Novel business models for accessible monoclonal antibodies for infectious diseases in low- and middle-income countries:
Recommendations from a multistakeholder meeting convened by IAVI, Unitaid, the Medicines Patent Pool, and Wellcome

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Monoclonal antibodies (mAbs) represent one of the most important medical innovations in modern pharmacology. They have become the standard of care for many cancers and autoimmune diseases in high-income countries and show considerable promise in the treatment and prevention of many infectious diseases, having a unique and complementary role with vaccines and small molecules across a range of use-cases. However, mAbs represent a relatively new technology with unique challenges. There is enormous global inequity in access to monoclonal antibodies, and a need for investment in novel strategies to address these inequities. Additionally, while mAbs have promise to prevent and treat infectious diseases – with recently approved mAbs for the prevention of respiratory syncytial virus (RSV) and promising mAbs for malaria and HIV in the pipeline – the current development pipeline remains insufficient. Of the first 100 antibody-based drugs approved in the US, 41 were for cancer treatment alone, a key public health priority, but only 7 were for any infectious disease (ID).[1]

Whilst R&D investment in ID mAbs has increased each year since 2016,[2] it has largely been focused on developing biodefense and outbreak pathogen products for stockpiling and use in high-income countries, which has not yielded broader access to innovations in highly endemic areas.[3] There has been limited investment in mAbs product development and optimization for use in low-resource settings, e.g., through yield optimization or lower dose/lower cost methods of administration. Market and policy barriers currently limit LMICs' access to existing mAbs for infectious diseases (ID mAbs) and further restrict the investment in developing new ID mAbs that target diseases of critical importance in LMICs. Challenges include a lack of coordinated end-to-end financing, as well as technical, manufacturing, regulatory, and implementation issues:

- The insufficient pipeline for ID mAbs reflects a lack of commercial incentives to invest in mAbs R&D and optimization for LMIC use.[4]
- The number of manufacturers globally, overall manufacturing capacity, and market competition is lower for biologics than for small-molecule medicines, given the market for mAbs is less mature and due to the increased complexity of manufacturing mAbs compared to small molecules.
- Manufacturing for mAbs is currently costlier than the manufacture of small-molecules, affecting how low prices can drop, even in a competitive marketplace.[4]
- Costs of manufacturing mAbs is affected by access and affordability of raw materials needed to make and purify antibodies (e.g. fetal bovine serum and protein A)
- Gaining regulatory approval for biosimilars is more complex than for small-molecule generics, mainly due to the historical requirement for comparative clinical trials and the limited experience of regulators with review of mAbs regulatory dossiers in many resource-limited settings.[5]
- Very few mAbs are included in donor and public sector financing and procurement platforms, limiting the ability to scale up mAbs access in resource-limited settings.
- Some inherent properties of mAb products (e.g., low-temperature storage requirements) can present challenges in resource-limited settings.

These issues must be urgently addressed to ensure the development of ID mAbs and their equitable access in LMICs.[4] In March 2023, IAVI, Unitaid, the Medicines Patent Pool, and Wellcome[A] – convened a consultation to explore novel business models to enable equitable access to mAbs in low- and middle-income countries (LMICs). The two-day meeting brought together over 100 participants (Annex 1) from diverse regions and fields, spanning scientific experts, biologics manufacturers, product developers, policy experts, global health funders, regulators, civil society organisations, and community representatives.

Consultation objectives and outputs

The objective of the consultation was to generate momentum and identify innovative partnership strategies for sustainable, affordable business models to improve access to ID mAbs in LMICs.

The intended outputs of the consultation were:

- Recommendations on viable and sustainable business model approaches for access to ID mAbs in LMICs
- Identification of priority interventions and enablers (voluntary licensing, market-shaping, de-risking incentives) to support innovative business models
- Cultivating strategic opportunities for novel business model partnerships and synergies

Disease and market archetypes

Different disease archetypes face different combinations of R&D, market, and access challenges and opportunities. Successful approaches to develop and supply mAbs to LMICs (viable "business models") may need to be tailored to address different market challenges. In order to guide discussions regarding relevant business models, the meeting conceptualized the different diseases, products, and market combinations in the following three groups:

- **Emerging and re-emerging infectious diseases** (EIDs), with a regional focus or pandemic potential and unpredictable demand, including Ebola virus and "Disease X" (unknown future pathogen)
- **Infectious diseases with burden predominating in LMICs**, including malaria, dengue, and rabies
- **Infectious diseases with significant burden in HICs and LMICs**, including RSV and HIV ("dual" market archetype)

Additionally, we considered a potential novel business model that could take a portfolio approach to addressing different disease and market combinations.

Box. Case studies of innovation in ID mAbs

Monoclonal antibodies for the prevention of malaria

Several mAbs are in development for use as malaria prophylaxis. All mAbs currently in development target the circumsporozoite protein (CSP), which is required for sporozoite entry into liver cells, in effect blocking the onwards spread of the disease (CSP is also the target of the approved WHO-recommended RTS,S/AS01 vaccine).[6,7] Candidates are in

[A] With funding support by Unitaid, Wellcome, the Bill & Melinda Gates Foundation and Medicines Patent Pool.

preclinical, Phase I, and Phase II development.[6–8] As one example, the L9LS mAb being developed by the US National Institute of Allergy and Infectious Diseases with additional funding from the Bill & Melinda Gates Foundation, demonstrated 88% protection against controlled human malaria infection in a Phase I trial. L9LS is delivered by a single subcutaneous injection, with pharmacokinetic modelling suggesting that protection could last for 6 months. Additionally, the Phase I results suggested that a dose as low as 1mg/kg could deliver a high level of protection.[7] Crucially for the context of developing sustainable business models, this low dose (potentially 20mg for a 20-kilogram 5-year-old child, once every 6 months) could enable relatively low cost of manufacture. Other candidates are in development.

Monoclonal antibodies for the treatment and prevention of respiratory syncytial virus

Respiratory syncytial virus (RSV) caused an estimated 101,400 deaths in children under 5 in 2019.[9] Palivizumab, first approved in 1998 is recommended for use in the first 1-2 years of life in infants at particularly high risk of severe RSV, mainly those born prematurely.[10] In key clinical trials, palivizumab reduced hospitalization rates by 55% compared to placebo, among children with prematurity or bronchopulmonary dysplasia, and reduced hospitalization days by 45% in children with congenital heart disease.[11,12] Palivizumab is administered as once-monthly injections during the RSV season, generally meaning 4-5 injections per season.

The high pricing of palivizumab, as well as lack of registration in some countries with high RSV incidence, such as China and Nigeria, currently limits access in LMICs.[4] The public-private partnership between Utrecht Centre for Affordable Biotherapeutics (UCAB), mAbxience, and WHO is developing a biosimilar that is expected to be 20 times less expensive (US$250 for five doses), and some manufacturers are targeting a price of US$5 per dose.[4]

Newer mAbs with improve product profiles for RSV prophylaxis have also entered the market. Nirsevimab (AstraZeneca), approved by the EMA in 2022 and the FDA in 2023, is a single-dose long-acting treatment that can provide seasonal protection against RSV and is being rolled out broadly in the US and EU.[13,14] Other candidates are in clinical development. Merck is advancing Phase 2b/3 clinical development of clesrovimab for prevention of RSV in infants and RSM01 is being developed by the Bill & Melinda Gates Medical Research Institute (GMRI).[15] GMRI have completed a Phase 1 trial in healthy adults and are now looking for partners to co-develop RSM01.

