director. Mitigating actions are aligned with and embedded within the Divisional and Departmental priorities.

- **Updated Risk Policy and Procedure:** The updated Risk Management Policy was approved by the Executive and Investment Committee in February 2024, and underpins the maturing Risk Management and Risk Management Framework in CEPI. It delineates clear roles, responsibilities and accountabilities at various levels within the organisation. The updated policy is supported by the Risk Management Procedure, also updated in 2023 and provides guidance on the Risk Architecture of CEPI- the roles, responsibilities, expectations, and linkages between the different functions within CEPI and the levels of risk management (organisations-portfolio-project). CEPI's Risk Management Policy can be found on CEPI's website.

The quarterly Risk report to CEPI Board and its sub-committee, the Audit and Risk Committee, continues to mature. The report provides not just an update on the top risks but keeps CEPI's governance appraised of emerging issues and the organisational response to them, and thus also serves as a decision-making tool.

5.2 Compliance

In 2023, CEPI continued to evolve its Compliance Programme. Activities undertaken and developments throughout the year include:

- **Third party due diligence and monitoring:** Building on the establishment of an enhanced Integrity Due Diligence process in 2021, CEPI continued to conduct robust and risk-based reviews of awardees. This included leveraging an in-house tool for screening and monitoring of all relevant entities, key individuals, ownership structures and ultimate beneficial owners, and sending 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, CEPI also formalised the Integrity Due Diligence process for suppliers and operated a risk-based approach to assessing integrity and human rights risk in these supplier relationships. Work was also started to develop a compliance audit programme, in collaboration with Partner Assurance.
- **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 has a sanctions compliance programme in place, which includes: 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. In 2023, CEPI instigated a sanctions risk assessment, working with outside counsel, to assess CEPI's policies and procedures and identify any areas for enhancement to strengthen compliance related to sanctions risk and take account of emerging and evolving sanctions compliance requirements.

- **Business integrity training:** In 2023, CEPI continued to roll out business integrity training to all new employees and long-term consultants. The training covers topics including Code of Conduct, Modern Slavery, corruption and bribery, gifts and hospitality, confidential information, whistleblowing and sanction requirements. CEPI 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 in-depth training sessions related to gifts and hospitality have been delivered across the organisation.
- **Human rights programme:** CEPI's human rights programme was further improved in 2023 based on the outcome of the Human Rights Impact Assessment (HRIA) which was completed in 2022. In 2023, CEPI continued to implement recommendations, including to ensure compliance with the Norwegian Transparency Act and the UK Modern Slavery Act. In June 2023, CEPI published its first annual statement under the Norwegian Transparency Act, which was combined with the UK Modern Slavery statement and sets out CEPI's key activities and ambitions to identify and mitigate risk in its third-party relationships.
- **Policy management:** CEPI's current policy framework is comprehensive and covers a broad range of organisational subjects. To further strengthen the policy framework, as well as ensure that changes in both CEPI's external and internal environment are addressed, a policy review was conducted in 2023 which identified several new policy requirements, as well as updates to existing policies. 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. To further support this, a comprehensive database of Investor Requirements was created and work is ongoing to ensure that these compliance requirements are met in both CEPI's policies and procedures and internal ways of working.
- **Data Privacy:** A new dedicated lead for Data Protection and Privacy led on the design and implementation of CEPI's Data Privacy Programme in 2023. This has comprised the implementation of a new Data Protection Policy, Data Classification Policy and Procedure, External Privacy notices and other related templates and guidance to support the organisation in complying with the relevant data privacy requirements.
- **Gender and diversity:** CEPI recognises that gender and diversity are critical factors in its work and is committed to integrating gender and diversity considerations into its strategy, governance, and operations, as well as its partnerships. Building on previous and ongoing initiatives relating to gender and diversity and as reported in the Diversity Equity and Inclusion Committee, CEPI is working to strengthen its approach to gender as part of a broader commitment to respecting and upholding human rights. In 2023, CEPI commissioned an external gap assessment looking specifically into the human rights-related requirements of its donors and how we can further strengthen compliance in these areas. The assessment will be completed in 2024 with findings to feed into an action plan to be implemented in mid-2024 over a 12–18-month period. Specific activities include increasing CEPI's accountability and transparency by developing indicators and targets to measure its progress and impact on gender and diversity, and reporting on them regularly and publicly, as well as enhancing policy and training on these topics.
- **Environment:** CEPI continues to review and monitor the carbon footprint generated by its international travel, in collaboration with its travel provider, and is identifying ways to mitigate this. In 2023, CEPI drafted an Action Plan for a Sustainability and Climate Change Strategy, structured into five phases, aimed at evaluating, strategising, implementing and enhancing CEPI's approach to environmental impact and climate risk. This plan integrates legal and investor requirements with CEPI's mission, prioritising actions based on risk assessment and available resources while emphasising Environmental, Social and Governance principles. This will be refined and delivered during 2024.

