WHO engagement in the ACT-Accelerator

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Emerging Biopharmaceutical Manufacturers Network

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Agenda

1. Introduction
2. Process of assessment of candidates
3. Market preparedness (supply at scale)
4. Access (equitable distribution)
5. Role of LMIC manufacturers as seen by WHO
6. Discussion

Goal of the ACT-Accelerator

to reduce COVID mortality & severe disease through accelerated development, equitable allocation & scaled up delivery of…

Vaccines

2 billion doses by the end of 2021

Therapeutics

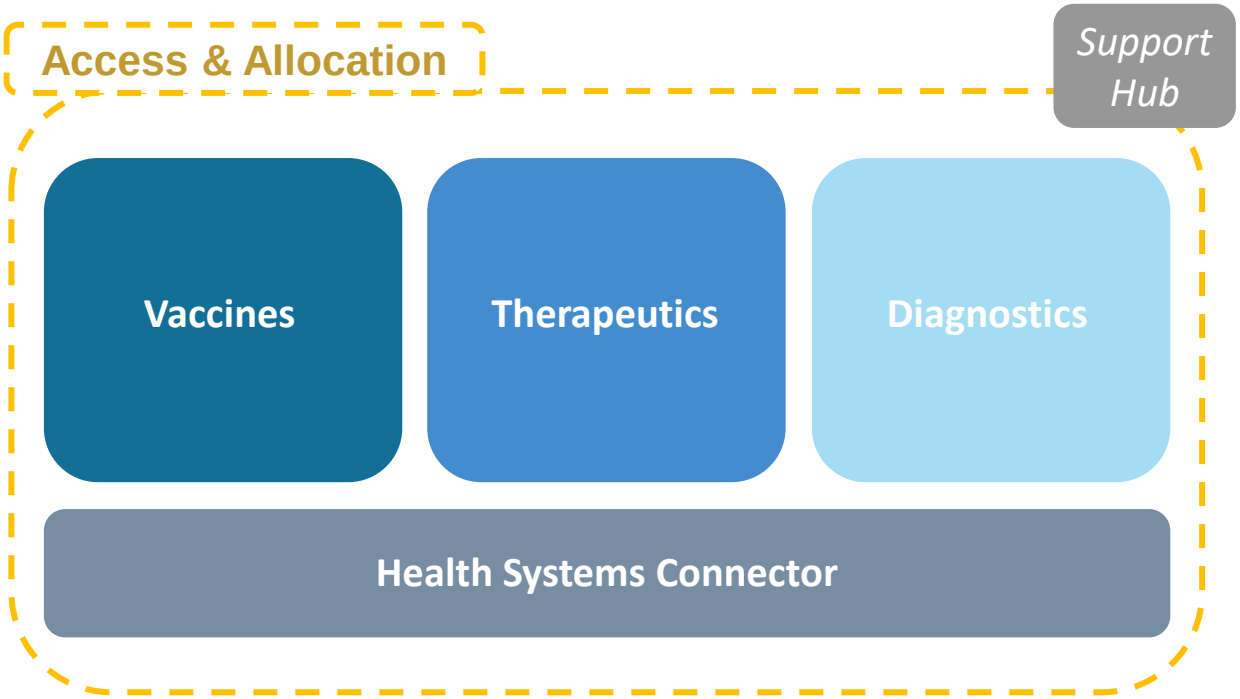
245 million courses by mid-2021

Diagnostics

500 million tests by mid-2021

…thereby protecting health systems & restoring societies & economies

Overview



- **3 vertical Pillars are the primary drivers** of ACT's product work
- A cross-cutting **Access & Allocation Workstream** delivers equity
- **A Health Systems Connector** drives optimal utilization
- **Support mechanisms** incl. 2 Special Envoys, ACT VCs, ACT Support Hub