It is also worth noting that a vaccine for maternal RSV vaccination (conferring protection to the newborn) has recently been approved.[16] The comparative cost-effectiveness, use cases, and preferences between maternal vaccination and prophylactic injectable mAbs will need to be evaluated.[17]

bnAbs for the prevention of peri- and post-natal HIV transmission

Broadly neutralizing antibodies (bnAbs) are antibodies that neutralize a wide range of different HIV-1 strains. bnAbs were originally isolated from people living with HIV and are now being investigated for use in HIV prevention and treatment.[18]

Numerous bnAbs for HIV prevention are being developed for adult and infant indications.[19] In particular, in the global health context, bnAbs have attracted interest for their potential as long-acting prevention for infants at risk of being infected with HIV,[20] a population for which there is a clear need for new prevention tools: There were 130,000 new HIV

infections in children in 2022[21] and over 70% of new infections among children arose from scenarios where the HIV prevention cascade wasn't fully delivered.[22]

bnAbs offer a range of advantages for the prevention of post and perinatal transmission.[23] Data from Phase 1 studies of multiple bnAbs suggest good safety and pharmacokinetics in infants, and infant macaque models suggest promising potential use both in prevention and post-exposure.[24,25] Due to most infant transmission occurring during the perinatal and breastfeeding period, a short-term preventive intervention could have life-long benefits. It is anticipated that HIV bnAbs will take the form of a long-acting injection, mitigating challenges with adherence compared to daily oral alternatives, and potentially facilitating integration into the standard vaccine schedule (WHO Expanded Program on Immunization). Modeling suggests bnAb prophylaxis for up to 18 months in infants known to be HIV-exposed at birth could reduce vertical HIV transmission by up to 42% relative to the standard of care alone depending on the setting, and would be cost effective.[26] With over 1.2 million newborns exposed to HIV each year, effective bnAbs for prevention of peri- and post-natal transmission would potentially have significant demand volume and significant potential health impact.[21]

Key questions and considerations for addressing the mAbs access challenges

The meeting considered key questions that will need to be answered to drive forward access to mAbs:

- What are promising access mechanisms, business models, partnerships opportunities, and enabling elements required to improve access to mAbs? How can we build and sustain effective end-to-end partnerships and political will to take this work forward?
- How do business models need to be adapted across market challenges for different disease contexts: mAbs for emerging infectious diseases with a regional focus or pandemic potential but unpredictable demand, mAbs primarily for LMIC markets, and 'dual market' mAbs for diseases with high prevalence in both HICs and LMICs?
- How can health systems be supported to implement broader use of mAbs?
- How can innovations in manufacturing technology be harnessed to lower the cost of producing mAbs, make production easier to scale and to expand to other geographies? What incentives can encourage manufacturers to adopt these innovations?
- What are industry and product developer perspectives on key barriers and enablers for affordable access to both currently marketed and novel mAbs in LMICs?
- How can industry be incentivised to develop and broadly commercialize ID mAbs for which the main market is in LMICs or to commercialize dual market mAbs in LMICs?
- What can be learned from the non-communicable disease (NCD) space in terms of access strategies?
- What role could LMIC-based mAb manufacturing play in increasing mAb access and meeting current and future domestic and regional market demand for ID mAbs of local relevance? What is required to advance capacity strengthening, technology transfer, and voluntary licensing for biosimilar development and manufacturing or mAbs regionally? Are there specific business models that could be used to sustain access to a portfolio of regionally manufactured mAbs of local relevance?
- What are the strategies, including but not limited to voluntary licensing, for intellectual property management that are compatible with global access to mAbs?

As more mAbs are developed for IDs with product profiles suitable for use in LMICs and novel business models which render them accessible, there is an opportunity to change the paradigm for access to mAbs for all indications, including for NCDs, for which access to mAbs is currently very limited.

Dismissing the need for expanded access to mAbs as an insurmountable challenge is not acceptable and does a disservice to the global communities who bear a disproportionate disease burden but currently face access barriers. As with the scale up of antiretroviral therapy for HIV treatment, pathfinders may be needed to provide proof of concept for the viability of sustainable access to life-saving commodities in resource-limited settings. Models that are successful in delivering a specific infectious disease mAb could provide a roadmap for working towards affordable mAbs for other indications. Embedding access considerations during the initial stages of product development is crucial but not sufficient. There is a vital need to define the models that will support mAbs reaching global market authorisation, implementation, and adoption for treating and preventing infectious diseases. Since the return on investment may not be immediate, global health actors may need to move forward with tackling this challenge "at risk".

The points below represent initial recommendations and proposals based on the key takeaways of the consultation's wide-ranging discussions. While they do not reflect commitments from the consultation co-convenors, they are intended as a starting point to guide more concrete discussions and action planning by a broader, global community of stakeholders. As a complement to this report, a manuscript summarizing key takeaways will be submitted for publication in a peer-reviewed journal.

Recommendations and proposals

An overview of the different disease archetypes, and the challenges and possible innovative business models for each, is provided in the Table 1. Detailed recommendations and proposals emerging from the consultation are categorized under four broad headings: 1) Partnerships & financing for innovation and optimization of mAbs for LMIC needs; 2) Intellectual property, voluntary licensing, and technology transfer[B]; 3) Regulatory pathways and strategies to facilitate mAbs availability; and 4) Market shaping, de-risking, and demand creation.

[B] Voluntary licensing is a mechanism for increasing access to a medicine, wherein patent-holders allow additional manufacturers to produce and sell generic or biosimilar versions of patented medicines in defined territories for specified uses, before patent expiry, through contractual agreements with such manufacturers. Technology transfer is a process wherein one drug manufacturer provides to another manufacturer documentation and process know-how, including expert human resources, training, and the physical transfer the needed cell lines, plasmids, and other necessary material.