5.3 Internal Audit / Partner Assurance

The Internal Audit and Partner Assurance (IA/PA) function is a critical aspect of an CEPI's governance and risk management framework. It provides an independent assessment of CEPI's financial reporting, and internal control systems, ensuring accuracy, compliance with laws and regulations, and adherence to established policies and procedures. CEPI's IA/PA function has continued to grow and evolve over the course of 2023 and reports to the Director of Governance, Risk and Compliance for administrative purposes, and to the Board Audit and Risk Committee for its functional role. A Head of function was appointed in March 2023 in addition to dedicated staff to manage internal audit and partner assurance activities. The IA/PA team focused on three priorities over 2023:

- **Evolution of the Assurance function:** IA/PA worked closely with an external consultancy firm to develop ways of working, templates and procedures to further mature the Assurance function within CEPI. External collaboration was sought to make sure all processes were aligned to industry and other internationally recognised guidance. A new Assurance Charter was developed and approved by the ARC providing a framework to govern all assurance activities. Furthermore, a new Audit Universe was created to guide the internal audit function, including in their assessment of risk, prioritisation of audit engagements and allocation of resources. Methodology to conduct internal audits was developed and rolled out to help ensure that all assessment work being conducted is consistence and reproduceable.
- **Internal Audit activities:** CEPI's Internal Audit team successfully conducted its first annual audit plan workshop in January 2023. The workshop was designed to facilitate development of full year assignment plan for 2024, and based on this assessment, seven audit topics were selected for 2024 along with three backups. The plan was submitted and approved by the Audit and Risk Committee in March 2023. Furthermore, two internal audit assessments were conducted in 2023 including an assessment of travel and expenses in CEPI. The outputs were shared with management with findings and agreed follow-up tracked until completion by Internal Audit, and updates provided to ARC on a quarterly basis.
- **Partner Assurance Activities:** In 2023, CEPI's Partner Assurance team completed six assessments of awardees, with outputs shared with both awardee and CEPI project teams. Agreed follow-up actions will continue to be monitored by the team until completion. The Partner Assurance assessment plan process has broadened to include not just the Finance team but also other functions within CEPI, namely Project Management Office, Compliance, and Project Leads. The assessment scope of partner assurance activities has thus been expanded to encompass both compliance with the CEPI agreement and CEPI policies, as well as financial testing.

5.3 Security and organisational resilience

CEPI is committed to maintaining a safe and secure working environment for employees, associates and partners. It does this by identifying and managing security risks relevant to CEPI's work. CEPI has a dedicated security and resilience function which leads CEPI's approach to resilience, including emergency response, crisis management, and business continuity, which are essential parts of CEPI's ability to minimise disruptions when facing extraordinary events and to respond to severe incidents and crisis situations.

In 2023, CEPI continued to mature its approach to security and resilience, with a focus on security for travel, events, and workplaces as well as business continuity and crisis management. Work was also started to develop a security strategy in relation to CEPI's investments, aiming to enable and support partners in taking on their own security responsibilities.

Appendices

Appendix 1: Organisational Update

A critical year of organisational transition and focus on investment management

2023 has been a critical year of transition during which CEPI has made significant progress, but has also grappled with organisational challenges, inherent to the changing global picture as the world exited the pandemic, due to its rapidly increasing size, and the broader scope of CEPI 2.0.