Vaccines, therapeutics & diagnostics are essential to global recovery

Lockdowns are not a solution

- Unsustainable in HICs / UMICs & unimplementable in LMICs

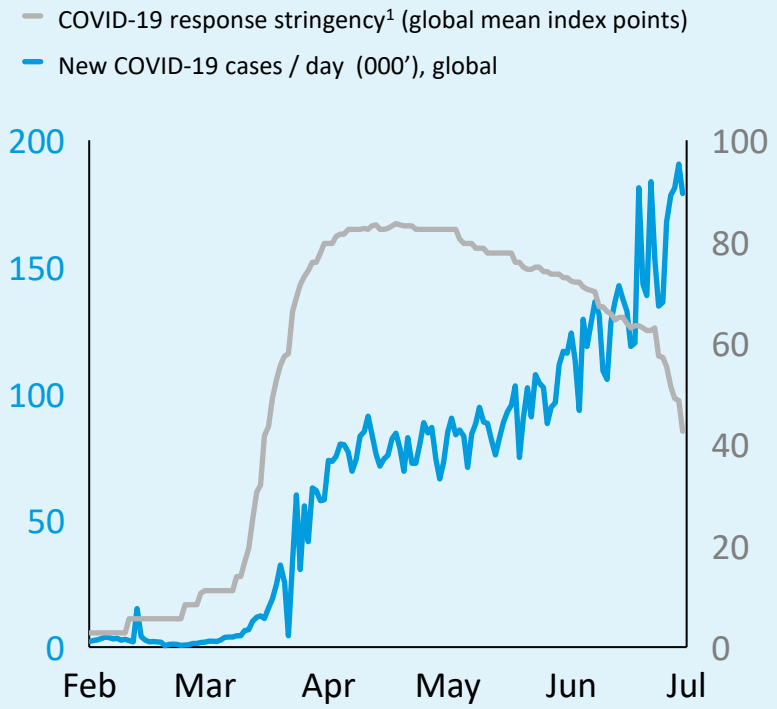
All populations are still at risk

- Serology data reveal massive immunity gaps everywhere

Countries can't beat COVID alone

- Interconnectivity undermines every country's emergence from lockdown

COVID is not coming under control



1. Based on University of Oxford's Coronavirus Government Response Tracker, "Stringency" measures the strictness of 'lockdown style' NPI policies that primarily restrict behavior

SOURCE: Oxford COVID-19 Government Response Tracker; WHO

Progress

Vaccines

- **9 vaccine candidates** already in portfolio
- **Broadest portfolio** across geographies & tech platforms
- **COVAX Vaccines Facility** launched (>170 countries, 70% global pop)

Therapeutics

- **1st new treatment secured** for LMICs (Dexamethasone)
- Key novel **drugs under evaluation**

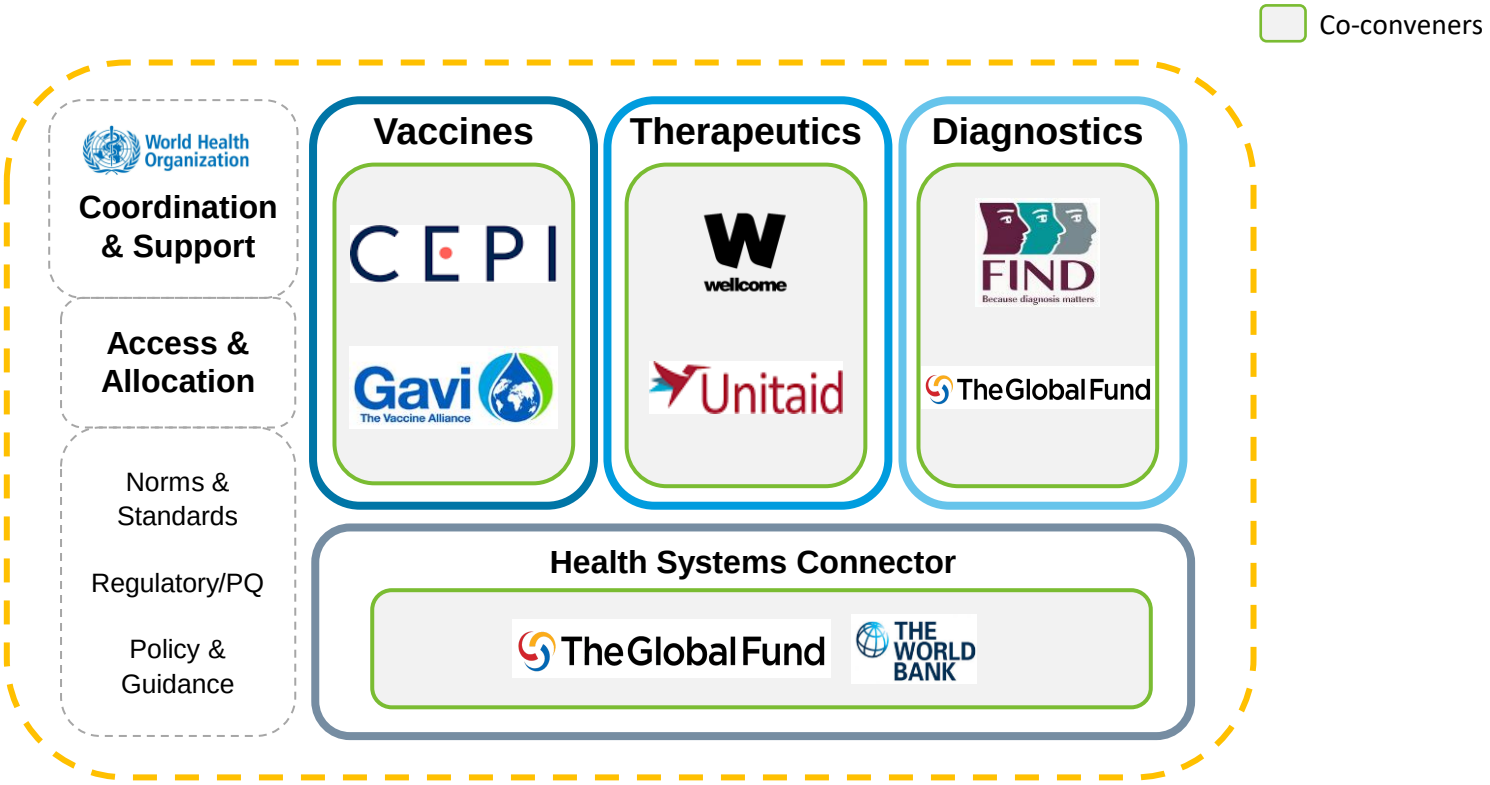
Diagnostics

- **50+ test kits** under evaluation
- **10+ million kits** procured (with Dx consortium)
- Promising **rapid Antigen diagnostic** test(s) identified