Table 1: Market challenges and potential business models for ID mAbs, in different infectious disease contexts

ID -market archetype	Example indications	Market challenges	Potential business models for increasing R&D	Potential business models for increasing access	Cross-cutting enablers
1. Emerging and re-emerging infectious diseases (EID)	Ebola virus Disease X (unknown future pathogen of pandemic potential)	• Unpredictable needs, often limited commercial markets and low volumes, except in the case of pandemics • National/regional outbreak responses generally driven by governments and humanitarian organizations • In some cases, may need to be stockpiled, for example, in a pandemic preparedness context, but access to stockpiled products is often not equitable • May need to rapidly deploy to low-resource settings, including for outbreak response	• Dual use as medical countermeasures (MCM) to unlock additional resources to incentivize R&D • Public sector/philanthropic funding to develop platform technologies that have both commercial, non-commercial/EID indications • Developing and stockpiling 'libraries' of promising investigational mAbs that have been taken through Phase 1, available for partners to rapidly advance through development as outbreaks emerge	• Public sector, end-to-end investment model to support mAbs access created • Investment in modular/decentralized manufacturing strategies that can meet regional needs • HIC subsidies or 'subscription' mechanisms that fund development/manufacturing of EID agents • Establishing manufacturing capacity to meet regular demand in LMICs and surge capacity to address outbreaks or biological security threats • Stockpiling	• Coordination among funders and other stakeholders to ensure end-to-end financing for new ID mAbs and find effective synergies and partnerships • Identification of 'champions' among governments, agencies, and funders • Identification of potential trailblazer mAbs, in alignment with priorities and preferences from affected communities and regions • Early-stage investments in product and manufacturing process optimization to support LMIC-friendly TPPs and affordability • Supporting both early- and late-stage coordinated clinical trial platforms in LMICs that can provide necessary evidence in affected communities, including in pandemics • Access considered early in the R&D process; access conditions tied to financing and collaboration models • End-to-end, stage-gated 'push' (grant) funding, and innovative 'pull' funding mechanisms such
2. Infectious diseases with high burden predominating in LMICs	Malaria Dengue fever Chikungunya	• Limited or no commercial market in UMICs/HICs • Large potential user population but concentrated in resource-limited settings • At scale, demand could outweigh supply capacity	• Criteria-based economic incentives for developers to optimize product profile and manufacturing process (e.g. market entry rewards or advance purchase agreements with volume guarantees)	• Grants and other funding conditional on inclusion of access provisions • Technology transfer to enable biosimilar manufacture for LMIC markets • Clear financing mechanism and market-shaping roadmap before start of Phase 3.	

		• Without optimization, Cost of Goods (COGS) may dictate a pricing floor that is unaffordable in LMICs			as advanced market commitments or market entry rewards • Product development partnership models (particularly for innovator products) • Voluntary licensing and technology transfer, where needed, and complementary access incentives and policies (such as use of TRIPS flexibilities) to enable biosimilar manufacture for LMIC markets • Advances in efficient and harmonized regulatory approaches • Procurement approaches that pool demand and decrease risk for manufacturers • Market-shaping mechanisms to stabilize demand and supply dynamics, such as advanced market commitments • High-quality demand forecasts based on key stakeholder consensus, incorporating market-shaping signals • Inclusive and needs-based approach • Awareness raising, community engagement, mAb health literacy, and advocacy to garner political will and support integration of mAbs into existing
3. Infectious diseases with "dual markets" (significant burden in HICs and LMICs)	RSV HIV Pathogens prone to antimicrobial resistance, e.g., pathogens causing neonatal sepsis COVID-19	• Significant commercial market in HICs, but HIC pricing unaffordable in LMICs, limiting access • Limited registration of originator mAbs in LMICs • mAbs not integrated into national insurance schemes or public sector financing in LMICs	• Grants or incentives for developing LMIC-adapted versions of products, where needed • Additional business models from archetypes 1 and 2 may be relevant to leverage based on the specific disease profile.	• Establishing a biosimilar market through voluntary licensing and technology transfer • Market segmentation through tiered pricing or 'second brands' • Additional business models from archetypes 1 and 2 may be relevant to leverage based on the specific disease profile.	

					financing and procurement mechanisms
Portfolio approach	Combined strategy to improve access to a selection of mAbs across the three categories above, possibly also adding a mAb for NCD treatment.	• Maintenance of manufacturing suites is very expensive. A consistent pipeline is needed to sustain production capacity. To enable production for smaller markets, a portfolio approach might provide a viable solution.	• 3-6 mAbs selected, as defined by regional or global priorities, to represent a mix of product types (including mAbs for established infectious diseases with high burden of disease/high expected volumes [groups 2/3]), mAbs for emerging infectious diseases with niche markets/low volumes and high uncertainty as those targeting potential pandemics (group 1), together with mAbs for non-communicable diseases. • Some of the mAbs in the portfolio included partially on the basis of having an established commercial market and stable demand for the product, which could thus provide a reliable income stream and potentially cross-subsidise manufacture of other products in the portfolio that have limited commercial markets. • Interventions such as support for technology transfer or pooled procurement initiatives to facilitate portfolio diversification and consolidate demand • Investment in production innovations to lower COGS to support affordability • Investment in modular/decentralized manufacturing strategies that can meet regional needs	

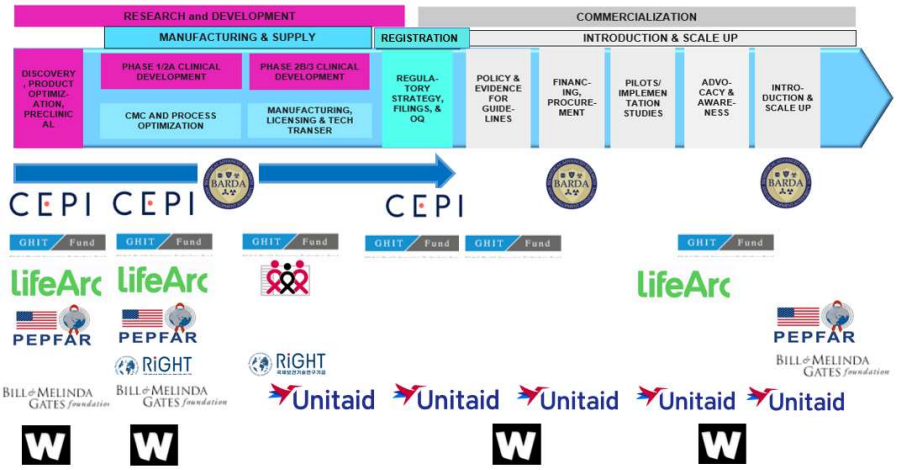
Key enablers for advancing access

Partnerships & financing for innovation and optimization of mAbs for LMIC needs

Coordination of funding

- Significant investments will initially be needed to increase R&D for ID mAbs and create mechanisms for equitable access. The financing needed can be broadly split into two categories: product-specific financing (e.g., investments in R&D, biosimilar development, and procurement) and cross-cutting financing (e.g. for regulatory system strengthening, voluntary licensing models, capacity building). Innovative financing models will be necessary and will likely require shared investments by governments, intergovernmental agencies, philanthropic foundations, and the private sector. International financial institutions may also play a role.
- Some funders may focus on upstream R&D and capacity building, while others may focus on market-shaping and providing market entry rewards or supporting procurement. Public and donor funding for mAbs product and process optimization, R&D, and technology platforms will be particularly important - with licensing, technology transfer, and access conditionalities - so that needed mAbs are widely and affordably accessible in LMICs. Incentives to support local manufacturing of mAbs should also be pursued. Coordination among relevant funders will be important to ensure 'end-to-end' financing. In some models, coordination between funders of mAbs for ID and NCDs may offer synergies, for example, in the 'portfolio' approach (Table 1). To help facilitate coordination, selected funders present at the Consultation mapped their active investments relevant to mAbs in Figure 1, below.
- A pooled funding source could offer one solution for ensuring adequate financing from discovery through to scale up and to avoid funding fragmentation, which makes seamless progression through product development to delivery difficult.