Following an analysis of the challenges CEPI was facing, CEPI's Executive Directors and new Extended Leadership Team have focused extensively on simplifying decision-making processes, clarifying roles and responsibilities of individuals and units within CEPI, promoting alignment across divisional and departmental boundaries, and – by focusing on delivery and adjusting systems and processes where necessary – improving planning and execution. Management identified the need to develop an integrated investment management capability and worked to establish this in the second half of the year.

The year-end accomplishments noted in this report speak to the fact that momentum is being regained and should be celebrated accordingly. This effort has required external support, benefited from the guidance of Board members and partners such as the Gates Foundation, and absorbed considerable Executive focus, but leaves CEPI in a much stronger position to deliver on its mission as it enters 2024.

Operational Agility Initiative

To understand the operational issues facing CEPI at this moment of its growth, the Voice of the Customer and Partner (VoCP) project was initiated in October 2022. The project aimed to understand the issues from both an internal and external lens. The objectives were to 1) create understanding of the current experience of awardees and partners when they work with CEPI, 2) identify insights from both an internal and external perspective and 3) create an actionable plan to address them for improvements in operational performance and customer experience, streamlining operations and measuring performance to ensure that CEPI remains a desirable and best-in-class partner in the wider global health community to prevent pandemics.

To execute the improvements identified in the VoCP project, the Operational Agility Initiative was created to drive people, process and technology improvements in the areas pinpointed by the exercise including in relation to Stage Gate Review process, awardee financial reporting and CfP grant applications. These improvements included simplified processes, improved awardee grant application templates, a workflow tool to speed up and track the approval process and a mentoring programme for new Project Leads and Project Managers. Additionally, awardee financial reporting has been reduced from quarterly to bi-annually to reduce burden.

In addition, a sprint was launched at the end of 2023 to focus on Investment Management, which led to the creation of the Investment Management System that helps monitor the financial progress of CEPI's projects with awardees. This has helped the organisation pinpoint areas where investments could be accelerated and to address operational issues blocking project progress.

A further example of how CEPI is streamlining and improving its internal processes includes the progress made in bringing in new partners. In October 2023, CEPI published a "Broad Call" for Innovations to Prepare for Future Epidemics and Pandemics CfP as a mechanism to attract innovative partners. This was an important step on the road to introducing more agile and fit-for-purpose processes.

The year ended with a significant uptick in spend relative to the forecast presented to the Board in September through rigorous attention to investment management. With the guidance of the Audit and Risk Committee, work has begun to implement the new risk management framework.

Looking forward to 2024, CEPI will:

a) maintain its focus on execution, systems, and processes;

b) improve strategic alignment, focus, and planning, towards a goal of delivering tangible results;

c) rigorously review its investment plan and timelines; and

d) with the Board and Investors, reflect on how to best advance CEPI's objectives within the CEPI 2.0 timeframe (2022-2026), taking the findings of the Midterm Review into account and considering whether any revisions to the KPIs are warranted.

Appendix 2: Monitoring, Evaluation and Learning

Two years ago, in the throes of COVID-19, CEPI began implementing CEPI 2.0 - its strategy for the second five-year business cycle from 2022 to 2026. A Theory of Change (ToC) for CEPI 2.0 was developed and piloted throughout the first two years of CEPI 2.0 strategic period to explain how CEPI's three key strategic objectives -PREPARE, TRANSFORM and CONNECT- were initially expected to be achieved, by providing details on anticipated outputs, outcomes and impacts. Outcomes and impacts are purposefully ambitious for this timeframe, to reflect the high levels of ambition of a relatively new organisation. While CEPI aims to contribute to the achievement of these outcomes and outputs, success or failure cannot be attributed solely to CEPI, as it is only one of the many actors working in the field and is part of a complex and dynamic ecosystem of vaccine R&D&M. More information on the CEPI 2.0 ToC and CEPI 2.0 key performance indicators (KPIs) can be found in the CEPI Results Framework.