Allocation

- **Equitable Access Principles** agreed
- **Draft Allocation Framework** issued for consultation

Partnership



Key success factors: deep engagement of Principals, integrated workplans & budgets, leveraging the best of each agency

Therapeutics Pillar progress

1

Monitored 1,700 clinical trials
~200 actionable readouts
25-30 priority assets

2

Invested $175M+ to address critical Research & Development needs

3

Developed Target Product Profiles to guide therapeutic development

4

Developed tools and approach to be ready to make anticipated investments

5

Identify interventions for affordability, access and regulatory for priority assets

6

Secured add. supply of Dexamethasone for LMICs in less than 20 days to cover 25-50% needs

Rapid evidence assessment

Aim: To conduct rapid evidence assessment of candidates

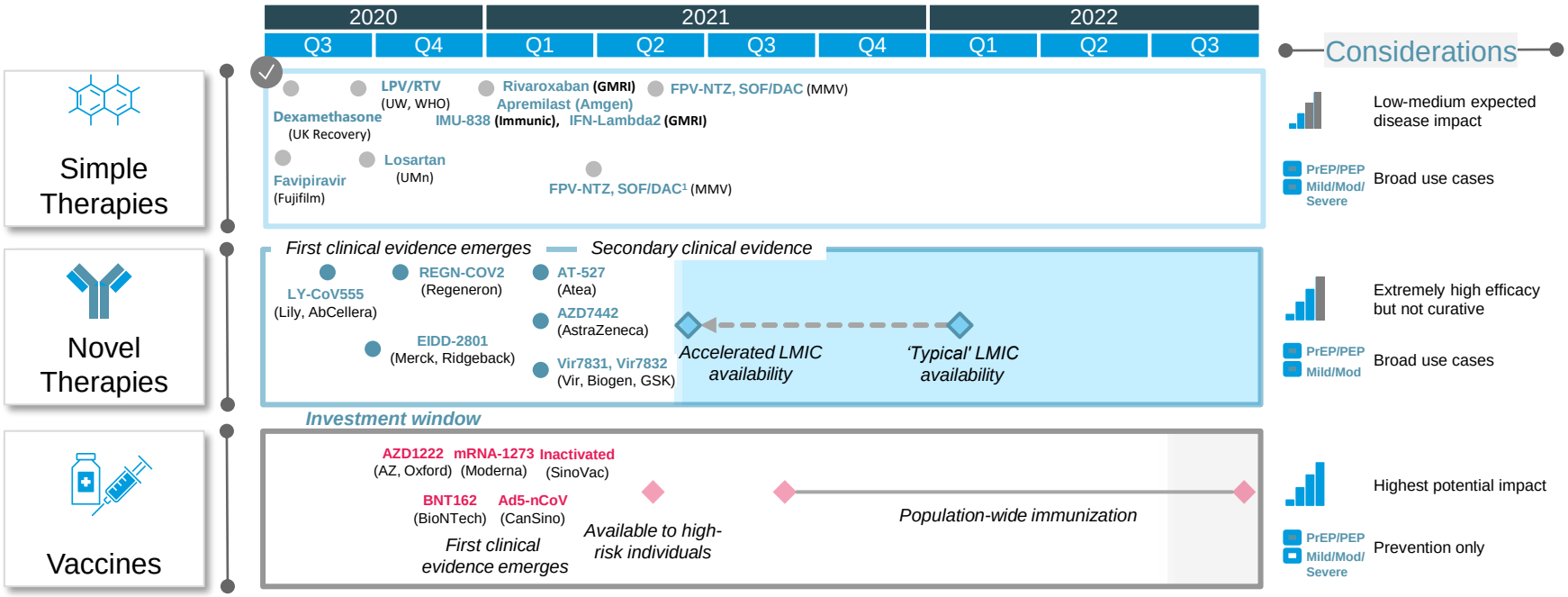
Core deliverables

- R&D progress for each candidate
- Validation of candidate list
- Identified suppliers