Figure 1. Active funding areas along the product development continuum (active investments of selected funders present at the Consultation only)[C]



[C] This graphic is not intended to be an exhaustive overview of currently available funding for mAbs, but rather an indicative illustration of areas along the product development continuum where a selection of funders present at the Consultation have active investments. Note that future investments in new areas that may be under consideration are not reflected.

Identification of "champions'

- The design and governance of initiatives to expand R&D and access to ID mAbs should engage with relevant communities and LMIC governments. This will be important, among other things, for R&D priority-setting, for ensuring effective plans for access, and for ensuring a long-term path to sustainability that is not reliant on donor funding.
- Initiatives will benefit significantly from having champions: this includes champion agencies, champion governments, champion funders, champion advocates, and champion products. A pilot project could be considered, focusing on one or a small number of 'champion' or trailblazer products. These pilots could aim for early impact and proof-of-concept for business models to expand access. Candidates for a 'champion' project could be ID mAbs that are already approved in HICs, such as palivizumab or nirsevimab for RSV; those in late-stage clinical development, like mAbs for malaria prophylaxis; and/or those in early development, such as bNAbs for the prevention of vertical transmission of HIV. Targeted enablers would be needed to accelerate access, depending on stage of product development.
- Prioritization of "champion" mAbs should take place through a consensus-based process bringing together communities, governments, intergovernmental agencies, and national agencies at the global, regional, and national levels. Once priorities are defined, these groups can work together in partnership to help design new financing initiatives, programmes, and partnerships to advance mAbs R&D and access.

End-to-end collaborative vision for access

- Product developers should collaborate with global health actors to develop access pathways for products. Working together, they must develop an 'access plan' for how products can be delivered affordably in LMIC health systems, strategies for ensuring timely availability, as well as consideration of the cost of goods, 'manufacturability', ease of delivery, and technology transfer early in the development and manufacturing processes. This may be especially relevant for ID mAbs that have significant HIC markets, as these mAbs may have been developed as commercial products only targeting high-income settings. An access-oriented approach should begin already in the early stages of development. As planning progresses, there should be access plans in place for each affected region.
- Organizations working on early-stage R&D for ID mAbs need a clear 'line of sight' to what financing and procurement mechanisms are available once their candidate mAb enters later stages of clinical development. High-quality demand forecasts and guarantees are key enablers. Similarly, target product profiles, such as those published by WHO for HIV, RSV, and malaria prevention mAbs,[28–30] are critical for directing R&D efforts and effective coordination of investments.
- Pharmaceutical companies and biotechnology SMEs should be encouraged to invest in the development of mAbs for infectious diseases and to collaborate with global health actors to enable equitable access. Strategies to broaden access to ID mAbs should aim to create win-win opportunities for the private sector. This will require identifying the incentives needed to bring private sector actors to invest in R&D for ID mAbs, and defining ways of collaborating that support broad LMIC access and enable transparency around manufacturing costs, drug pricing, and profit margins to make investments economically viable.

Investing in innovative research, manufacturing, and delivery approaches

- Funders, developers, and manufacturers of ID mAbs should leverage advances in technology and manufacturing strategies, which offer the prospect of lower COGS such as platforms for large scale manufacturing of mAbs in more agile manufacturing facilities,

as well as more disruptive approaches, including the use of next-generation platforms such as continuous manufacturing. Further on the horizon are alternative expression systems (e.g. manufacturing mAbs using plant expression systems or transgenic animals) and protein engineering. Optimized formulation (e.g., for improved stability such as by freeze drying, or subcutaneous formulations), and delivery strategies (e.g., nucleic acid encoded mAbs) could also improve manufacturing efficiency and lower COGS.[31] Dedicated funding may be needed to fully evaluate some of the newer manufacturing techniques.

- Decreasing the cost of manufacturing (COGS) for mAbs will be a key enabler for achieving affordable prices and expanding access and may be more important for ID mAbs for use in LMICs than for mAbs manufactured for high-income markets, where the ability to charge higher prices makes COGS relatively less important as a cost driver. Several aspects are important in reducing manufacturing costs:
    - Advances in manufacturing strategies have the potential to decrease COGS for mAbs.[32] As mentioned above, these can be divided into the nearer term possibilities of next-generation platforms and the longer-term exploratory approaches. Nevertheless, funding may be needed to support the establishment of newer, lower-cost manufacturing strategies that may carry greater risk of failure than more established approaches. Funders may need to absorb some of this risk and incentivise or subsidise the evaluation and adoption of innovative strategies that reduce COGS and invest in facilities that allow greater agility in meeting uncertain demand and switching from manufacturing one product to another. Support may also be needed for biosimilar manufacturers to switch to next-generation processes, as departure from the processes established for the reference products (originator antibodies) could pose challenges for biosimilar regulatory approvals. Regulatory authorities should anticipate the development of optimized manufacturing processes and devise regulatory standards and accelerated pathways that confirm safety, efficacy, and assured quality without creating unnecessary barriers.
    - Increasing the potency of antibodies could also reduce costs by enabling lower doses to be used and requiring smaller amounts per treatment course. In addition, such dose decreases could enable different delivery formats, for example subcutaneous delivery, moving away from infusions. Similarly, extending the circulatory half-life of the antibody can reduce costs per patient over time by reducing the overall number of doses needed.
- Platform trials could potentially support mAb development in LMICs (both biosimilars and entirely new mAbs) by sharing clinical trial costs and enabling testing in a variety of health system settings and countries, importantly including LMICs and endemic countries.[33,34] While platform trial designs have primarily been used to evaluate candidates in late-stage development, opportunities to apply platform trial approaches to earlier stages of development should also be explored. Linking platform trial sponsors to local/regional mAb biosimilar manufacturers that receive technology transfer for production could allow an ‘end-to-end’ approach to support regional access to innovations.
- mAb clinical trials should include all relevant populations, including those historically underrepresented in clinical trials, such as women, pregnant and lactating populations, elderly people, people with disabilities and co-morbidities, and children.
- In addition, necessary data for regulatory approval of regionally manufactured mAbs would be easier to collect if clinical trial capacity is reinforced in the region. Funders coordinating across the development pipeline for one disease (e.g., funding drug development projects acting on different pharmacological targets) could fund platform trials cooperatively, which would potentially enable more efficient testing of drug candidates from different projects.

- In addition, there is a need to strengthen the links between mAb discovery and clinical R&D, and between clinical development and mAb clinical supply. Synergies could be found between building LMIC capacity in ID mAb manufacturing and building regional capacity in discovery science, and research and development, both for mAbs development and for clinical research more broadly.