At the time of publication an independent midterm review (MTR) of CEPI 2.0 was underway. The outcome of this review is expected to be shared and published with relevant stakeholders, in the second half of 2024/ early 2025. The MTR will provide an independent assessment of CEPI's work, including tracking progress made against the KPIs until the end of 2023 and an assessment of the likelihood of CEPI achieving the initially envisaged outputs and outcomes by 2026. It is expected that the MTR will also identify key learnings from the first half of CEPI 2.0 strategic period and recommend adaption to be made to the ToC and associated results framework (including the KPIs) to better reflect the changes in the wider ecosystem and the latest shifts in thinking and approach since CEPI 2.0 was developed.

Notably, we anticipate changes will be needed to clarify ToC pathways, and building on the evidence and learnings, to update the ToC assumptions considering latest ecosystem developments. We will also need to consider the level of emphasis placed on COVID-19, which has naturally reduced over time; how CEPI's different investments build on each other; how the Strategic Objectives relate to and interlink with each other.

Any changes to these frameworks will be made in close consultation with stakeholders, including the Board, Investors and partners.

Table 2: Total Contributions and pledges by 31.12.2023 with expected received year (in USD million)

Investor	2017 - 2022	2023	2023 - 2026[1]	Total contributions & pledges[2]	% of Total contributions & pledges
European Commission	154.34	27.27	124.99	306.60	7.35%
Government of Australia	10.09	33.01	32.56	75.65	1.81%
Government of Austria	4.04	1.74	1.71	7.49	0.18%
Government of Belgium	6.04	-	-	6.04	0.14%
Government of Canada	88.79	15.13	60.11	164.02	3.93%
Government of Denmark	1.45	-	-	1.45	0.03%
Government of Ethiopia	0.30	0.10	0.20	0.60	0.01%
Government of Finland	7.58	1.06	3.21	11.85	0.28%
Government of Germany	654.68	-	42.81	697.49	16.71%
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	2.00	1.00	3.00	6.00	0.14%
Government of Italy[3]	21.88	3.90	13.38	39.15	0.94%
Government of Japan	231.27	103.00	187.00	521.27	12.49%
Government of Kuwait	10.00	-	-	10.00	0.24%
Government of Lithuania	0.11	0.11	-	0.22	0.01%
Government of Luxembourg	1.15	0.21	0.64	2.01	0.05%
Government of Malaysia[4]	2.00	1.00	-	3.00	0.07%
Government of Mexico	0.90	0.35	0.65	1.90	0.05%
Government of Netherlands	58.64	5.39	9.63	73.65	1.76%
Government of New Zealand	11.99	1.27	3.61	16.87	0.40%
Government of Norway	469.37	19.18	75.44	563.99	13.51%
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	2.01	6.00	9.00	17.01	0.41%
Government of Spain	-	-	80.27	80.27	1.92%
Government of Switzerland	21.10	-	-	21.10	0.51%
Government of the Republic of Korea	9.00	24.00	-	33.00	0.79%
Government of the United Kingdom	367.93	39.46	144.60	551.99	13.22%
Government of the United States of America	62.00	55.00	45.00	162.00	3.93%
Kingdom of Saudi Arabia	150.00	-	-	150.00	3.59%
Total Public Investors	**2,355.02**	**338.17**	**838.81**	**3,532.00**	**85.75%**

Investor	2017 - 2022	2023	2023 - 2026[1]	Total contributions & pledges[2]	% of Total contributions & pledges
Avast	8.00	-	-	8.00	0.19%
Bill and Melinda Gates Foundation	155.28	30.00	90.00	275.28	6.60%
Fidelity Charitable gift funds	1.49	-	-	1.49	0.04%
Goldman Sachs Gives	1.63	-	-	1.63	0.04%
Nestle	1.04	-	-	1.04	0.02%
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	88.57	42.28	150.67	281.52	6.74%
Other Private Investors and Philanthropies[4]	3.28	0.00	-	3.28	0.08%
Total Private Investors & Philanthropies	**273.93**	**72.28**	**240.67**	**586.88**	**14.25%**
Total Contributions & Pledges	**2,628.95**	**410.45**	**1,079.48**	**4,118.88**	**100.00%**

1) The payment schedules of several agreements signed in 2023 extend beyond 2026, including the contribution from the Government of Spain to be received via the International Finance Facility for Immunizations (IFFIm).