Current pipeline of therapies and articulation with Vx

Dynamic view as of August 25th

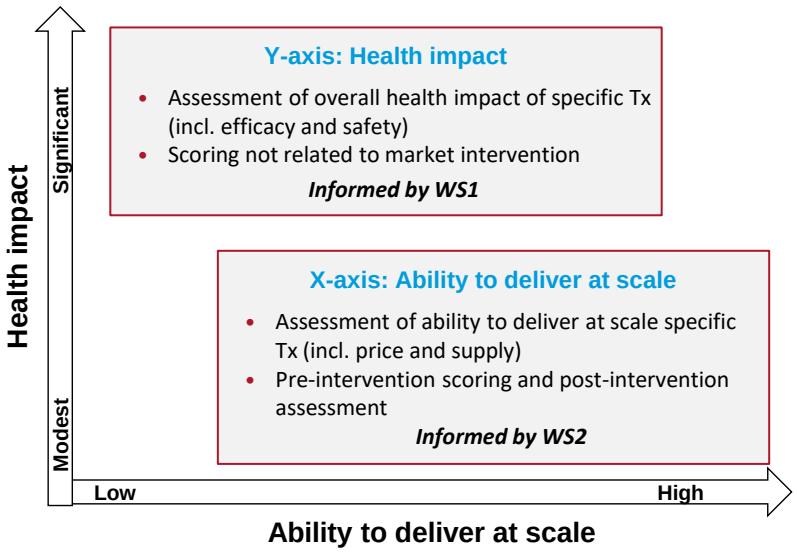
High-level pipeline of key clinical trials readouts and availability



Abbreviations: LPV/RTV: Lopinavir / Ritonavir FPV: Favipiravir; SOF/DAC: Sofosbuvir/Daclatasvir

Candidates are prioritized according to health impact and ability to be delivered at scale

The Tx candidates prioritization matrix evaluates health impact and ability to deliver at scale with …



Y-axis: Health impact

- Assessment of overall health impact of specific Tx (incl. efficacy and safety)
- Scoring not related to market intervention

Informed by WS1

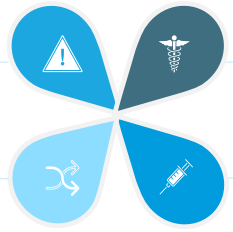
X-axis: Ability to deliver at scale

- Assessment of ability to deliver at scale specific Tx (incl. price and supply)
- Pre-intervention scoring and post-intervention assessment

Informed by WS2

… a Y-axis (health impact) scoring along 4 dimensions

Scoring (from 0 to 8)[1]



Safety
(-5 to +1 pts)

Clinical efficacy
(0 to +5 pts)

Drug-drug interactions & contra-indications
(-1 to +1 pts)

Formulation & administration
(-1 to +1 pts)

… and a X-axis (ability to deliver at scale) scoring along 5 dimensions

Pre-intervention scoring (from 0 to 10)

Regulatory status[2]
(0 to +1.5pts)

Intellectual property[2]
(0 to +1.5pts)

Supply capacity
(0 to +3)

Price
(0 to +3)

Ease of distribution
(0 to +1)

Post-intervention assessment (arrows)

High-level assessment of capacity to improve ability to deliver at scale after interventions on **IP / Regulatory status / Supply capacity / Price**

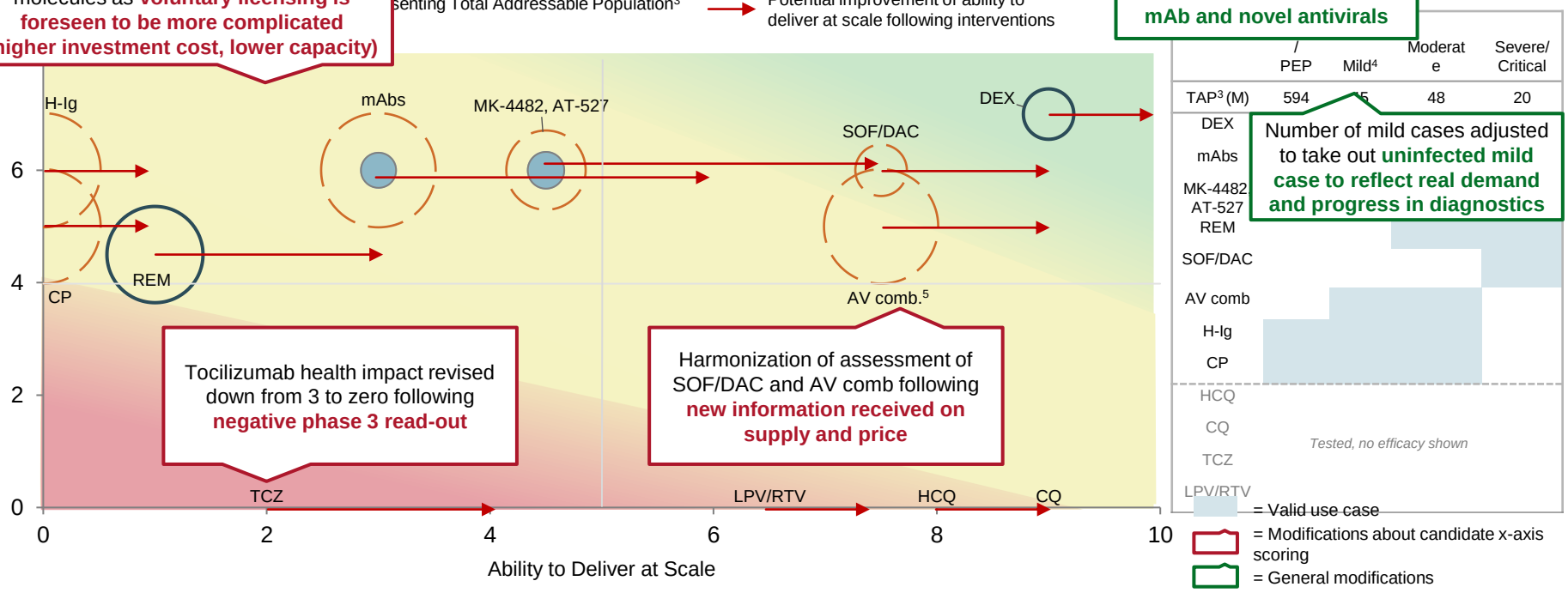
1. Any score below zero for health impact set at zero 2. The total potential score of regulatory status and IP is considered to have the same weight as pricing and supply capacity