Tailored business models for financing ID mAbs R&D (see also Table 1)

- Investments will need to be tailored to the different market challenges for different disease and product types. A coordinated system of grants for ID mAbs for LMIC contexts would provide 'push' funding, enabling R&D to begin where catalytic investments are needed. The development of mAbs for EIDs, in particular, is likely to require 'push' funding (grants) from foundations, governments, and international funders, as the commercial market may be very limited, and, in the case of planning for 'Disease X' as part of pandemic preparedness, unpredictable by definition.
- Viable business models need not be focused purely on the commercial drivers of success, but on the public health value proposition of products. Where needed, the public and philanthropic sectors must act in a complementary role with private sector actors to ensure viable models exist to advance the development, supply and widespread access to affordable mAbs that are meet health needs in low-resource settings.
- For mAbs for EIDs and IDs with disease burdens predominately in LMICs, product development partnerships (PDPs) could help effectively bring together funders, public and private sector organizations working along the product development continuum to coordinate a pipeline of numerous mAb candidates with a rigorous focus on target product profiles designed for LMIC access. This may be especially valuable for ID mAbs that have a limited commercial market and therefore a limited incentive for R&D investments in HICs.
- While outbreaks mostly occur in LMICs, HICs may have a significant interest in the treatment and prevention of EIDs, due to the potential of outbreaks spreading to HICs and the fact that many EID pathogens are considered risks for use as bioweapons. In the US, for example, the Strategic National Stockpile maintains significant volumes of treatments for certain EIDs (e.g. treatments for Ebola, smallpox, anthrax) as medical countermeasures (MCM).[35] The need for preventive agents and treatments for these pathogens could be addressed through a business model in which HICs subsidize (or 'subscribe to') mechanisms that provide supply to meet regular demand in LMICs while offering surge capacity to rapidly respond to HIC needs.
- Innovative financing strategies will be needed to subsidize other mAbs targeting EIDs that have a narrower use case, such as Lassa fever, that has limited pandemic potential and is less likely to pose a biowarfare threat.
- Libraries of promising drug (or vaccine) candidates could be developed and stockpiled, whereby public sector or philanthropic actors take a technology through Phase 1 to be rapidly taken over Phase 2 and further development as outbreaks occur. This approach could have synergies with the platform trials approach in enabling efficient and partially 'de-risked' clinical development.

Financing mechanisms and conditionalities

- 'Pull' funding[D] could play an important role in incentivizing R&D for ID mAbs. For example, large, centrally awarded financial incentives could be explored. Advanced market commitments (AMCs), involving a large up-front purchase commitment made while a product is still in development, have been extensively utilised for vaccine procurement, but have also been subject to critiques concerning some of their impacts on innovation and markets, including deterring further R&D and product optimization, as well as hindering the advancement of subsequent, more affordably priced entrants. Market entry rewards (MERs) for indications of relevance to LMICs should only grant a large lump sum 'reward' to any developer that brings to market a product meeting a specific TPP and in exchange for meeting access conditionalities. This financing mechanism has been widely recommended to incentivise antibiotic development,[36,37] and similar instruments could be designed to incentivise the development of mAbs for infectious diseases, provided TPPs are conducive to LMIC usage. For products that are in the late stages of development by commercial entities, pull funding may help incentivize the expansion of manufacturing capacity.
- Purchasing for a stockpile, as seen in the Ebola mAbs stockpile created by US BARDA,[38] can create some supply security and represents significant 'pull' funding. However, pull mechanisms alone are insufficient to guarantee access, as is evident by the lack of access to Ebola mAbs in LMICs. Pull mechanisms must therefore be linked with binding access provisions. These could include assurance of volumes to countries in need; affordability clauses; requirements for voluntary licensing, including through the Medicines Patent Pool (MPP); technology transfer; and other means to enable a sustainable and competitive market.
- For 'dual market' mAbs, grants, 'pull' incentives, or PDPs may help increase R&D for LMIC-adapted versions. In some cases, developers may only have made plans to register and market the product in HICs. In these cases, developers should be encouraged to either register the product in LMICs and offer affordable pricing in LMICs, or to grant a voluntary licence to enable additional companies to produce and sell the product affordably in LMICs. Experience from HIV treatment has shown that a strategy of voluntary licensing with low or no royalties, was acceptable to many HIC-based developers and effective in reducing costs and expanding treatment access to low- and lower-middle income countries with significant disease burden.[16] Additional incentives may nevertheless be needed to ensure that such sharing occurs for ID mAbs. And existing licensing models may need to be adapted to be effective for mAbs (e.g., with more emphasis on elements beyond patents, such as technology transfers).[4]
- Public sector or philanthropic financing and other support for the development of mAbs for IDs should include provisions that ensure an 'open science' approach to both the development and manufacture of mAbs. This could include, for example, early open-source publishing of research results; contributing to open compound libraries, provisions requiring the voluntary licensing of relevant patents; and committing to undertaking technology transfer to LMIC manufacturers benefiting from such licensing agreements. Broad dissemination of research results; increased scientific and product development collaborations; and sharing of research platforms, product- and process-related IP, and mAb technology platforms can all accelerate the availability and affordability of mAbs across LMICs. A more inclusive and sharing R&D ecosystem could

[D] 'Pull' funding describes an economic reward that is realized once a product is approved. Examples include an advanced market commitment, where a developer is guaranteed a certain procurement volume if the developed product meets certain criteria, or a market entry reward (prize) awarded by a funder upon developing a product meeting certain criteria.

realise the public health value of mAbs by supporting a move toward novel and more equitable business models.

Intellectual property, voluntary licensing, and technology transfer

Early planning for voluntary licensing and technology transfer

- If clear and sufficient market demand exists, increasing the number of manufacturers of ID mAbs could decrease prices through competition, increase global manufacturing capacity, and increase supply security (especially key in case of abrupt onset of demand like in pandemics). Voluntary licensing can also expand product availability into geographies in which originators lack commercial footprint or interest.
- A key enabler for this would be voluntary licensing of relevant IP and technology transfer from companies developing ID mAbs to biosimilar manufacturers early on. Technology transfer can reduce the cost and timelines of biosimilar development and reduce the risk of failure. It could also significantly reduce the cost and time needed for obtaining regulatory approval, e.g. by reducing up-front investments needed for developing a manufacturing process.[5]
- Experience with voluntary licensing to date illustrates that many large pharmaceutical companies are willing to share patent rights to enable generic manufacture, especially in low and lower-middle income countries where they lack commercial markets or for the purposes of meeting corporate social responsibility aims. Private sector entities that develop and manufacture mAbs should be encouraged to work with the MPP and product development partnerships to voluntarily license products to low-cost biologics manufacturers, ideally LMIC-based, and should undertake technology transfer, including the transfer of key materials such as cell lines, to enable increased global access at affordable prices.[5]

Incentive mechanisms and conditionalities

- Additional incentives may be needed to encourage the sharing of IP and technology transfer. Strategies to encourage these actions could include monetary incentives, conditionalities (for example, as part of grants or funding contracts), and political pressure (for example, high-level advocacy).
- A monetary prize has been proposed for companies that share IP licences to improve access in LMICs.[39] Companies may have a greater reluctance to share cell lines than they have for sharing patents, given that the recombinant cell line for a particular product could be reverse-engineered for other products: Similar to vaccine adjuvants and other technologies, the host cell line and vectors may have strategic value in other aspects of those companies' portfolios. As such, additional incentives may be needed to encourage such technology transfer.
- Companies may be more inclined to undertake technology transfer on products that are not a key driver of their commercial portfolio or have particularly high unmet needs in LMICs. Small and medium-sized biotechnology organizations may also be more ready to share assets when they do not have significant sales or manufacturing capacity in LMICs, or do not have plans for commercialization in LMICs.[5]