2) Includes pledges made through 31.12.2023. 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 2024 exchange rates.

3) Includes EUR 5 million contribution in 2021 received via the IFFIm.

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

5) Private Investors with contributions of less than USD 1 million are grouped under "Other Private Investors and Philanthropies".

Table 3: R&D&M Project disbursements 2023 per Strategic Outcome

Strategic Roadmap USD M	2023 Actual	2023 Budget	2023 Variance
1.1. End the acute phase of the COVID-19 pandemic	91.3	279.9	-188.6
1.2. Accelerate the development of vaccines and other biologic countermeasures against known high-risk pathogens	50.2	126.9	-76.7
1.3. Reduce the risk of further coronavirus pandemics	18.4	65.6	-47.1
2.1. Use vaccine prototypes and platform initiatives to give a head start on novel threats	25.7	96.1	-70.4
2.2. Scale enabling sciences to further accelerate vaccine development	20.2	52.5	-32.4
2.3 Transform vaccine manufacturing	3.4	13.9	-10.6
3.1 Secure financing for epidemic preparedness and response	-	-	-
3.2. Coordinate among key stakeholders to enable system readiness	1.7	10.2	-8.5
3.3. Equitable access principles as the foundation of any effective global response	13.8	20.9	-7.1
Total	**224.7**	**666.1**	**-441.4**

Table 4: CEPI 2.0 ODA eligible project disbursements per 31.12.2023

ODA Category USD million	ODA %	2023 Project disbursements
1. Priority pathogens	100%	15.8
2. BPCV	55%	10.7
3. Disease X – viral families	68%	1.6
4. Rapid response platforms for LMICs	100%	17.9
5. Monoclonal antibodies	100%	0.0
6. Manufacturing networks	100%	13.2
7. Manufacturing Innovations	68%	3.4
8. LMICs capabilities and engagement	100%	1.6
9. Benefits both PP and Disease X	90%	8.4
Total ODA eligible investments	**88%**	**72.6**

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

Table 5: Operating Expenses (Opex) 2023

Opex USD million	2023 Actual	2023 Budget	2023 Variance
Employment	35.4	38.7	-3.3
Consultancy	18.5	17.1	1.4
Travel	4.3	6.4	-2.1
Infrastructure	6.8	9.3	-2.5
Other	4.0	3.7	0.3
Total	**69.0**	**75.3**	**-6.3**

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. During November 2023, CEPI also set up a fixed income portfolio with Citibank to further spread its cash reserves and connected risk.

To cover operational costs and to minimise 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 4: Human Resources

CEPI has grown rapidly since the onset of the pandemic and the workforce has continued to develop to deliver on CEPI 2.0. Skills and capacity are built in CEPI's three main locations (Oslo, London and Washington D.C.). CEPI has also partnered with a company offering Employer of Record (EoR) services that enables engagement with workers across the globe to attract scarce resources. Deliberate and continuous efforts have contributed to developing CEPI's staff into a diverse and international group of employees.

CEPI's workforce increased from 212 employees at the end of 2022 to 259 employees by the end of 2023. This includes permanent and fixed-term employees and workers engaged through an EoR service, or on foreign payroll. Over the year, there were 67 starters and 20 leavers including 12 internal staff transferring from one CEPI office to another. In 2023, overall turnover was 8.9%, down from 13.1% in 2022 and comparable to the 8.8% rate in 2021. The peak in 2022 is consistent with trends elsewhere. CEPI is supported by a strong cadre of international expert consultants (not captured in the figures in this report) that serves to broaden CEPI's global reach and operational flexibility.

The CEPI workforce is global and the organisation's employees originate from 54 different countries. About 29% of the employees originate from the Global South. This number has steadily increased since CEPI launched: 13% in 2018; 22% in 2020, and 25% in 2021. CEPI is committed to continuing to improve this effort through extensive outreach activities and by leaning on partners with global reach. CEPI also aims to have a good gender balance at all levels of the organisation. The organisation currently has 63% female employees.