Priority candidates are identified by health impact and ability to be delivered at scale

Dynamic view as of August 31st

mAb ability to deliver at scale post-intervention revised down vs. small molecules as **voluntary licensing is foreseen to be more complicated (higher investment cost, lower capacity)**

Potential estimated need met added to **reflect potential effect of intervention on mAb and novel antivirals**

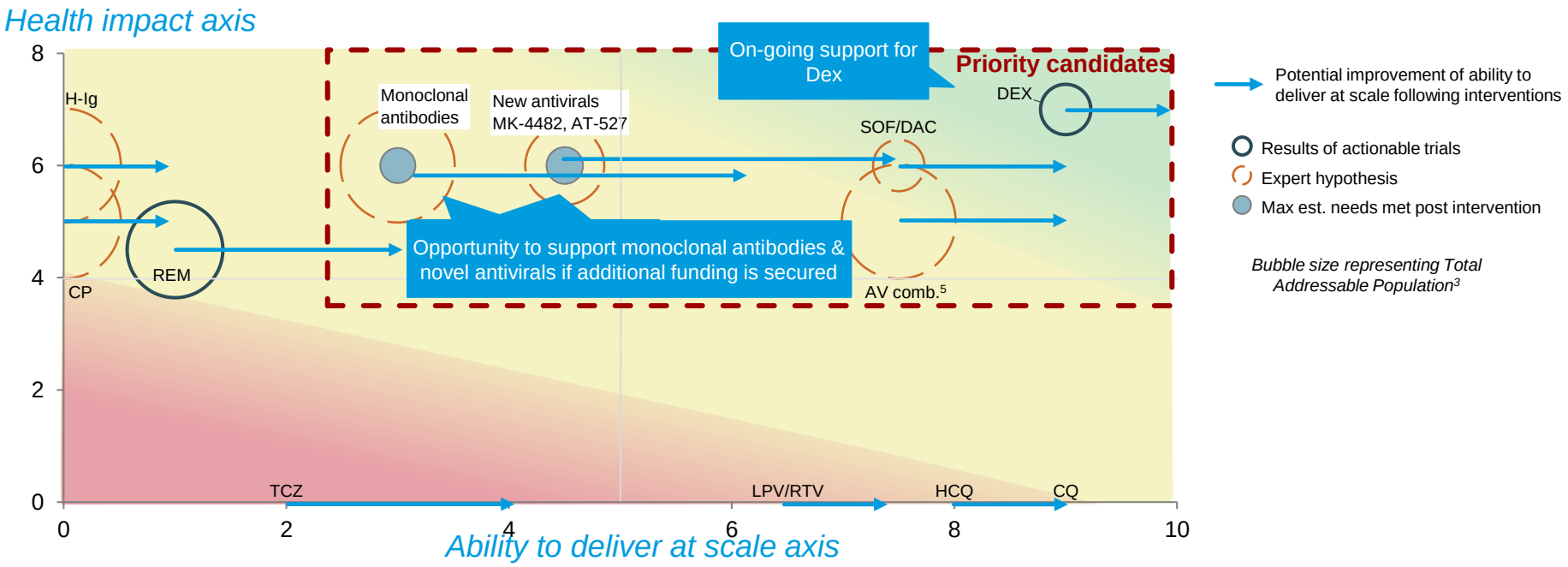


Abbreviations: **AV comb**: Antiviral combinations (includes Atazanavir/Ritonavir, Favipiravir, Nitazoxanide); **CP**: Convalescent Plasma; **CQ**: Chloroquine; **DEX**: Dexamethasone; **LPV/RTV**: Lopinavir/Ritonavir; **mAbs**: monoclonal Antibodies (includes REGN-COV2, LY-CoV555 and Astra Zeneca); **HCQ**: Hydroxychloroquine; **H-Ig:** Hyper-Immunoglobulin; **REM**: Remdesivir; **SOF/DAC**: Sofosbuvir/Daclatasvir; **TCZ**: Tocilizumab