- A 'hub-and-spoke' model[E], like the one currently employed in the mRNA Technology Transfer Programme, could be explored as a model for increasing mAbs manufacturing capacity globally. This model is particularly promising, because the partners receiving technology transfer from the hub promise to share their future innovations with each other, including with respect to process and product improvements and new disease mRNA vaccines and therapies. Relatedly, the feasibility of creating a central 'cell bank' to store validated cell lines used to manufacture certain mAbs for technology transfer should be explored to simplify cell line transfers, standardize sharing principles, and support coordination across stakeholders.
- Upper-middle-income countries (UMICs) typically face unique access barriers because they are at times not included in voluntary licenses. Some better-resourced UMICs have domestic biopharmaceutical manufacturing capacity, large domestic populations, ID burden, and health and industrial development budgets that can help create viable markets for locally made or imported (biosimilar) ID mAbs.
- Many countries have legal mechanisms that enable governments or courts to remove IP barriers to manufacturing a health product and to ensure supply availability, where needed to enable affordable and sufficient access, through compulsory licensing, provided for in the agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). However, compulsory licensing does not mandate technology transfer, and as a result, prospective biosimilar manufacturers can face considerable challenges in developing products and establishing manufacturing capacity. Additionally, a compulsory licence is limited to the country where it is issued, while voluntary licenses generally cover a large number of countries. Incentives should be created to encourage broad voluntary licensing, but compulsory licensing may be important where voluntary measures have failed and where there are pressing health needs.[40]
- More broadly, governments can support technology transfer for mAbs through legislation, policy, and financing. This approach combines health, science, and industrial policy and benefits from synergies across the three sectors. One example of this is in Brazil, where government technology transfer policy aimed at increasing local manufacturing capacity for mAbs has enabled technology transfer to public sector and local manufacturers for many key mAbs, including palivizumab, tocilizumab, trastuzumab, bevacizumab, rituximab, and adalimumab, among others.[41]

Regulatory pathways and strategies to facilitate mAbs availability

Supporting regulatory collaboration and mutual recognition

- Regulatory agencies with extensive experience in biologics, such as the FDA and EMA, together with the WHO Prequalification Programme, should support other regulators in reviewing dossiers of ID mAbs for regulatory approval. Engagement between mAb developers and regulatory agencies early in the development process allows alignment on the scientific protocol and data required to support rapid registration. Coordination between WHO policy processes and regulatory processes would be helpful to ensure that post-approval commitments are streamlined.

[E] A technology transfer hub brings together in one single place all the elements needed to establish the technology (including know-how, data, details on manufacturing processes, intellectual property, and training) and then transfers the fully validated manufacturing process to multiple secondary users. Recipients ('spokes') of technology transfer from 'hubs' would be equipped to manufacture (certain) mAbs to the highest quality standards and to enable their long-term sustainable operation by, among others, training local staff, establishing supply chains for consumables, and supporting the development of independent funding streams including through commercial sales.

- Strengthening regulatory networks with mutual recognition through mechanisms such as the African Medicines Agency, African Vaccines Regulatory Forum (AVAREF), and WHO Collaborative Registration Procedure (CRP) and can facilitate faster and broader approval of new mAbs. The WHO Prequalification of Medicines Programme and the European Medicines Agency's EU-Medicines for all procedure may provide important routes for accelerating regulatory approval of ID mAbs for use in LMICs, by working in close collaboration with a broader constellation of regional and national regulatory authorities.[42,43]
- Variation in biosimilars guidelines between countries, as well as requirements for domestic clinical trials in some countries, such as in India, pose regulatory barriers. This is especially important when numerous biosimilar manufacturers are based in these countries. Greater regulatory harmonization and discussions on the potential granting of clinical trial waivers when manufacturers use a process similar to the approved originator's process, would help in reducing these barriers.[5]
- For mAbs addressing epidemic or pandemic-prone pathogens or meeting unmet needs for priority diseases, expedited regulatory approvals (at the global, regional and national levels) should be pursued as early as possible.

Exploring novel regulatory approaches

- Greater use of pharmacodynamic markers and other non-clinical data for the 'bridging' of efficacy from a reference product may facilitate regulatory agencies' approval of biosimilars of ID mAbs , reducing costs and timelines. Experience in the use of 'immunobridging' for the approval of vaccines and to expedite new mAbs for COVID-19 against new emerging variants of concern (approval based on quantitatively comparing immune response markers in the blood between the original clinical data of an approved product and the proposed product) has provided additional momentum for these developments.[44,45]
- Given this, increasing use of *in vitro* (physicochemical) analytic techniques to support comparability of biosimilars to reference products, capacity-building and financing initiatives should ensure that relevant analytic equipment is included in their plans, including, potentially, financing and technology transfer to regional or local regulators to enable assessment of biologics.
- With the development of novel manufacturing platforms for mAbs, receptiveness among regulators towards approaches that can lower COGS will be important to allow rapid and wide adoption. Early coordination between developers and regulatory agencies will be important. Innovative regulatory incentives that could be leveraged to entice industry to take on manufacturing approaches to lower COGS and support TPP's aligned with the needs of resource-limited settings were suggested, however, further engagement with regulators and with industry to align on potential strategies would be needed.

Regulatory enablers for biosimilars

- Where there has been full technology transfer of a cell line and process for manufacturing a particular biosimilar mAb product, regulatory approaches could be developed that reduce data requirements compared to those for an entirely new biosimilar. This, in turn, would reduce costs and shorten timelines.[5]
- Biosimilar developers frequently face challenges in obtaining an originator product as an analytical comparator during manufacturing process development and for use in clinical studies to support a regulatory application,[46] and obtaining originator product for use as a comparator can make up a large proportion of biosimilar development costs.[5] Encouraging originator companies to provide, on reasonable terms, originator products for use in biosimilar testing, would help overcome this challenge. Alternatively, use of an approved biosimilar, if one exists, as the reference product instead of the originator

product could help overcome this challenge. In addition, access to reference product for biosimilar development should be included in access-oriented conditions in R&D grants.

Market shaping, de-risking, and demand creation

Market shaping and de-risking incentives

- For ID mAbs in clinical development, a roadmap for ensuring equitable access, including market shaping where relevant, should be developed from the earliest stages of R&D to help coordinate and guide developers and funders along the entire product development pathway.
- Successful business models for facilitating the development and manufacture of ID mAbs will depend on a mechanism for ensuring sufficient and dependable purchase volumes. For some products, a certain level of market demand will come from LMIC health systems undertaking normal procurement. Pooled procurement and centralized procurement similar to the models used by the Global Fund, the PAHO Strategic Fund, or UNICEF Supply Division, could be explored for ID mAbs to facilitate demand consolidation and increase bargaining power.
- For other EID mAb or an ID mAbs, demand might not be predicable or adequate to attract commercial investment. Additional market interventions may be needed to enable sustainable supply, such as advance purchase commitments with volume guarantees (which reduces the risk faced by manufacturers), donor-subsidies, or stockpiling.
- Pooled or centralized procurement approaches could help consolidate demand and facilitate broad geographic availability, particularly for small-volume mAbs. Pooled procurement strategies could be combined with the 'portfolio' approach described, and both could be facilitated by capacity strengthening investments. For example, a portfolio of 3-6 prioritized mAbs could receive focused funding for expanding manufacturing capacity (if and where required) and be the focus of a pooled procurement mechanism, whereby numerous countries with relevant health needs pool demand to procure the mAbs in the portfolio. This model would be most relevant if entirely new mAbs manufacturing facilities were being created, for example, to build regional manufacturing capacity.