The most important staff increase in 2023 was in the vaccine R&D division and notably in its Project Management Office, Regulatory Affairs and in Epidemiology teams. The Business Development team is being expanded significantly to support acceleration of deal sourcing, deal making and attention to end-to-end roles. With this growth came the need for enhancing internal support functions, improving risk management practices and implementing digital technology and information security arrangements commensurate with the organisation's size.

Appendix 5: CEPI Board Summary

CEPI's Board met four times in 2023 and there were 30 CEPI Board Committee meetings.

Administrative items

In the first half of 2023 there were the following changes to membership:

- Ichiro Kurane resigned after six years as an Investor Member of the CEPI Board
  - Dr Yasuhiro Suzuki was appointed as a new investor Board member
- New appointments were made:
  - Dr Mike Ryan was appointed as the new WHO representative on the CEPI Board
- Following recommendation from the Nominations Compensation Diversity and Inclusion Committee (NCDIC):
  - Dr Soumya Swaminathan was appointed to the Board for an initial two-year term, filling the seat vacated by Nisia Lima
- Prof Cherry Kang was appointed chair of the JCG, replacing Peggy Hamburg
  - Dr Jeanette Vega Morales was appointed to the CEPI Board
- Dr Jeanette Vega Morales replaced the seat that was left vacant by the departure of Prof Gagandeep (Cherry) Kang, who left her Board seat and transitioned to being Chair of CEPI JCG
- Dr Jeanette Vega Morales will serve an initial term of two years effective 2 June 2023, and was also appointed to serve as a member of the ARC.

Table 6: CEPI Board Members as of December 2023

Organisation/Affiliation	Name	Position
Independent Members		
	Jane Halton	CEPI Board Chair, Chair of EIC
LXI REIT PLC	Cyrus Ardalan	Chairman
Medicines for Malaria Venture	David Reddy	Chief Executive Officer
Center for Vaccine Development – Mali	Professor Samba Sow	Director-General
University of Chile and Doctor of Public Health, University of Illinois	Dr Jeanette Vega Morales	Medical Doctor and Pediatrician
Amref Health Africa	Dr Githinji Gitahi	Group CEO
MSSRF	Dr Soumya Swaminathan	Chairperson
Investor Representatives		
International University of Health and Welfare, Japan	Dr Yasuhiro Suzuki	President
Pharmaceutical and Medical Devices, 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
Gates Foundation, Gender Equality Division	Anita Zaidi	President
Non-voting Members		
Coalition for Epidemic Preparedness Innovations	Dr Richard Hatchett	Chief Executive Officer
Vicebio	Emmanuel Hanon	(Chair SAC) CEO
The Wellcome Trust Research Laboratory	(Cherry) Gagandeep Kang	(Chair JCG) Professor
Health Emergencies Programme, WHO	Dr Mike Ryan	Executive Director
World Bank (Health, Nutrition and Population)	Juan Pablo Uribe	(World Bank representative) Global Director

Board Effectiveness Review

An independent Board Effectiveness review was conducted by independent consultants Fidelio Partners in Q4 2023. The report was shared at the December 2023 Board Meeting along with management's initial response, with a follow up discussion held at the March 2024 Board Meeting.

Appendix 6: Summary of Scientific Advisory Committee

In 2023, CEPI's Scientific Advisory Committee (SAC) continued to meet on a roughly quarterly basis. Discussion topics included:

1. Critical landscape developments with a focus on monoclonal antibodies
2. CEPI's new Manufacturing and Supply Chain Division and strategy
3. Clinical preparedness
4. H5N1
5. Adjuvants
6. Broadly protective filovirus vaccines
7. Mucosal immunity and Controlled Human Infection Models
8. Optimising the composition of the Lassa portfolio
9. The Global vaccine library
10. CEPI's role in mpox

Table 7: Members of CEPI Scientific Advisory Committee as of December 2023

With 10 SAC members' terms ended in June 2023, CEPI launched an external call for new applications. Existing members were also invited to re-apply. Five of the existing members were renewed to June 2026, and five retired. A further nine new members* were also onboarded, bringing the total number of SAC members to 37.