Notes: Health impact score intended to inform ACT-A partnership prioritization of R&D and market preparedness interventions. Scoring is written for applicability to specific use cases of interest (PrEP, PEP, mild, moderate, severe) in LMIC settings, and will be updated to reflect latest standard of care

Priority candidates are identified by health impact and ability to be delivered at scale

Dynamic view as of August 25th



1. Actionable trials defined by ICMRA as randomized, Ph2/Ph3 or beyond trials with >250 enrollees per arm. 2. Expert hypothesis derived from consensus from technical experts based on results from non-actionable trials and analysis of mechanisms of action. 3.Total Addressable Population estimates treatment courses in LICs, LMICs, and UMICs excluding China; source: ACT-A Therapeutics Investment Case; BCG analysis. 4. assumes widespread availability of testing so treatments predominantly go to patients with confirmed infection. 5. Individual pre-intervention scoring of Nitazoxanide and Atazanavir/Ritonavir is +8.5 and Favipiravir +6.5

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Market preparedness

Aim: *To coordinate rapid allocation, deployment and scale up of recommended and quality assured therapeutics to support the COVID-19 response in LMIC.*

Core deliverables

- Allocation models
- Consolidated demand capture for supply constrained products
- Regular communication on status of consolidated demand, allocation and supply of supply constrained products
- Product-based deployment plans
- Quality assurance
- Coordinated procurement mechanism
- Supplier (existing and emerging) engagement management
- Delivery of products to countries and partners at scale and where applicable, in country distribution

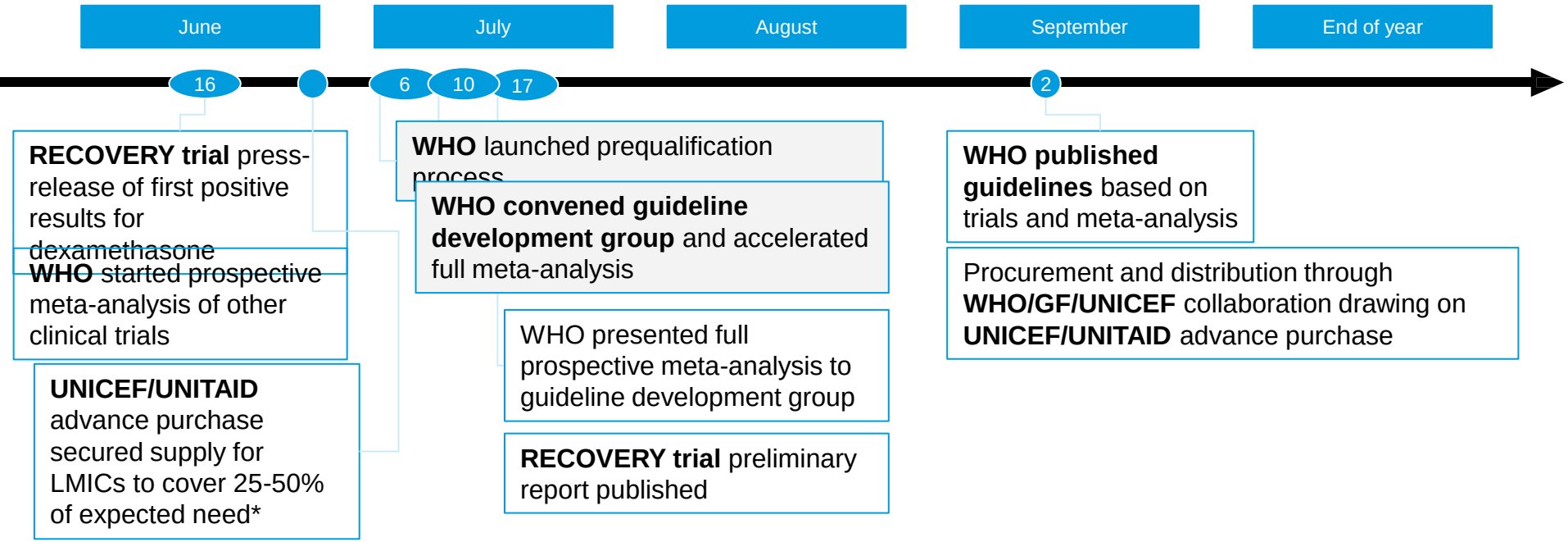
Market preparedness

- WHO clinical guidance (i.e. Corticosteroids);
- Ensure that all partners are included in the demand discussion (PAHO, UNICEF, GF, UNITAID, UNDP, WHO);
- Partners coordination to set up allocation plan for targeted products and further deployment (mainly from WHO Dubai and UNICEF warehouses)
- Discussion on forecast model;
- Learning from the diagnostics platform would be helpful for the therapeutics roll out
- Ensure regulatory convergence

WHO defines regulatory requirements, conducts evaluation processes and develops normative and standard-setting products for Tx