Demand creation and forecasting

- Detailed LMIC market intelligence, including demand projections and willingness-to-pay thresholds, will be necessary to support R&D investments, manufacturing strategies, as well as procurement and capacity-building initiatives. Demand forecasting is challenging and investments in ID mAb development and manufacture will still have significant inherent risks. Close cooperation between manufacturers, LMIC governments, and other funders will be important for dependable forecasting, and better defining the roles of global health actors in the development and dissemination of market intelligence will support a structured approach. Committed funding at risk for products that are critically needed could help mitigate start-up costs and potential losses to enable the portfolio-based approach (bundling of diverse mAbs as explained above). An initial focus on existing and authorized mAbs that are suitable for use in LMICs could provide proof of principle and help pave the way forward for future products.
- Local/regional political ownership of projects to expand the availability of ID mAbs are instrumental to drive forward the actions proposed here. The mAbs agenda should be integrated into regionalization and localization agendas, and governments and regional intergovernmental organisations should be involved as partners early on. Community and civil society engagement and mAb health literacy are central features of demand creation and will need to be systematically resourced by governments, intergovernmental organizations, and other partners. Work to support uptake of new ID mAbs in health systems will require planning efforts and advocacy for clinical adoption,

proper use, and equitable access. Public sector involvement could bolster political buy-in, sustainable financing, and the equitable sharing of risk. Public sector manufacturing could play a key role and has enabled local manufacture and expanded access in some settings, such as in Brazil, particularly for diseases such as regional EIDs that lack a commercial market.[47] Additionally, there are many opportunities for 'win-win' partnerships that offer new income streams for private partners, for example, through access to new markets, while expanding mAbs availability. The distribution of risk- and benefits-sharing between public and private partners must be fair and economically viable.

- Expanding the use of mAbs in LMICs will rely on products that meet health system parameters and address local/regional needs, national health strategy, donor and national funding, and regulatory capacity and data to support product implementation decision making. For clinical implementation, depending on the particular mAb and disease treated, it may also depend on factors such as the availability of diagnostic technology, clinician familiarity with the treatments, inclusion in clinical guidelines, and ability to arrange for product administration and follow-up. Investments in R&D to simplify administration (e.g., avoiding intravenous administration through long-acting sub-cutaneous injectable formulations) and improvements in logistical networks for health products at local and regional levels would reduce the costs of delivery faced by health systems and would likely improve uptake. Investments in health systems strengthening need to continue in parallel to investments facilitating access to mAbs.

Conclusions and next steps

Several streams of activity need to advance in parallel to make the vision of affordable and widely accessible mAbs a reality. An action plan for how to advance key recommendations to ensure a pathway to access could be developed, and a coordinating mechanism, such as a task team with equal representative buy-in from key stakeholder groups, could help to galvanise stakeholder interest and investment activities and track subsequent progress in advancing key recommendations.

Specific next steps to be undertaken by the convenors and participants of this workshop, along with a broader range of partners and stakeholders, include:

- Validating recommendations through tailored deep dives to include further perspectives on key topics, especially from additional LMIC stakeholders (including governments and communities) and industry representatives.
- Gathering additional perspectives, including from public health stakeholders in LMICs, to identify a small number of short-term proof-of-principle target mAbs across one or more disease areas,
- Aligning on and identifying funding for focused, coordinated actions by stakeholders across the full continuum to enable access to mAbs.
- A focus on cross-cutting interventions to be implemented that can enable equitable access to mAbs more broadly.

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References

1 Mullard A. FDA approves 100th monoclonal antibody product. *Nat Rev Drug Discov* 2021; 20: 491–5.

2 Policy Cures Research. G-FINDER data portal: tracking funding for global health R&D. https://gfinderdata.policycuresresearch.org/.

3 Torreele E, Boum Y, Adjaho I, *et al.* On the importance and challenges of global access to proven life-saving treatments for Ebolavirus – Authors' reply. *The Lancet Infectious Diseases* 2023; 23: 407–8.

4 Wellcome Trust, IAVI. Expanding access to monoclonal antibody-based products: A global call to action. 2020; published online Aug 10. https://cms.wellcome.org/sites/default/files/expanding-access-to-monoclonal-antibody-based-products.pdf.

5 Morin S, Segafredo G, Piccolis M, *et al.* Expanding access to biotherapeutics in low-income and middle-income countries through public health non-exclusive voluntary intellectual property licensing: considerations, requirements, and opportunities. *The Lancet Global Health* 2023; 11: e145–54.

6 Kayentao K, Ongoiba A, Preston AC, *et al.* Safety and Efficacy of a Monoclonal Antibody against Malaria in Mali. *N Engl J Med* 2022; 387: 1833–42.

7 Wu RL, Idris AH, Berkowitz NM, *et al.* Low-Dose Subcutaneous or Intravenous Monoclonal Antibody to Prevent Malaria. *New England Journal of Medicine* 2022; 387: 397–407.

8 Safety, Tolerability, Pharmacokinetics and Protective Efficacy of MAM01 in Healthy Adults - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05891236 (accessed June 21, 2023).

9 Li Y, Wang X, Blau DM, *et al.* Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. *The Lancet* 2022; 399: 2047–64.

10 Committee on Infectious Diseases and Bronchiolitis Guidelines Committee, Brady MT, Byington CL, *et al.* Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics* 2014; 134: 415–20.

11 The Impact-RSV Study Group. Palivizumab, a Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization From Respiratory Syncytial Virus Infection in High-risk Infants. *Pediatrics* 1998; 102: 531–7.

12 Feltes TF, Cabalka AK, Meissner HC, *et al.* Palivizumab prophylaxis reduces hospitalization due to respiratory syncytial virus in young children with hemodynamically significant congenital heart disease. *J Pediatr* 2003; 143: 532–40.

13 U.S. Food and Drug Administration. FDA Approves New Drug to Prevent RSV in Babies and Toddlers. FDA. 2023; published online July 18. https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-prevent-rsv-babies-and-toddlers (accessed Sept 27, 2023).

14 EMA. New medicine to protect babies and infants from respiratory syncytial virus (RSV) infection. European Medicines Agency. 2022; published online Sept 16. https://www.ema.europa.eu/en/news/new-medicine-protect-babies-infants-respiratory-syncytial-virus-rsv-infection (accessed Sept 27, 2023).

15 Safety, Tolerability, and Pharmacokinetics of RSV Monoclonal Antibody RSM01 in Healthy Adults - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05118386 (accessed June 22, 2023).

16 Pfizer. U.S. FDA Approves ABRYSVO™, Pfizer's Vaccine for the Prevention of Respiratory Syncytial Virus (RSV) in Infants Through Active Immunization of Pregnant Individuals 32-36 Weeks of Gestational Age. 2023; published online Aug 21. https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-abrysvotm-pfizers-vaccine-prevention-0.