Table 7: 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, NG	Alash'le Abimiku (renewed)
McGill University, CA	Amine Kamen*
Imperial College London, UK	Azra Ghani
Charité – Universitätsmedizin Berlin, DE	Christian Drosten
RH Solutions, FR	Dominique Maugeais
Vicebio, BE	**Emmanuel Hanon (Chair)**
Galveston National Laboratory/Institute for Drug Discovery, University of Texas Medical Branch, US	Gary Kobinger*
ModeX Therapeutics, US	Gary Nabel
Chinese Center for Disease Control and Prevention, CN	George Gao
KEMRI-Wellcome Trust Research Programme, KE and University of Oxford, UK	George Warimwe*
South African Medical Research Council, ZA	Glenda Gray*
International Vaccine Design Center, The Institute of Medical Science, The University of Tokyo, JP	Ken J. Ishii
IAVI, US	Kent Kester
Bharat Biotech International, IN	Krishna Mohan Vadrevu
Instituto de Biotecnología, Universidad Nacional Autónoma de México, MX	**Laura Palomares Aguilera (Vice Chair)**
Duke-NUS Medical School, SG	Linfa Wang
Arch Venture Partners, US	Luciana Borio
Institute for Protein Design, US	Lynda Stuart*
GHD|EMPHNET, BD	Mahmudur Rahman
Harvard T.H. Chan School of Public Health, US	Marc Lipsitch
Santa Casa de Sao Paulo School of Medical Sciences, BR	Marco Safadi
MJQuentinMillet Consulting, FR	Marie-Jose Quentin-Millet*
University of Virginia, US	**Michael King (Vice Chair)**
National Institute of Allergy and Infectious Diseases, National Institutes of Health, US	Paula Bryant (renewed)
Bill & Melinda Gates Foundation, US	Peter Dull
Paradiso Biologics Consulting, LLC, US	Peter Paradiso
WHO, US	Phil Krause (renewed)
Pasteur Network, FR	Rebecca Grais
Bright Global Health, US	Rick Bright*
Fondazione Biotecnopolo di Siena, IT	Rino Rappuoli
Cambridge University Hospitals Foundation Trust, UK	Sani Aliyu
University of Pennsylvania, US	Stanley Plotkin (renewed)
SUNY Upstate Medical University, US	Stephen Thomas
Gwynedd Consultancy Group, LLC, US	Vincent Ahonkhai*
Indian Institute of Science Education and Research, Pune, IN	Vineeta Bal
WHO	TBC (renewed)
Peking University, CN	Yunlong (Richard) Cao*

Appendix 7: Summary of the Joint Coordination Group

In 2023, CEPI's Joint Coordination Group (JCG) met twice to discuss topics including:

1. How JCG are partners revising PPR within their organisations for a post pandemic world
2. Critical points in the end-to-end process of vaccine development and delivery for enabling equitable access
3. CEPI's role in the R&D response to outbreaks
4. CEPI's role in vaccine introduction (particularly around Lassa and Chikungunya)

Table 8: Members of CEPI Joint Coordination Group as of December 2023

Members of CEPI Joint Coordination Group (December 2022)	
Organization / Affiliation	Name
Bill & Melinda Gates Foundation	**Gagandeep (Cherry) Kang (Chair)**
AVAREF	Chinwe Iwu-Jaja
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 Federation of Red Cross and Red Crescent Societies	Petra Khoury
Médecins Sans Frontières	Sidney Wong
UNICEF	Andrew Owain Jones
Wellcome Trust	Charlie Weller
World Health Organization	Ana Maria Henao Restrepo
World Bank	Magnus Lindelow

Reporting Period and Contact Information

Reporting period:	1 January 2023 – 31 December 2023
Date report submitted:	30 June 2024
Contact name:	Sally Girgis Hjoberg Head of Investor Relations
Postal address:	Post box 1030 Hoff, 0218 Oslo, Norway
Email:	ir@cepi.net
Website:	www.cepi.net

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