	Regulatory	Normative and standard setting
Objective	Support to countries for access to quality, safe and effective therapeutics in a timely manner through alignment of regulatory requirements and the use of reliance and collaboration in evaluation processes.	Support to countries through the provision of evidence-based recommendations for clinical practice or public health policy to achieve the best health outcomes possible.
Examples of key processes / tools	• Prequalification (PQ) • EUL (Emergency Use Listing) • Support to countries for regulatory pathways • Support to countries for oversight of safety, efficacy, and quality	• Ethics guidelines • Clinical guidance for COVID-19 including Living Guidance and rapid or interim guidelines • EML (Essential Medicines List)

Dexamethasone / corticosteroids – high-level status update



* Estimated volumes and % of need based on preliminary modelling and expectations for dexa use: 4.5m total over 6 months (3.4m severe, 1.1m critical). For planning, assumed 1/3 severe cases would be treated with injectable, 2/3 severe cases with oral; all critical cases with injectable. Actual volumes purchased a function of terms secured. As of 25 Aug 2020, approx. 2.9m treatment courses pre-ordered, delivery Aug 2020 through Mar 2021 (i.e., 33% of 12-month need based on initial modelling).

mAbs and novel antivirals - ACT-A seeking to invest for manufacturing capacity reservations and volume guarantees

Problem

Monoclonal antibodies and novel antivirals are expected to be the **most promising novel therapeutic** options but **we must act quickly and decisively** to accelerate global availability: **manufacturing capacity** for these treatment modalities is **scarce** and competition is fierce

Solution

ACT-A can reserve product-agnostic **manufacturing capacity and secure volume guarantees** to provide **affordable treatments** to **low and middle income countries** in 2021 and 2022

Impact

A first step to realize **rapid global and equitable access** to **cost-effective** treatment options for outpatients.

Ask

The Therapeutics Partnership needs **~$485mm in funding**, with funds set to be allocated to **Unitaid and UNICEF**, based on their comparative advantage to execute the interventions

The Global Allocation Framework builds on overarching principles and informs allocation mechanisms

A

Overarching principles for access

Global principles to ensure fair and equitable access to products

Presented in May 2020

B

Global Allocation Framework

A global Allocation Framework for all COVID-19 products

Final working draft shared on 9 August 2020

C

Fair and equitable Allocation Mechanisms

Mechanisms tailored for each product

Vx: finalized

Tx: Initial view Mid Oct 2020

Overarching principles to ensure equitable access to health products in the context of COVID-19

Solidarity: Joining forces to confront this unique challenge together and overcome this pandemic

Accountability: Clearly defined roles and responsibilities to ensure procedural justice

Transparency: To build and maintain trust

Responsiveness to public health needs: Health products are carefully selected and allocated to address the public health need

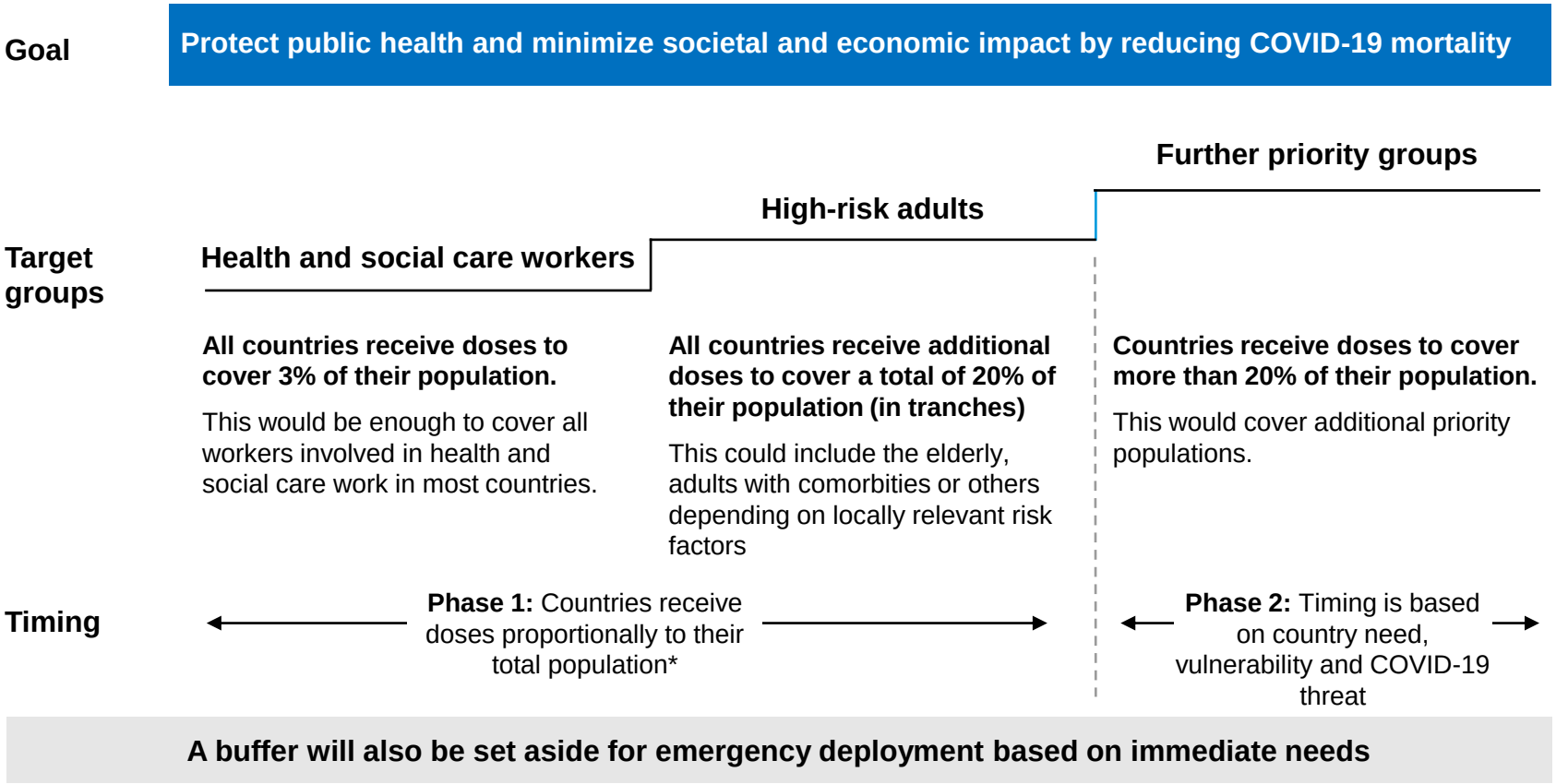
Equity and fairness: to inform the allocation process together with public health needs