17 Jorgensen SCJ. Nirsevimab: review of pharmacology, antiviral activity and emerging clinical experience for respiratory syncytial virus infection in infants. *Journal of Antimicrobial Chemotherapy* 2023; 78: 1143–9.

18 Landovitz RJ, Scott H, Deeks SG. Prevention, treatment and cure of HIV infection. *Nat Rev Microbiol* 2023; 21: 657–70.

19 World Health Organization. Pipeline for mAbs for infectious disease prevention. https://www.who.int/teams/immunization-vaccines-and-biologicals/product-and-delivery-research/monoclonal-antibodies-(mabs)-for-infectious-diseases.

20 Malhotra S, Baggaley R, Lynch S, Pérez-Casas C, Raphael Y, Stranix-Chibanda L. Antibodies for HIV prevention: the path forward. *J Int AIDS Soc* 2023; 26: e26097.

21 UNAIDS. AIDSinfo. https://aidsinfo.unaids.org/.

22 UNAIDS. 2023 Global AIDS Update: The Path That Ends AIDS. https://thepath.unaids.org/wp-content/themes/unaids2023/assets/files/2023_report.pdf.

23 Abrams EJ, Capparelli E, Ruel T, Mirochnick M. Potential of Long-Acting Products to Transform the Treatment and Prevention of Human Immunodeficiency Virus (HIV) in Infants, Children, and Adolescents. *Clinical Infectious Diseases* 2022; 75: S562–70.

24 National Institute of Allergy and Infectious Diseases (NIAID). Open-Label, Dose-Escalating, Phase I Study to Determine Safety and Pharmacokinetic Parameters of Subcutaneous (SC) VRC01, VRC01LS, and VRC07-523LS, Potent Anti-HIV Neutralizing Monoclonal Antibodies, in HIV-1-Exposed Infants. clinicaltrials.gov, 2023 https://clinicaltrials.gov/study/NCT02256631 (accessed Sept 25, 2023).

25 Hessell AJ, Jaworski JP, Epson E, *et al.* Early short-term treatment with neutralizing human monoclonal antibodies halts SHIV infection in newborn macaques. *Nat Med* 2016; 22: 362–8.

26 C. Alba, S. Malhotra, S. Horsfall, *et al.* Cost-effectiveness of broadly neutralizing antibodies for HIV prophylaxis for all infants born in high-burden settings. 2022. https://programme.aids2022.org/Abstract/Abstract/?abstractid=132.

27 Burrone E, Gotham D, Gray A, *et al.* Patent pooling to increase access to essential medicines. *Bulletin of the World Health Organization* 2019; 97: 575–7.

28 World Health Organization. Monoclonal antibodies for malaria prevention: Preferred product characteristics and clinical development considerations. 2023; published online April 20. https://www.who.int/publications/i/item/9789240070981.

29 WHO preferred product characteristics of monoclonal antibodies for passive immunization against respiratory syncytial virus (RSV) disease. https://www.who.int/publications-detail-redirect/9789240021853 (accessed July 4, 2023).

30 WHO preferred product characteristics for monoclonal antibodies for HIV prevention. https://www.who.int/publications-detail-redirect/9789240045729 (accessed July 4, 2023).

31 Van Hoecke L, Roose K. How mRNA therapeutics are entering the monoclonal antibody field. *J Transl Med* 2019; 17: 54.

32 Whaley KJ, Zeitlin L. Emerging antibody-based products for infectious diseases: Planning for metric ton manufacturing. *Human Vaccines & Immunotherapeutics* 2022; 18: 1930847.

33 World Health Organization. WHO COVID-19 Solidarity Therapeutics Trial. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments.

34 University of Oxford. RECOVERY Trial. https://www.recoverytrial.net/.

35 Lisa Schnirring. Project BioShield adds Ebola vaccines, drugs to US stockpile. CIDRAP. 2017; published online Oct 2. https://www.cidrap.umn.edu/ebola/project-bioshield-adds-ebola-vaccines-drugs-us-stockpile (accessed June 29, 2023).

36 The Review on Antimicrobial Resistance Chaired by Jim O'Neill. Tackling drug-resistant infections globally: final report and recommendations. 2016 https://amr-review.org/sites/default/files/160525_Final paper_with cover.pdf (accessed Feb 18, 2018).

37 DRIVE-AB. Revitalizing the antibiotic pipeline: Stimulating innovation while driving sustainable use and global access. 2018 http://drive-ab.eu/wp-content/uploads/2018/01/DRIVE-AB-Final-Report-Jan2018.pdf (accessed Feb 19, 2018).

38 Espeland EM, Tsai C-W, Larsen J, Disbrow GL. Safeguarding against Ebola: Vaccines and therapeutics to be stockpiled for future outbreaks. *PLoS Negl Trop Dis* 2018; 12: e0006275.

39 Shadlen KC. Accelerating pooled licensing of medicines to enhance global production and equitable access. *The Lancet* 2022; 400: 632–4.

40 World Health Organization, World Intellectual Property Organization, World Trade Organization. Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade. 2nd Edition. 2020 https://www.wto.org/english/res_e/booksp_e/who-wipo-wto_2020_e.pdf.

41 Pimenta MV, Monteiro G. The production of biopharmaceuticals in Brazil: current issues. *Brazilian Journal of Pharmaceutical Sciences* 2019; 55. DOI:10.1590/s2175-97902019000217823.

42 European Medicines Agency. Medicines assessed under the 'EU-M4all' procedure. https://www.ema.europa.eu/en/partners-networks/international-activities/medicines-assessed-under-eu-m4all-procedure.

43 World Health Organization. Pilot Prequalification of Biotherapeutic Products. https://extranet.who.int/pqweb/medicines/pilot-prequalification-biotherapeutic-products.

44 Doran Fink. Immunobridging to Evaluate Vaccines. 2021; published online Dec 6. https://cdn.who.int/media/docs/default-source/blue-print/doran-fink_4_immunobridging_vrconsultation_6.12.2021.pdf?sfvrsn=fd04428e_7.

45 European Medicines Agency, U.S. Food and Drug Administration. Summary report of the Joint EMA-FDA workshop on the efficacy of monoclonal antibodies in the context of rapidly evolving SARS-CoV-2 variants. 2023; published online Feb 8. https://www.ema.europa.eu/en/documents/report/summary-report-joint-ema-fda-workshop-efficacy-monoclonal-antibodies-context-rapidly-evolving-sars_en.pdf.

46 Rahalkar H, Sheppard A, Lopez-Morales CA, Lobo L, Salek S. Challenges Faced by the Biopharmaceutical Industry in the Development and Marketing Authorization of Biosimilar Medicines in BRICS-TM Countries: An Exploratory Study. *Pharm Med* 2021; 35: 235–51.

47 Scheinberg MA, Felix PAO, Kos IA, Andrade MDA, Azevedo VF. Partnership for productive development of biosimilar products: perspectives of access to biological products in the Brazilian market. *Einstein (São Paulo)* 2018; 16. DOI:10.1590/s1679-45082018rw4175.