Affordability: Consideration is given to pricing and procurement strategies to improve affordability of health products

Collaboration: Collaborative efforts amongst relevant global and national stakeholders is enhanced to accelerate and scale-up the response

Regulatory and procurement efficiency: Agile and comprehensive regulatory and procurement approaches are incorporated to improve timely access to safe, efficacious and quality health products for all countries in need

The Allocation Mechanism for Vaccines



*The fundamental principle applies that all countries receive doses at the same rate to the extent possible, notwithstanding likely practical limitations to be further worked out (e.g. minimum delivery volumes)

The initial thinking about allocation of therapeutics

Parameters to consider to define whether an allocation mechanism is needed

Intended Use	Setting	Type of Molecule	Time in the market	IP barriers
Secondary prophylaxis	Community/First level of care	Small	New	IP barriers
Reduce severity	Secondary/low complexity	Biological	Repurposed	No IP barriers
Reduce mortality	ICU			

Examplo 1: Dexamethasone

=> An allocation mechanism is not be needed

Intended Use	Setting	Type of Molecule	Time in the market	IP barriers	Strategy
Secondary prophylaxis	Community	**Small**	New	IP barriers	• **Reserved for severe cases: Quantification based on a small percentage of all COVID-19 cases** • **Suitable for High/low capacity settings: allocation across all countries** • **Small molecule: easy to scale up and local manufacturing, national, regional and global approach** • **Repurposed medicines: well known safety profiles and well established supply chain and other life cycle considerations should lessen concern for active PV and reporting** • **Not having IP barriers should facilitate affordability using market strategies**
Reduce Morbidity	Secondary/low complexity	Biological	**Repurposed**	**No IP barriers**	
Reduce mortality	**ICU**				

Examplo 2: Monoclonal Anti-bodies

=> An allocation mechanism may be needed

Intended Use	Setting	Type of Molecule	Time in the market	IP barriers	Strategy
Secondary prophylaxis	Community	Small	**New**	**IP barriers**	• **Reserved for severe/high risk cases: Quantification based on a small percentage of all COVID-19 cases** • **Suitable for complex care settings: allocation across all countries would require technical cooperation to increase capacity, monitor absorption capacity including cold chain** • **Biological: not easily to scale up, few countries with local manufacturing. Regional and global approach rather than national** • **New medicines: uncertainties on safety profiles and not established supply chain and other life cycle considerations. Requires appropriate PV and reporting after EU authorization** • **IP barriers may pose affordability barriers: pharma industry active engagement is a must**
Reduce Morbidity ?	Secondary/low complexity	**Biological**	Repurposed	No IP barriers	
Reduce Mortality ?	**ICU**				

Role of LMIC manufacturers

- COVID-19 pandemic has shown:
  - an insufficiency of the global manufacturing capacity and vulnerabilities in global supply chains
  - Countries who rely mostly on importation of medical products would be at risk for a lack of access to quality medical products
  - Market is different – countries that produce and those who do not procue
- Technology transfer can build capacity for production with quality takes time
- Quality assurance with local product can be a challenge – NRA and GMP

Need of a strong global coalition of generic manufacturers

Obrigada

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*These slides reflect the work of the ACT-A partners, in particular the Therapeutics pillar, co-led by UNITAID and Welcome Trust. Some of this information reflects the status quo at the date of the presentation or the date it was collected.